THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS,
PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

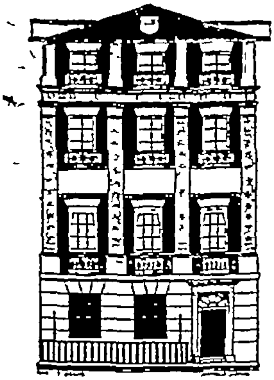
FOUNDED BY THOMAS WAKLEY IN 1823

VOL. No CCLX

VOLUME ONE
JANUARY-JUNE
1951

EDITOR
T F. FOX, M D, F.R C P

ASSISTANT EDITOR
E CLAYTON-JONES, M D



PUBLISHED BY
THE LANCET LIMITED
7 ADAM STREET, ADELPHI, LONDON, W C 2

CONCORDANCE

To enable the reader to determine at a glance the date and serial number of the issue of The Lancet containing the required page reference

Pages	Date of Issue	No	Pages	Date of Issue	No	Pages	Date of Issue
1–64	Jan 6	6645	539–596	March 10	6654	1025–1080	May 12
65–122	,, 13	6646	597–646	,, 17	6655	1081–1132	,, 19
123–180	,, 20	6647	647–698	,, 24	6656	1133–1186	,, 26
181–244	,, 27	6648	699–752	,, 31	6657	1187–1238	June 2
245–298	Feb 3	6649	753–806	April 7	6658		
299–358	,, 10	6650	807–862	,, 14	6659	1239–1286	,, 9
359–418	,, 17	6651	863–918	,, 21	6660	1287–1330	,, 16
419–480	,, 24	6652	919–972	,, 28	6661	1331–1374	,, 23
481–538	*March 3*	*6653*	*973–1024*	*May 5*	*6662*	*1375–1422*	,, 30

PRINTED BY
HAZELL, WATSON & VINEY LTD
LONDON AND AYLESBURY

RECENT HISTORY OF CORONARY DISEASE[1]

J N Morris
M A Glasg, M R C P, D P H
From the Social Medicine Research Unit, Medical Research Council

ORONARY heart-disease has emerged from obscurity e the first world war Angina pectoris has been gnosed more often, and coronary thrombosis, coronary lusion, and myocardial infarction have become estab ed as common disorders In England and Wales the adardised mortality from "diseases of the coronary eries and angina pectoris" following an even steeper rease, almost doubled between 1938 and 1948 In 8 the number of deaths so certified in persons under years of age was nearly 20,000 (Registrar-General 1–48)

f the increase is real, in whole or in part, it presents rucial problem for social medicine for causes may be coverable in changing ways of living, in people who changing in a changing environment To make its tribution social medicine can carry out case studies epidemiological inquiries The latter need their asurements as much as the former how much onary heart disease is there, and how much atheroma uch groups suffer more and which less, and in what cumstances of time, place, and society ? The present ort deals mainly with an attempt to devise a measure- nt of the prevalence of coronary atheroma in the pulation, and with the rather surprising results of its plication to the historical question But first the dence for the increase of coronary heart-disease will briefly re examined

Increase of Coronary Heart-disease

is exceedingly difficult to estimate how much of the rent increase of coronary heart disease represents ter prevalence, and how much is due to better nosis or to changing fashions in diagnosis Clinical rience unrelated to a defined population is necessarily rtain , but in the light of the long history of angina oris the impression of so many clinicians—e g ndy (1946), Hutchison (1950), Perring (1949), Yater l. (1948)—that the disease is commoner, and is earing in younger people, cannot be dismissed bably some of the increase shown in the Registrar eral's tables is due to a growing tendency to diagnose certify "coronary thrombosis," &c , instead of yocarditis," &c , but it is improbable in the light he published statistics, as illustrated in fig 1, that is the whole story (see also Ryle and Russell 1949) real test of field inquiry into the quality of certifica- practices in this very confused area has not, however, n tried

EVIDENCE FROM NECROPSIES

ecropsy findings are another source of information, these have been insufficiently studied Because of nature of ischæmic heart-disease such records are ilable in two places—the coroner's court and the pital

dden Death

schæmic heart disease may be the commonest cause death now discovered by the coroner's pathologist (Simpson 1947, 1950) A sample analysis of its most obvious manifestation, spontaneous rupture of a cardiac ventricle in the elderly, from the coroners' records of Cardiff, Liverpool, the East and West districts of London, and Manchester shows an increase, at 60–74 years of age, from 18 cases in 1932 to 47 in 1949 This represents an increase of more than twice, when the local losses of population as well as the general ageing trend are considered It is unlikely that changes during this short period in the conditions under which this kind of case was brought to medicolegal necropsy (some tending to raise the number, others to lower it), and in the quality of the pathological practice, could have explained so big an increase[2] Clearly the condition is no longer a curiosity, though it can only be appreciated in the coroner's court Krumbhaar and Crowell (1925) collected fewer than 600 cases in their review of the literature from 1872 In England and Wales it may be estimated on the above figures, and on similar ones obtained from other parts of the country, that there were quite possibly more than 600 cases at the age of 60–74 in the one year 1949[3]

HOSPITAL PATHOLOGY

A wider view of the problem, however, is necessary, and a longer perspective , and here only hospital records can help One hospital has been studied in particular Before the first world war the pathological department of the London Hospital (table I) had, on average, one or two necropsies a year with a recent coronary thrombosis and/or acute cardiac infarction Since then the number has risen considerably, the increase being fairly uniform after 35 years of age and in both sexes. There are two trends of interest in the table the over all increase of six or seven times, and the steeper incline during and immediately after the first war compared with later (fig 2). The average annual proportional increase from

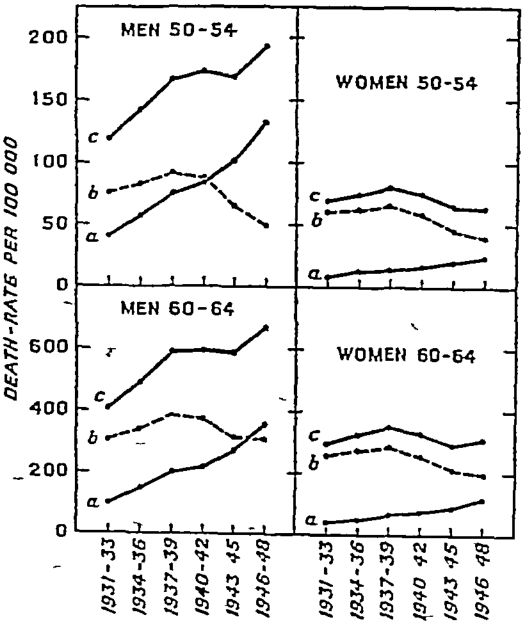


Fig 1—Mortality from heart-diseases at ages of 50-54 and 60-64 in men and in women (data from Registrar-General 1931-48) : *a* diseases of coronary arteries, angina pectoris ; *b*, chronic myocardial diseases, but including myocardial infarction , *c*, sum of *a* and *b*

---

[1] 'Coronary disease' is taken here to include (1) coronary atheroma (atherosclerosis) and (2) coronary, ischæmic (arteriosclerotic) heart-disease particularly the syndrome of thrombosis, occlusion, and infarction, and its variants 'Ischæmic' heart-disease is the most accurate term, but 'coronary' heart-disease is convenient and in too common use to be discarded

[2] Bedford's (1933) analysis of the cases "B(rought) I(n) D(ead)" to the General Infirmary in 1910–30 indicates that coronary heart-disease increased $2^1/_2$–3 times in Leeds Unfortunately this series cannot be continued to date

[3] 128 cases in a population of about 9,000,000, and including only those reported to the coroner

1907–14 to 1919–23 was about five times greater than that from 1919–23 to 1944–49. These figures seem clear enough, but it is difficult to assess material drawn from so long a period, and, before we accept the trends of table I as evidence of long-term and short term increases in the prevalence, other possibilities must be considered

Interpretation of Data

The first possibility, of course, is that the increase is not real but merely reflects better post mortem diagnosis This is an unlikely explanation There is abundant evidence throughout the forty years that the department was fully aware of the relation of infarction to thrombosis, of myocardial fibrosis to gradual occlusion, and of the topical pathology of ostial stenosis and infarction from embolism, as indeed were many pathologists last century —see Herrick (1942), Parkinson and Bedford (1928), Willius and Dry (1948) But what makes these figures important is that, unlike other series of this kind, they are based on the *routine* examination at necropsy of the myocardium *and* of the coronary arteries over the whole period Moreover Prof H M. Turnbull, director of the department, was making a special study of atheroma and arterial disease in general during 1907–14 (Turnbull 1915) The possibility that cases were overlooked is therefore small, and the earlier material is as likely to be reliable as the later As an additional precaution the records were scrutinised, and only definite unequivocal cases with either or both of these two obvious macroscopic conditions were included—i e, only such of the more modern cases as, it may be presumed, any competent pathologist conducting the necessary routine examination, at any time, would have recognised In this way some allowance could be made for the greater interest in coronary heart disease of recent years—though Sir James Mackenzie was in charge of the cardiac department before the 1914–18 war (Mackenzie 1914)—and for the stimulus of more frequent clinical diagnosis There is also probably a keener appreciation today of the very recent infarct, and of the possible significance of coronary stenosis and occlusion without definite recent thrombosis or obvious infarction, in cases of sudden and unexplained death The clinical position has changed entirely in recent years [4] (indeed there may be a problem today of overdiagnosis rather than underdiagnosis), but it is unlikely that there is any readier recognition of the two selected post mortem ma tions It is of interest, too, that the incidence of after 1912, after 1925, and before 1939 shows no evi that the papers of Herrick (1912) or McNee (19 the keen interest of the 1930s seriously affected particular experience The increase began about thus antedating Herrick's second (1919) paper

TABLE I—DEATHS FROM CORONARY HEART DISEASE IN THE LONDON HOSPITAL

Years	Average no of necropsies per year at age of 35–70			
	Males		Females	Total
	Recent coronary thrombosis*	Acute myocardial infarction†	Both‡	
1907–14	1 1	0 25	0 25	1 6
1915–18	2 25	0 5	0 75	3 5
1919–23	3 4	1 6	0 8	5 8
1927–31	3 6	1 2	1 4	6 2
1935–39	4·4	1 8	1 8	8 0
1944–49	5 5	3 0	2 0	10 5

*Fresh unorganised thrombus with or without acute infarction

†Or necrosis or rupture due to coronary atheroma without recent thrombosis (though there was often evidence of *old* thrombosis)

‡Recent coronary thrombosis and acute myocardial infarction

Cases of coronary embolism occlusion by atheromatous debris and with syphilitic aortitis have been excluded

Cases with recognised diabetes have been included in 1907–14 there was 1 in 13 cases in 1944–49 there were 7—3 in 53 men, and 4 in 12 women

The fact of an increased number of cases seems establ but this does not necessarily indicate greater prevale the disease, though it is the obvious explanation. The p tion served by the hospital might have increased six or times at all ages or, more likely, in the older ages Tl no hint of this in the number of admissions, which mi some circumstances reflect such an increase The Regi General's censuses of 1911, 1921, and 1931 show that the population of the relevant ages changed little from 19 1921, and it is now much smaller than it used to be (Regi General 1947, 1949), and the order of increase sho table I obtains for local cases drawn from the neighbo as well as for the total number of cases

The main difficulty, however, in this kind of probl that of changes in the hospital's admission policy (influe for instance, by the development of the cardiac depart causing a greater proportion of the available cases attracted to the hospital, and consequently a genuine in in numbers which may not be due to greater prevalence in population served This would be less likely to happen the "emergencies" of coronary heart-disease than wi more chronic condition like bronchogenic carcinoma (\ in addition, recognition and therapeutic possibilities varied over the years) Moreover, about a third of the p cases both in 1907–14 and 1919–23 were "B I.D" The is interesting because selective factors almost ce operated in the later years of 1907–49 (Parkinson and Be 1928), when the pathological experience increased rela little, whereas almost as certainly they did not operate earlier years, when it was increasing substantially

It seems likely, therefore, that table I illustrates increase in prevalence, especially from 1907–1 1919–23, but there is no point in labouring such argu and trying to use these figures as a *measure* o increase [5] It should be possible to gather similar evid at least of the larger infarcts, from other hospitals there was interest in these conditions In Guy's Hos for instance, there were 3 such cases in 1910–14 10 in 1919–23

CONCLUSION

There is no "correct" answer to this kind of hist question in the absence of elementary information, a period of time, about the basic ratio and in parti about the denominator of the basic ratio

$$\frac{\text{Number of phenomena, cases, deaths, \&c}}{\text{Population in which these are occurring, \&c}}$$

—the "&c" referring to such details as sex and Bits and pieces of evidence, singly not of high qu

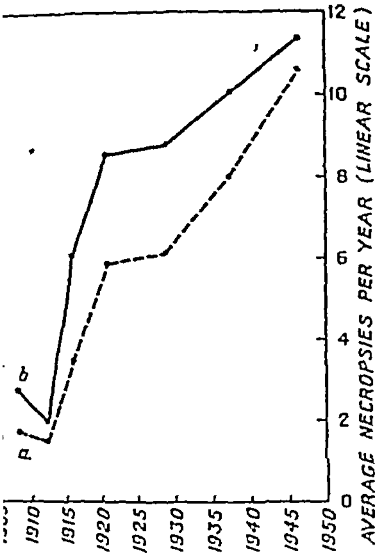
---

[4] The death certificates of 12 of the 13 cases of 1907–14 were traced at Somerset House In 4 of the 10 with coronary thrombosis at necropsy this was mentioned on the certificate Of the 2 with infarction alone, 1 was ascribed to "angina pectoris, syncope" but the infarct was not mentioned

[5] The usual method of dealing with such a problem be to calculate the ratio of

$$\frac{\text{Necropsies with coronary heart-disease}}{\text{All necropsies}}$$

This ratio, for males aged 35–69, was 0·6% (of a to 2000) in 1907–14, 2 6% (of 947) in 1919–23, an (of 860) in 1944–49—i.e, the annual rate of incre again about five times as great from the first t second period as from the *second to the third* Bu method is of doubtful validity It ignores the very changes that may have occurred in the denomina e g, the decline of mortality of infectious disease generally it assumes that apart from a real change i prevalence of the disease (the numerator), all the factors discussed above that might affect the nume and/or the denominator have changed in time s to affect them proportionately, or to an ascerta different degree This is an assumption indeed, whereas it may be possible, as in the present instan estimate the broad effect of these selective and factors on the numerator it is usually impossib impracticable to do so, except in the short run, for multiple conditions comprising the denominator o be put together in the hope of obtaining the facts. In the present instance most of the evidence in the same direction the conjunction of clinical, ation, coroners', and hospital experience suggests that there has been a true increase in the prevalence of coronary heart-disease during this century Such hospital evidence as this suggests further that coronary thrombosis and myocardial infarction, clearly described clinically only shortly before the 1914-18 war and not commonly diagnosed till after it, may have been rare before it (Brooks 1906, Mackenzie Norris 1911), and did not become common till after he biggest increase may have been in 1917-23 If s so, the scepticism of some contemporary clinicians the increase of coronary heart disease would partly stified, for this may have taken place mainly in the ience of a previous generation, whereas in their hese conditions have throughout been common



-Deaths from recent coronary thrombosis acute myocardial infection at the age of 35-70 en and in women (data from necropsies at London Hospital) *a* linear scale *b*, loga nic scale (equal vertical distances represent l percentage changes)

History of Coronary Atheroma

onary heart disease is associated generally with iced coronary atheroma, the latter is considered the underlying lesion and the former to be a lication of it The usual explanation of the increase heart disease is by an increase of the atheroma, has never been proven Coronary atheroma is on in the adult population and is progressive ously it is important to examine the course of the oma during the years in which there is evidence the heart disease increased For this purpose an ator of the prevalence of coronary atheroma in the ation is needed, and one that can be projected back the first world war There is only one possible e for such an indicator No study of people now could help, nor can death certificates be of any use investigation could be made from necropsy records mples of the population, but no such material is able for any period Sufficiently comprehensive ers' records do not exist, so far as I am aware The native therefore remains of investigating the problem hospital necropsy material, or not at all, and the suitable hospitals are large academic institutions the condition of the coronary arteries has been ded routinely over many years As already mend, the London Hospital is such a hospital, and the y was therefore carried out there

MATERIAL AND METHODS

iere are two aspects of the indicator which is needed what can be taken to represent the population at ? and (2) what can be used as the measure of nary atheroma ?

Defining the Population General

It is never justifiable to assume without examination that any hospital data are a cross section of the general population in any respect—hence the discussion of table I to establish whether the large changes in it reflect even broadly the course of events in the general population As regards coronary disease for instance, hospital necropsy material may be classified, by main cause of death, as follows

Group A Deaths from Coronary Heart disease —Table I illustrates the more dramatic manifestations of these There are also a smaller number of cases without definite recent thrombosis or acute infarction, and of more insidious forms of ischæmic heart disease which are relatively unimportant in the ages studied

Group B Deaths from Conditions Associated with Coronary Disease, especially hypertension (with or without chronic nephritis) and its complications, deaths from arterial degeneration in other sites and cases with diabetes

Group C Deaths from Other Conditions, the remainder, and great majority of necropsies Deaths from a wide variety of conditions—malignant disease, infections, injuries and operations rheumatic and pulmonary heart-disease, &c

The present problem is to estimate the prevalence of coronary atheroma in the whole population, those with coronary heart disease, those with conditions associated, and the majority But it is impossible to obtain or to set up a representative sample of any such whole population from hospital necropsy material which even at best, is typical only of the recently dead, who form a small and special part of it Groups A, B, and C cannot simply be added together, because, whereas patients with coronary heart disease may form only 1% of the middle aged population as a whole, group A may constitute almost any fraction of the necropsy material, depending on factors already discussed The same objection applies to the use of group B as a measure of those in the population who have hypertension or other associated diseases What can be done, however, is this Groups A, B, and C conform broadly to the relevant categories in the population, and it is therefore possible to use them as indicators of what is happening in these categories without implying that the fraction each group forms of the necropsy material bears any relation whatever to the fraction its corresponding category forms of the whole population Later, so far as is necessary, an attempt can be made to estimate the true size of the various categories to obtain a view of what is happening in the whole population

Group C does not at first sight represent any kind of population But if the assumption can be made that there is no particular association either positive or negative between deaths (and necropsy) from cancer or infections, &c, and the state of the coronary arteries such a miscellaneous collection may be considered typical at least of the great mass of the ' hospital class of the population living as well as recently dead so far as the coronary arteries are concerned, and an adequate sample for this study In some of the cases there may be conditions predisposing to coronary atheroma, in others conditions protecting from it on balance these, on the whole will tend to cancel out—or so it is postulated This is certainly a big assumption

Alternatively since the problem is an historical one analysis of the findings in such a collection as group C is worth while if the lesser assumption can be made that any association there may be between such deaths and the condition of the coronary arteries has not altered materially in the last forty years, changes found in the coronary arteries of this group will therefore not be due to the main conditions causing death, but will reflect changes occurring generally in the population These are the kinds of assumption that need to be made if hospital data are to be usable in this kind of investigation (and indeed, often as " control ' material at all)

The condition of the coronary arteries in group B deaths can be taken to indicate what is happening in the minority of the population with predisposing conditions used in this way, as explained it does not matter for the moment whether the group is too large or too small in relation to the prevalence of these conditions in the total population

Finally, as regards group A, no conceivable increase in the numbers with coronary heart disease (e g, an increase from 0·1% of the middle aged population before the 1914–18 war to 1·0% now) could materially affect any totals of atheroma found from the analysis of the 99% or so covered in groups C and B—even if it is assumed that almost all of such sufferers had advanced degeneration. So group A may be safely ignored in this part of the study

Defining the Population Particular

The study was carried out on the remarkable collection of post mortem reports of the London Hospital The records were sorted A, B, and C, as described Group A cases were put aside and have been dealt with already Group B, forming rather less than 10% of the remainder in both sexes and in both periods, were kept separate from group C forming over 90% Where the allocation was in doubt cases were relegated from C to B, and from C and B to A It was decided to concentrate on the extremes of the 1907–49 span, over which the increase of coronary heart disease is most certain Two six year periods were therefore studied in detail—1908–13 and 1944–49 In both periods the majority of patients dying in the hospital were brought to necropsy though the proportion was greater in the earlier period

Standardisation

It is necessary to assure that the groups being compared were as like as possible—i e, to "standardise" them This involved a consideration of what is known or thought to be important in the development of coronary atheroma Standardisation was straightforward for sex and age A sample study of the occupations of the dead persons did not suggest that there has been any important change in the social status of this "population" in the past forty years of course there has been some change, but it is still predominantly classes III–V (skilled semi skilled, and unskilled workers) An attempt was made to standardise for broad ethnic groups by using religion as an indicator, but this was unsuccessful, there is no doubt that the proportion of Jewish patients in both periods is higher than in the general population but I did not form the impression that there had been any change that might matter The addresses of the 1908–13 patients, like their religion were not available, so no estimate of possible changes in the local proportion or of the urban/rural ratio was practicable

A few other technical points may be mentioned here Preliminary inspection showed that there was little change (a slight rise) in the average body weight between 1908–13 and 1944–49, this factor was therefore ignored The heart weight was recorded in each case No attempt was made to allow for the presence or absence of congenital abnormalities of the coronary circulation or of clinical coronary heart-disease incidental to the main condition from which these persons died the former was not considered sufficiently important, and it would have been quite impracticable to assess the latter, the assumption had to be made that any such cases were similarly distributed in the different periods

Dr W W Woods has been carrying out or supervising a large number of the necropsies since 1911, but routine initialling of the reports was not begun till much later Dr Woods and Prof D S Russell s reports alone were analysed for the 1944–49 figures in this part of the study, mostly they were by Dr Woods There was no particular selection in these cases In the 1908–13 period two methods were used (1) one in three samples were drawn for ages 30–49 and (2) the total number was analysed for ages 50–69

The Indicator of Atheroma

It was necessary to choose a simple measure that sorted the records into meaningful categories at least of slighter and of more severe coronary atheroma, in which the differentiation was unequivocal and comparable for different periods, and which involved a minimum of interpretation by myself After much experiment a report of calcification in the atheromatous lesions was finally adopted as the indicator of "advanced" atheroma, of protracted and/or severe degeneration, as indeed it is so regarded in the hospital This divisor being used, doubt about their appropriate category arose in only a small minority of the these were distributed as follows When coronary atheroma was described merely as " and when, as also occasionally happened, hæmorrhage, stenosis, or occlusion was reported accompanying calcification, the grading was " In the remainder of this paper the term " atheroma" refers specifically to the above three tions "Slight" atheroma was scored "early" fatty lesions, as were also, without much some "nodular" and "atrophic" lesions in So few cases at any age were specifically stated free from atheroma—well under 5% at 50–69 that such were considered "early" for the comparisons

A more difficult problem arose, particularly in when there was no specific statement on the condition coronary arteries in the summary reports available In all of these cases there was an obvious cause of death were commoner at younger ages, and the general of the condition of the arterial system was usually slight" or "slight" atheroma It therefore seemed to include those 'not stated" in the totals when the tion of advanced atheroma was calculated—i e, it was in effect that they were "early" The negligible where it was clear that the heart had not been were ignored

The technique of routine examination of the arteries with scissors has not altered materially period under review Naked-eye descriptions used To preserve homogeneity I extracted, and classified all the reports myself, and as a precaution earlier and later years were scored al The simplified procedures used meant sacrifice of diagnostic refinement for the sake of parability, but, as so often happens, the problem to find the perfect method but the best that is

CONDITION OF CORONARY ARTERIES 1908–49
GROUP

Group C is a representative sample of the of the population as regards their coronary art so it is postulated Tables II and III assemble for this group, and fig 3 illustrates them the main findings

(1) Coronary atheroma visible to the naked eye the great majority of persons after the age of 40

TABLE II—PREVALENCE OF CORONARY ATHEROMA IN
AGED 30–70 AT NECROPSIES IN THE LONDON

Age group (yr)	No of cases								
	In 1908–13					In 1944–49			
	Early atheroma*	Advanced atheroma†	Not stated‡	Total	Proportion of total with advanced atheroma	Early atheroma*	Advanced atheroma†	Not stated‡	Total
30–34	40	0	14	54	0%	14	0	0	14
35–39	44	1	13	58	2%	25	0	1	26
40–44	58	3	14	75	4%	40	0	5	45
45–49	63	6	15	84	7%	45	0	3	48
50–54	167	46	38	251	18%	59	3	2	64
55–59	136	45	19	200	23%	46	7	2	55
60–64	83	58	16	157	37%	61	20	3	84
65–69	52	60	4	116	52%	52	21	1	74
Total	643	219	133	995	Standardised rate at 50–69 years 30·4%	342	51	17	410

* Fatty lesions (or nodular or atrophic, and the few with no

† Lesions with calcification (or ulceration hæmorrhage occlusion and described merely as severe)

‡ No specific statement in the reports on the condition of the arteries

These cases form group C Deaths from coronary heart from hypertensive disease from arteriosclerosis in other with recognised diabetes are not included

2) The amount of advanced atheroma, as defined, reases with age in both sexes

3) There has been no deterioration in the coronary eries of the population in the period 1908–49, as indicated the proportions of advanced cases in this series, and using *methods described*

4) There was in this series less advanced atheroma in 4–49 than in 1908–13 in both sexes and at all relevant es[6]

(5) There is no evidence in these tables that advanced eroma is appearing at younger ages than formerly On e contrary, the male rates of advanced atheroma in 4–49 resemble those occurring in age groups at least e years younger in 1908–13, and the female rates those curring in age groups at least ten years younger

he decrease may be summarised by calculating a dardised rate of advanced coronary atheroma at 9 years of age based on the age distribution of the ulation of England and Wales in 1947 This rate for es was 30 4% in 1908–13 and 16 0% in 1944–49, and females 25 9% in 1908–13 and 7 5% in 1944–49 The iction in males was 47% and in females 71%—i e, e was less advanced atheroma in females in both ods, and a greater reduction in them (fig 3)

E III—PREVALENCE OF CORONARY ATHEROMA IN FEMALES GED 35–70 AT NECROPSIES IN THE LONDON HOSPITAL

e up r)	No of cases									
	In 1908–13					In 1944–49				
	Early atheroma	Advanced atheroma	Not stated	Total	Proportion of total with advanced atheroma	Early atheroma	Advanced atheroma	Not stated	Total	Proportion of total with advanced atheroma
-39	32	0	19	51	0%	25	0	2	27	0%
-44	34	0	11	45	0%	24	0	1	25	0%
-49	37	1	6	44	2%	24	0	5	29	0%
-54	94	11	18	123	9%	34	0	3	37	0%
-59	53	17	12	82	21%	32	1	3	36	3%
-64	46	25	10	81	31%	41	4	2	47	9%
-69	28	32	3	63	51%	20	6	0	26	23%
tal	324	86	79	489	Standard 50–69 25 9%	200	11	16	227	Standard 50–69 7 5%

See footnotes to table II

DISCUSSION OF THESE FINDINGS

he trend shown in tables II and III was unexpected as seems to be the case, there has been an increase of onary heart disease, explanation of this by an increase oronary atheroma conjures up a picture of progressive dening in the arteries of the population that would alarming However, the picture is not so self evident terms of the natural history of ischæmic heart disease, more generally in terms of the emerging knowledge of nutritional relations of atheroma or of the falling th rates of older people, that close proof is not required ore it can be accepted It was nevertheless surprising find this suggestion of an actual decrease in atheroma, the more because the same material showed the pected increase of the heart disease I have been able to find any corroboration in the literature, ough some senior pathologists have remarked in sonal discussion on the apparent decrease of "pipe m" or "ossified" coronary arteries

It is necessary now to scrutinise the present findings, k out weaknesses, and, if possible, disprove the trends own by the tables Three possible sources of error at least need to be considered (1) advanced atheroma may have been understated in 1944–49, (2) or overstated in 1908–13, and (3) the choice of methods may be unsound

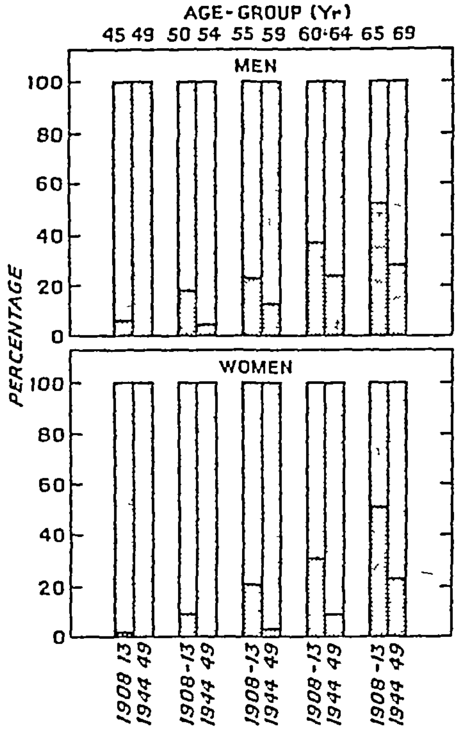


Fig 3—Prevalence of advanced coronary atheroma at the age of 45-70 in men and in women (data from necropsies at the London Hospital): each hatched column shows percentage of age-group with advanced atheroma.

Experimental Error

This may be considered in relation to the first of these possibilities It probably is (and was) small, calcification is easily recognised, omission to record it when observed is unlikely to have increased with the growing interest in coronary disease, in general the reports of 1944–49 are fuller than those of 1908–13, and the proportion 'not stated" is smaller, as against the heterogeneity of the earlier reports, the later are by two—mostly by one—senior and increasingly experienced pathologists In my own analysis of the records, methodology apart, little more than an ability to read—and a lot of patience—was needed

Seesaw Effect?

The total of advanced atheroma in 1908–13 may have been artificially inflated at the expense of 'early' atheroma on the one hand, and of coronary heart-disease on the other What has happened the latter argument would run, is merely that coronary thrombosis and cardiac infarction were usually overlooked in 1908–13 and hence not reported The underlying severe atheroma however, *was* noticed and reported and in consequence included in the 1908–13 parts of tables II and III, whose totals of advanced atheroma were thus exaggerated A review of the material along these lines should exclude the very obvious infarcts, and reasons have already been given why it is unlikely that coronary thrombosis was so overlooked To deal thoroughly with this problem would take much arithmetic, a prospect that arouses little enthusiasm, but fortunately it is unnecessary If the most extreme position is taken for the moment and all cases of table I are added to tables II and III, it can readily be seen that even then the total volume of advanced atheroma in 1944–49 would not equal that of 1908–13[7] In the females such a redistribution would not make any material difference Among the males the new "total" of advanced atheroma still remains short

This null hypothesis" in terms of complementary effects may be generalised Theoretically it is possible that the total volume of severe atheroma in the population has remained the same, or has even increased but that this is obscured because so many more with the atheroma are developing and

---

The reduction is unlikely to have occurred by chance P≤0 002 in males and 0 008 in females, on a method testing the weighted sum of the differences a transformation having first been used to make the distribution more nearly normal

[7] Putting the matter simply, it may be said that about 50 male cases would be needed to raise the level of advanced atheroma in 1944–49 to that of 1908–13, and about 35 female In fact there were in this Woods and Russell series 33 and 7 respectively (Table I includes all the 1944–49 cases of coronary heart disease, those examined by other pathologists also Omission of the less definite cases from table I, as described, does not affect this conclusion)

dying of ischæmic heart disease, being transferred, as it were, from tables II and III to table I This is unlikely to be true, because the order of decline of atheroma suggested by tables II and III is so much greater than any conceivable increase in the heart-disease Thus, among males aged 60–64, advanced atheroma (table II) fell from about 37%, or 370 per 1000, to about 24%, or 240 per 1000—i e , by about 130 per 1000 But *mortality* from coronary heart-disease in the general *population at this age (fig 1) even now is nothing like 130* per 1000—it may in fact be about 7 per 1000 Indeed the total mortality of males aged 60–64, from all causes, is less than a quarter of 130 per 1000 Another inquiry being carried out in this unit suggests that the *morbidity* is perhaps 10 or 12 per 1000 Therefore, if table II is at all representative and gives any kind of picture of changes that have taken place in the prevalence of advanced atheroma, such an explanation is inadequate

Choice of Methods Validation

The methods used in the present study may be wrong An important element in the relation of atheroma to heart disease may have been missed in the selection of the ratio of calcification to fatty lesions as the indicator The thickness of the intimal lesions, for example, may be more relevant Moreover, this definition is static and *structural , but it was impracticable to devise a more* functional one in terms of arterial narrowing, not to say efficiency of the coronary circulation and myocardial nutrition The decrease in calcification may be a special phenomenon not exemplary of atheroma in general, and as such important, or not It was impossible to inquire into the existence of different types of atheroma (Duguid 1949, White and Ferrero 1949) Further, the *constitution* of group C may be unsound

A partial answer can be given to some of these points from the internal evidence As a test of whether group C as a whole has no particular association with coronary atheroma, it was broken down into two malignant disease, where there is least reason to suspect such an association, and the miscellaneous remainder The results are of the same order in both subgroups, in both periods,[8] thus supporting the proposition that group C may be regarded as typical of the great mass of the population so far as the coronary arteries are concerned As regards the reliability of the indicator of atheroma used, it may be said that the pattern of tables II and III was stable , it emerged after only a quarter or so of the work had been done and did not change Moreover the *regularity* of the pattern, the progression with age in both sexes and in both periods, and the uniformly heavier incidence in males up to the age of 65 suggest that the criteria adopted discriminated real properties of the material and consistently separated the slight from the more severe atheroma The rarity of stenosis and occlusion without it may be adduced in validation of the use of calcification as " indicator," and it may be added that ischæmic heart disease in this series is associated with atheroma that has progressed to calcification in some part of the coronary system (though not necessarily in the lesions that form the basis of the thrombosis)

CORONARY ARTERIES IN HYPERTENSION

There is no doubt about the association of hypertension with coronary heart disease (Friedberg 1949), and, though its association with coronary atheroma has possibly been overemphasised in the past (Harrison and Wood 1949), conceivably there may have been an increase in coronary atheroma restricted to, or mainly in, the hypertensive members of the population In that event tables II and III, by omitting many of the cases with serious hyper tension (these were excluded to group B), may be begging an important question The simplest way to deal with this would be to add the appropriate number of with hypertension to tables II and III, and to c new inclusive rates of advanced atheroma , the " priate " number (since it is postulated that tables III are representative of the great mass of the popu in respect of their coronary arteries) being that would occur in a sample of the general population *age structure of tables II and III This aspect* problem has already been discussed The trouble i despite its importance, the prevalence of hypert in the population is unknown, and it is impossi estimate the appropriate number for the correc tables II and III

This discussion, however, may safely be cut sho males the standardised rate (on the basis a described) of advanced coronary atheroma for d from hypertensive disease in group B was 40·3% 1908–13 (59 cases) and 32 1% in 1944–49 (23 c i e , it does not seem that correction of table II for tension could have turned its downward secular tre or even kept it level There were only 14 female ca group B in 1944–49, so another expedient had adopted Heart weight may be used as a crude indi of " incidental " hypertension in necropsy mat especially if deaths from valvular and pulmonary h diseases are excluded The group C material (table was therefore reclassified by heart weight into t above 11½ oz and those of 11½ oz or less, and cases with the heavier hearts were added to the fe *group B data Advanced atheroma (standardised)* this composite " hypertensive " group was 32 3% 1908–13 (103 cases) and 14 3% in 1944–49 (37 c Again it does not seem that the reduction in the ge prevalence of advanced atheroma in the population w is suggested by fig 3 is invalidated by the inabilit make due allowance for the prevalence of hyperte in the population[9]

---

[8] Standardised rate of advanced atheroma in deaths from malignant disease at 50–69 years of age

	1908–13	*1944–49*
Males	26 3% (230 cases)	15 3% (137 cases)
Females	22 4% (136 cases)	4 9% (84 cases)

[9] The proportion of heavier hearts was similar in both and in both periods, in the range of about 12% *age of 50–54 to about 35% at that of 65–69* In also the standardised rate of advanced atheroma i heavier hearts declined from 36 4% in 1908–13 (174 to 21 1% in 1944–49 (59 cases) In males 13½ oz taken to be the critical heart weight

This sketchy treatment of hypertension and its rel to coronary disease is intended only to meet this limited and specific problem There is more adv atheroma in those with hypertension, and the dec was less in them A simple sum, however, shows tl the males it would be necessary for the great maj of the adult population to have become seriously hy tensive before the volume of advanced athero 1944–49 could reach the level of 1908–13 through mechanism *Possibly there has been some increa* hypertension in recent years which may be related t increase of coronary heart-disease , but, though hy tension may be as lethal as cancer or infection, impossible to estimate its prevalence during the forty years It would not be worth trying to draw conclusions, in so chronic and multiform a disorder, the numbers of cases over the years brought to necro as was done in *table I* with a much simpler prob The only community indicator available is mortality intracranial vascular disease, and this has changed l during the period in which coronary mortality has so steeply (Registrar General 1931–48) (It may course, be possible to study further the prevalenc hypertension in the population from a detailed consid tion of heart weight and arterial hypertrophy as fo at necropsy)

Incidentally these findings provide another valida of method and dispose of another obvious weaknes the present study—the allocation of cases to group and C If we disregard for the moment the rights wrongs of the ratios of the groups, the addition of all tl group B cases to group C in 1944–49 would still le the totals of advanced atheroma very short of those group C alone in 1908–13

Associated Conditions

ses in which diabetes was recognised were also excluded oup B The prevalence of diabetes, however, is so much ler than that of coronary atheroma in these necropsies the general population, that this relatively minor aspect e problem may be safely ignored [10] Similarly none of the conditions with hypercholesterolæmia or the diseases bly associated with coronary atheroma—e g, Paget's se and fatal arteriosclerosis elsewhere—is or was suffi ly common to need consideration in this type of munity study

CONCLUSION

hatever the clinical situation coronary atheroma well recognised at the London Hospital before the world war The evidence here does not suggest that e has been any increase of atheroma—any progressive moration in the coronary arteries of the population ng the past forty years On the contrary there seems be less of advanced coronary atheroma now than ierly Since the decrease was seen in both the normo- ive majority and the hypertensive minority of the ulation, the relative sizes of these is in the present iection unimportant [11]

(*To be concluded*)

ASPIRATION TREATMENT OF PERFORATED ULCERS

A FURTHER REPORT

HERMON TAYLOR
M.A, M D, M Chir Camb F R C S
EON TO THE LONDON HOSPITAL, AND TO KING GEORGE HOSPITAL, ILFORD

CCASIONALLY during the last half century obtuse ents have refused operation for their perforated ulcers have yet recovered In 1935 Wangensteen advised nst operation on gravely ill people whose admission ospital had been delayed For such cases he recom- ided continuous gastric tube drainage, to promote or upport natural closure of the perforation, and he others since have reported on patients saved in way From time to time, at emergency operations, found that the perforation has been sealed by inous adhesion to the liver or omentum, and, to justify surgeon in staying his hand, the loose term "leaking foration" has crept into the literature to include a up of cases in which leakage has in fact ceased. etimes, too in routine operations on ulcers, upper ominal adhesions round cellulose particles have ne witness to a past perforation which has healed hout being recognised, though the patient, under s examination, may recall a particular and atypical t of "ulcer" pain

hus it has been recognised, though tardily, that a foration may close spontaneously But the therapeutic pects have been obscured by the outlook and train- of the average surgeon in acute abdominal work dramatic nature of the case, the sudden pain, the conception of the gaping hole in the stomach, the satisfaction of closing it, the recognition by relatives and by authority that the surgeon has not shirked his duty but has taken the risk (!)—all these things have made it difficult for the young surgeon, to whose lot these cases mostly fall, to conceive any other course than immediate operation for all perforations whatever the hazards Nevertheless, the fact is that a perforation will certainly close itself if the stomach is promptly emptied and kept empty, so that neither fluid nor gas passes through the aperture Professor Wangensteen recognised this simple truth, as well as the enormous defensive and recuperative power of the peritoneum after contamination, but he confined its application to late cases

It was not till 1939 that Mullen, of Seattle, applied Wangensteen's principle to early cases of frank perforation Having treated 8 patients without a death, he cautiously addressed the Seattle Surgical Society on the subject, with the result that a further 19 were treated by his colleagues Of these 19, 1 was moribund on admission and died but 2 died who had been in good condition with recent perforations and who could have been expected to recover after operative treatment There is no doubt that failure in these 2 cases was due to inadequate gastric decompression—a subject discussed later in this paper Dr Mullen, however, feared the indiscriminate application of a method subject to such errors, and abandoned it without publishing his work No notice seems to have been taken of the fact that the total mortality—3 deaths in 27 cases—was actually below that of surgical treatment at Seattle at the time In 1945 Bedford Turner treated 6 cases of acute perforation by gastric suction without fatality, but he did not follow up this work after completing his resident appointment at the Royal Sussex County Hospital, Brighton

THE KING GEORGE HOSPITAL EXPERIMENT

Seven years ago I began independently to try the method at King George Hospital, Ilford, for reasons which have already been explained (1946) At that time the general mortality of operation for perforated peptic ulcer lay between 12% and 20% At York, Visick (1946) put it at 20%, and in Glasgow Illingworth et al (1944) at 14% The Radcliffe Infirmary 19%, Hackney Hospital 17% King George Hospital 18%, and the London Hospital 17% were remarkably uniform results for Southern England in the period 1940–45 In the United States Luer (1949) quoted 18% for St Louis City Hospital, in 1938–48, DeBakey and Odom gave 17% in a review for 1940, and Black and Blackford found 12% for 1945

In our preliminary work at King George Hospital we treated 28 cases, with 4 deaths Of the patients who died, one was moribund from the start, and another collapsed with a massive pulmonary embolism A third died from the results of an ill conceived intercurrent operation, and the fourth from re perforation following inadequate gastric decompression Nevertheless our results were better than previous surgical results at the hospital, and could obviously be improved by the lessons we had learnt We therefore decided to continue with what was perhaps the first sustained attempt to work out on a hospital scale the risk, the complications, and the implications of a policy of treating perforated ulcers by aspiration instead of operation

Object in View

We set ourselves to show that gastric aspiration could be relied on to close the perforation in the bulk of cases, and that, where it failed, recourse could still be made to operation without material increase of risk Our intention was to avoid those deaths which followed the pulmonary, cardiovascular, and surgical complications of the operation itself, and which accounted for more than half the surgical case mortality Our target, an

---

The prevalence of diabetes among men, as judged from Ministry of Food data is well under 1%, and among women somewhat higher but still less than 1% (Stocks 1949) Compare the prevalence of coronary atheroma (tables II and III)

It should be possible to repeat these observations else where—e g, on the contemporary prevalence of advanced atheroma The warning must be given that historical study of atheroma is likely to be rewarding only where there has been routine description of the lesions over a long period (Willius et al 1933) In view of the growing interest in coronary disease and the possibility of changing standards it is impossible to interpret series that do not record the condition of the arteries in all or a large proportion of necropsies, or which do not routinely describe the actual lesions in them (see Levy et al 1934) easy one in 1946, has been greatly diminished by the remarkable fall in operative mortality in general, and for perforated ulcer in particular, since that time The reasons for this are the general use of antibiotics, the expansion in the science of anæsthesia, and the newer techniques in abdominal wound closure and postoperative care Thus, in Cincinnati, McElhinney and Holzer (1948) have reduced the operative mortality of perforated peptic ulcer from 21% to 11% and McElhinney (1949) reported only 4 deaths in his last 64 cases In this country Avery Jones, Parsons, and White (1950) write of a fall in operative mortality from 27 to 4% in the last ten years, but their series of 490 cases included 36 patients (with 32 deaths) who were not operated upon, either because the perforation was not diagnosed, or because they were considered too ill

Difficulties in Assessment

The difficulty of reaching sound conclusions is indicated in the last phrase, for the mortality from perforated ulcer under either method of treatment is influenced by many extraneous factors Old people run more risk than the young, women more than men, gastric perforations more than duodenal, late cases more than early ones If one adds the special circumstances affecting the practice of individual surgeons, it is clear that the excellent results of their personal operations cannot be generally applied, since they exclude the patients whom they thought too ill for operation as well as those they were not called to see Even with hospital figures, a clear distinction must be made between operative mortality and total mortality For example, I have quoted the figure of 17% operative mortality for perforated ulcer in the London Hospital for 1940–45 During that time there were also 11 patients too ill to be operated on, all of whom died, but their records are not included in the surgical mortality figure, which could therefore be misleading in loose argument It is debatable whether Avery Jones and his colleagues make the practical problem of treatment easier by including also the undiagnosed cases demonstrated post mortem, but their work has done much to promote the necessary sense of perspective It is evident that comparison of the results obtained by the conservative policy at King George Hospital with the results of the operative method elsewhere are admissible only if the latter include the whole practice of a hospital, night and day, treated by the entire staff Even then, conclusions must be modified by geographical and social factors, for the results in a compact residential area, with excellent transport and general practitioner services, will be better than those in a hospital less fortunately placed

Preliminary Conclusions

A number of points are already clear from our preliminary observations in 1946 and the experience of other workers since that time No cases should go untreated for lack of transport facilities, but aspiration on the spot is better than a long journey and delayed surgery In hospital, any patient who has to wait for his operation—because he is in poor condition, or for any other reason—must have his stomach emptied and kept empty during the waiting period Operation must not be performed where it would be attended by serious risk from advanced age or associated disease, all such patients could be treated by aspiration

These conclusions apply to cases treated in unfavourable conditions The object of the present study is to present for comparison the results of the aspiration method in conditions which were perfectly suitable for surgery The question is not one of mortality alone Fit young people nowadays run little risk to life from either method, and from this point of view there may be little to choose between the two But into the scales of judgment must be thrown a certain incidence of morbidity and disability which are weighty conside
early in an active career One may include such
as wound hernia, activation of latent phthisis, int
obstruction by bands or adhesions, and other
of the operation itself This is by no means a ne
factor, for example, in the early tentative days
King George Hospital experiment, some of th
preferred to continue the practice of immediate ope
on their cases The small group of 7 operated
which thus arose comprised 1 death, 3 une
recoveries, and 3 survivals with complications
latter included a severe atelectasis and pneumo
one case, and re suture of a ruptured wound with
hernia in another, while the third patient had to
a second operation to relieve intestinal obstructi
to an intestinal kink, and was left with an inc
hernia Clearly it is but half the tale to record
patients survived !

The deeper one delves into these complexitie
more obvious becomes the need for each hospi
have a policy, and for the results to be studied cli
as well as statistically Two alternative polici
available—to operate on all cases that are not too
and to aspirate the remainder, or to aspirate all s
cases but be prepared to intervene surgically
need arises At King George Hospital we have a
the second course, based on the following appre
of the pathological process at work

THEORETICAL CONSIDERATIONS

In the absence of treatment, death is or
caused by absorption of toxins from the infected
toneal fluid In practice therefore the important c
estimation to be made is the intensity of the toxic
and it is useful to distinguish three degrees

In the *first stage* infection has not yet taken pl
there is therefore no toxicity The question is
one of closing the perforation in the best way,
prefer to keep the stomach empty by aspiratio
allow it to close itself This method avoids the
effects and dangers of operation Antibiotics m
given prophylactically with advantage but are
essential

In the *second stage*, ordinarily at about twelve
infection is established and toxic absorption has
menced, but there is still time to deploy antibi
arrest the infection, and one can still rely on n
processes to eliminate the toxins—provided no reinf
occurs Absence of reinfection can be ensured by k
the stomach empty by aspiration, and where the p
is a serious surgical risk this may be the best
However, excess of infective fluid renders the perito
less capable of the firm adhesion required to sea
perforation, and trouble may arise later from poc
of fluid In a healthy subject, therefore, operat
suture the perforation and to allow proper toilet
peritoneal cavity may well provide smoother and
convalescence

In the *third stage*, ordinarily at twenty-four hour
system is overwhelmed with toxins from the fl
peritoneal cavity Our immediate concern is no l
to kill organisms or stop the perforation, the ne
to arrest at once any further absorption of toxi
removing the fluid from the peritoneal cavity The pa
is necessarily too ill for full scale operation, but
pelvis and renal pouches can be drained through
incisions under local anæsthesia, while reinfection
the perforation is prevented by continuous aspirati
the stomach

Many factors influence the speed at which the perit
crisis develops—the size of the perforation, its rel
to the pylorus, the nature and amount of the ga
content, and the kind of micro organisms which
dominate The intensity of the pathological pro
therefore, ranges widely at one end of the scale i
small duodenal perforation in a healthy person wit
empty stomach and good protective rigidity, whi

other is the large gastric perforation in an elderly ale or flabby alcoholic with a full stomach and a r abdominal wall The very late case is, therefore, necessarily the very toxic case, and herein lies explanation of the rare success of simple aspiration the treatment of neglected cases, first described by ngensteen It was Illingworth however, who first nted out that an untreated patient alive three days r perforating had a rather better chance of survival a one admitted after twenty four hours—a paradox ccord with this appreciation of the processes at work

Nevertheless, in most cases the time factor is the t important consideration Gastric aspiration is ful at all stages, but it will be noticed that the ective is different in early and late cases In an early e aspiration is employed to promote prompt sealing the perforation It may do this in an infected case, s, but its object here is rather to prevent reinfection the peritoneal cavity, whether the perforation closes once or later With effective aspiration the perforation comes innocuous and can be discounted while undivided tention is given to the condition of the patient and the ritoneal cavity (So far from gastric contents draining to the peritoneal cavity, the reverse is often seen in ese patients with gross peritonitis the gastric aspirate ing at first identical in character with the fluid scharged from the abdominal drainage tubes)

GENERAL MANAGEMENT OF CASES

The great majority of cases arriving at hospital are in e early non toxic phase These we have treated by e aspiration method outlined in my original paper, nd they have made an uneventful recovery Their ogress is very carefully observed, especially in the st twelve hours, and we are prepared to open the bdomen if a steady rise in pulse-rate suggests a virulent fection, or throws doubt upon the diagnosis By means f X rays we look for any increase of subdiaphragmatic as, which would indicate failure of the perforation to lose We are on the watch for localised collections of uid which might become infected and require evacuation Ve think we have learnt most of the tricks of the small ndwelling naso-œsophageal gastric tube how it may e held up at the cardia and deceive the unwary by llowing the aspiration of a test drink, how it may ink itself in the stomach and prevent aspiration, but et allow water to be injected down it as a spurious est of its patency We have come to the conclusion hat the only way to be sure that the gastric aspiration s what it seems to be is to employ radio-opaque tubes which will reveal their position on radiography We are not content unless the position is correct and aspiration produces *some* fluid however little, and can recover a test drink. Gas or fluid must be absent from the stomach, and the quantity of intraperitoneal air must be seen steadily to decrease as the days pass It will be observed that X ray control plays a large part in the management of the cases

We have eschewed all attractive pieces of constant suction apparatus, which cannot report failure to the ward sister, and we have learnt the value of aspiration at regular intervals and the opportunities they provide for repeated observation of the patient In lonely far off places the doctor would have to be content with much less than this, and indeed the method can be reduced to simple terms by which the patient can himself aspirate his stomach. We have done this as a matter of interest at King George Hospital, but the best results are obtained only after the most careful instruction of the nursing staff, who have the fundamental responsibility of ensuring that the gastric aspiration is faultless This presents no difficulty to an experienced ward sister, but great watchfulness is required at every stage, and the success of the treatment depends on the attention and enthusiasm devoted to it

ERRORS OF DIAGNOSIS

Two perforations were not diagnosed. One patient with predominantly right sided pain was operated on as an acute appendix, and a duodenal perforation was exposed and sutured The other was treated conservatively as a case of cholecystitis Radiography was undertaken for gall stones, but revealed instead a tell tale layer of gas between liver and diaphragm Both these patients did well

More important for my thesis are errors in the opposite sense—cases misdiagnosed as perforations In my original paper I mentioned the recovery of a patient with acute cholecystitis who was thought to have a perforated ulcer and was treated by gastric aspiration The importance of this was pointed out immediately by Professor Grey Turner (1946) " Let us accept " he said in effect, " that a patient with a perforated ulcer can be saved by this means without operation, and let us suppose that the method becomes widely applied How many patients will there then be, wrongly diagnosed as perforations, who will lose their lives because the abdomen was not opened and the true cause of the emergency found and dealt with ? " That was a serious criticism of the whole policy, and to estimate its gravity we have been careful to record all cases of erroneous diagnosis At King George Hospital since 1946 our diagnosis of perforation has been correct in 73 cases and incorrect in 4, which I record in detail

1 One patient was thought to have done very well with aspiration of the perforation " until four weeks later when the truth was revealed by a second attack with jaundice ! An uneventful cholecystectomy ensued

2 A man of 63 with a known ulcer admitted with acute pain was aspirated for fifteen hours Continuing pain and a rising pulse rate led to operation which disclosed a perforated appendix The patient did well

3 A man of 40 with six hours abdominal pain, and right-sided tenderness and rigidity was subjected to gastric aspiration on a diagnosis of perforated ulcer Rapid subsidence of abdominal pains and the appearance of signs at the right base soon demonstrated that he had a right basal pneumonia and pleurisy with referred pain He did well but it was fortunate that no operation had been performed

4 The fourth patient, a rather ill man of 56, was admitted four hours after sudden abdominal pain. Gastric aspiration was instituted but was abandoned because the pulse rate rose from 90 to 130 in the next two and a half hours. Operation thereupon revealed a fæcal peritonitis, spreading from the right flank which was thought to be appendicular in origin. The patient lingered for thirty six days on antibiotic therapy, with drainage of abdominal abscesses as they presented successively in the pelvis, the left flank, and under the diaphragm until death supervened from exhaustion and toxæmia Necropsy showed a plastic peritonitis with multiple pockets of pus and fistulæ to the colon. The appendix stomach, and duodenum were normal and it was considered that the initial fæcal peritonitis had arisen from perforation of the right colon, perhaps from a foreign body perhaps through a diverticulum. Few patients recover from such a condition.

If we include the cases at King George Hospital before 1946, the facts may be summarised as follows During seven years, in a 200 bed general hospital in a London suburb, 106 cases were diagnosed by the resident staff as perforated ulcers, and treated mostly by gastric aspiration in preference to operation Of the 106 patients 5 were suffering from other diseases and 1 of them died In this case the delay in operating occasioned by the misguided aspiration of the stomach for two and a half hours was a factor, though a small one, in the fatal issue Against this may perhaps be set the case of basal pneumonia in which the period of aspiration provided an opportunity to correct the diagnosis, with avoidance of operation The possibility of clinical error cuts both ways and raises also the question of the number of patients wrongly diagnosed as perforations who lose their lives because the abdomen is opened too hastily Gastric crises, coronary occlusion, dissecting aneurysm, basal pneumonia with pleurisy, and pancreatitis are all acute medical conditions for which operation may be mistakenly undertaken

However this may be, the broad conclusion to be drawn from our experience seems to be that if the policy of aspirating perforated ulcers justifies itself on its merits, the risk of accepting it on grounds of possible error of diagnosis is not substantial

The discussion of errors of diagnosis would not be complete without mention of Sister Miller's sign Sister Miller is in charge of the casualty department of King George Hospital, and she has observed that those patients do well whose pain is rapidly relieved by the initial evacuation of the stomach in her department We have learnt to reconsider the diagnosis very carefully when Sister Miller is not happy about a case

RESULTS OF TREATMENT

Cases with Respiratory Infections

Of the 73 cases of actual perforation admitted to the hospital in 1946–50, 8 were associated with acute respiratory disease, and 4 of these showed radiological opacity in the lung fields on admission It is my impression, and it may be a fact, that the incidence of perforated ulcer rises during epidemics of influenza or coryza Certainly patients with quiescent ulcers tend to relapse if they get a cold in the head, and it is probable that acute ulcers also arise in patients with coryza and that a few of them proceed at once to perforation

Recovery from both perforation and respiratory infection was uneventful in 6 cases, though 1 of the patients was found to be tuberculous and was later referred to sanatorium A 7th case did well after drainage of an empyema The 8th patient actually recovered from his perforation only to die of his lung condition

The perforation occurred two days after the onset of a diffuse bronchopneumonia The radiograph showed bilateral basal consolidation of the lungs as well as air underneath the diaphragm An elderly man he improved under treatment, collapsed with a melæna and rallied with transfusion A subphrenic collection of fluid was thought to be a respiratory handicap and was drained The abdomen was now soft and the patient was on milk feeds, but cyanosis deepened, dyspnœa increased, and he died of right heart failure after nine days Necropsy showed a firmly closed duodenal perforation, fibrinous exudate below the diaphragm, but no peritonitis Death was due to myocardial degeneration, adhesive pericarditis and consolidation of both lungs Clearly the aspiration treatment had given him the best chance of recovery

None of these 8 patients with respiratory infections could have done better with operation, and some of them might have done worse

Other Associated Disease

Other sporadic cases of associated disease to which the same comment may apply are a uræmic man of 65 whose bladder was enlarged to the umbilicus, and a man aged 77 with coronary thrombosis whose perforation was confirmed by intraperitoneal gas Both these patients recovered In 2 instances the perforation occurred in a carcinoma of the stomach

One of these patients a woman recovered from the perforation but developed ascites during convalescence Exploration showed a gastric cancer covered with organising fibrin and widespread peritoneal carcinomatosis The other cancer patient was an old man of 81 with a twenty hour perforation and gross peritonitis He was operated upon at once, appeared to recover from the infection but died of exhaustion at the end of a week

Cases Operated Upon

Surgical intervention of major or minor degree was undertaken in 9 cases In 2 the operation was immediate The first patient was the aged man just mentioned The second was a diabetic of 56 with a forty-eight hour perforation and gross peritonitis This desperately ill man was treated by gastric aspiration and the insertion under local anæsthesia of drains into the right and left renal pouches and into the pelvis He died without material improvement two days later Necropsy showed an unsealed gastric perforation and total peritonitis

A man of 60 was operated upon after three hours' aspiration because he had a rising pulse rate and because he had perforated while eating a large meal His stomach was found to have been effectively emptied by the large gastric tube, and his lesser curve gastric perforation was already sealed by a delicate fibrin layer under the liver There was little peritoneal fluid and we came to the conclusion that the rise in pulse rate had been emotional in origin He made an uninterrupted recovery

Three minor operations were undertaken late in convalescence in order to drain local collections of fluid from the right renal pouch or subphrenic space Through a one inch incision under the right ribs a finger was inserted and gently advanced, separating the tissue planes until the fluid was reached A tube was then inserted and the skin closed round it This minor procedure was usually undertaken because of the development of mild fever, which might indicate early infection of the fluid collection There were other cases in which an area of persisting tenderness after the subsidence of the main peritonism suggested that a collection of fluid might be present, but these all resolved spontaneously It is likely that transient encystment of small collections of sterile fluid is a regular feature in the resolution of the peritoneal disturbance

Air swallowers

The remaining operations were on patients afflicted with air swallowing, either as an established habit or perhaps induced by the presence of the indwelling naso œsophageal catheter My first contact with this complication was in a case at the London Hospital (This case and others which occurred sporadically elsewhere than at King George Hospital are not included in this series because their treatment was not undertaken as a matter of hospital policy I have felt it important to keep the present experiment absolutely controlled at King George Hospital until the issue is clear)

The patient was a man of 50, with a six hour duodenal perforation and coincident acute bronchitis Treated with penicillin and by the aspiration régime he did well constitutionally His temperature and respiration rate subsided and he talked and smiled and read the newspaper His indwelling gastric tube produced small quantities of clear juice, but he astonished everyone with the enormous distension of his abdomen On the third day he was taken to the theatre and a small incision was made below the right ribs, whereupon his pneumoperitoneum collapsed like a pricked balloon Coils of intestine picked out of the abdomen at random for inspection showed a glistening peritoneum of normal pink colour No further exploration was made and the patient returned to bed The next day his abdomen was distended again though his excellent condition was unchanged Pondering this conundrum at the bedside, I observed the man swallow a gulp of air and it was clear that the swallowed air was passing from the stomach through an unsealed perforation into the peritoneal cavity It appeared that he could swallow air faster than it could be aspirated and that the surface tension of the bubbles in the narrow lumen of the naso œsophageal catheter was sufficient to prevent escape of gas between aspirations The small tube was therefore replaced by a stomach tube the size of a finger, which was left in place for twenty four hours The distension subsided, the perforation sealed, and the patient made a good recovery The site of the ulcer and its adhesions to the liver were subsequently confirmed at operation for persisting ulcer symptoms

Importance of X ray Control

This was the first occasion on which I met a perforation which failed to close with small tube aspiration It demonstrated in a remarkable way the innocuous character of the unsealed perforation, despite the continued escape of air, provided all *fluid* is removed from the stomach so that none is available to pass the gap into the peritoneal cavity Manifestly, however, such a situation is unstable and dangerous, since gastric aspiration is never absolutely reliable, as events at King George Hospital show

A man of 53, with a four hour duodenal perforation was treated in the usual way and for three days appeared to do well His condition then deteriorated, with pyrexia and a slowly rising pulse rate, while the gastric aspirate became dark and copious I was asked to see him on the seventh day, when he was quite ill Reviewing the radiographs of the abdomen, it was found that pictures taken on the third day showed more gas under the diaphragm than the film taken on the first day The significance of this had not been appreciated The patient had swallowed air, a fact confirmed by the ward sister, his perforation had been kept open by the gas and peritonitis had developed apparently by the fourth day An operation was carried out to drain the peritoneal cavity, but the patient died some hours later

The lesson did not sink in, and we are ashamed to report that soon afterwards an almost identical series of events occurred in another patient, which also ended fatally

The strict rule was therefore made that every patient treated by aspiration must be radiographed on the second day, and that if the film showed more gas under the diaphragm than was seen in the radiograph taken on admission, the abdomen was to be opened at once This occurred in the very next patient, again an air swallower with a duodenal perforation The second day showed an increase of gas below the diaphragm, operation was performed after thirty hours, an unsealed perforation was sutured, the pelvis was drained, and the patient made a satisfactory recovery One other patient was operated on for rapidly increasing gas beneath the diaphragm associated with a rising pulse after four hours' aspiration Again an unsealed perforation was sutured and the patient did well

I have recorded this episode in detail because of its unexpected nature It remains to be seen to what extent the swallowing of air constitutes a danger now that we are aware of it So far it appears that the risk from escape of air through an unsealed perforation is not great for twenty four to forty eight hours, provided the fluid contents of the stomach are removed by the indwelling tube But once the state of affairs has been recognised, operation should be undertaken immediately It is worth noting that the two fatal cases described to me by Dr Mullen are very like our air swallowers One of them was found to have an increase of gas under the diaphragm some days after the onset and died on the ninth day The evidence in the other case is not complete but is rather similar

" *Shock* "

Another patient died from a cause which has remained obscure

A woman of 32, rather frail and undernourished was admitted with a two hour perforation, a pulse rate of 120, and a cold clammy skin She was treated in the usual way by aspiration and penicillin, but developed a rapidly progressive circulatory collapse, with a profound fall in blood pressure, and died in twelve hours All that was found post mortem was a prepyloric perforation completely closed by fibrinous attachment to the liver and a minimal peritoneal reaction with a few ounces of turbid fluid Unfortunately the fluid was not cultured, but there was no suggestion in the appearances that virulent infection had taken place

A similar clinical picture with a more fortunate ending was seen later in the series, again a woman in collapse with a blood-pressure of 90/56 six hours after a perforation The abdominal condition responded to the aspiration, but she lay for a long time in a feeble state and was not well enough to go home till five weeks had passed Desmond (1950) in London, McElhinney and Holzer (1948) in Cincinnati, and Luer (1949) in St Louis have all described cases like these Though the perforation is recent, a shock like state develops rapidly and inexorably, the patient fails to respond to resuscitation and dies in a short time, having given no opportunity for surgical intervention Whatever the explanation, it is clear that in our fatal case operation would have achieved nothing, since the perforation was sealed and there was little fluid to remove from the peritoneal cavity

Fatal Cases

There is 1 other fatal case to mention—an old man of 81 with a three day perforation who died within twenty four hours The total of 7 deaths in the series of 73 cases may thus be recapitulated as follows

Two air-swallowers peritonitis
One shock
One bronchopneumonia pericarditis (perforation intercurrent and recovered from)
Three perforations over 24 hours
  Diabetic 48 hour perforation
  Senile 72 hour perforation ,
  Senile 30 hour perforated carcinoma

The development of the conservative method must accept responsibility for the deaths of the air swallowers, but clearly the others could not have benefited in any way from major surgery even had this been possible

Successful Cases

When we have been depressed by our 2 mistakes we have been borne up by the thought of the number of gravely ill patients among the 65 survivors whose chance of life has not been prejudiced by the additional burden of an operation If in writing this account, I have dealt at length with our problems and failures, it is because more can be learnt from them at this stage than from inadequate statistics But I should not do justice to my colleagues and assistants if I were to leave the impression that we have been indulging in a sort of clinical tight rope walk with the patient's life in suspense On the contrary, in a young healthy person nothing could be more uneventful than a typical perforation treated by aspiration The patient is put to bed having had his stomach emptied promptly on arrival at hospital and being already easier with his morphine In six hours he says that his pain is better, next day he is sore but can move about, the day after that his tube is out and he is on medical treatment just as if he had been admitted with a non-perforating acute extension of the ulcer The safeguards and examinations described are carefully practised, but in the main they yield quite negative results Indeed, my chief anxiety these last six years has been lest the routine nature of these cases should lull the staff into an easement of the vigilance so necessary to detect at once the case that goes wrong I think that might be a fair comment on the episode of the air swallowing

EXPERIENCE OF OTHERS

From personal contacts and a study of the literature I have been able to collect the following 555 cases from the United States, France, Holland, and England

	Cases	*Deaths*
Mullen (1950) Seattle	27	3
Bedford Turner (1945) Brighton	6	—
Lane (1950) Baltimore	79	1
Visick (1946) York	14	3
Seeley et al. (1950) U S Army	83	4
Quénu (1950), Paris	17	1
Iselin et al (1950) Nanterre	19	1
Swynghedauw (see Quénu 1950) Lille	8	—
Truscott and Withycombe (1950) Cambridge	20	3
Gill and Jenkins (1950) Guildford	24	4
Stead (1951), London	46	5
Bloem (1950) The Hague	6	1
Dodd (1950) London	10	—
Bullough (1950) Manchester	95	7
Hermon Taylor (1946) London	28	4
Hermon Taylor (1951) London	73	7
	555	44

It will be seen that 555 patients survived and 44 died Of the deaths 22 were in cases known to be hopeless on admission and too ill for operation (Visick 2, Gill and Jenkins 3, Mullen 1, Bloem 1, Stead 4, Seeley et al 3, Hermon Taylor 4, Bullough 4) There may have been others In 6 more cases death is known to have resulted from a cause unconnected with the choice of treatment—namely, pulmonary embolism, delirium tremens, pneumonia, shock Manifestly, whatever the ultimate therapeutic pattern, the hard core of inevitable deaths will persist The remaining 16 deaths represent the first returns of a new method, creditable themselves, and capable of improvement as the special problems that arise are recognised and dealt with

What is advocated, and what is reported, in this article is not the treatment of all perforations by aspiration regardless of circumstances There is no question of comparing a consecutive series of aspiration cases with a similar series operated on What is recommended is that the bulk of cases should be treated by aspiration as a policy, with operation reserved for the failures such as air swallowers, patients who cannot be intubated or are uncontrollable, cases with severe initial peritoneal contamination, and possibly others

SUMMARY

101 cases of perforated ulcer have now been treated by the aspiration method at King George Hospital, Ilford This paper analyses the second group of 73 cases

Of these 73 patients, 2 were lost through air swallowing, the steps required to deal with this complication are described The other 5 fatal cases were not related to the method of treatment Several patients were saved by aspiration who would have been serious operation risks

With 1 doubtful exception, no patient admitted as a surgical emergency lost his life because it was the policy to aspirate such of them as were diagnosed as perforated ulcers

Perforation of an ulcer is a complication which has lost its desperate character The protection afforded to the patient by maintained emptiness of the stomach allows time for each case to be considered on its merits No case should blindly be subjected to immediate operation

The first step in the treatment of any perforated ulcer under any circumstances is prompt evacuation of the stomach In the further treatment of most perforations, continued aspiration of the stomach is the method of choice, operation being reserved for special circumstances

I wish to record my appreciation of the judgment and skill of Mr C P Allen F R C S, and Mr J F R Bentley, F R C S, in treating these patients To my house surgeons and to the sisters and nurses of King George Hospital whose enthusiasm for this method of treatment has been the largest factor in its success, I should like to express my deep gratitude

REFERENCES

Bedford Turner E W (1945) *Brit med J* i 457
Black B M Blackford R F (1945) *Surg Clin N Amer* 25 918
Bloem T (1950) Personal communication
Bullough A S (1950) Personal communication
DeBakey M Odom C B (1940) *Sth Surg* 9 425
Desmond A (1950) Personal communication
Dodd H (1950) Personal communication
Gill W C, Jenkins T P N (1950) *Brit med J* i 488
Illingworth C F W Scott L D W Jamieson R A (1944) *Ibid* i 618 655
Iselin M Peret S Toutain J M (1950) *Mém Acad Chir* 76, 323
Jones F A Parsons P J White B (1950) *Brit med J* i 211
Lane J (1950) Personal communication
Luer C A (1949) *Surgery* 25 404
McElhinney W T Holzer C F Jun (1948) *Surg Gynec. Obstet* 87 8,
— (1949) Personal communication
Mullen B P (1950) Personal communication
Quenu J (1950) *Mém Acad Chir* 76 226
Seeley S et al (1950) In the press
Stead J R St G (1951) *Lancet* i 12
Taylor Hermon (1946) *Ibid* ii 441
Truscott B M Withycombe J R F (1950) *Ibid* i 894
Turner G G (1946) Personal communication
Visick A H (1946) *Lancet* ii 941
Wangensteen O H (1935) *Minn Med* 18 477

CONSERVATIVE TREATMENT OF PERFORATED PEPTIC ULCER

J R St G Stead
F R C S
SURGEON, HACKNEY HOSPITAL, LONDON

The evolution and technique of the conservative treatment of perforated peptic ulcer have been described by Hermon Taylor (1946), and he has now set out his results up to date (Taylor 1951)

The conservative method has been used at Hackney Hospital in selected cases during the past two years The 76 consecutive cases described here were not segregated, and were treated by the two general surgical firms without special facilities The cases are classified, according to treatment, in table I

Untreated Cases

3 patients were admitted moribund They were aged 61, 89, and 78 Treatment was clearly impossible, and they died after 15 minutes, 4 hours, and 8 hours The diagnosis was confirmed at autopsy 2 further cases were not diagnosed before death

Conservative Treatment

During the greater part of the period under review, both surgical firms treated all cases conservatively unless certain indications for operation were present, Of altogether 50 patients treated conservatively, 38 were fit for operation and 12 were unfit for operation

PATIENTS FIT FOR OPERATION

Diagnosis—In 32 of the 38 patients who, though fit for operation, were treated conservatively, the diagnosis of perforation was confirmed by the radiological demonstration of gas under the diaphragm In 2 of these 32, subsequent radiological examination showed no evidence of ulcer, on the basis of probability these cases are classified as duodenal ulcers In the remaining 6 there was conclusive clinical evidence of perforation, but free gas was not demonstrated, each, however, had radiological evidence of peptic ulcer and 4 subsequently underwent partial gastrectomy, at operation the appearances were consistent with a recent perforation

Management—One firm gave penicillin only, and the other used penicillin and sulphamerazine The results were not significantly different Before radiological examination the patient's stomach was aspirated, to check the diagnosis and the position of the Ryle's tube and the efficacy of the aspiration The radiograph sometimes revealed free fluid in the peritoneal cavity, and this was an indication for particularly close observation Patients were reviewed 4–6 hours after treatment was begun The initial dose of morphine did not mask the

TABLE I—TREATMENT OF 76 CONSECUTIVE CASES OF PERFORATED PEPTIC ULCER

Treatment	No of patients	No of deaths
Nil		
Moribund on admission	3	3
Undiagnosed antemortem	2	2
	5	5
Conservative		
Fit for operation—		
Gastric ulcer	3	nil
Duodenal ulcer	35	1
Unfit for operation—	3	3
Gastric ulcer	9	1
Duodenal ulcer		
	50	5
Operative	21	2
Total	76	12

pain in those whose response to aspiration was unsatisfactory, and such patients were operated on within 6 hours of admission. In successful cases repeated doses of morphine were usually unnecessary.

No rules can be laid down for the duration of aspiration and the time for starting feeds. The period of rest in bed, and the length of stay in hospital (average 19 days) were the same as in uncomplicated operation cases, and any time saved by the conservative method was due to the absence of complications.

Complications.—Freedom from complications is recognised as one of the chief advantages of the conservative method. In this group the most common complication was thrombophlebitis. No serious pulmonary complication was seen. There was 1 case of progressive pneumoperitoneum.

Case 1.—A man, aged 61, perforated less than 1 hour before admission. After 48 hours the abdomen was tense and tympanitic although the general condition was satisfactory and flatus had been passed. Radiological examination showed gross *pneumoperitoneum* with *no distension* of the gut. Through a 2 in. incision in the midline, under local anæsthesia, the abdomen was deflated. There was a small quantity of turbid free fluid, and matted coils of small gut were seen. The fluid was reported sterile. On the day after operation the abdomen again became tense and radiological examination showed that the gut was distended. The ileus eventually subsided and the patient recovered. Subsequent radiological examination after a barium meal showed a deformed duodenal cap and a normal small gut.

Since the distension was progressive, the perforation either remained unsealed or re-opened, but the source of the free gas is unknown. If swallowed the air should have been removed from the stomach by aspiration and the radiograph does not show gas in the stomach. There was, however, gas in the small intestine, and it is perhaps more probable that this was the source of the increasing quantity of gas in the peritoneal cavity. Whatever the source of the free gas, this patient owes his recovery to the resistance of his peritoneum rather than to the efficacy of the treatment.

Mortality.—There was 1 death in this group.

Case 2.—A man, aged 40, had suffered from indigestion for 15 years; radiological examination at another hospital was negative. He perforated 4 hours before admission. He was a moderately well nourished man in severe pain with cold extremities. Pulse-rate 84 per min.; blood-pressure (B.P.) 130/70 mm. Hg. Heart and lungs clear. Abdomen: board-like rigidity in epigastrium and down right side; liver dullness diminished. No tenderness on rectal examination. Radiological examination: "considerable quantity of gas under diaphragm on both sides."

Conservative treatment was instituted. After 8 hours the abdomen was softer, and 4 hours later the patient was *apparently comfortable*. *24 hours after* admission his general condition was satisfactory. The rigidity had greatly diminished, and there was tenderness only in the epigastrium; there was, however, obvious distension. 48 hours after admission aspiration was discontinued and feeds by mouth started.

Progress appeared satisfactory until the 5th day when the abdomen became more distended and gastric aspiration produced 47 oz. of dark bile-stained fluid in 24 hours. The bowels were open on the 6th day, but the distension was not appreciably reduced. The patient became confused and had hallucinations, and the peripheral circulation failed. He died on the 7th day after admission. Necropsy report: "general peritonitis; unsealed perforated duodenal ulcer." The ulcer was chronic, and involved the anterior and superior aspect of the first part of the duodenum. The peritoneal cavity contained a quantity of purulent fluid.

In this case conservative treatment failed, and there had been no contra-indication to operation. The early *progress* was typical of a successful case and suggested that the ulcer had become sealed. Possibly aspiration was stopped too soon and distension re-opened the perforation.

Comment.—In this group of 38 patients sealing of the perforation failed twice, although only 1 patient died. Until the cause of these failures is known, and shown to be avoidable, there must be some anxiety attached to the use of the method; for when it was obvious that the perforation had not remained sealed it was too late for operative treatment effectively to control infection, and the issue depended entirely on the patient's resistance. This failure-rate in a large series of *early operable* cases might condemn the method despite its advantages to the majority of patients.

TABLE II—DATA ON 12 CASES UNFIT FOR OPERATION AND TREATED CONSERVATIVELY

Case no.	Age (years)	Site of ulcer	Hours after perforation	Associated conditions	Result	Remarks
6	44	S	6	—	Died after 10 days	Peripheral circulatory failure on admission
7	77	D	4	—	Died after 30 days	
8	67	S	3	Hæmorrhage, bronchitis	Died after 30 hrs	
9	60	S	24–48	Hypertension, emphysema	Died after 30 hrs	Failed intubation
10	71	D	24 +	—	Recovered	Dehydrated; circulatory failure on admission
11	54	D	12–24	—	,,	Dehydrated
12	64	D	1	Recent massive hæmorrhage	,,	Perforated in ward while under treatment for hæmatemesis
13	71	D	5	Prostatic obstruction	,,	
14	74	D	12	Bronchitis	,,	
15	46	D	6	Active pulmonary tuberculosis	,,	
16	62	D	9	Inop. rectal carcinoma	,,	
17	63	D	24 +	—	,,	

D = duodenum S = stomach

PATIENTS UNFIT FOR OPERATION

Of the 50 patients treated conservatively, 12 were regarded as unfit for operation either on account of the effects of the perforation or on account of associated disease (table II). The group is of interest because many surgeons consider that conservative treatment should be limited to such cases.

Diagnosis.—Of the 12 patients in this group, the diagnosis was confirmed at autopsy in 4. Of the survivors 3 had free gas and free fluid under the diaphragm and required peritoneal drainage, while 5 had no radiological abnormality, but at subsequent operation the appearances suggested a recent perforation; in 1 of these there was pus surrounding the duodenal ulcer.

Management.—The management was modified according to the condition of the patient. 5 (with normal radiological appearances) progressed uneventfully on conservative treatment. The 3 cases requiring drainage are summarised below.

Case 3.—A man, aged 71, who had perforated over 24 hours previously, rather unexpectedly responded to aspiration and rehydration. After 48 hours he had a grossly distended silent abdomen with an obvious collection of free fluid in the peritoneal cavity. Under local *anæsthesia* a small incision was made below the right costal margin, and aspiration produced 80 oz. of clear green fluid, which was reported sterile. Later, a pelvic abscess developed, which drained spontaneously per rectum. The patient was ultimately discharged.

Case 4.—A woman, aged 54, having perforated about 17 hours previously, was dehydrated and the abdomen was grossly distended. After routine treatment a localised-collection of turbid fluid (reported sterile) was aspirated from the right hypochondrium under local anæsthesia The subsequent course was uneventful

Case 5 —A man aged 63, admitted over 24 hours after perforation with obvious peritonitis, was treated conservatively and developed a right subphrenic abscess which was drained during the 2nd week The further course was uneventful

In cases 3 and 4 the initial conservative treatment was followed by a trivial operation, a formal laparotomy and suture under general anæsthesia must have involved a greater risk In both, the removal of the fluid not only reduced the risk of infection but also appeared to relieve the ileus

Mortality —Of the 4 deaths in this group, 1 was probably avoidable though in this case the gastric perforation was of a type in which the postoperative mortality is high

Case 6 —A man, aged 44, had 20 years history of indigestion, and had been invalided from the Army on account of *duodenal* ulcer 24 hours of anorexia and pain was followed by perforation 4 hours before admission The patient was profoundly shocked pulse rate 120 per min, poor volume Abdomen generalised board like rigidity The stomach was aspirated and intravenous saline and dextrose commenced After 9 hours there was no improvement, B P 76/60 4 pints of plasma were given, with improvement in the peripheral circulation, but it was not until 24 hours after admission that the B P rose to 110/75 Treatment was continued as for general peritonitis Although distension was relieved and the bowels became active the patient's condition deteriorated progressively Bronchopneumonia was the immediate cause of death Autopsy report "Perforated *gastric* ulcer, general peritonitis, bronchopneumonia"

The patient was so shocked on admission that plasma was indicated in the first instance However, the response, though slow, was complete and the circulation was restored Aspiration was begun immediately and failed to prevent or control purulent peritonitis This type of case, which is of considerable importance, will be discussed further

The remaining 3 deaths were, in my opinion, unavoidable, but as others may disagree the essential features are described

Case 7 —A man, aged 77, had perforated 4 hours before admission, site of ulcer unknown He was a pale, frail looking old man with a dry tongue and cold extremities Pulse rate 96 per min, B P 200/100 Abdomen generalised board like rigidity With routine conservative treatment his condition improved and the abdomen became soft, bowel function returned Radiological examination on the 3rd day showed gas and a fluid level under the right diaphragm This fluid became infected and a subphrenic abscess formed, with a right pleural effusion and bronchopneumonia in the right lower lobe Gross œdema was present over the sacrum and lower ribs The patient's condition deteriorated and he died on the 30th day after admission Autopsy showed perforation of a duodenal ulcer, and confirmed the other clinical findings

Case 8 —A man, aged 67, was unable to give a history which was obtained from his wife For 10 years he had had "bronchitis" following appendicitis and peritonitis He was always poorly with occasional epigastric pain relieved by powder 4 days before admission he had severe abdominal pain with watery vomits 3 days before admission he had melæna with nine stools in 24 hours and became very pale and ill He perforated 3 hours before admission On admission he was pale and collapsed Pulse rate 120 per min B P 120/60 Heart enlarged, obvious dyspnœa and bronchospasm Abdomen rigid Gastric aspiration produced chocolate coloured fluid tinged with red Blood transfusion was commenced 6 hours after admission the patient collapsed and became comatose, B.P 72/42 He never regained consciousness although the circulation improved and the B P rose to 115/70 He died 30 hours after admission Autopsy report "Perforated gastric ulcer fibrinopurulent peritonitis, bronchopneumonia"

Case 9 —A man, aged 60, had for 3 months had substernal pain with loss of weight 27 hours before admission he began to have severe epigastric pain, which was unrelieved by morphine He was extremely ill, with dry and brown tongue and scarcely palpable pulse, B P 118/80 Lungs crepitations at both bases Abdomen rigid Radiological examination showed gas under diaphragm In this case all attempts to pass a Ryle's tube failed Intravenous plasma was given without improvement in his general condition, and operation was not considered justifiable The patient died after 36 hours Autopsy showed fibrinopurulent peritonitis, and two perforated chronic gastric ulcers, one of which was subjacent to the cardia, fibrous scar in hypertrophied myocardium The close proximity of the ulcer to the cardia may have explained the failure to pass the tube, which was a unique experience in this series

In these cases it was believed that there was no alternative to conservative treatment, although in case 5 survival for a month in spite of a subphrenic abscess may suggest that in the first instance the patient was a reasonable operative risk

Cases Treated By Operation

In my opinion the reported results did not justify conservative treatment of a consecutive series of cases A "safety first" policy was adopted, and certain indications for operative treatment were recognised (table III)

FAILURE OF CONSERVATIVE TREATMENT

When conservative treatment is succeeding aspiration of the stomach greatly relieves the pain, and within a few hours the abdominal rigidity diminishes in extent and degree, receding from the left to the right iliac fossa, and then up the right side to the epigastrium The patient's colour improves, and his agonised expression changes to one of resignation, if not of contentment

TABLE III—ANALYSIS OF 21 CASES OF PERFORATION TREATED SURGICALLY

Reason for operating	No of patients	No of deaths
Failed conservative treatment	4	nil
Diagnosis in doubt	6	1
Inexperience of conservative method	3	1
Gross pyloric obstruction	1	nil
Routine	7	nil
Total	21	2

The indications for abandoning the conservative treatment were (1) persistent or recurrent severe pain, and (2) extension of the area of tenderness and rigidity These are more useful indicators than the pulse and temperature, significant changes in which usually lag considerably behind local pathological changes 4 patients were operated on because progress under conservative treatment was unsatisfactory In 2 cases the perforation appeared to be unsealed at operation In all, the postoperative course was uneventful

DIAGNOSIS IN DOUBT

6 patients were operated on because the diagnosis remained in doubt Acute appendicitis was the alternative diagnosis in 4 In the 5th, a woman, aged 81, perforated diverticulum was regarded as the more likely diagnosis, but it was obvious on opening the abdomen that the free fluid came from the stomach or duodenum As a lower abdominal incision had been made it was decided to close the wound and treat the perforation conservatively rather than prolong the operation The further course was uneventful

Case 18 —The 6th patient was a man, aged 84, with a vague history and obvious general peritonitis His general condition was thought to be fair The diagnosis was in doubt, and laparotomy was decided on Before the peritoneum was opened the patient died Autopsy report Perforated duodenal ulcer general peritonitis

It is not claimed that this patient would have done well on conservative treatment

INEXPERIENCE OF CONSERVATIVE METHOD

Assistants with no experience of the conservative method were instructed to operate on cases of perforated ulcer when advice was not available This occurred 3 times, including the first 2 cases of the series, 1 patient died

Case 19 —A man, aged 54, had perforated 6 hours previously His general condition was satisfactory, there were classical signs of perforation. The induction of anæsthesia by a casualty officer occupied 40 minutes owing to considerable difficulty with intubation, and relaxation was unsatisfactory throughout the operation The perforation was sutured and the fluid aspirated from the peritoneal cavity The postoperative course was stormy, and the patient died on the 10th day Autopsy report "Bilateral pulmonary collapse with bilateral bronchopneumonia" No purulent peritonitis or ileus present

In this case conservative treatment would probably have been successful Conservative treatment by an inexperienced surgeon is probably safer than operative treatment with an inexperienced anæsthetist

PYLORIC OBSTRUCTION

In 1 case perforation followed 2 weeks of frequent projectile vomiting, which had resulted in dehydration and emaciation The reasons for deciding on operative treatment, after rapid rehydration, were (1) his condition had undermined his peritoneal resistance, (2) the escaping fluid was likely to be heavily infected, and (3) it was uncertain whether gastric aspiration would successfully control ileus in the presence of gross pyloric stenosis At operation the pylorus was grossly stenosed, the perforation was sutured, but gastro enterostomy was not performed For the first few days after operation there was considerable gastric residue without bile, but when further operation was being seriously considered bile appeared in the aspirate His subsequent progress was slow, but on discharge from hospital he had gained weight and felt well enough to refuse further surgical treatment

ROUTINE OPERATION

One surgical firm adopted the conservative method some months after the series commenced, and the 7 "routine" cases are included only because they occurred during the period under review As far as is known, there was no contra indication to conservative treatment in these cases

Results

The mortality in the whole series was 15 8%, excluding the 5 untreated patients, the mortality is 9 7% This result compares favourably with the mortality of 17% in a series of 80 cases operated on at Hackney Hospital between October, 1945, and October, 1948 In these two series the patients came from the same community and were treated under similar conditions The mortality of the 50 patients treated conservatively was 10%

The results in cases of duodenal ulcer were

Treatment	*No of patients*	*No of deaths*	*Mortality (%)*
Conservative	44	2	4 5
Operative	19	2	10 5
Total	63	4	6 3

Thus of the 59 survivors 42 (71%), including 9 complicated cases, have been spared a general anæsthetic and formal laparotomy with their associated discomforts and complications Of the 4 deaths, 2 must be regarded as avoidable, 1 was treated conservatively (case 2), and the other by operation (case 18)

The results for gastric ulcer were

Treatment	*No of cases*	*No of deaths*
Conservative	6	3
Operative	2	nil
	8	3

Of the 3 deaths in cases treated conservatively, 1 (case 6) was due to failure of the method or its application, and 2 (cases 7 and 8) were regarded as unavoidable

Discussion

This series, though numerically insignificant, illustrates the problems, failures, and successes of the conservative treatment of perforated peptic ulcer The problems are concerned with diagnosis, treatment, and the selection of cases

DIAGNOSIS

The diagnostic problems may be considered from three aspects (1) the proof of perforation of a peptic ulcer, (2) the differentiation between gastric and duodenal perforation, and (3) the differentiation between perforated peptic ulcer and other acute conditions ✓

Proof of Perforation —All the patients in this series are believed to have had a perforated peptic ulcer Free gas under the diaphragm has been taken to indicate that the stomach or duodenum has perforated The quantity of free gas does not necessarily indicate the prognosis, since it is not a reliable measure of the extent or the virulence of the peritoneal contamination The demonstration of free fluid is a much more valuable indicator Of the patients treated conservatively 47 were submitted to radiological examination, free gas was present in 38, and fluid in 19 Radiography is not decisive when negative In the first place, it is difficult to place a patient in great pain in the most favourable position for demonstrating gas, and secondly, an apparatus requiring only a short exposure is necessary to obtain a satisfactory film of a patient whose rapid, shallow, and painful respiration prevents him holding his breath for a long exposure A merely confirmatory radiograph may be taken after the stomach has been emptied and pain further relieved by morphine, but in doubtful cases this procedure may not be justified

In 10 patients treated conservatively, all of whom survived, radiography was either not available or failed to demonstrate gas, 8 of these had subsequent operations at which the surgeon was satisfied that there had been a recent perforation

Differentiation of Gastric and Duodenal Perforation — The number of gastric perforations treated conservatively is much smaller than that of duodenal perforations There are a priori grounds for anticipating less satisfactory results with conservative treatment of gastric perforations, since the peritoneal contamination is usually more extensive and more virulent This more severe assault on the peritoneum is due to the larger size of the perforation and to the absence of the barrier formed with duodenal perforation by the spastic pylorus, which divides the stomach contents from the perforation With a large gastric perforation removal of excess fluid and food debris may be essential, although the peritoneum may be able to neutralise the fluid which has escaped through a small hole in the stomach Moreover, there may be a limit to the size of the hole which can become sealed before further infection occurs

If the treatment of a gastric perforation is to differ from that of a duodenal perforation, the two types must be differentiated from each other This could not as a rule be done with confidence The history and physical signs are often inconclusive, the precise results of previous radiological investigation (if any) are usually not known by the patient, and when a definite radiological diagnosis is available, it is not infallible (case 6)

Further experience may show that small gastric perforations through which little fluid escapes do as well with conservative treatment as do duodenal perforations from which they are clinically indistinguishable.

Large perforations associated with gross contamination are unlikely to be controlled by conservative measures, these require operative treatment Profound shock and the radiological demonstration of quantities of free fluid may be the indications for operation Thus as an indication for the method of treatment the site of the ulcer is less important than the extent and virulence of peritoneal contamination

Differential Diagnosis—That non operative management may increase the risks if the diagnosis is wrong has been appreciated In almost 80% of the patients treated conservatively in this series radiography confirmed the diagnosis beyond reasonable doubt, and when the radiographic appearance was normal, anxiety stimulated a careful review of the signs and symptoms

Hæmorrhage and strangulation of a viscus are probably the most urgent indications for laparotomy, but they are seldom likely to be mistaken for a perforation General peritonitis from causes other than perforation might benefit from aspiration, chemotherapy, and rehydration for a few hours before operation Acute cholecystitis and acute pancreatitis are not urgent emergencies even if operation is regarded as the treatment of choice in the acute phase Acute appendicitis is the commonest source of danger, and in this series 4 cases were operated on because the condition could not be excluded (a 24 hour radiological service was not available at the time) but in the ulcer age group a 6 hour delay in operating for acute appendicitis is unlikely to be fatal

When perforation of a peptic ulcer is regarded as an absolute indication for urgent operation, doubtful cases will be submitted to laparotomy Sometimes, however, the alternative condition either contra indicates operation, or is more satisfactorily treated after investigation and preparation Confidence in the conservative régime has the advantage of providing time to establish the diagnosis and to apply deliberate treatment

Maingot (1948) has estimated that 90% of perforated peptic ulcers are diagnosed correctly It does not appear reasonable, therefore, that diagnostic difficulties should dictate a form of treatment which is not necessarily suitable for every case The expediency of laparotomy is acknowledged, but it is unjust to condemn the conservative management of a perforated ulcer because it does not cure acute appendicitis or an internal hernia The risks of incorrect diagnosis are reduced to justifiable proportions if three precautions are observed (1) routine radiography, (2) careful observation during the first 6 hours, and (3) laparotomy when a condition requiring urgent operation cannot be excluded In this series, 6 patients (less than 10%) were operated on because of diagnostic difficulties, and the number would have been fewer had a radiological service always been available The diagnosis of perforated peptic ulcer was confirmed at autopsy in all cases where death took place after conservative treatment, and no patient died from another condition because he had been treated conservatively in the first instance

Treatment—Clearly the therapeutic measures which constitute 'conservative treatment' have a limited influence on the natural course of the disease *An empty* stomach is not essential for the sealing of an ulcer, particularly if the perforation is in the duodenum, a spastic pylorus is the natural barrier between the stomach contents and perforation of the duodenum, and with spontaneous cure this barrier has sufficed In several successful cases in this series the stomach was not kept empty, despite the most conscientious efforts There are several reasons for this (1) it is almost impossible to ensure that the end of the tube remains at "the bottom of the sump", (2) a patent tube may not function under negative pressure, (3) the time and patience required f ficient aspiration cannot always be given by an staff (continuous suction is, in my opinion, less efficient than repeated aspiration) Moreover, there is evidence that if a duodenal perforation does not become sealed, the fluid escaping during the stage of ileus is foul intestinal contents This contamination cannot be prevented by gastric aspiration as the fluid escapes before it regurgitates into the stomach It cannot, therefore, be claimed that aspiration prevents the escape of fluid from a perforation, although in the early stages it may limit the quantity that escapes

The second therapeutic measure is the administration of chemotherapy to control infection in the contaminated peritoneal cavity One team gave penicillin only to 26 cases treated conservatively A localised abscess developed in 2 cases, in each of which perforation had taken place more than 24 hours before 3 other patients had local *aspiration of fluid on the 2nd, 3rd, and 6th* days after perforation, and in each case the fluid was reported sterile, but it is difficult to believe that all the organisms present were sensitive to penicillin The decision not to operate at all when the perforation is sealed was a logical step forward after closure without drainage had proved so satisfactory There is, however, a limit to the quantity of irritating or infective fluid which the peritoneum can successfully neutralise, even with the assistance of chemotherapy, and when this quantity is exceeded the excess should be removed

The third, and possibly the most effective, therapeutic measure is the control of ileus Whether peritonitis is chemical or bacterial, ileus develops, and when much fluid is present paralysis and distension of the gut may be extensive and long continued Efficient management of this complication is, therefore, as essential with the conservative method as it is after operation

Selection of Cases—The following indications for operation are suggested

1 Where the surgeon is inexperienced Experience is required both to reduce the risk of error in diagnosis, and for the observation of cases during the first 6 hours

2 With failure of the conservative method On account of our ignorance of the conditions necessary for sealing of the perforation, and doubt as to whether gastric aspiration fulfils these conditions, cases have to be judged individually Signs of failure should be recognised while operative treatment can still be effective

3 With gross peritoneal contamination When the patient is profoundly shocked and does not respond rapidly to the relief of pain by aspiration and morphine gross contamination of the peritoneum is probably present, and operation should be undertaken when the patient has been resuscitated Aspiration of the irritating fluid may prove an essential part of restorative treatment, and even while shock persists aspiration of the fluid under local anæsthesia may be justifiable Although such cases are more likely to have a gastric perforation, it is the effects of the perforation rather than its site that indicate the *method of treatment*

4 Where the diagnosis is in doubt If a condition requiring urgent operation cannot be excluded laparotomy is indicated

The results in 39 consecutive cases treated by one firm, according to the principles outlined above, are shown in table IV

TABLE IV—RESULTS IN 39 CONSECUTIVE CASES TREATED BY ONE SURGICAL FIRM

Treatment	No of patients	Free gas present	No of deaths
Conservative			
Good risk cases—			
Duodenal ulcer	18	18	0
Gastric ulcer	2	2	0
Poor risk cases—			
Duodenal ulcer	5	3	0
Gastric ulcer	1	1	1
	26	24	1
Operative	13		2
Total	39		3*

* Mortality 7 6%

The death in the group treated conservatively was case 9 The 2 deaths in the operation group (cases 18 and 19) have already been commented on, and were unconnected with the use of the conservative method These results are no worse than those of many operation series, and 66% of the patients avoided a major operation under general anæsthesia

Summary

Of 76 consecutive cases of perforated peptic ulcer, 50 were treated conservatively with 5 deaths, 4 of which were of patients rated unfit for operation

With conservative treatment routine radiographic examination is essential Cases of general peritonitis in which free gas is absent, and those in which free fluid is demonstrated, require particularly careful assessment

Conservative treatment is practicable without specialised facilities, but it demands constant supervision by an experienced surgeon, notably during the first 6 hours, by the end of which time it is usually possible to tell whether this method is succeeding

The conservative method is still on trial, and the indications for its use are not yet established.

I wish to thank Mr W E Tanner, F.R.C S, for his criticism and encouragement and Mr J C Gillies F.R C.S E., for allowing me to include his patients in the series I wish also to acknowledge the judgment and skill of Mr R F Read, F.R.C.S., and Mr H M Jamison, F.R.C.S, who were responsible for the successes in this series I am grateful to Dr H P Kent, who kindly reviewed the X ray films

REFERENCES

Maingot R (1948) Abdominal Operations New York p 303
Taylor H (1946) *Lancet* ii 441
— (1951) *Ibid* i 7

MEASUREMENT OF HEART SIZE

Geoffrey Bourne
M.D Lond, F R C.P
PHYSICIAN IN CHARGE OF THE CARDIOLOGICAL DEPARTMENT, ST BARTHOLOMEW'S HOSPITAL, LONDON

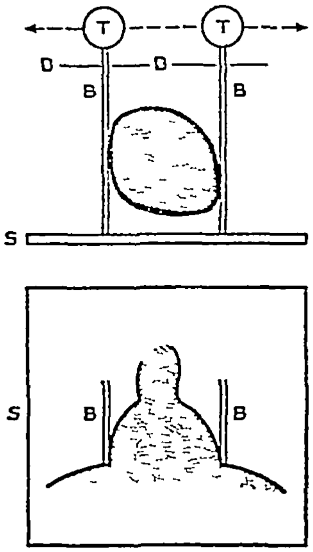
B G Wells
M.D Lond M.R C.P
CHIEF ASSISTANT TO THE DEPARTMENT

In the diagnosis, prognosis, and observation of progress in heart disease no fact is of more importance than the size of the heart Many methods of mensuration have been in use In early days percussion and palpation had to be relied upon, but radiology as an exact method has largely superseded these in cardiac clinics, except for patients who are too ill to move from bed, or too remote from apparatus Various methods of X-ray estimation of heart size have been employed, including the taking of a 6 ft film and various types of mechanical orthodiagraphy

We show here the value of a simple method of measurement and prove that it is reliable within narrow limits The method is not new but seems to have fallen to some extent into disuse

METHOD

The apparatus consists of a standard X-ray screening set but must be of the type in which the tube and shutters may be moved horizontally or vertically while the screen remains stationary This is in contrast to the more usual arrangement in which the tube and screen are coupled so that the tube may not be moved without moving the screen with it The vertical and horizontal shutters have separate controls The patient is placed standing behind the screen and facing the examiner, and his position is adjusted, by palpation of the shoulders, chest, and hips, so as to ensure that the transverse plane of the chest is parallel with the screen He is told to lean firmly forwards and to press the shoulders and upper part of the chest as near to the screen as possible, the arms hanging to the side He is also told to stand with the feet firmly apart to prevent swaying



The narrow beam (B) from the movable tube (T) is reduced to a narrow slit and passes forwards touching the left and right borders of the heart, on to the screen (S)

When adequate visual accommodation has been reached, and a general view of the chest obtained, the vertical shutters are closed until the field is rather less than an inch wide The tube and shutters are moved until the right border of the heart lies in the centre of this narrow vertical field The position of this border is marked on the screen by a vertical grease pencil line The tube and shutters are now moved until the left border of the heart is in the centre of the field, and this border is marked in a similar way (see figure) It is advisable to return to the right and left borders again to confirm that the marks are still accurate, because the patient may have moved Further precautions must be observed to obtain an accurate result Measurement is taken after a full easy inspiration at the end of which the breath is not held in The patient is asked to "breathe deeply into the stomach," and by observing the diaphragm it can be confirmed that the depth and character of the inspiration are natural and full The heart is measured in diastole Systole does not seem to influence the position of the right border to any appreciable extent, but on the left side there may be in some cases nearly a centimetre difference between the two cardiac phases The mark of the grease pencil on the right border will be made at a level slightly higher than that on the left, but the error so introduced into the transverse measurement can be kept to 0 1 cm or so

DIFFICULTIES

Certain difficulties are met with in an occasional case Slight scoliosis may cause the right border of the spine to protrude further to the right than the right border of the heart This was met with once in the investigation

The presence of a triangular pad of epicardial fat between the outer and lower edge of the heart shadow and the diaphragm may introduce difficulty, particularly on the left side, but recognition of this is usually sufficient to make it possible to visualise the edge of the left ventricle without trouble

The right border of the heart is in some people extraordinarily translucent to X rays, but here again care in the observation of shadow movement is nearly always sufficient to guard against error

Patients must understand very definitely that they must not move, and the best way of ensuring stability is by reiterating to them that they must keep the upper part of the chest and the shoulders leaning firmly forwards against the screen

In a few stocky adipose individuals the diaphragm may be so high that its shadow actually bisects the transverse cardiac diameter at a level which makes accurate transverse measurement difficult

ADVANTAGES

The advantages of the method are that, if the screening-room is adjacent to the examination room, the physician can screen his own cardiac patients readily, and the screening becomes part of the clinical investigation The method is rapid, and no expenditure on films is required The method is superior to that of a 6-ft film taken by a technician in the X ray department, for in such a film it is unknown whether the heart is in systole or diastole, and holding the breath for the exposure may possibly alter the size of the heart Moreover, the difficulty experienced by many patients in obeying instructions about breathing is apparent on screening such patients, and their misunderstandings can more easily be corrected

ACCURACY OF METHOD

To prove the degree of accuracy of the method 53 persons were investigated, giving a total of 159 separate cardiac measurements The experiment was done with batches of five or six people at a time Three separate measurements were recorded in each case, and these were made in an order which was scrambled by the other member of the experimental team on each occasion In this way the investigator making the measurement remained ignorant of the identity of the subjects and of the order in which they were being placed behind the screen Care was taken that the subjects were not recognised, and a definite numerical figure of transverse diameter was noted after each experiment, the measurement being recorded at the time by the other member of the team

RESULTS

The differences between the highest and lowest of the three separate "blind" measurements were as follows

Difference (cm)	*No of cases*	
0 0	1	49
0 1	3	
0 2	7	
0 3	12	
0 4	9	
0 5	9	
0 6	8	
0 7	2	4
0 8	1	
0 9	1	

In 77% of the 159 measurements of heart size the divergence between the three separate measurements was 0 5 cm or less, and in 92% it was 0 6 cm or less When it is realised that this error includes possible variation in the localisation of both the right and the left borders, the general accuracy of the method becomes still more striking These results were obtained "blind" If, in routine clinical work, three similar measurements are taken they can be further checked if a significant error between two or more results is found Further accuracy should then be obtainable

EFFECT OF CHANGE IN POSTURE ON CARDIAC MEASUREMENT

One source of error in anteroposterior screening and measurement of the heart is due to the patient's chest being not quite parallel to the screen To test whether slight inaccuracy in this position could introduce serious error, measurements were made first with the patient as straight as possible , secondly with the patient turned slightly towards the left anterior oblique position with the left shoulder touching the screen and thirdly with the patient rotated in the direction of the right anterior oblique position so that the right shoulder touched the screen In neither of these two semilateral positions was the rotation great, but in each of them it was sufficient to be easily detectable by the hands of the examiner Slight rotation towards the left anterior oblique position in 17 cases showed an increase in 3 only and a decrease in 14 In only 1 case showing an increase was this significant, 0 7 cm In the other 2 it was negligible, 0 1 and 0 2 cm Of the 14 cases showing a decrease in size, 8 showed a decrease which was insignificant (0 3 cm or less) and 6 showed a measurable decrease, the figure varying between 0 6 cm and 0 9 cm The fact that so many showed a decrease, even though this was small in more than half of the cases, is possibly of some significance Rotation towards the right anterior oblique position showed an increase in 7 cases and a decrease in 5 In 4 cases there was no change The discrepancy of one case in the total number examined in this position was due to the fact that in one person the slightest degree of rotation towards the right caused the right border of the heart to be obscured by the vertebral column, which showed some scoliosis The increase in this position in 2 cases measured 0 6 cm , in 5 cases it measured 0 5 cm or less The decrease in size in this position in all 5 cases was less than 0 4 cm

Thus in both semi oblique positions there was a significant increase in only 3 cases out of 33 measurements, this increase being about 0 6 cm The decrease in size on turning towards the left anterior oblique position is presumably due to the fact that the long axis of the transverse cardiac diameter lies roughly in this direction It is essential in cardiac mensuration to ensure that the patient is accurately facing the screen, but deviation from exact accuracy to a degree so slight as not to be detectable seems not to influence the accuracy of measurement to any significant degree This positional source of possible error is common to all methods of radiographic heart measurement

CONCLUSION

It is of great importance that there should be available in cardiological departments apparatus capable of measuring accurately and rapidly the size of the heart The form of apparatus used in this series of experiments seems to provide these necessary qualities

By careful measurement of the heart it can be determined in all cases whether the organ is of normal size, by comparing the figure with the theoretically normal figure of such tables as those of Hodges and Eyster (1924), in which allowance is made for the patient's age, height, and weight Furthermore, the measurement of the heart at intervals of months or years provides invaluable information regarding diagnosis and prognosis By routine numerical estimation of the transverse diameter of the heart, reinforced by screening in the oblique position, the examiner's opinion about the size of the patient's heart becomes progressively more accurate and reliable

REFERENCE

Hodges P C Eyster J A E (1924) *Amer J Roentgenol* 12 259

DIAMINODIPHENYLSULPHONE IN THE TREATMENT OF LEPROSY

JOHN LOWE
M D Birm M R C P
SPECIALIST, NIGERIA LEPROSY SERVICE LEPROSY SETTLEMENT,
UZUAKOLI, EAST NIGERIA

A PAPER published some months ago (Lowe 1950) described our experience during 1948 and 1949 with diaminodiphenylsulphone (D A D P S), given by mouth, in leprosy , a preliminary report had been published previously (Lowe and Smith 1949)

In general, the use of sulphone was held to be a great advance in the treatment of leprosy , the treatment was effective in all types of active leprosy and D A D P S was found to be much the cheapest sulphone to use and probably the most effective Two modes of administration were recommended (1) daily treatment with 100 mg a day for two weeks followed by 200 mg a day for two weeks and thereafter 300 mg a day and (2) twice weekly treatment with 100 mg. doses in the first week, 200 mg. doses in the second week, and so on to 500 mg. doses in the fifth and following weeks. These doses were found to be the largest that were well tolerated by African patients. The dosage was discussed, and the question was raised whether a dose of 300 mg. a day was necessary or desirable; it was suggested that "the best standard dose may be less than our present 300 mg."

Since that paper was written D.A.D.P.S. treatment has been rapidly extended to over 500 patients; further studies have been made of the dosage in relation to therapeutic and toxic effects, and the findings are presented here.

TOXIC EFFECTS

The toxic effects of D.A.D.P.S. are of the same nature as those encountered with other sulphones, and they are no more common than with other sulphones given in their usual doses. In the minimisation of toxic effects, gradual induction of sulphone treatment is of paramount importance.

Anæmia

A fall in hæmoglobin levels is the almost invariable accompaniment of sulphone treatment of any kind. This fall usually lasts a few weeks, and then the level becomes stabilised in Africans at about 11 or 12 g. per 100 ml., though in well nourished persons it may be higher. A fall to below 9 g. per 100 ml. is an indication for a temporary cessation of treatment or a reduction in dose.

The anæmia produced by sulphones is said to be mainly hæmolytic in origin. It seems more than possible, however, that other factors contribute, such as iron deficiency and vitamin deficiency, for sulphones may interfere with iron absorption (Brownlee 1948), and may also reduce "refection" of vitamins in the gut. The administration of iron in the form of ferrous sulphate seems to help considerably in the maintenance of hæmoglobin levels. If the anæmia were purely hæmolytic, this should not be so. Some workers have recommended yeast preparations, but we have found them unnecessary, and are thus saved much trouble and expense in treating our very large number of cases.

In a few of our patients sulphone treatment has been rendered difficult by the presence of persistent anæmia associated with the liver dysfunction, possibly nutritional in origin, which is so common in our Africans; but on the whole anæmia has caused little trouble in our patients.

Experiments made here have shown that a gradual induction of treatment with D.A.D.P.S., more gradual even than that outlined in the previous report, can reduce the already low incidence and degree of serious anæmia.

Sulphone Dermatitis

About 2% of patients treated with D.A.D.P.S. on our original dosage have developed a generalised dermatitis caused by sensitisation. Unless the drug is stopped, the dermatitis may proceed to exfoliation and may even cause death; for not only the skin but also the mucosæ of mouth, larynx, respiratory tract, pharynx, and gastro-intestinal tract may be affected. A roughly similar incidence of dermatitis has been seen here with proprietary sulphones. Anti-histamine drugs are of great value in the treatment of this dermatitis.

Three striking facts about sulphone dermatitis are: (1) it always appears in the first six weeks of sulphone treatment or not at all; (2) it usually appears when the dose of sulphone has been raised above its initial level of 100 mg. a day; and (3) any attempt to start treatment with larger doses than usual, or to increase the dose more rapidly than usual, is immediately followed by a rise in the incidence and severity of dermatitis.

These facts suggest that the risk of dermatitis may be reduced by maintaining the initial dose for six weeks—i.e., until the period of possible dermatitis is past. When 200 patients were experimentally treated on this modified régime, there were only 2 cases of dermatitis.

Sulphone Psychosis

It is believed that this is the first published report of sulphone dermatitis. During 1948 and 1949, when 'Sulphetrone' was the main sulphone used, two patients complained of disorientation and other minor psychological disturbances, but no connection between this condition and sulphone treatment was apparent. Late in 1949 and early in 1950 when D.A.D.P.S. was being increasingly used, and experiments with high doses of D.A.D.P.S. were in progress, several cases of psychosis were observed, and it became clear that sulphones can produce a psychosis. The following 6 cases were all in African patients.

Case 1.—A man with lepromatous leprosy was treated with D.A.D.P.S., rising to 300 mg. a day, for eight months, and in the ninth month with 400 mg. a day. After a month on 400 mg. a day he complained of confusion and restlessness and said that the drug was "upsetting his brain." Treatment was stopped, and recovery was complete in a month. The patient has since taken 300 mg. a day for six days a week for several months with no further psychosis. He is an intelligent educated African. There is a reliable history of a previous attack of psychosis while he was receiving hydnocarpus oil.

Case 2.—A highly educated and intelligent but highly strung man, with some emotional instability accentuated by worry about his disease, was treated with the usual doses of D.A.D.P.S. rising to 300 mg. a day for four months, and thereafter with 400 mg. a day for two months, followed by 500 mg. a day for two months. No toxic signs appeared. He then reverted to the standard 300 mg. a day; and a month later, in the ninth month of treatment, he became very restless, talkative and finally wildly excited and confused. This condition lasted several weeks, and later gave way to depression and retardation of mental and physical activity. The psychosis thus took the form of manic depressive insanity. After four months recovery is not yet complete.

Case 3.—A man with tuberculoid leprosy was treated with D.A.D.P.S. with the dose increased at twice the usual rate, 100 mg. a day for a week only, 200 mg. a day for a week, and 300 mg. a day in the third week. In the third week the patient's liver and spleen were found to be enlarged and jaundice developed, and during the first nine months treatment was temporarily suspended twice for periods totalling several weeks. In the ninth month the normal dosage of 300 mg. a day was being given, when the patient developed a psychosis and became restless, talkative, and confused. The psychosis had religious manifestations (the patient was under the influence of a fanatical religious sect). Treatment was stopped, and within a month the patient became normal and has remained so. Treatment has not been resumed, since the disease is inactive.

Case 4.—A woman with tuberculoid leprosy, emotionally unstable, and worried by her separation from her young baby, was treated with D.A.D.P.S. in the usual dosage. In the ninth month she became restless and unmanageable, refused food, and became melancholic and depressed, weeping incessantly. Treatment was stopped. In three weeks she became normal, and treatment was resumed at 100 mg. a day. In two weeks the psychosis recurred, but it disappeared on cessation of treatment. A month later sulphetrone treatment was started and the dose raised to 3 g. a day. The psychosis recurred again, and is only now subsiding three weeks after the third cessation of treatment.

Case 5.—A woman with lepromatous leprosy started D.A.D.P.S. treatment on the usual dosage and after three weeks, while on 200 mg. a day, developed high fever (105°F) of unknown origin and a psychosis which was attributed to the fever She became restless, talkative, and incoherent Treatment was stopped, and the fever and psychosis subsided A month later treatment was restarted at 100 mg a day, and in two days the fever and psychosis recurred Treatment was stopped for another month Treatment was then resumed with small doses of sulphetrone (1 g a day), and so far there has been no recurrence The patient is of a psychotic type

Case 6 —A boy, aged 14, was treated with D A D P S *on our usual dosage rising to 300 mg a day* Treatment continued for four months, when the boy said that the drug was affecting his brain, and that he was confused and could not remember where he was and what he was doing Treatment was stopped, and the psychosis disappeared in two weeks Treatment has not yet been resumed

These 6 cases have occurred among 350 patients at present being treated with D A D P S here In 200 other cases being observed by us elsewhere, and being treated with lower doses, no psychosis has yet occurred In three years' experience of sulphetrone treatment of over 250 patients we have seen only 2 mild cases of psychosis, but a few have occurred in other leprosy institutions in Nigeria Psychosis seems to be more common and severe *during* D A D P S *treatment than during sulphetrone treatment*

Of the 6 cases, 3 occurred on abnormal dosage, either higher or more rapidly increased than usual, 1 occurred during a high fever of doubtful origin apparently precipitated by sulphones, and 2 occurred in the course of normal treatment, without other factors operating A psychotic background was present in at least 4 of the cases Psychosis tended to occur in the more highly educated and sensitive patient, apparently being rare in the ordinary simple Africans

5 of the cases occurred during a period of four months at the end of 1949 and the beginning of 1950 when D A D P S was being given seven days a week 4 of the cases occurred in the ninth and tenth months of treatment In the last four months, since treatment was reduced to six days a week only 1 further case (case 6) was seen, and that was a very mild case If further cases occur, we shall consider the advisability of reducing our maximal dose from 300 to 200 mg a day No case of psychosis has yet been seen on our modified D.A D P S treatment as outlined above

Dr B D Molesworth has told me that in Malaya he has seen a few mild cases of psychosis during sulphone treatment, but only in patients showing some mental instability before treatment

Erythema Nodosum Leprosum

This condition can hardly be classed among the toxic effects of sulphones, since it sometimes occurs naturally in lepromatous leprosy It can be precipitated by various drugs—e g, potassium iodide—and by procedures such as smallpox vaccination It is common during sulphone therapy, about 30% of lepromatous cases developing it at some time during treatment It is characterised by malaise, fever, and painful and tender areas of inflammatory induration in the skin and subcutaneous tissue The leprous lesions also often show *acute inflammation, in the skin lesions this may* be of little import, but in leprous nerves, eyes, and other vital tissues it may do serious damage

This condition is not of bad prognostic import often improvement becomes well marked only after several such incidents, which usually last only a few days It is desirable, however, to try to ensure that these incidents are relatively mild and not too frequent, and here again a more gradual induction of treatment and a lower standard dose may help considerably We now have, here and elsewhere, over 300 patients on D A D P S treatment with a dosage of 200 mg a day There is strong evidence that the incidence and severity of this "reaction" is lower than in those on the higher dosage

In the treatment of the "reaction" the injection of an antimony preparation—e g, 'Fantorin'—has been found of value by us and by others (Wolcott 1947) In ordinary "reaction" with skin manifestations we have found anti histamine drugs of little value In some cases with neuritis, however, which may be intensely painful and distressing, anti histamine drugs sometimes seem very effective We have used 'Phenergan,' 1 tablet given on going to bed at night, it causes too much giddiness to be used in ambulant patients Phenergan may also be useful in some cases of leprous iritis

DOSAGE

Though in the leprosy settlement at Uzuakoli, with fairly close medical supervision, the dosage previously recommended, rising to 300 mg a day, is still being maintained for most of our patients, we have been experimenting with different dosages which may be found more easily practicable in certain circumstances

Here in Nigeria D A D P S therapy in leprosy institutions with resident medical officers is now rapidly developing Moreover, a rapid extension of sulphone treatment to outstations and leprosy isolation villages with no resident medical officer and only occasional visits from such an officer is being planned Here and elsewhere in Nigeria over 1000 patients are already being treated with D A D P S, and within a few months treatment is expected to start in several thousands more In these circumstances, close medical supervision being impossible, it is considered advisable to reduce the possibility of toxic effects to an absolute minimum To meet this situation, the following two treatment régimes are suggested

(1) *Twice weekly treatment*, with doses starting at 100 mg and rising by steps of 100 mg each week to 400 mg twice a week in the fourth week this dosage to be maintained if possible as long as treatment lasts

(2) *Daily treatment* for six days a week, the dose being 100 mg a day for the first six weeks, and then 200 mg a day

Patients on twice weekly treatment receive a dose of freshly prepared ferrous sulphate mixture containing gr 20 of ferrous sulphate on each treatment day For patients on daily treatment the dose of ferrous sulphate is gr 10 daily

Either of these two régimes should be found practicable in patients in countries such as India, where the dosage previously recommended is often not tolerated A recent personal communication from Mr M Smith, B SC, suggests, however, that for Indian patients the dosage must be still further reduced if serious anæmia is to be prevented The reasons for this are not clear, and further study is needed

Both of these dosage régimes have the following advantages The incidence and severity of anæmia are considerably reduced, particularly with the twice weekly treatment The incidence and severity of sulphone dermatitis is probably reduced, though it is not entirely prevented, occasional cases of dermatitis having been seen on both these régimes Twice weekly treatment should reduce the danger of continuing the administration of sulphone in the presence of dermatitis The dermatitis often takes two or three days to develop completely, on twice weekly treatment, therefore, any sulphone dermatitis which arises should be obvious before the next dose is due

It seems probable that psychosis will be rare or unknown on the revised régimes, no case has yet been seen, but the modified treatment has not been in use long enough to make this fact significant since psychosis has been seen usually in the ninth or tenth month of treatment

"Reaction" is likely to be less common and less severe on the revised dosage régimes

Experience previously reported led to the statement 'Improvement is not proportional to the size of the dose Our patients on 400 and 500 mg a day are not so far showing an appreciably more rapid response than those on lower doses" Further experience has confirmed this view The higher dose moreover, tends to produce psychosis and the greatest daily dose in any circumstances should not exceed 300 mg But does the proposed reduction to 200 mg reduce therapeutic effectiveness? To this question no definite answer can yet be given All that can be said is that good results are being observed here on 200 mg a day, and even 100 mg a day, and a correspondent has written that even 50 mg a day is an effective dose

In lepromatous cases in which very long treatment is needed and improvement is slow but sure years of experience will be needed before the most effective dose can be determined

In tuberculoid cases however a response to treatment is seen in a few weeks or months Evidence obtained here in such cases indicates that there is little if any difference between the speed of response in patients treated with 100 200, or 300 mg a day The response is definitely quicker with daily treatment than with twice-weekly treatment, but this may be of little practical importance It might mean that the treatment of this form of leprosy would take perhaps 18 months instead of 12–15 months, and even this is not at all certain

CONCLUSIONS AND SUMMARY

The dosage of D.A.D.P.S previously recommended is still being maintained here in African patients with little trouble and with good results For widespread use in Nigeria with little medical supervision two modified treatment regimes with a reduced daily dosage are recommended one for treatment on six days a week with doses rising to 200 mg a day, and the other for treatment twice weekly with doses rising to 400 mg a day This reduced dosage, or even a still lower one should be useful in other peoples—e g, Indians—who are reported to tolerate sulphones less well than Africans The reduced dosage does not seem to be appreciably less effective

It is of vital importance that D.A.D.P.S treatment for leprosy which is believed to be the first reasonably effective and widely applicable treatment, should be adopted for general use in a form which gives the *widest* possible margin of safety compatible with therapeutic efficacy Suggestions are made here to meet this need, and the toxic effects anæmia, allergic dermatitis, psychosis, and 'reaction' (erythema nodosum) which may still be encountered are described

The cost of D.A.D.P.S for the treatment of a patient on the modified dosage suggested is 6–9 shillings a year

POSTSCRIPT

Since this article was drafted I have read an article by Floch and Destombes (1949) recommending treatment with daily doses of D.A.D.P.S 200 mg by mouth. They have treated 101 cases since November 1948 They also mention injections of 200 mg every day of 400 mg every other day and of 600 mg twice a week Their work was almost simultaneous with ours and neither we nor they knew of the others work.

REFERENCES

Brownlee G (1948) *Lancet* ii, 131
Floch H Destombes P (1949) *Int J Leprosy*, 17 367
Lowe, J (1950) *Lancet* i, 145
— Smith, M. (1949) *Int J Leprosy* 17 181
Wolcott R R (1947) *Ibid* 15 380

HÆMOLYTIC ANÆMIA DURING TREATMENT OF LEPROSY WITH DIAMINODIPHENYLSULPHONE BY MOUTH

REPORT OF A CASE

K. RAMANUJAM
M B Madras
ASSISTANT DIRECTOR OF LEPROSY RESEARCH GOVERNMENT OF MADRAS

MICHAEL SMITH
B Sc Lond
BIOCHEMIST BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION, KING INSTITUTE OF PREVENTIVE MEDICINE MADRAS

IN view of recent reports (Lowe and Smith 1949, Lowe 1950) of the treatment of leprosy with diaminodiphenylsulphone (D.A.D.P.S.) given by mouth the following case record is of interest and suggests that the administration of D.A.D.P.S in the doses indicated may not be without serious toxic effects

CASE-RECORD

A male Indian aged 36, in good physical condition, had had leprosy for three years During the past year his lesions had become worse

On admission there were several erythematous infiltrated plaques on the right cheek right buttock arms, and back. The lesions were well defined and anæsthetic The left great auricular nerve one of the supraclavicular nerves on the right side and both peroneal nerves were thickened No enlargement of the liver or spleen was detected by palpation Major tuberculoid (major lepride) leprosy was diagnosed The lesions were negative to standard methods of examination, and the histological picture was that of a reactional tuberculoid (major lepride)

Investigations —Examination of the blood showed red cells 4 600 000 per c.mm. Hb 13·6 g per 100 ml plasma bilirubin within normal limits, and no methæmalbumin. Liver function tests (thymol turbidity and alcohol turbidity) were normal The urine on three successive days contained no urobilin (Schlesinger)

Treatment —The patient was given D.A.D.P.S 0·1 g daily for thirteen days 0·2 g daily for ten days, and 0·3 g daily for thirteen days

Progress —Thirty five days after the start of treatment—i.e, on March 21 1950—the patient complained of nausea, weakness low fever and constipation. A Schlesinger test for urobilin was strongly positive for the first time Owing to an oversight D.A.D.P.S treatment was continued for a further thirty six hours and the blood sulphone level was 1·3 mg per 100 ml This figure is considered to be within the normal limits for D.A.D.P.S (Smith 1949) The treatment was discontinued on March 23 the patient having taken a total of 7·1 g of D.A.D.P.S., and on the same day the patient was admitted to the hospital ward in a toxic condition with much vomiting, a coated and dry tongue and extreme asthenia His temperature was 101·4°F His spleen extended 1 in. below the costal margin and was soft but not tender His liver was not palpable

Investigations —A blood-count showed red cells 4 200 000 per c.mm. Hb 12·7 g per 100 ml reticulocytes 27% white cells 16 600 per c.mm (polymorphs 51% lymphocytes 33% eosinophils 3% monocytes 13%) The polymorphs showed a pronounced shift to the left no malaria parasites were seen, the plasma bilirubin level was 2·6 mg per 100 ml, and a test for plasma methæmalbumin was strongly positive Liver function tests (thymol turbidity and alcohol turbidity) were normal the urine contained large amounts of urobilin (Schlesinger — —) but no bilirubin On March 27 six days after the onset bile pigment appeared in the urine for the first time

Progress —On March 28 the conjunctivæ were obviously icteric, the patient appeared completely exhausted, and the spleen and liver were tender soft, and enlarged The patient's daily temperature was varying between 99° and 103·4°F, the peak being reached at about 4 P.M. Examination of the blood showed red cells 3 000 000 per c.mm., Hb 12·7 g per 100 ml (* error due to presence of bile pigment) plasma bilirubin 7 mg per 100 ml and methæmalbumin present. The urine contained urobilin and bile pigment

March 30 the patient was apyrexial but the liver and spleen were still enlarged and tender and the icterus was deepening A blood-count showed red cells 2 900 000 per c.mm. Hb 9·3 g per 100 ml white cells 12 000 per c.mm (neutrophil polymorphs 50%, lymphocytes 40%, monocytes 10%, eosinophils 0) The shift to the left was no longer appreciable, the blood DADPS level was 0 35 mg per 100 ml

April 4 the icterus was perceptibly decreasing, and the patient s general condition was much improved The liver was still palpable and tender but the spleen was no longer palpable The urine still showed a trace of bilirubin

April 10 the patient was well No bile pigment was present in the urine, but Schlesinger s test for urobilin still continued to be positive The blood still contained a trace of DADPS

April 25 the patient was discharged

May 11 investigations showed red cells 4,800,000 per c mm , Hb 12 6 g per 100 ml , no evidence of any liver dys function (thymol turbidity, alcohol turbidity, and intravenous hippuric acid test), and no urobilin in the urine

May 15 an attempt was made to start treatment again, but after three daily doses of DADPS 25 mg the patient complained of headache and backache and his urine again contained large amounts of urobilin (Schlesinger + +) Although neither liver nor spleen was palpable, the attempt to estimate the hippuric acid synthesising power of the liver (Quick's intravenous test) had to be discontinued because of a severe attack of shivering during the intravenous injection of sodium benzoate

DISCUSSION

Acute hæmolytic anæmia was diagnosed because (1) at the outset the laboratory findings of methæmalbuminæmia, bilirubinæmia, reticulocytosis, and urobilinuria obviously indicated hæmolysis, (2) DADPS is known to be hæmolytic, and (3) one of us (M S) had experienced similar cases undergoing DADPS therapy in West Africa

Although infective hepatitis is not uncommon in India, this was not accepted as the diagnosis, because of (1) the initial enlargement of the spleen and the clinical toxic symptoms, (2) the absence of bile in the urine during the initial stages, and (3) the absence of any indication of involvement of the liver from liver function studies Further, leucocytosis and anæmia are not usually observed in infective hepatitis

Clinically, the initial enlargement of the spleen and the toxic symptoms presenting themselves at the onset did not suggest infective hepatitis, but this diagnosis was considered and ruled out when the jaundice became apparent, because of the incidence of this condition in India

Hæmolysis was not severe in the present case, causing only a total drop of 1,700,000 red cells and of 4 3 g of hæmoglobin per 100 ml The clinical symptoms were severe, however, and the jaundice lasted for a shorter time than is usual in infective hepatitis The possibility that infective hepatitis had supervened on hæmolytic anæmia seems to be ruled out by the fact that the liver function tests were within normal limits The recurrence of what we thought were prodromal signs of hæmolysis when the patient was again given small doses (25 mg) of DADPS may have been due to a sensitivity to DADPS, or possibly the patient had not fully recovered from the previous attack

SUMMARY

A case of hæmolytic anæmia during DADPS therapy is reported

The initial laboratory evidence was a sudden strongly positive Schlesinger test for urine urobilin Methæmalbuminæmia, bilirubinæmia, urobilinuria, and a decrease in red cells and Hb were observed No evidence of any liver dysfunction, either during or subsequent to the jaundice, was discovered

We wish to draw attention to the possibility of hæmolytic jaundice when DADPS is given by mouth We regret that, owing to the distance from a fully equipped laboratory, more detailed tests were impossible

Our thanks are due to the medical superintendent of Government Lady Willingdon Leprosy Sanatorium Chingleput Madras, and his staff for their assistance Dr R G Cochrane for his criticism and assistance with the preparation of this paper, the staff of the research department at the sanatorium for their cooperation, and Dr Mungavin, of Imperial Chemical Industries, for his active interest and help One of us (M S) wishes to thank the British Empire Leprosy Relief Association for facilities enabling him to make this study

REFERENCES

Lowe J (1950) *Lancet* i 145
— Smith M (1949) *Int J Leprosy*, 17, 181
Smith M (1949) *Leprosy Rev* 20 78

EFFECT OF POSTOPERATIVE BED REST AND EARLY AMBULATION ON THE RATE OF VENOUS BLOOD-FLOW

H Payling Wright
B Sc , Ph.D Lond , L M S S A
RESEARCH ASSISTANT, OBSTETRIC UNIT

S B Osborn
B Sc Lond , A Inst P
PHYSICIST

Denise G Edmonds
TECHNICAL ASSISTANT

UNIVERSITY COLLEGE HOSPITAL AND MEDICAL SCHOOL

The measurement of the rate of blood flow over a limited section of the circulatory system has been attempted in many ways , these have been reviewed by *Bellis (1943)* The most usual method has been to introduce intravenously some substance which produces an observable reaction in the subject immediately on its arrival at some site in the body remote from that of the injection For example, cyanide has been used to determine the arm carotid or foot carotid time, since by stimulating the respiratory centre it causes the subject to gasp when it reaches the brain , or saccharin may be injected, the end point being the sensation of a sweet taste at the moment that the substance in the blood reaches the capillaries of the taste buds Such methods are not wholly satisfactory, since the section of the circulatory system over which the rate of flow is measured includes the pulmonary vessels and is therefore subject to various extraneous complicating factors Personal errors may be introduced by the observer, who must note the reaction in the patient, and also, with some methods, by the patient when he indicates the end points Moreover the sites at which recognisable reactions can take place are few These methods nevertheless give comparative measurements of the rate of blood flow under varying conditions, provided that those conditions influence a sufficient proportion of the circulatory path under observation , where the altered conditions are confined, as they often are, to a limited section of the vascular circuit, however, they tend to be obscured

With the introduction of radio isotopes, techniques have been devised which are both more flexible and precise The instant of first arrival of a radio isotope introduced into a vein in an extremity can be detected with objective precision at any proximal point in the vessel By the suitable arrangement of injection and recording sites the mean rate of flow in cm per sec over any desired section of the vein may be determined with considerable accuracy In the present study these technical methods were applied to the problem of venous stasis in the limbs of patients during the postoperative period

METHOD

The technique used was the same as that reported previously (Osborn and Wright 1949, Wright et al 1948, 1949, 1950) A small volume (0 2–1 0 ml) of radioactive isotonic saline solution containing 2–10 µc Na^{24} per ml was injected intravenously in the extremity (foot or hand) under standard conditions of temperature and posture The time of the first arrival of the isotope

TABLE I—AVERAGE RATES OF VENOUS FLOW IN AMBULANT AND IN NON-AMBULANT PATIENTS

Day	Rate of flow (cm per sec.)			
	Leg		Arm	
Preoperative	4·5 ± 0·24 (103)		10·0 ± 0·87 (45)	
During anæsthesia	6·2 ± 0·55 (37)		—	
Postoperative	Group 1 (Ambulant)	Group 2 (Non ambulant)	Group 1 (Ambulant)	Group 2 (Non ambulant)
1–3	4·8 ± 0·85 (6)	4·2 ± 0·65 (20)	—	11·9 ± 1·64 (12)
4–6	5·0 ± 0·54 (9)	3·8 ± 0·49 (24)	10·3 ± 1·04 (5)	10·5 ± 0·38 (7)
7–9	5·5 ± 1·14 (19)	2·9 ± 0·32 (23)	11·1 ± 1·09 (6)	8·4 ± 1·74 (14)
10–12	7·1 ± 0·29 (24)	2·8 ± 0·37 (15)	—	7·6 ± 1·11 (13)
13–15	5·6 ± 0·51 (21)	2·7 ± 0·29 (16)	11·5 ± 1·01 (7)	7·5 (3)
16–18	4·7 ± 0·39 (15)	2·9 ± 0·41 (7)	10·3 ± 1·23 (13)	—
19 +	5·2 ± 0·56 (25)	3·9 ± 0·39 (13)	10·2 ± 1·19 (10)	8·9 ± 1·61 (6)

Numerals in parentheses indicate number of observations

at the proximal end of the limb was detected by a screened Geiger Müller counter placed over the femoral triangle for the leg and in the axilla for the arm. An electric circuit was devised that provided a kymograph tracing on which was recorded the moment of the injection, the instant at which the radioactive material reached the counter, and a suitable time scale. From the times thus recorded and a knowledge of the distance between the injection site and the window of the counter shield, the mean rate of venous flow up the limb could be calculated.

MATERIAL

117 surgical patients were investigated preoperatively and at weekly intervals during convalescence. Records were obtained from 42 of these at the end of the operation while the patient was still anæsthetised in the theatre. Since anæsthesia was produced by various means and combinations of drugs and for differing times, no conclusions can be drawn as to the effects of different anæsthetics on the flow rates.

For the analysis of the data obtained during the postoperative period, observations were separated into two main divisions: (1) those made on patients who were ambulant (walking) at the time the record was taken, and (2) those made on patients who had remained uninterruptedly in bed since the operation. Thus the data from any single patient would be included in group 2 so long as they remained continuously in bed, but from the day of ambulation onwards their records would be included in group 1. The progressive transference of patients from group 2 to group 1 will be apparent in table I. The distribution of cases in these two groups at the tenth postoperative day was as follows:

	Ambulant	*Non ambulant*
Hysterectomy	20	9
Colporrhaphy	7	31
Amputation of cervix	2	1
Ventrisuspension	1	1
Repair of rectal fistula	1	1
Gastrectomy	1	3
Myomectomy	8	—
Ovicystectomy	3	—
Salpingectomy	3	—
Dilation and curettage	3	—
Sterilisation	2	—
Thyroidectomy	2	—
Excision of thyroid cartilage	1	—
Osteomyelitis of jaw	1	—
Ureteral transplantation	1	—
Resection of gut	1	—
Dental cystectomy	1	—
Radical mastectomy	1	—
Cholecystectomy	1	—
Correction of hallux valgus	—	1
Inguinal herniotomy	—	3
Vulvectomy	—	1
Drainage of psoas abscess	—	1
Lobectomy	—	1
Carcinoma of œsophagus	—	1
Prostatectomy	—	1
Compound fracture of tibia and fibula	—	1
Total	60	56

A further division of cases has also been included. It was shown previously (Wright et al. 1950) that, in pregnancy, retardation of venous flow in the legs was first apparent during the second trimester. In the present series, therefore, observations on the venous flow in the legs of patients with pelvic tumours which gave rise to masses greater in size than a sixteen-week pregnancy were considered separately throughout as group 3.

RESULTS

The average mean flow rates in both arms and legs, together with their standard errors, are set out for groups 1 and 2 in table I. The figures in parentheses give the numbers of individual observations.

Where the total numbers were too small for their standard errors to have significance, these have been omitted. Observations made in the postoperative period have been grouped into three-day periods so that the numbers in each shall be sufficient to allow of statistical treatment.

The data from table I are set out graphically in fig. 1. The mean rate of venous flow in both the arms and the legs (curves B) of the patients continuously confined to bed (group 2) showed a progressive slowing until the fifteenth day; in other words, there was a generalised venous slowing in the limbs and presumably, therefore, in the circulation as a whole.

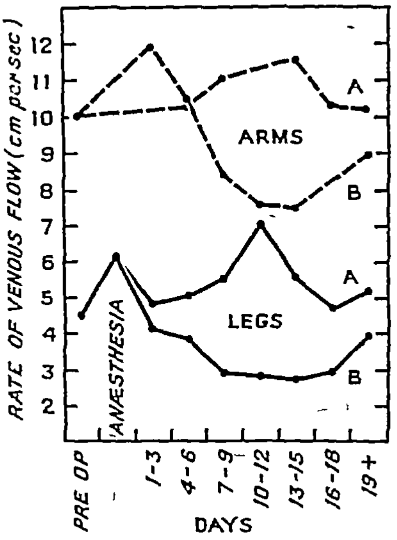


Fig. 1—Average rates of venous flow on various days in arms and legs of 103 surgical patients. A, ambulant. B, non-ambulant.

In group 1 no such slowing in either the upper or the lower limb (curves A) was apparent; indeed there was an increase in the flow-rate which was most marked in the legs and which reached a maximum ten to twelve days after operation. A similar though smaller change in flow rate occurred in the arm.

In group 3 there was a somewhat different finding. The figures are set out in table II and fig. 2. The initial flow rate in the legs was significantly slower than for the main groups and corresponded closely to those previously reported for women sixteen weeks pregnant. These tumour-bearing patients showed an increase of flow rate under anæsthesia similar to that in groups 1 and 2, and this was followed by a return to about the initial figure within a few days Those patients who became ambulant (curve A) showed, by the tenth day, an increase in leg venous flow rate almost identical with that in group 1, but those who were confined to bed (curve B) also showed an increase, but to a lesser and only doubtfully significant degree

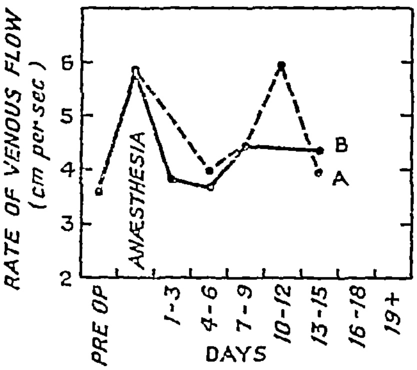


Fig 2—Average rates of venous flow on various days in the legs of 19 patients from whom large pelvic masses were removed A, ambulant B non ambulant.

So that the relative changes in flow rate for the various groups should be more easily appreciated, the figures are set out in fig 3 as percentages of the initial rates for groups 1 and 2 —i e, 100% is taken as 4 5 cm per sec for legs, and 10 0 cm per sec for arms

DISCUSSION

Since the time of Virchow the importance of venous stagnation as a factor in the onset of thrombosis has frequently been emphasised Should the venous flow become abnormally slow during the postoperative period, probably the effect of the increased numbers (Dawbarn et al 1928) and adhesiveness (Wright 1942) of the platelets, and the increase in erythrocyte sedimentation rate (Austoni 1936) would more readily promote thrombus formation at any point of intimal damage The modern treatment of surgical patients by early ambulation is mainly based upon the belief that the venous return from the legs is retarded during the second week after operation in those who are confined to bed, and that this stagnation coincides with the maximal thrombogenic changes in the blood.

So much importance has been attached by some clinicians to the early mobilisation of patients that the American Medical Association (1944) devoted a session to a symposium on the "Abuse of Bed Rest," and other workers have drawn attention to the dangers of venous stagnation (Newburger 1943, Borgstrom 1950) Nevertheless the evidence on which is founded such wholehearted support for the early ambulation of surgical patients is still slender It is based mainly on clinical considerations and observations, the patients' subjective feelings, and certain statistical surveys (Schumacher 1927, Leithauser 1943, Canavarro 1946, Lam and Hooker 1946, Westerborn 1946) which show that the incidence of thrombosis and embolism is less in those patients who have been moving actively soon after operation Such statistics are, however, difficult to interpret, because the seriously ill patient, or one in whom a superimposed infection is present, is more likely both to be kept in bed and to develop thrombosis In some reports, moreover, it has been shown that early ambulation alone does not wholly obviate thrombo-embolism (Blodgett and Beattie 1946, 1947, Powers 1947).

TABLE II—AVERAGE RATES OF VENOUS FLOW IN LEGS OF WOMEN WITH PELVIC TUMOURS

Day	Rate of flow (cm per sec)	
Preoperative	3 6 ± 0 38 (19)	
During anæsthesia	5 8 ± 1 54 (5)	
Postoperative	Ambulant	Non ambulant
1–3	—	3 8 ± 0 17 (6)
4–6	3 9 ± 0 [illegible]4 (5)	3 7 ± 0 6[illegible] ([illegible])
7–9	4 4 ± 0 56 (6)	4 4 ± 1 3 ([illegible])
10–12	5 9 ± 1 [illegible]9 (8)	—
13–15	3 9 ± 0 96 ([illegible])	4 3 (2)

Numerals in parentheses indicate number of observations

There are, however, certain studies on rates of venous blood-flow which have a direct bearing on the practice of early ambulation Frimann Dahl (1935), using serial phlebograms, showed that both in normal persons confined to bed and in surgical patients in the preoperative period, the flow in the femoral and saphenous veins was so greatly retarded that stagnation might be almost complete Since there was no comparable stasis in the upper limb, he concluded that its occurrence in the legs resulted from (1) raised intra abdominal pressure, (2) inactivity, and (3) the formation of venous eddies at the sapheno femoral junction

Further blood flow estimations have been made in the postoperative period by other workers Webb et al. (1936), using the saccharin method, and Bellis et al. (1943), using cyanide, reported a decrease of several seconds in flow time immediately after operation Their measurements were made within the first forty eight hours, while the patients temperatures were raised and they were still receiving sedatives These factors were considered to have affected their findings Kvale et al (1940) and Smith and Allen (1940), on the other hand, also using the cyanide method, found that from the third postoperative day onwards the foot carotid time was prolonged, from a preoperative mean value of 35 sec it had increased to a mean value of 57 sec by the tenth day These observations were later supported by those of Bjork and Strombeck (1945), who measured the flow time daily after operation by the injection of fluorescein, timing its appearance in the patient's lips The times recorded by Kvale et al (1940) and Smith and Allen (1940) seem to correspond fairly well to ours when allowance is made for the more complex vascular pathway over which they made their measurements They found little change in the flow time in the upper limb (arm carotid time, pre op ≓ 19 sec , tenth day post op = 25 sec), but this may be due to the failure of their method to disclose changes in venous flow rate which are shown clearly by our technique As can be seen in fig 3, the change in the arm flow rate is small relative to that in the leg

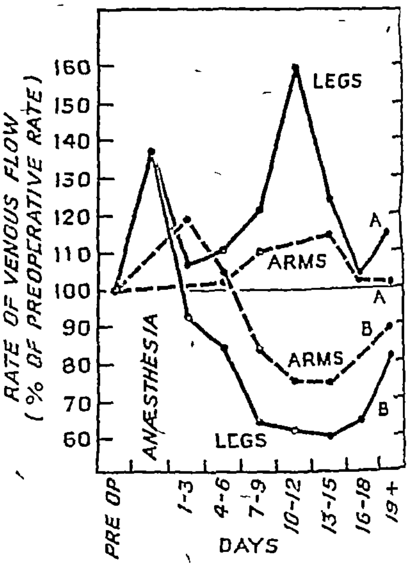


Fig 3—Average rates of venous flow on various days expressed as percentages of the preoperative rate of flow in arms and legs of surgical patients A ambulant B non ambulant.

Since in the present series there is a preponderance of patients who underwent operations for colporrhaphy in the non ambulant group and for hysterectomy in the ambulant group, it might be argued that the type of operation was the determining factor which influenced the degree of stasis developing during convalescence That no such bias is significant, however is shown by the fact that, when each of the more common types of operation in this series is analysed separately the same differences in rates of blood flow between ambulant and non-ambulant patients were found within them as in the whole groups

It seems likely from our observations, which confirm those made by other workers using different methods, that the immobilised patient undergoes a progressive slowing of the venous flow in both legs and arms during the postoperative phase, though that in the lower limbs is much the more pronounced Moreover, the present figures also indicate that in ambulant patients, in whom such circulatory changes have not hitherto been reported, venous flow rates exhibit an acceleration just at that time when such patients are most vulnerable to the other factors which contribute to thrombus formation The comparison of leg flow rates in groups 1 and 2 can leave little doubt of the advantage to the patient so far as this aspect of postoperative care is concerned

As might have been expected from our previous observations on pregnancy and ascites, the venous flow rates in the legs in patients with pelvic tumours were abnormally slow when first examined In those who were permitted early postoperative walking the venous flow began to accelerate by the fourth day and thereafter followed the same course as in the group of mobile patients as a whole Those confined to bed, however, also showed an acceleration over their preoperative time by the tenth day, but this was less than in the ambulant patients of the same type The removal of the pelvic mass, which we believe acts as a mechanical obstruction to the venous return from the legs, adversely affected the blood flow in the lower limbs of these patients to as great an extent as did the enforced immobilisation

SUMMARY

1 Venous flow rate in the limbs of 117 surgical patients were measured on different days after operation

2 In patients who were ambulatory during convalescence, no slowing of venous flow was apparent in either leg or arm In patients confined to bed, a reduction of flow rate, which was most marked at ten to twelve days after operation, was found

3 Changes in flow rate were always greater in the leg than in the arm

4 Observations on patients from whom pelvic masses were removed suggested that the alleviation of intra abdominal pressure had a greater influence than post operative ambulation on venous flow rate

5 The importance of venous stasis in relation to postoperative thrombosis is discussed

We wish to thank Prof W C W Nixon and Prof R S Pilcher for permission to examine their patients This work has been supported by a grant from the Medical Research Council

REFERENCES

American Medical Association (1944) *J Amer med Ass* 125 1075
Austoni B (1936) *Arch Soc ital Chir* 42 624
Bellis C J (1943) *Surgery* 13 27
— Doss A K., Craft, C B (1943) *Ibid* p 35
Bjork V O Strombeck J P (1945) *Nord Med* 26 878
Blodgett J B Beattie E J (1946) *Surg Gynec. Obstet* 82 485
— — (1947) *Ibid* 84 716
Borgström S (1950) *Acta chir scand* suppl no 150
Canavarro K. (1946) *Ann Surg* 124 180
Dawbarn R Y Earlam F Evans W H (1928) *J Path Bact* 31 833
Frimann Dahl J (1935) *Acta chir scand* 76 1
Kvale W F Smith L A Allen E V (1940) *Arch Surg* 40 344
Lam C R Hooker D H (1946) *Ann Surg* 123 221
Leithauser D J (1943) *Arch Surg* 47 203
Newburger B (1943) *Surgery* 14 142
Osborn S B Wright H P (1949) *Brit J Radiol* 22 110
Powers J H (1947) *Amer J Med* 3 224
Schumacher P (1927) *Arch Gynäk* 129 929
Smith L A Allen E V (1940) *Arch Surg* 41 1377
Webb G Sheinfeld W Colin H (1936) *Ann Surg* 104 460
Westerborn A (1946) *Nord Med* 29 347
Wright H P (1942) *J Path Bact* 54 461
— Osborn S B Edmunds D G (1948) *Lancet* ii 767
— — — (1949) *J Obstet Gynæc* 56 36
— — — (1950) *Surg Gynec Obstet* 90 481

AN EXPERIMENT ON THE TRANSMISSION OF COLDS

C H ANDREWES
M D Lond F R C P, F R S

J E LOVELOCK
Ph D Lond

T SOMMERVILLE
M D Edin

From the Common Cold Research Unit (National Institute for Medical Research), Harvard Hospital, Salisbury

THERE is a strong body of evidence that the common cold is an infectious disease caused by a virus or a group of related viruses Opinion is sharply divided on the relative importance of coarse droplets droplet nuclei, and indirect manual transfer in the transmission of the disease from person to person (Andrewes 1949) The elucidation of these problems has an obvious bearing on what methods might be employed for the control of the spread of the disease

Study of the natural methods of transmission of infection in colds has proved difficult Experiments at the Common Cold Research Unit, Salisbury, using volunteers after three days' isolation, were unsuccessful because of the low incidence of takes in the groups exposed to infection In one test only 1 of 19 normal people who lived for some hours with cold sufferers contracted a cold, in a second test none out of 4 so exposed, in a third test 1 out of 5 All these colds were ' pedigree " colds which had undergone several person to person passages at Salisbury by intranasal inoculation In addition one natural "wild" cold failed to pass to any of 5 normal people

On the other hand, numerous observers attest that small groups living in isolation for some months acquire greatly enhanced susceptibility to colds, so that most of them develop symptoms shortly after making contact once more with "civilisation" The Norwegian explorer Adolf Hoel (quoted by Høygaard 1939) stated that Arctic explorers commonly caught colds on returning home even after as short an absence as three to four months After such relatively short absences, however, the colds thus caught were milder and shorter than after longer expeditions Such reports encouraged us to hope that a small party isolated for about three months might acquire sufficient susceptibility to permit studies of the methods of spread of cold infection

The experiment to be described was designed to determine the effective routes of person to person transmission of colds As will appear, the original objective was not attained but other interesting and unexpected findings make the attempt seem worth recording

THE ISLAND EXPERIMENT

We were fortunate in learning through Dr Fraser Darling, of an island, Eilean nan Ròn, lying about 1½ miles off the little port of Skerray on the north coast of Sutherland This island has a number of well built stone houses on it, but had been uninhabited for twelve years, the population having left it from pressure of economic circumstances It is owned by the Duke of Sutherland, who kindly allowed us to use it for purposes of this experiment Eilean nan Ròn is rather over a mile long, under a mile wide and is bare, mostly covered by moorland Picturesque cliffs surround it, but there is a landing place from which a flight of steep steps leads to the plateau on top of the cliff

Early in July, 1950, 12 volunteers landed on the island for three months' stay, most of them were students from Aberdeen With them were landed camp equipment, stores and all necessities, so that no personal contact between them and the mainland should be necessary for about three months A small radio transmitter and receiver kept them in daily communica tion with the mainland On three occasions shepherds visited the island to attend to the sheep grazing there, but they made no contact with the volunteers

Preliminary Isolation Period

The volunteers were left in otherwise complete isolation from July 12 to Sept 19, 1950 (ten weeks) At the very beginning a small outbreak of colds occurred One man had a cold on arrival (July 8), another case occurred on July 9, and 3 more on July 11 These rapidly cleared up and no more occurred during the isolation period

Period of Experiment

On Sept 19, the party of 12 separated into three groups of 4, A, B, and C These thereafter lived and cooked for themselves in separate buildings, not closer together than 50–100 yards The island was divided into three territories to one of which each party was restricted On that day (Sept 19) 2 of us (C H A and J E L) landed and joined party C to see whether normal cold free people could "carry" cold virus in their respiratory tracts or elsewhere on their persons and so convey infection to the "islanders" One of us had not had a cold for about five, the other for about eleven, months No colds developed as a result of this contact by the evening of Sept 23

On Sept 23, one of us (T S) arrived with 5 others, all 6 had been inoculated intranasally at Aberdeen on Sept 19 with one of our "pedigree" virus strains from the Salisbury unit On arrival on the island, 4 of these subjects had already got colds, in the other 2, colds were doubtful, but they developed well later The cold strain used (Pool 96) had the following history cold washings from a child aged four years were diluted 1 in 100 with saline and passed intranasally to 6 people, 2 of whom developed colds, washings from 1 of them were inoculated into thirteen day chick embryos amniotically, after five days' incubation at 36 5°C, amniotic fluid was harvested, this induced a definite cold in 1 of 4 inoculated volunteers, four further human passages from him were carried out and gave "takes" in 10/18, 9/20, 5/10, and 5/6 persons respectively This last passage (Pool 96) giving 5/6 takes at Salisbury was the one taken to Aberdeen At each passage, washings were stored at −76°C for some days It may be mentioned that on a number of occasions we have produced colds with fluids from eggs inoculated amniotically, but have not done so with sufficient regularity to convince us that we have cultivated a virus

EXPERIMENTS TO STUDY THE ROUTES OF TRANSFER OF INFECTION

Indirect Contact

The 6 "colds" spent three hours in a room of group A's house in the absence of the party themselves During their occupation they were liberal in the way they disseminated nasal discharge on playing cards, books, cutlery, handles of cups, letters, chairs, door handles, and tables Care was taken to avoid contact with any of the 4 members of group A or to allow the possibility of direct aerial transmission of particles from the respiratory tract With this object the occupied room was aired by opening doors and windows for half an hour between departure of the "colds" and reoccupation of this room by party A These then occupied the room for three hours, freely handling the objects contaminated by the cold cases

Exposure to Airborne Particles

The 6 "colds" occupied a sealed room with party B, they were separated from them by a blanket stretched across the room but not reaching to floor or ceiling During three hours exposure, the cold cases talked freely, coughed occasionally, and were induced to sneeze frequently with snuff Group B remained silent and neither coughed nor sneezed Air collected by means of a slit sampler revealed that a satisfactory number of small airborne particles passed over the blanket to group B

Direct Contact

Group C (who had previously been exposed to the 2 normals) lived and ate with the 6 "colds" from Sept 23 to 26, when 5 of the 6 "colds" left the island The 6th (T S) remained with party C till the end of the experiment (Oct 4)

Results

Much to our surprise no colds had developed in any of the 12 exposed "islanders" by Sept 29 It was particularly unexpected that none of party C caught colds, though very fully exposed

COMPARISON OF INFECTIVITY OF NATURAL AND INDUCED COLDS

After the failure to obtain "takes" from exposure to induced colds we decided to conduct an experiment to compare the infectivity of natural and induced colds We succeeded in learning of a crofter with a cold on the adjacent mainland, he came across to the island for the day on Sept 29 and gave an opportunity for the spread of his cold to party B, living with them and talking round a fire for two periods of two hours each He had developed the cold five days earlier (Sept 24), when he arrived it was at the mucopurulent stage and there were signs suggesting mild frontal sinusitis He was still blowing his nose occasionally but not coughing or sneezing

Later, on Sept 29, 4 more people arrived, having been inoculated with colds induced by Pool 96 in Aberdeen on Sept 25 2 of them had good colds, the other 2 were apparently incubating them, as they developed after they landed Party A was "challenged" by direct exposure to these 4 colds The total period of exposure was six hours, composed of three hours on the evening of Sept 29 and three hours on the morning of Sept 30 In the morning session only 3 of the cold cases were used for the "challenge"

Party C was exposed both to the natural cold (for about three and a half hours) and by living with the second lot of induced colds for four days (up to Oct 3)

Results

Of the 4 of party B exposed to the natural cold 3 developed typical colds, 1 started on the night of Oct 2–3, the other 2 on the morning of Oct 4 Again, no colds were induced in party A by exposure to induced colds The contrast is rendered less clear cut by the failure of colds to develop in any of party C, exposed to both natural and induced colds One of them did, however, develop a cold 36 hours after leaving the island (Oct 6) this was possibly contracted on Oct 3 from one of party B

After history

Two weeks after their return to their homes only 1 member of group A had developed a cold and 2 members of party C Altogether 6 of those isolated for three months failed to develop colds either when exposed on the island or within a fortnight of returning to the mainland

DISCUSSION

The abundant field information on the increased susceptibility to colds induced by a period of isolation is too seldom precise and quantitative No great administrative difficulties need be encountered in arranging for careful tests of the question Unfortunately, three months is the longest period for which, in Britain it is practicable to obtain volunteers from among students on vacation, and it seems that ten weeks' isolation is not adequate to induce uniform susceptibility It is possible that a few people act as carriers of cold virus and that presence or absence of one of these in a small group might determine whether such a group became rapidly and uniformly susceptible

Our results suggest that there is a difference between natural and artificial colds as regards infectivity Full exposure of 8 previously isolated persons to 10 induced colds, both in their incubation and fully developed stages, failed to reveal one instance of natural "jumping" of infection, on the other hand, one natural cold, even though it had reached its fifth day, and was no longer active, induced colds in 3 out of 8 persons after an exposure of only three and a half hours

A difference in spreading power between the natural and propagated colds is perhaps attributable to attenuation of the infective agent by the artificial manner of its transfer or as a result of storage This is not certain, however, for the crofter's cold may not have been due to the same type of organism as that in Pool 96, though the infections in both instances were fairly typical colds Loss of "jumping" power on passage through the natural host has of course its parallel in what was seen when variolation was practised The Hampstead strain of ectromelia virus has also lost much of its infectivity after years of laboratory passage Shope (1934) has reported similar behaviour on the part of *Hæmophilus influenzæ suis*

SUMMARY

A group of 12 persons after complete isolation for ten weeks did not show greatly enhanced susceptibility to natural acquisition of common cold infection A cold virus had been artificially propagated in normal persons by intranasal inoculation and in addition had apparently survived one amniotic passage in fertile hens' eggs, this virus still induced colds in 15 out of 16 persons on intranasal inoculation but it failed to be transmitted by natural contact In contrast a natural "wild" cold did spread to 3 of 8 subjects

We wish to thank His Grace the Duke of Sutherland for allowing us the use of Eilean nan Ròn, Mr and Mrs F J Betteridge who worked so hard on the island to make the expedition run smoothly, the other volunteers who came to the island for longer or shorter periods, departments of the Royal Navy the Royal Air Force, the Ministry of Health and the General Post Office for the loan of equipment or help in other ways, and many other persons too numerous to mention individually, for helpful coöperation

REFERENCES

Andrewes C H (1949) *Lancet* i 71
Hovgaard A (1939) *Ibid* i 245
Shope R E (1934) *J exp Med* 59 201

BACTERIAL VARIANTS IN PATIENTS TREATED WITH CHLORAMPHENICOL

A Voureka
M.D Athens
From the Wright-Fleming Institute of Microbiology, St Mary s Hospital Medical School, London

In cultures made from the urine of several patients under treatment with chloramphenicol for urinary infections atypical bacterial colonies developed, examples of which are described below Some of these strains could be identified as variants of the original infecting organism

Case 1 —Before treatment was begun cultures of this patient s urine grew typical colonies of *Pseudomonas pyocyanea*

During the first three days of chloramphenicol treatment the number of colonies isolated diminished, and on the fourth day the urine seemed to be sterile On the fifth day however colonies again appeared on plating on blood agar the colonies were small 0 5–1 0 mm in diameter, greyish, opaque, dry, and extremely rough with a lobate ragged periphery When picked off they left an impression on the plate They had a membranous consistence, resembling small pellicles, and could not be emulsified Microscopically they consisted of motile slender gram negative bacilli

They produced a diffusible green pigment on agar and in broth, where they formed a surface pellicle The morphology of the colony remained unchanged through 19 subcultures, whereas when left on the plates at room temperature the colonies soon became large and confluent, with a rich mucoid consistence Subcultures from the edges, which seemed even more mucoid, grew the same tiny rough dry colonies

At the 19th subculture, besides the small rough colonies, some larger ones with mucoid periphery appeared, and on further subculture these gradually assumed the appearance of normal *Ps pyocyanea* The small rough colonies of the 19th subculture bred true through another 10 subcultures, when some mucoid variants appeared again

Similar dry pellicle like colonies were isolated from swabs of the patient s hands These colonies grew on 1% cetrimide agar, produced on agar and in broth a diffusible green pigment soluble in chloroform and in water, formed a surface pellicle in broth, liquefied coagulated serum and gelatin, consisted of gram negative motile rods, and had the characteristic odour of *Ps pyocyanea* These are the characteristics of *Ps pyocyanea*, and, since repeated subculture produced mucoid variants which eventually became indistinguishable from that organism, the culture was identified as *Ps pyocyanea*

Case 2 —Before treatment with chloramphenicol was begun this patient s urine grew a coliform bacillus and *Ps pyocyanea*, the characters of which were noted Twice a day during treatment samples of mid stream urine were plated, and the sediment was examined

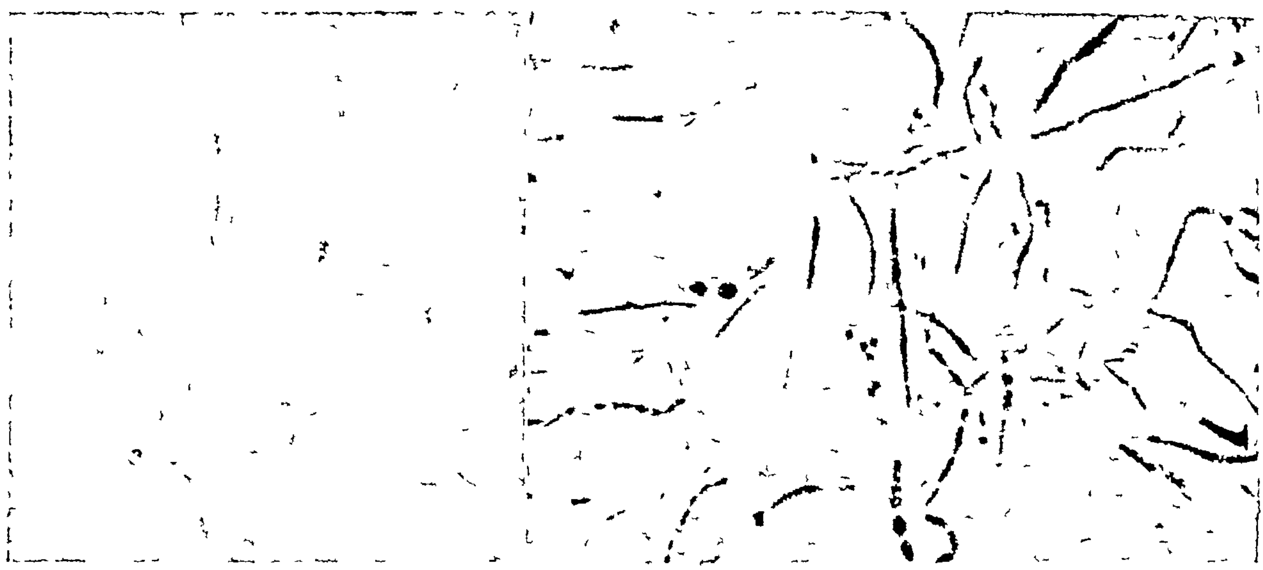
After the patient had received 2 g of chloramphenicol in one day the sediment contained chains of cocci, bacilli, some diplobacilli, motile single bacilli, and some long thick rods On plating the urine yielded hæmolytic coliform colonies consisting of gram negative motile bacilli *Ps pyocyanea* seemed to have vanished

On the fourth day of chloramphenicol treatment, however, besides the typical coliform colonies, other types appeared Some were tiny colonies, 0 5 mm in diameter, circular dome shaped with glistening surface transparent, and easy to emulsify They formed a uniform turbidity in broth The growth consisted of gram negative non motile bacilli After a few subcultures on normal laboratory media these reverted to typical coliform colonies

Colonies of another type also appeared These were dry and rough produced a diffusible green pigment on agar and in broth, and in all respects were similar to, and behaved like, the small colonies isolated in case 1 which had been identified as of *Ps pyocyanea*

Case 3 —Before treatment, cultures of this patient s urine yielded colonies identified as a coliform bacillus When he had received 9 g of chloramphenicol in 72 hours another specimen of urine was plated After 24 hours, on blood-agar, this had grown a few barely visible colonies which, on further incubation, enlarged and became like those of a streptococcus Unstained preparations examined by phase contrast showed a mixture of types There were chains of small cocci the size of streptococci Some chains consisted of small and large cocci, and others had a large bulb at one end or in the middle Other chains consisted of bulbs of different sizes, or of a mixture of bulbs, cocci and rods There were also bacillary chains in some of which, the individual members were of equal size whereas in others there were both small rods and large swollen ones Giant bizarre forms of different shape, size, and thickness (see figure) were also present Most of the organisms were gram negative, but a few were gram positive

The tiny colonies were transplanted into broth, and after 48 hours incubation there was a very poor granular growth consisting of the same pleomorphic population To exclude the possibility that the culture was a mixture of different organisms a slide serum agar culture was prepared with a highly diluted inoculum This was placed on the warm stage, and under phase-contrast microscopy a chain of small cocci was chosen and left to grow After overnight incubation the chain had *increased in length, but instead* of cocci the additional members were bacilli. Then, with a micromanipulator, individual members from the coccal and bacillary chains as well as representative types from all the abnormal forms, were isolated and left to grow in droplets of broth in the oil chamber The bulbous and giant forms did not divide Some became slightly larger, and in some bulbous chains one or two additional members appeared, but all these forms lysed



(a) (b)

Pleomorphic culture obtained in case 3 Unstained bacteria seen by phase-contrast microscopy (a) × 2000; (b) × 1200

without further multiplication in spite of repeated attempts However, all the other organisms, coccal or bacillary, reproduced the original pleomorphic picture, including the bulbous and giant forms

When left on the plates at room temperature, some of the tiny colonies became smoother and much larger (some fifty times their original size) Subculture from these large colonies, after they had been left for a month at room temperature, again produced a poor granular growth in broth, though richer than the first, and small colonies on blood agar though slightly larger and smoother than the originals Microscopically there were the same bizarre forms and chains On repeated subculture the tiny colonies reproduced the same pleomorphic population, with a slight progressive reduction in the ratio of abnormal large bulbous forms to coccal and bacillary chains

With the gradual disappearance of the large non viable forms the colonies enlarged until, after repeated subculture over months, they lost all resemblance to the original hardly visible colonies which required enriched media for growth After a few hours' incubation they now gave a rich growth on blood agar as well as on agar The colonies were very rough and the size of normal coliform colonies In broth they produced both definite turbidity and a granular sediment The organisms have, however, kept their peculiar pleomorphism, though the large bulbous forms are now rare and many diplobacilli have been added to the population

Serological reactions showed that the original coliform and the pleomorphic strain had some antigenic constituents in common, but the latter was very rough and only occasionally gave good emulsions so its serology could not be more thoroughly studied

Cases 4, 5, and 6—These were patients with coliform infections of the urinary tract After treatment with chloramphenicol organisms very like the pleomorphic strains described above were isolated from their urines Very large doses of these organisms were injected intraperitoneally into mice without any obvious ill effect, whereas much smaller doses of the original strains killed the animals

In subsequent experiments in vitro an organism similar to the pleomorphic strains was also obtained by subjecting *Bact coli* to the combined action of chloramphenicol and antiserum Other variants, isolated by the same process, are described in an accompanying paper

CONCLUSIONS

Organisms obtained from the urine of patients receiving chloramphenicol treatment sometimes show profound morphological and cultural alterations, which may include loss of virulence, and may be lasting or transient

The emergence of organisms with altered characters is important, in that the infecting organism, although still present, might escape observation When they revert to the normal these variants may be responsible for relapses They may also be significant in the detection of carriers

PRODUCTION OF BACTERIAL VARIANTS IN VITRO WITH CHLORAMPHENICOL AND SPECIFIC ANTISERUM

A VOUREKA
M D Athens

From the Wright Fleming Institute of Microbiology, St Mary's Hospital Medical School, London

THE observation that atypical colonies, breeding true through a series of subcultures, could be isolated from the urine of patients treated with chloramphenicol led to an attempt to induce similar changes in vitro by subjecting bacteria to the action of chloramphenicol The organisms chosen for these studies were strains of a coliform bacillus isolated from two untreated patients whose urine was later found to yield atypical colonies when chloramphenicol treatment was being given

Chloramphenicol Alone

Young broth cultures of these strains were used to inoculate broth tubes containing chloramphenicol in concentrations ranging from 2 to 250 μg per ml Throughout 2 weeks' incubation samples of these cultures were removed twice daily for examination by phase contrast microscopy and inoculation into broth and on blood agar

No growth was apparent in the tubes containing 16–250 μg of chloramphenicol per ml, but direct preparations showed rods many enlarged up to five times the original size, which on plating yielded normal colonies, mostly smooth but with occasional rough smooth types No other abnormality was noticed No forms like those obtained from the urine of the treated patients or any other sort of stable atypical colonies were obtained throughout the whole experiment

Chloramphenicol and Specific Antiserum

It was then thought that special conditions in the body might have influenced the production of these forms, and the combined action of chloramphenicol and specific antiserum was therefore investigated The organism studied was *Bact coli* D433, for which a strong antiserum was available (agglutination 1 1600) and under the combined action of this antiserum and chloramphenicol alterations were obtained in both the colonial and the cellular morphology of the bacteria

This paper deals particularly with the variants which have been reproduced through a sufficient number of subcultures to be regarded as stable The intermediate stages have also been carefully studied in an attempt to define the way in which these variants arise The observations seem to support the assumption that, in some cases at least, variants are a result of injury to the normal parent cell

The technique most often successful in producing variants was as follows

Broth containing 250 µg of chloramphenicol per ml is inoculated with a small inoculum (0 01 ml per ml) of an 18 hours' broth culture of *Bact coli* D433 After 24 hours' incubation an equal volume of the antiserum is added and the culture further incubated This procedure seems to give variants more regularly than when the antiserum is added at the same time as the chloramphenicol Samples are examined daily by phase-contrast microscopy and planted into broth and on blood agar Variants are usually isolated some time within 1–6 days, mostly within 24 hours

Control experiments with *Bact coli* D433 in broth in chloramphenicol alone or in antiserum alone, failed to yield stable atypical colonies on subculture Experiments starting from whole cultures as well as from single cell cultures were carried out, but the results were the same

FINDINGS

Fresh Preparations Viewed by Phase contrast Microscopy

A few hours after the addition of antiserum, the culture consists of greatly swollen cells arranged singly, in chains, or in masses of entangled chains As further hours pass the bacteria show increased damage The masses seem to fuse progressively as if the bacterial walls have melted The single bacilli are greatly swollen and practically round, their lining membrane is no longer sharply defined but looks hairy, as if it is deteriorating and about to disintegrate Still later, only severely damaged round bodies and masses of tiny particles can be seen

Subcultures in broth or on blood-agar give one of the following three types

Type 1—Granular growth in broth, consisting usually of a mixture of forms most of the cells are in bacillary form, some being larger than normal, chains of bacilli a few chains of coccal forms, and some large lanceolate diplococcus like organisms are also present Plating on blood agar yields mostly normal coliform colonies, but small shiny dome shaped colonies are also present On further incubation very tiny colonies become visible, and these on subculture give usually a mixture of small shiny dome shaped colonies and a range of very tiny ones, some moist and others dry, just visible with the hand lens The moist colonies reproduce usually as a mixture of small shiny dome shaped colonies and dry colonies, whereas the very tiny dry colonies bred true forming variants, one example of which will be called variant α (fig 1)

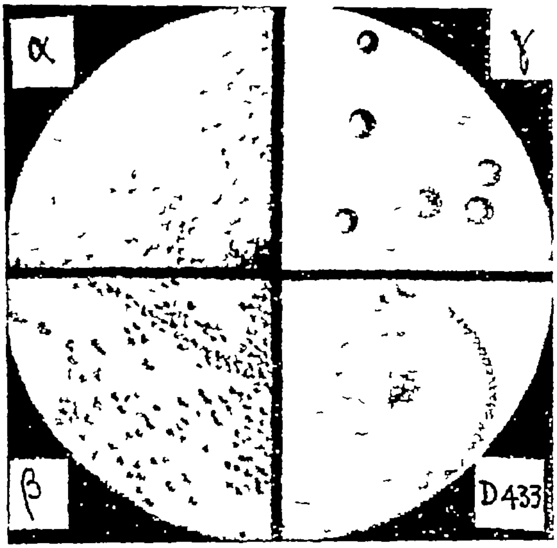


Fig 1—Colonies of variants α β and γ and of *Bact coli* D433 on same serum agar plate

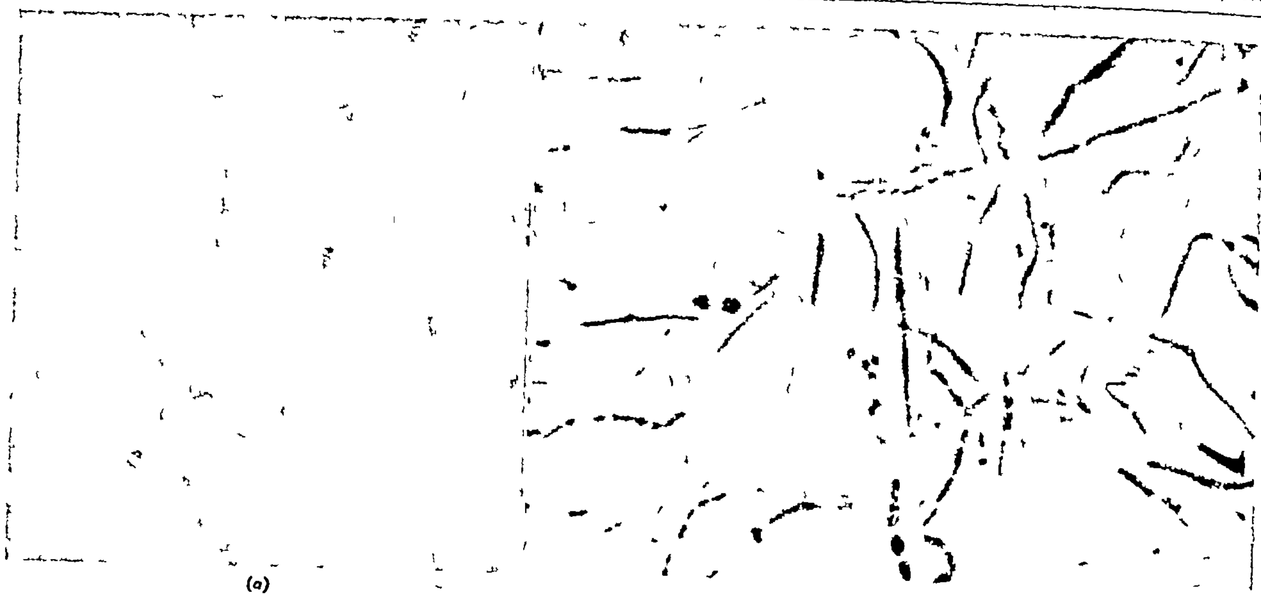
Type 2—Very poor granular growth in broth, hardly visible before 48 hours incubation, consisting of an extensively damaged population Most cells are grossly enlarged and misshapen The prominent forms are large about the size of red blood cells, and shaped like lanceolate cocci or diplococci and large club shaped bacteria These monstrous forms reappear throughout many subcultures then gradually the rate of growth increases and the cells are smaller but retain their pleomorphism

On repeated single cell cultures the giant forms do not divide, some grow a little more before lysing, but they all lyse without multiplying From smaller healthier looking cells, however, all the range of the giant cells is reproduced

On blood agar type 2 yields a mixture of colonies of sizes ranging from very tiny to forms looking like typical colonies of enterococcus (fig 1) Some produce a greenish discoloration of the blood, others a complete hæmolysis All types may be present on the same plating On old plates the colonies enlarge up to ten or twenty times their original size, they are

TABLE I—AGGLUTINATION AND ABSORPTION OF AGGLUTININS

Antigens used	Dilutions of antiserum to *Bact coli* D433						
	1/100	1/200	1/400	1/800	1/1600	1/3200	Control
Serum unabsorbed							
D433	++++	++++	++++	++++	++++	+	–
α	++++	++++	+++	++	+	–	–
β	++++	++++	++++	++++	+++	+	–
γ	++++	++++	++++	+++	++	±	–
Serum absorbed by D433							
D433	–	–	–	–	–	–	
α	+	±	–	–	–	–	
β	–	–	–	–	–	–	
γ	–	–	–	–	–	–	
Serum absorbed by α							
D433	++	++	+	–	–	–	
α	++	+	+	–	–	–	
Serum absorbed by β							
D433	–	–	–	–	–	–	
β	–	–	–	–	–	–	
Serum absorbed by γ							
D433	+++	+++	++	++	+	+	
γ	+	+	–	–	–	–	



(a) (b)

Pleomorphic culture obtained in case 3 Unstained bacteria seen by phase-contrast microscopy: (a) × 2000; (b) × 1200.

without further multiplication in spite of repeated attempts However, all the other organisms, coccal or bacillary, reproduced the original pleomorphic picture, including the bulbous and giant forms

When left on the plates at room temperature, some of the tiny colonies became smoother and much larger (some fifty times their original size) Subculture from these large colonies, after they had been left for a month at room temperature, again produced a poor granular growth in broth, though richer than the first, and small colonies on blood agar though slightly larger and smoother than the originals Microscopically there were the same bizarre forms and chains On repeated subculture the tiny colonies reproduced the same pleomorphic population, with a slight progressive reduction in the ratio of abnormal large bulbous forms to coccal and bacillary chains

With the gradual disappearance of the large non viable forms the colonies enlarged until, after repeated subculture over months, they lost all resemblance to the original hardly visible colonies which required enriched media for growth After a few hours' incubation they now gave a rich growth on blood agar as well as on agar The colonies were very rough and the size of normal coliform colonies In broth they produced both definite turbidity and a granular sediment The organisms have, however, kept their peculiar pleomorphism, though the large bulbous forms are now rare and many diplobacilli have been added to the population

Serological reactions showed that the original coliform and the pleomorphic strain had some antigenic constituents in common, but the latter was very rough and only occasionally gave good emulsions, so its serology could not be more thoroughly studied

Cases 4, 5, and 6—These were patients with coliform infections of the urinary tract After treatment with chloramphenicol organisms very like the pleomorphic strains described above were isolated from their urines Very large doses of these organisms were injected intraperitoneally into mice without any obvious ill effect, whereas much smaller doses of the original strains killed the animals

In subsequent experiments in vitro an organism similar to the pleomorphic strains was also obtained by subjecting *Bact coli* to the combined action of chloramphenicol and antiserum Other variants, isolated by the same process, are described in an accompanying paper

CONCLUSIONS

Organisms obtained from the urine of patients receiving chloramphenicol treatment sometimes show profound morphological and cultural alterations, which may include loss of virulence, and may be lasting or transient

The emergence of organisms with altered characters is important, in that the infecting organism, although still present, might escape observation When they revert to the normal these variants may be responsible for relapses They may also be significant in the detection of carriers

---

PRODUCTION OF BACTERIAL VARIANTS IN VITRO WITH CHLORAMPHENICOL AND SPECIFIC ANTISERUM

A Voureka
M D Athens
From the Wright Fleming Institute of Microbiology, St Mary's Hospital Medical School, London

The observation that atypical colonies, breeding true through a series of subcultures, could be isolated from the urine of patients treated with chloramphenicol led to an attempt to induce similar changes in vitro by subjecting bacteria to the action of chloramphenicol The organisms chosen for these studies were strains of a coliform bacillus isolated from two untreated patients whose urine was later found to yield atypical colonies when chloramphenicol treatment was being given

Chloramphenicol Alone

Young broth cultures of these strains were used to inoculate broth tubes containing chloramphenicol in concentrations ranging from 2 to 250 µg per ml Throughout 2 weeks' incubation samples of these cultures were removed twice daily for examination by phase contrast microscopy and inoculation into broth and on blood agar

No growth was apparent in the tubes containing 16–250 µg of chloramphenicol per ml, but direct preparations showed rods, many enlarged up to five times the original size, which on plating yielded normal colonies, mostly smooth but with occasional rough smooth types No other abnormality was noticed No forms like those obtained from the urine of the treated patients or any other sort of stable atypical colonies were obtained throughout the whole experiment

Chloramphenicol and Specific Antiserum

It was then thought that special conditions in the body might have influenced the production of these forms, and the combined action of chloramphenicol and specific antiserum was therefore investigated The organism studied was *Bact coli* D433, for which a strong anti-ageing, unsuitable temperature or pH, or exposure to bacteriophage, chemicals or X rays

As regards the emergence of variants α, β, and ι, the simplest explanation would be that they are present in undetectable numbers in the original culture as a result of a spontaneous mutation and that through the process used they are selected and their further growth is favoured

Selection and favoured growth, however, are highly improbable in most of the present cases because (1) most of the variants were more sensitive to the mixture of chloramphenicol and antiserum than was the original strain, (2) most of the variants needed a large number of subcultures to give a fair growth on normal laboratory media on which the original strain would grow readily and profusely, and (3) a whole range of variants with markedly different characters can be obtained from a freshly isolated single cell culture, and, whereas many variants may belong to the same group and have closely similar characteristics, no variant is an exact replica of another

The emergence of variant β is particularly suitable for study Variant β is produced by steps by survival of healthier bacteria out of an obviously " ill " population As has already been shown by single-cell culture, the giant individuals which, in the first subcultures, form the greatest proportion are cells doomed to death They cannot divide, they grow up to a point and lyse, and single-cell cultures of other almost " healthy " looking members illustrate the way these giant cells appear

It seems as if these healthy looking bacteria carried in themselves an important defect which made them produce monsters One has the impression that the organisms were very ill and perhaps just escaped an almost deadly injury, they survived, but the injury provoked in the cell lasting alterations which caused the progeny to differ from the original strain

The non-viability of most of the progeny of the cells accounts for the very poor growth, especially following the first isolation, whereas on repeated subcultures the healthiest individuals survived, the viable proportion of the progeny increased, the giant cells disappeared, and the growth improved A particular phase of growth during the action of the poisonous agent might have been responsible for the difference in characters among the variants obtained, or different mechanisms might have been involved. Whereas there is no clue to how variants α and ι arose, the changes described in type 2 strongly support the claim that variant β was the result of a mutation induced by a profound disturbance or injury of a vital element in the " reproductive system " of the cell.

If chromosomes and genes in bacteria are to be accepted (there is strong evidence that they should), a change in a gene or in a block of genes may lead to the production of daughter cells with altered characters The range of types obtained unpredictably in these experiments could then be linked with the range of alternative types, the " alleles " to which a gene can unpredictably mutate

The profound injury inflicted on the cell by chloramphenicol and antiserum might provoke the strong disturbance necessary to evoke a change in the genes and thus induce mutation Possibly this mechanism does not differ fundamentally from that responsible for " spontaneous mutation "

Klimek et al (1948) Bellamy and Klimek (1948), and Gale and Rodwell (1948) have described a staphylococcus which, when rendered highly resistant to penicillin, has the morphology of gram negative rods and pleomorphic cocci. This organism I found to be very sensitive to potassium tellurite, to which ordinary staphylococci are highly resistant The findings here and similar work done on a penicillin resistant staphylococcus suggest that a double process may have been involved in the production of their variant (1) selection of a resistant organism, and (2) injury to the cell by the high concentration of penicillin

CONCLUSIONS

Alterations in morphology, sugar fermentations, resistance to inimical agents, and antigenic structure can be induced in *Bact coli* D433 by treating cultures with specific antiserum and chloramphenicol

Some synergism exists between chloramphenicol and antiserum, since a combination of the two seems to have a more potent effect on the cells than either has alone

Resistance to chloramphenicol and to penicillin vary independently and must therefore have separate genetic locations

Gram staining, sensitivity to penicillin, and resistance to potassium tellurite are correlated, but the correlation is not absolute

These variations, which range from changes in antigenic structure to a complete change of characters, might illustrate the evolution from one serological type to another, or from one species to another

Studies of the avirulent variant and its reversion to the normal might help to explain variations in virulence

I am indebted to Mr Ben May, of Alabama, for financing this work and for providing the micromanipulator without which accurate results could not be obtained, Dr Pierre de Fonbrune of Paris, for teaching me to use his micromanipulator, Dr Joan Taylor for providing *Bact coli* D433 and its antiserum, Sir Alexander Fleming and Prof Robert Cruickshank for their valuable advice, and Mr T Jefferies for the photographs

REFERENCES

Bellamy W D Klimek J W (1948) *J Bact* 55 153
Gale E F Rodwell W (1948) *Ibid* p 161
Klimek, J W Cavallito C J Bailey J H (1948) *Ibid* p 139

Medical Societies

ROYAL SOCIETY OF MEDICINE

What is General Practice ?

THE society's new section of general practice held its first scientific meeting on Dec 20, with Dr G F ABERCROMBIE, the president, in the chair

Dr G O BARBER said that the question which had been asked during the formation of the section was " What is general practice ? " So it seemed logical to try to define the difference between medicine as practised by the general practitioner and medicine as practised in the hospital by the specialist

General practice was such an individual matter that each practitioner was bound to have a different concept of his work. As a young man, Dr Barber had just joined a practitioner who had been in the district for forty years when he overheard a patient say " I don't hear very good reports of this young man, I hear he has to examine people before he knows what's wrong with them " He thought at the time " I'll show them " It took him many years to realise that he was wrong then, and that the old lady was right He did not mean that the general practitioner should not examine patients and keep records, but the good G P, living with his patients and knowing the details of their lives, got so intimate a knowledge of them that often his examination of them simply confirmed the impression he got as they walked into the consulting room General practice was, in one sense, being with one's patients

Medicine in hospital was medicine in vitro, while general practice was medicine in vivo The general practitioner was the naturalist stalking his prey in the jungle, whereas the hospital consultant only examined his specimens in the zoo The essence of general practice was studying man as a natural animal, in his environment In general practice one had the advantage of knowing round and dome shaped, and have a wavy appearance Variant β belongs to type 2

Type 3 —The growth in broth is again hardly visible before 48 hours' incubation but is less granular than in type 2 On blood agar type 3 gives very small streptococcal like colonies (fig 1) some of which produce hæmolysis These colonies breed true for a great number of subcultures (over 200) and do not change on old plates The morphology of the cells—elliptical coccobacilli or short fusiform bacilli—also remains constant from the first subculture Variant γ is an example of type 3 It arises abruptly, in contrast with variant β, which one seems to be able to watch developing After a large number of replatings, however, the rate of growth of variant γ increases, as happens with all the variants described Growth appears earlier, the colonies are larger, and rods are seen among the population These larger colonies are sometimes surrounded by a rough flat margin which occasionally spreads like a film Occasionally, on platings from old broth cultures there was a thin film of growth covering most of the blood agar plate, on subculture this film grew typical γ colonies

As has been mentioned, all these variants grow very poorly for a number of subcultures after their first isolation On nutrient agar the growth is even poorer, and for this reason blood agar has been used in these experiments

TABLE II—SUGAR FERMENTATIONS OF *Bact coli* D433 AND OF VARIANTS α, β, AND γ

Strain	Lactose	Glucose	Dulcitol	Mannitol	Saccharose
Bact coli D433	+	+	−	+	+
Variant α	+	+	−	+	−
β	+	+	+	+	+
γ	+	+	−	+	+

+ acid and gas

After a variable number of replatings larger colonies appear in cultures of variants α and β, and these eventually revert to coliform colonies indistinguishable from those of the parent strain After some 200 subcultures in one year, variant γ has not yet reverted to normal Larger and smoother colonies have, however, been obtained in some platings, and the population consists mostly of bacilli and some longer rods Growth on moist plates favours reversion

Characters of Variants

Gram staining —The variants so far described are gram negative

Virulence —Intraperitoneal inoculations of large doses of these variants had no ill effects on mice, whereas smaller inocula of the original strain killed all the inoculated mice and the organism was recovered from their heart blood

Serological reactions —All the variants are agglutinated almost to titre by the antiserum to the original *Bact coli* D433 The finding of complete or almost complete cross absorptions proves that variants α and β are antigenically closely related to the parent strain whereas the partial absorption obtained with variant γ suggests that one or more of its antigenic constituents are lacking or changed (table I)

Sugar fermentations —Variant γ ferments the same sugars as the original strain, but variant α does not ferment saccharose and variant β ferments dulcitol thus differing from *Bact coli* D433 (table II)

TABLE III—RESISTANCE TO INIMICAL AGENTS

Strain	Greatest concentrations permitting growth			
	Penicillin (units per ml)	Potass tellurite	Chloramphenicol (µg per ml)	Streptomycin (units per ml)
Bact coli D433	50	1/320 000	6	3
Variant α	50	1/40 000	24	3
β	6	1/2500	3	3
γ	12 5	1/640 000	0 75	>1 5

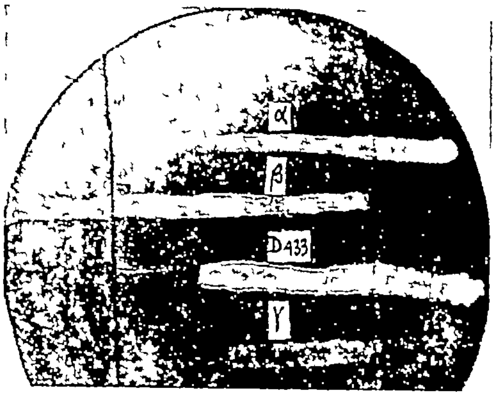


Fig 2—Resistance of variants α, β, and γ to potassium tellurite 1/100,000 (on left) and to penicillin 50 units per ml (on right) compared with that of *Bact coli* D433

Resistance to inimical agents —As table III and figs 2 and 3 show variant β is more sensitive to penicillin and more resistant to potassium tellurite than the original strain. Variant α shows increased resistance to potassium tellurite, but it is also more resistant to penicillin whereas variant γ is more sensitive to all the drugs used All the variants except α are either equally sensitive or more sensitive to chloramphenicol than the original strain Of the many variants isolated, some of which closely resembled variant α, it was the only one resistant to chloramphenicol It may have originated, by selection, from a cell of high resistance to chloramphenicol—indeed in a freshly isolated single cell culture it was found that the cells often differed in their resistances to chloramphenicol

Variants were also obtained from a strain of *Salmonella typhi* and a penicillin resistant staphylococcus, but these will be dealt with elsewhere

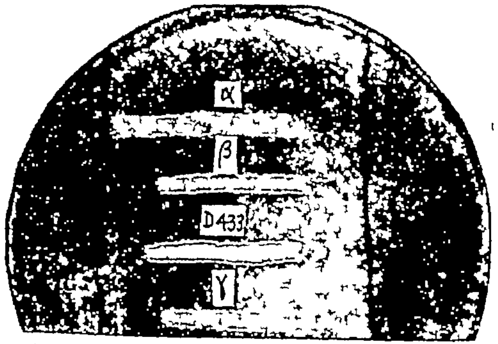


Fig 3—Resistance of variants α, β, and γ to streptomycin 500 units per ml (on right) and to chloramphenicol 100 µg per ml (on left) compared with that of *Bact coli* D433

There have also been isolated, in experiments using *Bact coli* D433, atypical colonies which have not yet been identified

DISCUSSION

The action of chloramphenicol and antiserum on a specific strain of *Bact coli* has led to the appearance of atypical colonies diverging greatly from normal but whose relationship to the original strain has been established through reversion to the normal or through serological reactions

These changes need not be specific to chloramphenicol and antiserum Any agent causing the cell an injury or a disturbance of the same degree will probably lead to the production of similar variants All variants described by different workers have been obtained from cultures submitted to unfavourable conditions, such as

Dr Delisle Gray said that young men in hospital did not know what general practice was Before specialising, they should learn what general practitioners did they should first spend 6–12 months in general practice

Dr Barber made it clear that he had not suggested that the general practitioner should not examine the patient , but that without the case history the examination might be futile When the practitioner came into a home he should bring a therapeutic influence, but anxiety was likely to return after he left Here the bottle of medicine was valuable as an emblem of his continuing authority

Reviews of Books

Medical Treatment

Principles and Their Application Editor Geoffrey Evans f r c p , consulting physician, St Bartholomew's Hospital London Butterworth 1951 Pp 1398 £5 5s

At a time when so many new drugs and methods are being introduced, it requires both skill and courage to produce a book on medical treatment—skill in selection and courage in rejection Dr Geoffrey Evans has exercised both virtues, and, marshalling a team of more than fifty contributors, has produced a volume likely to prove a standard work of reference for doctors throughout the world The series of monographs, covering the whole field of medical treatment, reflect the enormous advances that have been made during the past few years The information is up to date, including such topics as 'Aureomycin' and chloramphenicol, aminopterin, vitamin B_{12}, the rice diet, and the treatment of acute renal failure by intragastric drip , and though the articles naturally vary both in form and quality, all of them are practical Some, such as that by Professor Haddow on the chemotherapy of cancer are fully annotated reviews , others, such as an excellent section on diseases of the gall-bladder by Dr E R Cullinan, are based on personal practice and unsupported by references Dr Paul Wood presents a clear and reasoned account of the treatment of heart disease, and the chapter on pulmonary tuberculosis by Dr Robert Coope and Mr Price Thomas is worthy of its authors Sections on geriatrics, rehabilitation, and the treatment of dental sepsis are included , and dermatology, pædiatrics, the tropical diseases, and industrial hazards are expertly discussed

Since treatment is not stereotyped, it is inevitable that certain statements invite criticism It seems a pity, nowadays, still to recommend an acid ash diet in the prevention of renal calculi, to surround adiposity with an aura of mystery, and even to refer to the use of autogenous vaccines in the treatment of intestinal toxæmia. Many physicians would not agree that the mercurial diuretics are reliable in the treatment of the œdema of type II nephritis, and the usual dosage of penicillin in subacute bacterial endocarditis is now higher than that recommended These are, however, minor points , and we welcome a book that deserves, and is sure to receive, an enthusiastic reception

Congenital Heart Disease

(2nd ed) J W Brown, m d Lond , f r c p , physician to the Grimsby General Hospital London Staples Press 1950 Pp 344 30s

Since the first edition of this book appeared ten years ago the advances in diagnosis and treatment of congenital heart-disease have been so remarkable that Dr Brown has seen fit to rewrite most of it , his bibliography of over 700 references bears witness to the work this has entailed For the most part he considers cyanosis a useful guide in classification, and thus follows Abbott , but he points to the tendency in congenital heart lesions towards anatomical adjustment and adaptation In a useful chapter on differential diagnosis he emphasises the value of the early history, such as routine school-entrance records provide, and a proper appreciation of physical signs His wide experience of school-children adds weight to the statement that current views on prognosis of the cyanotic group require revision , puberty is not always an adverse factor in such cases, yet the significance of a rising blood-count is serious He advocates regular periodical observation of children with congenital heart disease so that cardiac enlargement can be assessed, but he decries an unnecessarily gloomy outlook Valuable advice is given on the general care of patients, on their education, and on their management when pregnant Though evidence is conflicting, he firmly believes that maternal rubella in the first three months of pregnancy is so important that therapeutic abortion in such cases is justified

The many cardiologists and practitioners who have eagerly awaited this second edition will not be disappointed by it

Chemotherapie der Tuberkulose mit den Thiosemikarbazonen

Gerhard Domagk and others Stuttgart Thieme 1950 Pp 405 D.M 60

The object of this work is to review the experimental and clinical results obtained with the thiosemicarbazones in the treatment of tuberculosis Three chapters are by Domagk the first two on the bacteriology and pathology of tuberculosis, while well presented, include a number of unjustifiably dogmatic statements , the third gives the experimental results obtained with the drug The other chapters deal with clinical results in various forms of tuberculosis skin, upper respiratory, glandular, intestinal, genito urinary, osteo articular, and pulmonary (four chapters) Each author gives his own experience , there has been no combined study of dosage and duration of treatment The best chapters are by Kalkoff, on skin tuberculosis (a remarkable study), and by Malluche, on the local treatment of cavities In pulmonary tuberculosis the results are suggestive but by no means conclusive, and the work is far from reaching present standards required for the evaluation of chemotherapy On the other hand the production of the book—the paper, the print, and the quality of the illustrations—surpasses anything nowadays seen in this country

Essential Urology

Fletcher H Colby, m d , chief of the urological service, Massachusetts General Hospital Baltimore Williams & Wilkins London Baillière, Tindall, & Cox 1950 Pp 580 61s 6d

This sound book is intended for the senior student The teaching is essentially practical and good illustrations abound Few will disagree with the author's condemnation of the various ingenious but dangerous rigid stone-extractors for the cystoscopic manipulation of ureteric calculi, or with his candid admission that many cases of chronic prostatitis are resistant to all known forms of treatment We confidently recommend the work

The Alkaloids

Chemistry and Physiology Vol I Editors R H. F Manske , H. L Holmes New York Academic Press 1950 Pp 525 $10

This is the first of a series of four volumes, to which it seems that a fifth, on the pharmacology of the alkaloids, may be added

Volume I is divided into seven sections each written by an expert The first two deal with what may be called the natural history of the alkaloids thus R H F Manske describes their botanical distribution, and gives lists of natural orders and botanical families of alkaloid yielding plants, with charts of these orders, based on Hutchinson's diagram suggesting probable lines of evolution in flowering plants Manske hints at the possibility of a classification of plants on the basis of their chemical components He also discusses, evidently from practical experience, the isolation of the mixture of alkaloids usually present in a plant, and the separation and purification of its components W O James surveys critically the results of many workers bearing on the problems of where, how, and why biogenesis of alkaloids occurs in plants The remaining sections are chemical all five are written by chemists, primarily for chemists, and as the case history When the student as a clerk took a patient's history at the bed side, the answers he got were really the patient's impression of the answers, in general practice the doctor knew these answers from his own observation Living in the neighbourhood, the practitioner gained a knowledge of his patient by observing his heredity as well as his environment—which was very important knowledge when the stress syndrome began to develop One often observed in different members of a family a tendency to break down in the same way

There were two conflicting views of the scope of general practice One was that as medicine and surgery and the allied specialties became more and more complicated, the general practitioner must become an intelligent signpost to the outpatient departments Dr Barber believed the opposite to be true He believed that it was the general practitioner's duty to oversee the specialist investigations, and when he passed on a patient to a specialist or a hospital department, it was part of his duty to see that the specialty was applied properly and according to the patient's needs The practitioner should not think "Oh, I've sent him to hospital Now I can forget about him until he comes back" Whether a patient was well or ill, he should have a general practitioner who felt responsible for him Such over all responsibility sometimes took the general practitioner a good deal away from academic medicine, but this responsibility for the patient in sickness and in health was the *driving force* of general practice The emergency call *might* be for something trivial But general practice consisted not so much in treating the triviality which caused the panic in the home and perhaps the neighbourhood, as in treating this "herd panic" This was especially true of births and deaths At the birth of a first baby *not only* the mother but the expectant father and the grandparents needed treatment, and the handling of *them* should be as effective as that of the confinement Death, too, did not affect only the person who was going to die The practitioner could make all the difference between a never forgotten blow and an event that drew together the remaining members of the family

It could be argued that general practice was degenerating into the treatment of trivialities, and in this case general practice would be humdrum but worthy But Dr Barber did not believe that any case was trivial, for the triumph of general practice was in sifting trivialities

General practice would always be what the individual practitioner made of it it was his own conception of his duty to his patients

Dr J D Simpson remarked that the responsibility borne by the general practitioner differed from that borne by his hospital colleagues He should have a special knowledge of the environment of his patients, for the treatment of a given condition varied in relation to the person's immediate circumstances Thus the doctor must be prepared to accept greater risks for the man having his "last shot" at a university scholarship than he would for a boy who was taking one part of his first M B from school at the age of 16 The question of fitness for athletics was often put to the general practitioner If called on to make a decision on behalf of the team by the captain, he must decide the risk to the patient and to the side For example one more dislocation would not do great harm to the good rugger player who had already dislocated his shoulder twice, but the side might lose him early in the game One transient loss of consciousness did not justify a diagnosis of epilepsy, and in these circumstances electro encephalography would, in nine cases out of ten, confuse the issue as would the administration of phenobarbitone "to stop any further fits" How much better and more courageous to tell the patient that "it was a faint," and to wait without giving drugs till the next attack, which might never happen Sometimes the doctor might be wrong but the number of patients he would save from fear of a disease which they had not got would amply justify his action He must, of course, tactfully stop them indulging in particularly dangerous activities

A special subject of research gave the practitioner additional incentive and interest His opportunities for research were twofold First, there was the long term collection of cases of a particular disease, for this he must keep a nosological record—a list of patients who had had the disease When planning an investigation, he should first seek a statistician's advice Secondly, there was the recognition of clinical syndromes during epidemics

In summary, the general practitioner must be expert in the environment of his patients, and he should not fear to accept responsibility which will save his patients anxiety

Dr C M Billington thought there was no good in going back to the family doctor of 1884, who had little armament except love, it was necessary to look at what the general practitioner could do to produce health, either on his own or in a team This was a new concept

Dr E P Scott recalled that Mackenzie did his work on digitalis when a general practitioner at Burnley He was sorry that the expression "family doctor" had gone out It would have been a pity if the artist had labelled that famous picture "The General Practitioner" instead of "The Doctor"—and much worse *if he had* made it, as it might become, "General Medical Operative"

Dr E B Rayner said that when the general practitioner passed his patient on to the hospital service he too often did not—for reasons well known—pass on sufficient information

Dr Laurence Dulake regarded the general practitioner as the only "proper doctor"—all the rest were incomplete doctors The object of general practice, as he saw it, was to give people another chance An old doctor had told him that G P s fell into two classes—the "pooh poohers" and the "tut tutters" Dr Dulake did not hold with "tut tutting" out loud, but he would prefer to know, by examination, whether a patient was epileptic or not He found that about 60% of patients suffered from gross psychological disorder Linkage with psychiatrists in the neighbourhood was useful for the general practitioner

Dr D M Hughes thought that general practice was the practice of being a "doctor" A specialist was not a doctor in the traditional sense, he wanted to practise medicine as an intellectual pursuit and incidentally to help the patient and doctor Dr Hughes was not saying that one concept was higher than the other, but the two were different

Dr Lindsey Batten *also* pointed out that general practitioners were the *only people* in the profession who looked after the whole patient He did not think this could be done by *teams* *it had* essentially to *be* done by the individual One job of the general practitioner was to explain to the patient what was the matter with him, a complaint about hospitals was that the patient often came out without ever learning the nature of his illness The general practitioner had not only to introduce the specialist to his patient but in a sense to protect the patient from the specialist

Dr M C Andrews limited as far as possible, the number of consultants he called in so that they got to know not only the patients but himself and his attitude to the patients

THE LANCET

LONDON SATURDAY, JAN 6, 1951

Peace at Home

LOOKING back over the past five years, we may agree that the main achievement of the Labour Government has been to redistribute the national wealth without using or evoking violence. The war, which made it necessary to increase the social rights of the ordinary citizen, created also the feeling of comradeship that has permitted an increase by consent. Those who were relatively rich, whether in possessions or position, have yielded much with a good grace because they too have thought it right that, in a people so united in adversity, every family should henceforth be sure of help against illness or poverty. Through social security an ideal has been largely realised, and this country no longer consists of DISRAELI's two nations. Yet somehow we lack a corresponding sense of success, of coöperation, of responsibility, and of hope. With world peace in deepening peril our rulers may well find it hard to inspire such hope and unite us in strenuous work to raise the quality of our national life. But sometimes it seems that everyone now sets too little store by unity; indeed that, reversing the usual practice, we engage in controversy at home to take our minds off what is happening abroad.

These generalisations can be applied to the particular case of the National Health Service. We could and should be proud that in troubled times the medical services of this country have not only been maintained but in places already extended; and doctors who have suffered in the process should at least derive some comfort from the knowledge that vast numbers of people are thankful to be able to get medical care without direct payment. Yet few of those who work the service feel that they are taking part in a great new venture in which thought and endeavour will bring steady improvement. Social historians will probably attribute the establishment of the N.H.S. to a masterly mixture of courage and compromise, of planning and improvisation; and they will be astonished that so much was done so fast. But those of us who are living through the social history are conscious more of the soluble problems that remain unsolved, of the faults that remain unrectified, of the limits set on progress, and of the absence of coherent policy. Delays would be tolerated if we were sure of every question being considered on its merits after full examination of the facts by those most likely to understand them; but clearly this ideal state of affairs has not been reached. Where all should be loyally pursuing one aim—to give the public the most useful service that can be devised for the available money—we have instead an atmosphere of conflict, with somewhat arbitrary decisions on one side and a tendency to threats on the other. Moreover the conflict is acquiring a political flavour; for one outcome—and cause—of the maladjustment between the British Medical Association and the Minister of Health is that the chief representative organisation of the profession appears to have abandoned its political neutrality, and thereby prejudiced its status in negotiation. Everyone knows that frank expression of differing opinions is a necessary preliminary to decisions, and it is useless to pretend that differences do not exist; but if the public is to be served, and medicine to be advanced, the Ministry and the profession must work together to that end, and not in general opposition to one another. If it is to acquire the unity it needs, the health service must be kept, as far as possible, out of party politics.

As far as possible. What does this mean? One must admit at once that a service of this kind has to operate within the bounds of political decisions. First and most obviously there is the Chancellor's decision on what sum can be found to finance it. But there are also many others. The proposal, for example, to charge patients for board and lodging in hospital is really a proposal to collect more money from the public for the benefit of the service, and an additional levy of this kind could be imposed only if the Government thought fit. Again, it may seem to the medical profession that the large sums now spent on providing spectacles and dentures could more profitably be used elsewhere—for instance, in enlarging specialist services. But in the last resort it is the function of the Minister, not of the profession, to decide what the public shall be given; and he would be within his rights if he formed the opinion that actually people gain more from being able to bite their food, or read their newspaper (though possibly Mr. BEVAN would not choose this example) than from having a ventriculography or even a thoracoplasty in their last illness. Equally we should be entitled to reply that if the service does not employ diagnostic and therapeutic methods of the latest type, and provide for their development, medicine in this country will stagnate, and in the end the public will be the losers. Likewise we can object to the demand for dentures being met at the cost of a preventive dental service for children. The truth is that the Minister's decisions, though political in the sense that they are not technical, should be based not on what the public wants but on what it *needs*—taking a long view. Though he must bear the responsibility for the decisions, and present them to the Cabinet and the country, he ought to have the help of a body charged with forming and continually reviewing the policy on which the service shall develop, the priorities to be given to its various projects, and the effect of one decision on another. Mr. BEVAN has a remarkable knowledge of the service and has championed it successfully against the Treasury in a way that a less powerful Minister could never have done. The Ministry deserves credit for accomplishing an administrative transformation of quite appalling complexity. But the Minister and civil servants, if left to themselves, may well put public demands before public needs, and they are tempted to solve their urgent problems empirically without reference to a general plan. The recent memorandum on registrars is an example of an important decision taken without enough discussion of its consequences, not least of which has been the alienation of some of the service's strongest supporters and keenest workers.

such are well done They will be useful to research workers on alkaloids, and can be cordially recommended to advanced students, being rich in accounts of interesting reactions and of the ingenious methods by which the structures of alkaloids are being determined

The Health of the People

S Leff, M D, medical officer of health for Willesden London Gollancz 1950 Pp 288 12*s* 6*d*

"This," says the wrapper, "is in effect a comprehensive survey of all aspects of the health, living and working conditions and medical services of the people of this country" But Dr Leff's conception of "The People" is something much less than the whole population, it is rather an economic class, coterminous, at widest, with the wage-earners and their dependants and contrasted throughout the book with the "well to-do," with whom they are seen to be in constant and inevitable opposition The health with which the book is concerned is that neutral state for which we make Ministers and medical officers responsible, good health and the healthy find little mention Dr Leff's real subject is rather the relation of the community to those of its citizens who, for one cause or another, need material assistance He shows very convincingly how lamentably we always have fallen short of supplying the needs of the sick, the poor, the old, the crippled, and, in some respects, the wage earners of our population For any who may believe that we have, or have nearly, provided for our dependants, especially for the sick in mind or body, this book should prove a valuable corrective, and it will also administer a cold douche to the *laudator temporis acti* But not all will feel that the cupidity of the "well-to-do" and the existence of vested interests are almost the sole cause Are not apathy, dullness of soul, reluctance to face formidable difficulties, and plain laziness—qualities in which no class has a monopoly or even a priority—at least as much to blame? Dr Leff believes that our present National Health Service may fail to supply the People's needs because of "centralised bureaucracy in Whitehall and bureaucracy of technicians [i e, 'doctors and specialists'] at all levels of administration" His remedy is reform and revival of local government and the transfer of administrative power from the "technicians" and other appointed members to the "elected representatives of the People" The book would be more persuasive if it were less bitter, and harped less on one string

Der Film als Experiment und Heilmethode

Jaromir Lhotsky, Prof O Pötzl Vienna Maudrich. 1950 Pp 136 ÖS 30

The title arouses expectations which the contents do not satisfy The first two chapters are concerned with the psychology of films and "the problem of film-experience" The theoretical requirements for experimental application of films to scientific study are then very briefly stated, a chapter on objective methods of recording psychological phenomena is interpolated, and a short account is given of some technical points in cinematography, using 16 mm film The study of normal and abnormal psychology by means of the film is then systematically reviewed, but too cursorily to be of value, even the investigations which Dr Lhotsky himself made in mental hospitals are little more than listed Allusion is also made to the possibilities of applying the film to vocational selection and "lie-detecting," and the lines of possible development are sketched out The book is suggestive rather than informative

A lengthy appendix, by Professor Pötzl, contains an essay which he wrote in 1938 on the comparison of films with dreams He examines the vivid optic hallucinations of drunkards, which are seen in three dimensions in delirium tremens, whereas when they occur in acute alcoholic psychosis they are two-dimensional Pötzl carried out tachistoscopic experiments on a patient with this condition who had had, years before, a hemianopsia from cerebral syphilis it was possible to excite a series of hallucinatory pictures in the section of the visual field previously affected by the hemianopsia A number of these tachistoscopic experiments are described, in which dream pictures were evoked, and Professor Pötzl analyses, in an intricate and somewhat obscure argument, the cerebral determinants of the movements and time relations evident in these visual phenomena

Traité du pneumothorax extra-pleural

P le Foyer and E Delbecq with the collaboration of M Bertheau, M Bidermann, A Garnier, L Giaccardo, and G Larraud Paris Doin 1950 Pp 367 Fr 2500

In this monograph the authors consider all aspects of extrapleural pneumothorax, emphasising perhaps the surgical side, and the complications, rather than the problems of selection, though these are certainly not ignored It is a comprehensive and thorough work freely illustrated, and for those who do not read French with much accuracy there is a summary in English at the end of each chapter or section The names and experience of the two authors are sufficient evidence that this is an authoritative work, though naturally it contains views with which other experts would not always agree

A Short Textbook of Radiotherapy for Technicians and Students

J Walter, B M, M.R C P, D M.R.E, consultant radiotherapist and deputy medical director, Sheffield National Centre for Radiotherapy, H Miller, M.A., PH.D. F INST.P, physicist to the centre London J & A Churchill 1950 Pp 444 28*s*

This small textbook fulfils its purpose and can be recommended to all radiographers who intend to sit for the Society of Radiographers' certificate in radiotherapy The physical section gives a lucid account of those parts of a difficult subject which all who use X rays and radioactive substances must not only learn but understand A short biological and pathological introduction leads to the methods used in treatment Here it has been more difficult to select suitable material, but on the whole the choice and presentation is good The initiative of the authors will be welcomed by those who have to teach therapy to radiographers

---

Principles of Medical Statistics (London *The Lancet* Pp 282 10*s* 6*d*)—The fifth edition of Prof A Bradford Hill's book differs in only one major respect from the fourth In response to a real need for worked examples of the statistical methods outlined in the main text, he has included a number of questions against which the student can test his understanding The model answers, which are given in some detail, considerably enhance the didactic value of this addition to a book which has become the standard introductory text on statistics for the medical investigator

Common Skin Diseases (9th ed London H K. Lewis. 1950 Pp 505 25*s*)—The new edition of this standard textbook by Dr A. C Roxburgh contains much new material on anti histamine drugs, dimercaprol, mepacrine, penicillin dermatitis, and other topics Work on penicillin and calciferol has been brought up to date, and a note has been added on the use of streptomycin in intractable lupus vulgaris. The book has been thoroughly revised, and the illustrations—some coloured, many plain, and all good—have been augmented by three new ones

Collected Papers by Sigmund Freud (Vol 5 London Hogarth Press 1950 Pp 396 25*s*)—Edited by James Strachey these are miscellaneous papers published between 1888 and 1938 The piety of psycho analysts has ensured that everything written by the founder of their branch of knowledge should be available, in the original German and in translation It is remarkable that the rather fugitive papers collected in this volume contain so much that is not only of historical interest but enlarges our knowledge of Freud's outlook and illuminates some obscure corners of psycho analytic theory Besides encyclopædia articles and other concise expositions, there are random notes, little more than occasional jottings, and considered statements of a problem (as in paper 30, on the termination of analysis) Freud, we are told, once said to an intimate 'I am not a Freudian myself' The reader often has cause in reading these papers, to recognise Freud's freedom from the pedantry and conceit sometimes disclosed in the writings of his followers In this final volume of the canon he emerges once more as a man of lofty mind with a constant singleness of purpose in all his studies and reflections

THE LANCET

LONDON SATURDAY, JAN 6, 1951

Peace at Home

LOOKING back over the past five years, we may agree that the main achievement of the Labour Government has been to redistribute the national wealth without using or evoking violence The war, which made it necessary to increase the social rights of the ordinary citizen, created also the feeling of comradeship that has permitted an increase by consent Those who were relatively rich, whether in possessions or position, have yielded much with a good grace because they too have thought it right that, in a people so united in adversity, every family should henceforth be sure of help against illness or poverty Through social security an ideal has been largely realised, and this country no longer consists of DISRAELI's two nations Yet somehow we lack a corresponding sense of success, of coöperation, of responsibility, and of hope With world peace in deepening peril our rulers may well find it hard to inspire such hope and unite us in strenuous work to raise the quality of our national life But sometimes it seems that everyone now sets too little store by unity, indeed that, reversing the usual practice, we engage in controversy at home to take our minds off what is happening abroad

These generalisations can be applied to the particular case of the National Health Service We could and should be proud that in troubled times the medical services of this country have not only been maintained but in places already extended, and doctors who have suffered in the process should at least derive some comfort from the knowledge that vast numbers of people are thankful to be able to get medical care without direct payment Yet few of those who work the service feel that they are taking part in a great new venture in which thought and endeavour will bring steady improvement Social historians will probably attribute the establishment of the N H.S to a masterly mixture of courage and compromise, of planning and improvisation, and they will be astonished that so much was done so fast But those of us who are living through the social history are conscious more of the soluble problems that remain unsolved, of the faults that remain unrectified, of the limits set on progress, and of the absence of coherent policy Delays would be tolerated if we were sure of every question being considered on its merits after full examination of the facts by those most likely to understand them, but clearly this ideal state of affairs has not been reached Where all should be loyally pursuing one aim—to give the public the most useful service that can be devised for the available money—we have instead an atmosphere of conflict, with somewhat arbitrary decisions on one side and a tendency to threats on the other Moreover the conflict is acquiring a political flavour, for one outcome—and cause—of the maladjustment between the British Medical Association and the Minister of Health is that the chief representative organisation of the profession appears to have abandoned its political neutrality, and thereby prejudiced its status in negotiation Everyone knows that frank expression of differing opinions is a necessary preliminary to decisions, and it is useless to pretend that differences do not exist, but if the public is to be served, and medicine to be advanced, the Ministry and the profession must work together to that end, and not in general opposition to one another If it is to acquire the unity it needs, the health service must be kept, as far as possible, out of party politics

As far as possible What does this mean? One must admit at once that a service of this kind has to operate within the bounds of political decisions First and most obviously there is the Chancellor's decision on what sum can be found to finance it But there are also many others The proposal, for example, to charge patients for board and lodging in hospital is really a proposal to collect more money from the public for the benefit of the service, and an additional levy of this kind could be imposed only if the Government thought fit Again, it may seem to the medical profession that the large sums now spent on providing spectacles and dentures could more profitably be used elsewhere—for instance, in enlarging specialist services But in the last resort it is the function of the Minister, not of the profession, to decide what the public shall be given, and he would be within his rights if he formed the opinion that actually people gain more from being able to bite their food, or read their newspaper (though possibly Mr BEVAN would not choose this example) than from having a ventriculography or even a thoracoplasty in their last illness Equally we should be entitled to reply that if the service does not employ diagnostic and therapeutic methods of the latest type, and provide for their development, medicine in this country will stagnate, and in the end the public will be the losers Likewise we can object to the demand for dentures being met at the cost of a preventive dental service for children The truth is that the Minister's decisions, though political in the sense that they are not technical, should be based not on what the public wants but on what it *needs*—taking a long view Though he must bear the responsibility for the decisions, and present them to the Cabinet and the country, he ought to have the help of a body charged with forming and continually reviewing the policy on which the service shall develop, the priorities to be given to its various projects, and the effect of one decision on another Mr BEVAN has a remarkable knowledge of the service and has championed it successfully against the Treasury in a way that a less powerful Minister could never have done The Ministry deserves credit for accomplishing an administrative transformation of quite appalling complexity But the Minister and civil servants, if left to themselves, may well put public demands before public needs, and they are tempted to solve their urgent problems empirically without reference to a general plan The recent memorandum on registrars is an example of an important decision taken without enough discussion of its consequences, not least of which has been the alienation of some of the service's strongest supporters and keenest workers such are well done They will be useful to research workers on alkaloids, and can be cordially recommended to advanced students, being rich in accounts of interesting reactions and of the ingenious methods by which the structures of alkaloids are being determined

The Health of the People

S LEFF, M D, medical officer of health for Willesden London Gollancz 1950 Pp 288 12*s* 6*d*

"THIS," says the wrapper, "is in effect a comprehensive survey of all aspects of the health, living and working conditions and medical services of the people of this country" But Dr Leff's conception of "The People" is something much less than the whole population, it is rather an economic class, coterminous, at widest, with the wage earners and their dependants and contrasted throughout the book with the "well-to-do," with whom they are seen to be in constant and inevitable opposition The health with which the book is concerned is that neutral state for which we make Ministers and medical officers responsible, good health and the healthy find little mention Dr Leff's real subject is rather the relation of the community to those of its citizens who, for one cause or another, need material assistance He shows very convincingly how lamentably we always have fallen short of supplying the needs of the sick, the poor, the old, the crippled, and, in some respects, the wage earners of our population For any who may believe that we have, or have nearly, provided for our dependants, especially for the sick in mind or body, this book should prove a valuable corrective, and it will also administer a cold douche to the *laudator temporis acti* But not all will feel that the cupidity of the "well-to do" and the existence of vested interests are almost the sole cause Are not apathy, dullness of soul, reluctance to face formidable difficulties, and plain laziness—qualities in which no class has a monopoly or even a priority—at least as much to blame? Dr Leff believes that our present National Health Service may fail to supply the People's needs because of "centralised bureaucracy in Whitehall and bureaucracy of technicians [i e, 'doctors and specialists'] at all levels of administration" His remedy is reform and revival of local government and the transfer of administrative power from the "technicians" and other appointed members to the "elected representatives of the People" The book would be more persuasive if it were less bitter and harped less on one string

Der Film als Experiment und Heilmethode

JAROMIR LHOTSKY, Prof O PÖTZL Vienna Maudrich 1950 Pp 136 ÖS 30

THE title arouses expectations which the contents do not satisfy The first two chapters are concerned with the psychology of films and "the problem of film-experience" The theoretical requirements for experimental application of films to scientific study are then very briefly stated, a chapter on objective methods of recording psychological phenomena is interpolated, and a short account is given of some technical points in cinematography, using 16 mm film The study of normal and abnormal psychology by means of the film is then systematically reviewed, but too cursorily to be of value, even the investigations which Dr Lhotsky himself made in mental hospitals are little more than listed Allusion is also made to the possibilities of applying the film to vocational selection and "lie-detecting," and the lines of possible development are sketched out The book is suggestive rather than informative

A lengthy appendix, by Professor Pötzl, contains an essay which he wrote in 1938 on the comparison of films with dreams He examines the vivid optic hallucinations of drunkards, which are seen in three dimensions in delirium tremens, whereas when they occur in acute alcoholic psychosis they are two-dimensional Pötzl carried out tachistoscopic experiments on a patient with this condition, who had had, years before, a hemianopsia from cerebral syphilis it was possible to excite a series of hallucinatory pictures in the section of the visual field previously affected by the hemianopsia A number of these tachistoscopic experiments are described, in which dream pictures were evoked, and Professor Pötzl analyses, in an intricate and somewhat obscure argument, the cerebral determinants of the movements and time relations evident in these visual phenomena

Traité du pneumothorax extra-pleural

P LE FOYER and E DELBECQ with the collaboration of M Bertheau, M Bidermann, A Garnier, L Giaccardo, and G Larraud Paris Doin 1950 Pp 36[illegible] Fr 2500

IN this monograph the authors consider all aspects of extrapleural pneumothorax, emphasising perhaps the surgical side, and the complications, rather than the problems of selection, though these are certainly not ignored It is a comprehensive and thorough work freely illustrated, and for those who do not read French with much accuracy there is a summary in English at the end of each chapter or section The names and experience of the two authors are sufficient evidence that this is an authoritative work, though naturally it contains views with which other experts would not always agree

A Short Textbook of Radiotherapy for Technicians and Students

J WALTER, B M, M.R C P, D.M R E, consultant radiotherapist and deputy medical director, Sheffield National Centre for Radiotherapy, H MILLER, M A., PH.D., F INST P, physicist to the centre London J & A Churchill 1950 Pp 444 28*s*

THIS small textbook fulfils its purpose and can be recommended to all radiographers who intend to sit for the Society of Radiographers' certificate in radiotherapy The physical section gives a lucid account of those parts of a difficult subject which all who use X rays and radioactive substances must not only learn but understand A short biological and pathological introduction leads to the methods used in treatment Here it has been more difficult to select suitable material, but on the whole the choice and presentation is good The initiative of the authors will be welcomed by those who have to teach therapy to radiographers

---

Principles of Medical Statistics (London *The Lancet* Pp 282 10*s* 6*d*)—The fifth edition of Prof A Bradford Hill s book differs in only one major respect from the fourth In response to a real need for worked examples of the statistical methods outlined in the main text, he has included a number of questions against which the student can test his understanding The model answers, which are given in some detail, considerably enhance the didactic value of this addition to a book which has become the standard introductory text on statistics for the medical investigator

Common Skin Diseases (9th ed London H K Lewis 1950 Pp 505 25*s*)—The new edition of this standard textbook by Dr A C Roxburgh contains much new material on anti histamine drugs, dimercaprol, mepacrine, penicillin dermatitis, and other topics Work on penicillin and calciferol has been brought up to date, and a note has been added on the use of streptomycin in intractable lupus vulgaris The book has been thoroughly revised, and the illustrations—some coloured, many plain, and all good—have been augmented by three new ones

Collected Papers by Sigmund Freud (Vol 5 London Hogarth Press 1950 Pp 396 25*s*)—Edited by James Strachey these are miscellaneous papers published between 1888 and 1938 The piety of psycho analysts has ensured that everything written by the founder of their branch of knowledge should be available, in the original German and in translation It is remarkable that the rather fugitive papers collected in this volume contain so much that is not only of historical interest but enlarges our knowledge of Freud s outlook and illuminates some obscure corners of psycho analytic theory Besides encyclopaedia articles and other concise expositions, there are random notes, little more than occasional jottings, and considered statements of a problem (as in paper 30, on the termination of analysis) Freud, we are told once said to an intimate I am not a Freudian myself' The reader often has cause in reading these papers, to recognise Freud s freedom from the pedantry and conceit sometimes disclosed in the writings of his followers In this final volume of the canon he emerges once more as a man of lofty mind with a constant singleness of purpose in all his studies and reflections possible by emptying the stomach and then keeping it empty to prevent any further leak from the perforation and so allow it to seal naturally If such a course can be shown to be no less successful than operation its advantages are great Operation should always be avoided if other measures will suffice Quite apart from fatalities, abdominal operations may cause such complications as incisional hernia (of which "burst abdomen" may be reckoned a fulminating variety) and intestinal obstruction due to adhesions, to say nothing of the inconvenience caused to the surgeon performing a subsequent operation by the scarred abdominal wall and peritoneal adhesions There is, however, one advantage that a non operative method might at first sight seem to offer but which the aspiration treatment of peptic ulcer denies us An experienced surgeon must be at hand throughout the management of these cases and particularly in the first six hours, for in certain circumstances operation must after all be undertaken without further delay The folly of entrusting the conservative treatment to an inexperienced surgeon is emphasised by STEAD, whose article also appears in this issue he believes that an inexperienced surgeon will do better to operate provided a good anæsthetist is available

There are serious objections to this new method of treatment One of the weightiest is the possibility of mistaking the diagnosis and so failing to operate on cases, such as acute appendicitis, in which early operation is essential TAYLOR claims that his experience silences this criticism, for he has had only 4 cases in which the original diagnosis of perforated peptic ulcer was later proved wrong In 2 of these cases the conditions turned out to be of a sort prohibiting or at least not requiring surgery, but in the other 2 a necessary operation was slightly delayed It may well be, as TAYLOR says, that in these 2 cases the delay in operation made no difference, but few surgeons will feel entirely reassured that on other occasions similar cases might not turn out worse With the aspiration method the position of the patient seems rather precarious Like the diver on the bottom of the sea, his life depends utterly on an uninterrupted flow through a long flexible tube The difficulties of ensuring that aspiration is continuously effective are serious if surmountable , and most surgeons would prefer the single, final stopping of the leak which only operation can secure Another serious objection —not mentioned by TAYLOR or STEAD—is the necessity of keeping the patient in bed and relatively still for several days while the perforation is sealing The importance of early mobilisation is now generally recognised, and it must be noted that one of TAYLOR's early cases died of pulmonary embolism. In studying the results of conservative treatment and comparing them with operative results, a serious difficulty must be faced In an operative series every diagnosis is established by operation in a non operative series the diagnosis rests on radiological and clinical findings Positive radiological evidence can usually be accepted as conclusive , but sometimes this evidence is uncertain , and in about one-third of the cases it is negative It is true that in many of these cases the presence of an ulcer is subsequently proved, and in some an operation may later show that perforation has taken place , yet in an important proportion of the cases proof of perforation is lacking , and we feel that this somewhat reduces the significance of the mortality figures The gross mortality of TAYLOR's 101 cases was a fraction under 11% From other sources he has collected a further 454 cases, and the mortality for the whole series is just under 8%, which certainly compares favourably with most published figures for operative treatment By analysing the mortality figures and excluding cases moribund on admission and those with other diseases which have contributed to the fatal issue, a net mortality percentage much more favourable to the conservative method may be arrived at but such adjusted figures are not acceptable In the contest between rival treatments the prize can be awarded only to the competitor who wins from scratch The comparisons, moreover, must be contemporary, and it may be misleading to judge the results of conservative treatment against those of surgery in the years before 1945 We may say that the exponents of the conservative treatment have made a case for their method as a safe alternative to surgery, and in particular they have shown how much can be done for the patient who is too ill for operation , and great credit is due to these surgeons for their courage and vision But they have certainly not yet proved that aspiration is better than suture

In the last few years there has been a sharp reduction in the mortality of many different abdominal operations, and the suture of perforated peptic ulcer has shared in this improvement In 1939 SANGSTER[3] reported 100 perforations with 24 deaths , in 1948 he reported 105 with only 4 deaths[4] At a meeting of the surgical section of the Royal Society of Medicine on Dec 6, Prof DIGBY CHAMBERLAIN reported the results of 1622 cases treated during the years 1930–49 The over-all mortality was 17 9% (including the cases too ill for operation), but in the last two years the mortality was only 6% and 7% The Central Middlesex Hospital[5] results are similar and in some ways more impressive In the last three years 165 cases were admitted and 11 died—a gross mortality of 6 6% Although this figure must be accepted as it stands, it is important to note that of the 155 cases operated on only 2 died AVERY JONES and his colleagues[6] have reported a larger series from the Central Middlesex Hospital which shows how striking was the steady improvement in results over the ten years 1938–48 —and this despite a great increase in the proportion of aged people It is not possible to demonstrate conclusively what is the cause of this improvement, but there is strong evidence that antibiotics and improved anæsthesia are the main factors, with better postoperative care (including early rising) and advances in surgical technique (such as the avoidance of drainage) also helping In this country in the past few years the general standard of emergency surgery has been raised by the presence of more surgical registrars in the hospitals, and its results have much improved because skilled anæsthetists, using modern methods including muscle relaxation, are on hand to help them It remains very doubtful whether conservative treatment, even conducted by an experienced unit, is equally safe for the patient, and we endorse the opinion that, until the facts are clearer, it should be

---

[3] Sangster A H *Lancet* 1939 ii, 1311

[4] Sangster A H *Ibid* 1948 ii, 289

[5] Doll R Personal communication

[6] Jones F A Parsons P J White B *Brit med J* 1950 i 211

To give a sense of united effort two things are necessary first, the representatives of those who work the service must join with the Ministry in forming a development policy against which any proposed action can be tested, and secondly every member of the service must know that all constructive suggestions have attention at a high level This dual need was recognised in the original scheme, when great significance was attached to the creation of a Central Health Services Council to advise the Minister [1] But unhappily the council, despite much good work by its *standing committees*, has so far failed to fulfil its main functions As it has made no attempt to evolve a general policy, and as its very existence is commonly forgotten, it serves neither as the mind nor as the mouthpiece of the service, though it should be both For these shortcomings there are two reasons First, the Ministry has a long record of ignoring its advisory committees, and the Central Health Services Council, modestly disclaiming a position of leadership, has been content to accept the minor, if useful, duty assigned it—that of giving technical advice on single subjects This handicap might be overcome by a more forceful disposition on the part of the council itself, but we should still be left with the second cause of failure, which depends on principles rather than personalities The reason why members of the service know little or nothing about the labours of the C H S C is that its proceedings (apart from an annual report subject to the Minister's censorship) are confidential The argument in favour of this arrangement is a strong one—namely, that if the council's meetings were public, or if it issued its opinions to the press, the Minister would never feel able to consult it on delicate subjects before a decision was reached, and might well refuse it the full information it must possess if its conclusions are to have weight Time may show that the advantages of this secrecy are being bought too dearly it might be more healthy to have a more representative and less confidential council, able to argue publicly with the Minister, so that the reasons for and against his actions would be plain to all concerned Meanwhile the least the Ministry should do is to give the fullest possible publicity to the work of the council, allowing it to issue frequent statements on the advice it has given, and sometimes to invite expressions of opinion by members of the service on subjects on which it is about to deliberate

After its inevitably shaky start, the National Health Service badly needs a period of consolidation, and one of the things to be consolidated is the morale of those who work it If a sense of confidence and purpose and hope is to be created, they must feel that it has a development policy, and that its decisions are based on that policy and on equity—not on hard bargaining, and certainly not on party politics Moreover, they must understand what the policy is, and be enabled to influence those charged with forming and reviewing it If the Minister and some of the profession's spokesmen would cease blaming each other for the imperfections of a service which is being constructed with fair success in extraordinarily difficult circumstances, there would be more time for explanation to the participants, both lay and medical, and more pride in what has been done In determining future policy, the really big issues could be faced more squarely, and we might gradually get rid of the idea that organisation is always something imposed unnecessarily on "us" by "them" The National Health Service is part of this country's endeavour to devise a way of life in which rational planning is combined with a high degree of personal freedom Such an experiment, we are rightly reminded,[1] is a daring novelty compared with the authoritarian régimes which have been customary through the ages *and still dominate half the world To make it succeed* we need more than peace abroad We need at home the kind of peace that is manifest in discussion without discord

Treatment of Perforated Peptic Ulcer

"THE perforation of a gastric or duodenal ulcer i one of the most serious and most overwhelming catastrophes that can befall a human being The onset o the symptoms is sudden, the course rapid, and, unles surgical measures are adopted early, the disease hasten to a fatal ending in almost every instance" Lor MOYNIHAN's striking words,[2] written a quarter of a century ago, are in the main true today except that surgical measures now have a respectable rival In *the attempt to lower mortality two main lines* may be followed elimination of the faults of operative treatment, and a trial of non operative measures

In medicine no treatment can succeed which doe not act in concert with the natural curative processes of the body, and the best method of treatment wil often be the one which unobtrusively supports and directs these processes and avoids violent and artificia intervention There is good evidence that the body can seal a perforation in a peptic ulcer by the deposition of fibrin and the apposition of an adjacent viscus—commonly the liver or the omentum Indeed, most posterior penetrating gastric ulcers have harmlessly perforated, the perforation being, so to speak, walled off before it occurred But even free anterior perforations not uncommonly seal themselves spontaneously and the incident can only be inferred from the finding at some subsequent operation of extensive peritoneal adhesions with perhaps encysted cellulose particles, and of an ulcer or its scar adhering to the liver or omentum In these cases the diagnosis of perforation was never made at the time it took place It is indeed often very difficult to distinguish clinically between a perforation and a severe attack of ulcer pain Many orthodox surgeons recognise this type of self sealing perforation by speaking of a "leaking" ulcer and withholding operation, also operation is regularly withheld from patients with perforated ulcers who are too ill to stand it and occasionally recovery has been reported The deliberate exploiting of the natural sealing process in patients who are fit for, and according to accepted practice urgently require, operation is of course, a different matter, but both in this country and in America conservatism of this sort now has its advocates Among the most persuasive of these is HERMON TAYLOR, who reports in this issue a series of cases treated by what he calls the aspiration method He maintains that half the operative mortality is due to complications of the operation itself, and that it is

---

[1] Williams F *News Chronicle*, Dec 28 p 2

[2] Moynihan B Abdominal Operations 1926 vol i p 223

These stimulating papers will no doubt be followed by further observations on the same lines Already VOUREKA's work has thrown light into several obscure corners For instance two out of three of her variants in the end reverted, partly at any rate, to the parental pattern It seems to follow that whatever were its characters when it emerged from the bowel, *Bact coli* D433 has found in captivity the way of life best suited to our artificial culture media

---

Annotations

BACTERIUM VERSUS VIRUS

JUST as greater fleas have lesser fleas upon their acks to bite 'em, so pathogenic bacteria going about heir lawful occasions in a human host are often plagued by still smaller organisms, the virus particles of bacteriophage, which produce disease in the bacteria and possibly, sometimes) restrict their activity enough to allow their host to recover Attempts have been made, though without convincing success, to apply bacteriophages in therapeutics The existence of a converse antagonism between bacterium and virus is usually gnored Yet the late Professor Twort remarked, in a popular article, that " In test tube experiments it is easy to arrange conditions so that a bacteriophage will kill off its host, the bacterium, but it is equally easy to arrange another set of conditions in which the bacterium will kill or inhibit its invading bacteriophage " This article has prompted Mrs Wooster, in our correspondence columns, to suggest the use of bacteria for controlling virus diseases

If we take *Bacterium coli* and one of its spherical phages (T6) as examples of the proposed contestants, the dimensions of these organisms, as given by Putnam,[1] are about 2 5 × 1 μ for the bacterium and about 50 mμ for the phage The contest will therefore be comparable if not to man against flea, at least to man against cockroach Some pathogenic viruses would be smaller (e g , poliomyelitis about 10 mμ) and some larger (e g , rabies and herpes 100–150 mμ) than the coliphage But the attractive picture of a large anthropoid bacterium chasing an elusive swarm of cockroach like viruses and finally annihilating them one by one is grossly misleading The hope would be that the bacteria by their growth and excretions might so modify the phage's environment that its continued existence became impossible This may be easily done in the test-tube but would be far more difficult in the body, where there are physiological mechanisms to keep the environment constant and any drastic change is likely to do more harm to the host's cells than to the virus Most viruses, such as those of poliomyelitis or hepatitis, are embedded in the tissues, where it would be undesirable if not impossible for bacteria to pursue them Perhaps viruses which attack cells on exposed surfaces, like herpes or the viruses causing respiratory infections, would be more accessible, but a further difficulty would be that the virus particles live and multiply *inside the cells* and exist outside only in the brief periods of passing from one cell to another Invasion of the tissue cells by bacteria, even if they come as well meaning scavengers, is not a contingency that anyone will contemplate with equanimity

However, before we condemn the proposal out of hand, we should perhaps recall how ridiculous it would have seemed, not many years ago, to enlist the help of green moulds in combating puerperal fever or pneumonia, yet *Penicillium notatum* was soon to be our most valued ally We in England sometimes accuse our American cousins of allowing enterprise to outstrip judgment—of wasting too much time, effort, and money in exploring fool ideas that any sensible Englishman could have told at the start were unsound and impracticable But now and again some fool idea, British or American, leads to a brilliant discovery, and the sensible Englishman is left to ponder whether his vaunted critical faculty is really such a reliable guide after all

---

[1] Putnam F W *Science* 1950 111, 481

SOME TUBERCULOSIS FIGURES

To say we are neglecting the tuberculous is to pluck monotonously at a single string, possibly we can appreciate the note more fully by attending to its overtones Dr F J W Miller,[1] bringing up to date his figures already published,[2] reports that, in Newcastle upon Tyne in the ten years 1939–49, tuberculosis was the greatest single cause of death in childhood, that deaths of children formed almost 10% of the total mortality from this disease, and that tuberculosis is responsible for nearly a quarter of all deaths between the ages of one and fifteen years This might be less serious than it sounds if the Newcastle death rate from tuberculosis was low but it is high compared with that of the country as a whole, having been, in 1949, 75 per 100,000 population for respiratory tuberculosis—against less than 50 for England and Wales Dr Miller illustrates the undue loss of children by comparing the figures for Newcastle (population 270,000) with those of Ealing and Acton (population 212,000) in Newcastle, in 1942–45 inclusive, 1177 people died of tuberculosis 130 of them being children, in Ealing and Acton only 450 people died of whom 18 were children—giving respective rates of 48 children and 8 children per 100,000 population Moreover the death rate in Newcastle, as compared with *such other large cities as Birmingham and Manchester,* is especially high among children of school age Dr Miller infers that the high childhood mortality means the presence of a large number of infective adults in this overcrowded city

In Glasgow the picture is possibly more sombre still Dr Stuart Laidlaw[3] notes that the number of new cases of pulmonary tuberculosis notified in 1949 was 2829—the highest figure recorded since 1910—and that 540 (19%) of those affected were children under the age of fifteen There were, moreover, 12,000 people on the tuberculosis register—3000 more than before the war Again overcrowding must be a potent factor in the spread of the disease, for " more than half the families in Glasgow are living in one or two apartment houses " What life in such conditions means, in terms of proximity, is illustrated in the Newcastle report, where the spread of an ordinary respiratory infection through a tenement is described

> In this house rooms were let to 7 families, who combined to make a total of 13 adults, 6 children aged two to five, and 3 infants A baby living in an attic with her parents developed pneumonia, four weeks later her mother—much given to visiting her neighbours—developed a cold At the same time a three year old on the ground floor developed bronchitis, while a few days later her infant sister had pneumonia A family of 4 on the same floor all developed respiratory illness and soon afterwards another baby in the house developed pneumonia, while her mother followed suit with a sharp cold

It is not difficult to apply the moral of this story to a more serious infection The point is brought home even more forcibly by Dr Laidlaw's study of the home conditions of 2674 Glasgow patients with pulmonary tuberculosis 1300 of these—nearly half—shared their beds with others, only 444 had a bed to themselves, and only 930—just over a third—had a room to themselves Domiciliary treatment can hardly hope to succeed in regarded as an experimental method to be left to those who are making a trial, with full knowledge of the risks, under entirely favourable conditions

---

[1] Annual Report of the Medical Officer of Health for 1949 Newcastle upon Tyne Pp 217

[2] *Lancet* 1949, ii 274

[3] Annual Report of the Medical Officer of Health for 1949 Glasgow Pp 302

The successful suture or sealing of a perforation is often not the end of the story According to ILLINGWORTH et al,[7] within one year 40% relapse (20% severely), and 70% relapse (50% severely) within five years Moreover hæmorrhage shortly after perforation is an important factor in the immediate mortality Another serious possibility[8] is the mistaking of perforated carcinoma for a simple ulcer (the distinction may be very difficult to recognise) or the development of carcinoma in a simple ulcer after perforation The difficulty of diagnosing carcinoma at an operation for perforated ulcer suggests that the majority of carcinomas which perforate are small and have not produced metastases, and are therefore resectable In such cases postoperative (or post-aspiration) investigations may not suggest the diagnosis of carcinoma, and the dreadful truth will reveal itself too late These considerations raise again the question of gastrectomy as the immediate treatment of perforation For years eminent Continental surgeons have advocated this procedure, but British surgeons have not been convinced Now that the mortalities of gastrectomy and of suture for perforated ulcer have dropped so low, gastrectomy for perforation should perhaps be reconsidered, for it could prevent most of the continued disability from chronic ulcer and some of the deaths from carcinoma

Bacterial Oddities Produced By Chloramphenicol

ANTIBIOTICS sometimes have odd effects on the shape, size, and cultural characters of bacteria in vitro In this issue, Dr VOUREKA, of Athens, working at St Mary's Hospital, Paddington, describes how her interest in these bizarre forms was aroused by the strange behaviour of urinary bacteria from patients under treatment with chloramphenicol After a few days of this treatment the urine appeared to be sterile, but if the drug was continued the *Ps pyocyanea* and *Bact coli* previously present reappeared in cultures swollen and distorted, producing colony forms widely different from those seen when they were first isolated Similar morphological oddities have been observed in cultures of other organisms under the action of other antibiotics, and two of the many explanations put forward[9] are (1) that they are bacterial cells which have lost their ability to divide though retaining their power to grow, and (2) that the antibiotic has interfered with the formation of the bacterial cell wall but otherwise has allowed growth to proceed

In her second paper VOUREKA describes in vitro experiments with *Bact coli* D433, done with the aim of elucidating these observations Cultivation in broth plus chloramphenicol alone produced bizarrely distorted organisms, but most of their colonies were normal in appearance When a specific antiserum and chloramphenicol were added to the culture medium the grotesques became still more varied, and pairs or chains of coccal forms were now seen besides the swollen and misshapen ones Growth was always poor and sometimes invisible, and subcultures on solid media (without antiserum or chloramphenicol) gave a scanty growth distinguished by at least three small colony forms bearing no resemblance to the parent strain All these exhibited a remarkable stability in up to 200 further subcultures, though there seemed to be an increasing tendency for the colonies to revert to their original size and shape

The bacterial variation following exposure to antibiotics which has received most attention, because of its practical implications, is the acquisition of drug resistance This is now generally looked on not as a mutation but as an effect of the selectiv survival of the most resistant members of the origin population Since high natural drug-resistance pr sumably depends on some metabolic peculiarity, is not surprising that the hyper-resistant organism occasionally possess minor aberrations in oth characters[10] It is not easy to explain why some these artificially produced resistant strains retai *their resistance through multiple subcultures in* medium free from antibiotic, whereas some do not VOUREKA's grotesques differ from the original strai in other features besides shape, size, and colony form and they retain these differences for many generations Serologically they are almost but not quite identica with their parent They have lost their virulence fo mice but have acquired the ability to ferment som sugars *Their resistance to other inimical* substance —penicillin and potassium tellurite—has changed, bu the changes are neither constant nor rational Mos surprising of all, far from being less sensitive t chloramphenicol than their parent they are equall or more sensitive It is difficult to think that change like these have arisen by the selection of strain better able to withstand the adversity of life wit chloramphenicol VOUREKA ascribes the changes t a true mutation, and though this must be only guess it is a not unreasonable one Most of wha we know about bacterial inheritance has been seen through several layers of glass, very darkly, bu there must be some part of the bacterial cell housin genes that determine its inherited characters In hostile but not quite lethal environment it may b possible to effect a change in the genes which wi alter the characters of the organism for man generations Botanists accept as a matter of cour the multiplication of genes known as polyploid effected by the action of colchicine—there was eve a chance at one time that the production of penicilli by *P notatum* could be increased in this way—an similar natural sports, usually sterile, are known a high in the animal kingdom as the *mollusca* Perhap these mutations, if they are such, are commoner tha we think Every day uncountable numbers o bacteria must be brought near to death from pheno poisoning, but few bacteriologists examine the survivors It may be that such variants are more ofte seen among parasitic organisms—there is certainl wide variation in the colonial forms of *Bact col* recovered in a routine laboratory

---

[7] Illingworth C F W Scott L D W Jamieson R A *Ibid* 1946 i 787

[8] Doll R *Ibid* 1950 i 215

[9] Eisenstark A Ward C B jun Kyle T S *J Bact* 1950 60 525

[10] Crofts J E Evans D G *Brit J exp Path* 1950 31 550 Johnstone K I Crofts J F Evans D G *Ibid* p 562 Hunter M F Mudd S Woodburn M A *J Bact* 1950 60 315

The problem of serum neuritis became more complicated during the late war when a number of cases were reported Thus from the Middle East Burnard and Fox[6] and Spillane[7] recorded the condition (under the name of localised neuritis of the shoulder girdle) as occurring without administration of serum, in his forty six cases Spillane found no time relation between the administration of vaccines or sera and the development of paralysis Weinstein[8] recorded sixteen similar cases among American military personnel, again in none of these had serum been administered within the previous three months, but all had had prophylactic injections of typhoid or typhus vaccine 1–12 weeks before the onset of the illness Parsonage and Aldren Turner[9] reported on 136 cases of the same condition, to which they gave the purely symptomatic name of neuralgic amyotrophy The record of previous inoculations was investigated in 67 of these, the number inoculated within the preceding four weeks was 11, of whom 6 had been inoculated within the previous fortnight They found however, that in no less than 66 of the 136 cases the condition had developed intercurrently in hospital Cases of neuralgic amyotrophy without any time relation to serum or vaccine administration are still occasionally seen in this country and have also been reported from Scandinavia[10] and France[11]

This condition and serum neuritis differ in several ways from anterior poliomyelitis The onset is afebrile and is not accompanied by the constitutional and meningeal symptoms of poliomyelitis, the pain at the onset is severe and localised, which is on the whole uncommon in poliomyelitis, where pain is usually more generalised even though the subsequent paralysis is localised, commonly sensation is impaired, particularly in the distribution of C5 segment, and the cerebrospinal fluid (C.S.F.) has been normal in the majority of cases where it has been examined in the acute stage The pathology and ætiology of neuralgic amyotrophy remain obscure, but the clinical picture is exactly comparable to that of serum neuritis, and probably the two disorders have a similar basic pathology Since there is a possibility that neuralgic amyotrophy may be precipitated by vaccine inoculation, care should be taken, and the C.S.F. examined, before atrophic paralysis following inoculation is attributed to anterior poliomyelitis

ON THE RECORD

THE Royal College of Physicians has published in book form the reports of its fifteen special committees which sat between 1942 and 1947 to consider a wide range of subjects of public and professional importance[12] These have already had considerable influence, and some of them should have more The one on medical education was notable as a bold effort to free the curriculum from the accretions of ages, and in general from the obsession that a doctor cannot be safely loosed on the public unless he has had lectures on every conceivable subject—though he need *understand* nothing This report was responsible for the " pre registration resident year," which is in due course to be introduced under the new Medical Act, but the college seems to have had in mind an assistant residentship, or scarcely paid post under the supervision of a senior resident, whereas nowadays the scheme is generally regarded merely as a means of ensuring that before undertaking independent practice all doctors shall hold a house appointment The report on the design of dwelling houses starts off in rather pessimistic vein, but in its latter half it proceeds to some first class social medicine Taking them all round, the reports are further evidence that the Royal College of Physicians, when it is given the chance, can rise to the occasion as a source of sound well considered advice In his introduction, Lord Moran, president from 1941 to 1950, points to its long record of service of this kind, which we hope and believe will continue and increase

DISSEMINATION OF THE MENINGOCOCCUS

IN both world wars cerebrospinal fever (meningococcal meningitis) became epidemic among recruits in Service establishments This, together with advances in the serological typing of meningococci and the advent of chemoprophylaxis, led Aycock and Mueller[1] to make a long and continuous study, from 1941 to 1945, of carrier rates in relation to the incidence of the disease in two American army establishments

Thirty years ago Glover[2] postulated a rise in the meningococcal carrier rate to 20% as a pre epidemic danger point and suspected a relation in the army between this rise and overcrowding in sleeping huts During the inter-war period, however, Dudley and Brennan[3] found that in Naval establishments persistently high carrier rates (54%) might obtain without clinical attacks, and clinical attacks occurred despite very low carrier rates. Furthermore, carrier rates were as high among senior ratings with spacious quarters as among recruits whose sleeping accommodation was much inferior Early in the late war Fairbrother[4] suggested that fatigue was more important than overcrowding in predisposing to clinical attacks, especially among recruits from rural districts, whose natural immunity was likely to be low

Aycock and Mueller discount altogether the effect of overcrowding They found that the disease is fairly uniformly distributed throughout the U S.A during years of high and low prevalence alike Plotting of reported cases during the period 1915–48 showed an undulating curve of increases and decreases, each extending over a period of 6–11 years, with peaks in 1918, 1929, 1936, and 1943 This rhythmical variation is a continuing phenomenon, and is not due to independent seasonal epidemics, since the rhythm during the epidemic season varies with that in the inter epidemic summer months But the pattern of periodicity differs from that of such " immunising infections " of childhood as measles, chickenpox, and diphtheria With these, an epidemic is terminated by the " exhaustion of susceptibles " and recurs only when enough non immunes have once again accumulated Thus Aycock and Mueller deny that natural immunity following exposure shapes the epidemic pattern of meningococcal meningitis, season is responsible, they find, only for secondary fluctuations in the longer cyclic curve, and there is no single cause for either

Using a method for prolonging the viability of the meningococcus on nasopharyngeal swabs, similar to that described by Downie,[5] these workers have compared the carrier rate of various serological types among seasoned troops and recruits, and they suggest that the carrier-rate among the latter may represent that of the civil population—a view later supported by swabbings of Harvard medical students In the two military groups the total carrier rates and their type-composition were essentially the same, and there was no indication of the seasonal variation which obtains for clinical attacks But, whether in the army or the civilian population, type composition is not stable, the carrier-rate for one type may increase while the rates for other types are stationary or declining Aycock and Mueller believe that these changes, which are not sudden or frequent, are natural such conditions, and protection of contacts becomes a mockery The acute need for more treatment beds in Glasgow is illustrated by the statements that, in spite of the rise in incidence, the number of cases under treatment in hospitals and sanatoria was no greater than in 1948, and that though there were only 351 deaths in institutions, as compared with 486 in 1948, this was mainly because advanced chronic cases could not gain admission They were at home, of course, sometimes infecting others

---

[6] Burnard E D Fox T G *N Z med J* 1942 41 243

[7] Spillane J D *Lancet* 1943, ii 532

[8] Weinstein E A *Arch Neurol Psychiat* 1947, 57 369

[9] Parsonage M. J Turner J W A *Lancet* 1948 i 973

[10] Hook O *Nord Med* 1949, 42 1662

[11] Alajouanine T Thurel R Blatrix C *Rev neurol* 1950 82 279

[12] A limited number of copies are available on application to the college

[1] Aycock W L Mueller J H *Bact Rev* 1950 14, 115

[2] Glover J A *Spec Rep Ser med. Res Coun Lond* no 50 1920

[3] Dudley S F Brennan J R *J Hyg Camb* 1934 34 525

[4] Fairbrother R W *Brit med J* 1940 ii 859

[5] Downie A W *Lancet* 1940 ii 36

These two reports remind us tellingly that tuberculosis is a social disease In overcrowded cities we can only hope to check its widening course by providing more houses or more beds—but preferably both

STERILISATION LAWS

THE sterilisation of certain classes of mentally or eugenically defective patients, which recurs, along with euthanasia, as a subject for ethicomedical debate in England, has been practised in the State of North Carolina since 1933, when the General Assembly regularised an earlier measure which had been ruled unconstitutional on appeal Woodside gives an account [1] of this experiment in action which is likely to interest both the opponents and the advocates of eugenic sterilisation

The North Carolina sterilisation law is a fair specimen of American State eugenic legislation Under it, sterilisation proceedings may be initiated by the head of any State penal or charitable institution, or by the county senior welfare officer, and action is mandatory upon these officials if a written request is presented by the next of kin or guardian of the patient The Eugenics Board, which administers the hearing of petitions for sterilisation, may act only in cases of mental disorder, feeblemindedness, or epilepsy (Voluntary sterilisation at the request of the normal patient is left to the discretion of the surgeon and has nothing to do with the eugenic laws) Detailed medical and social reports and the sworn consent of the patient, unless he or she is a minor, an inmate of a State mental institution, or of unsound mind ("certified"), are required No other eugenic or social reasons are recognised Failing the consent of the relatives, action can proceed at the discretion of the board, but with full rights of appeal to the superior court of the county, and only minors or the insane can be sterilised without their own consent Appeal to the courts, while it is the normal democratic safeguard, is possibly less adequate than Woodside suggests, since the appellants are almost uniformly feebleminded and underprivileged, but, as she points out, the use or abuse of the law depends on the spirit in which it is carried out, and the North Carolina law has not so far produced any flagrant injustice In this respect it is less open to criticism than other American State laws which prescribe compulsory sterilisation for delinquents and sexual deviants, sometimes without reference either to the non-hereditary nature of the complaint or to the emotional attitudes of courts

Since 1907, when Indiana introduced a sterilisation law, 49,207 sterilisations have taken place in the United States, 2152 being in North Carolina Most of these cases were among the group likely to benefit most, the feebleminded To the high grade female defective, incapable (as is often the case) of learning or maintaining contraception, sterilisation may mean a freer life, since the administrative argument for inpatient confinement is removed, while for the community the eugenic benefit is evident Woodside cites work done by herself and Eliot Slater confirming the tendency to consortive mating in the unintelligent, and with defectives this is even more prominent While many defectives are incapable, both biologically and psychologically, of safe parenthood, they may none the less be capable of proving happy and affectionate wives, and it is doubtful whether the restriction of rights involved in voluntary sterilisation is anything like as grave as that implied by restrictions on the "emotional contacts of the female patient" on licence from English institutions

One extraordinary feature of the North Carolina scheme is that only institutions with surgical facilities can really apply it at their discretion, for no funds exist for extramural operations On the wider issue, Woodside describes the possibilities of voluntary sterilisation in relation to current attitudes and prejudices in the public North Carolina has remarkably advanced provisions for contraceptive instruction, but many patients seem unable to take full advantage of them and benefit greatly by sterilisation once its nature and purpose, together with its lack of effect on sexual performance, have been explained to them In multiparæ in poor health or bad economic circumstances, sterilisation increases orgasm capacity in proportion as it reduces fear of conception

Studies of this type provide informative material on which to base our own views of the future of sterilisation Most English workers would feel that the legal denial of voluntary sterilisation to the individual is irrational, and that sterilisation of high grade defectives, based on persuasion, is eugenically desirable Compulsory powers will always, however, be rightly suspect in this country, especially when they are used, or may be used, to provide an easy administrative answer to a psychiatric problem Some of the American States have already provided experience from which we may be able to profit as time goes on

SERUM NEURITIS AND RELATED CONDITIONS

THIS year, apparently typical anterior poliomyelitis has been described in children inoculated within the previous 3–4 weeks with pertussis vaccine or with a mixture of this and diphtheria toxoid [1], and in the majority of these cases paralysis was maximal in the limb which had been inoculated A statistical study [2] confirms that during the 1949 epidemic this phenomenon was too common to be attributed to chance

Since Thaon's [3] report in 1910, atrophic palsy of one or both shoulder girdles has been recognised as a rare complication of the administration of serum [4] Serum neuritis has most commonly followed injection of tetanus antitoxin, but it has also been seen with diphtheria antitoxin and other sera The clinical course is fairly uniform, starting usually 5–10 days after administration of the serum At the onset there may be serum sickness and urticaria Severe pain is felt in the region of the scapula and upper part of the arm The pain lasts from a few hours up to a few days and is accompanied by atrophic paralysis of some of the shoulder-girdle muscles and at times slight sensory changes, usually on the outer side of the upper arm The distribution of the muscle involvement is usually radicular, the muscles supplied by C5 and C6 roots are commonly involved, but sometimes isolated muscles alone are paralysed, and the condition may be bilateral Winkelman [5] has recorded four similar cases with onset 7–14 days after smallpox vaccination Usually serum neuritis is ascribed to allergic œdema of the perineural tissues, but this explanation is unproved type were sufficiently alike for the data from them to be pooled. The exceptions were the two E N T wards which differed considerably—either in their practice or possibly in the type of patient admitted. One general surgical ward appeared to practise a high degree of early ambulation compared with the other wards of the same type. Leaving these exceptions on one side we were left with a sample of 522 patients drawn from twenty-one wards, distributed as follows six general surgical wards (155 patients), six general medical wards (167 patients), four gynæcological wards (109 patients) six obstetrical wards (antenatal 41 patients puerperal 50 patients). The estimates finally obtained, after adjustment, are set out in tables I–V.

---

[1] *Sterilisation in North Carolina* By MOYA WOODSIDE, research assistant Institute for Research in Social Science University of South Carolina London Oxford University Press 1950 Pp 236 20s

[1] McCloskey, B P *Lancet* 1950 i 659 Martin J K *Arch Dis Childh* 1950, 25 1 Geffen D B *Med Offr* 1950 83 137

[2] Hill A, Knowelden J *Brit med J* 1950 ii 1

[3] Thaon P *Sem méd Paris*, 1910 30 513

[4] Allen I M *Lancet* 1931 ii 1128 Kennedy F *Amer J med Sci* 1929 177 555 Woolling K R Rushton J G *Arch Neurol Psychiat* 1950 64 508 Thompson A R Tombleson J B L *Brit med J* 1949 i 1013

[5] Winkelman N W *Arch Neurol Psychiat* 1949 62 421

Table I shows that under early ambulation the number of bedfast patients in the general surgical wards would be reduced to less than a third of the present value, and the number of fully ambulant patients would be increased by about two thirds. The data also suggest that the adoption of early ambulation would give an increase of about 10% over the current rate of throughput.

Table II shows that under early ambulation the number of bedfast patients in the general medical wards would be reduced to rather less than half the present figure, and the number of fully ambulant patients would be more than doubled. Here it seems that the adoption of early ambulation would give an increase of nearly 10% over the actual current rate of throughput.

In the gynæcological wards (table III) the number of bedfast patients would be reduced under early ambulation to little more than a third of the present figure and the number of fully ambulant patients would be nearly doubled. An increase of about 10% over the current rate of throughput could be expected.

TABLE III—GYNÆCOLOGY 109 PATIENTS

Category	I (%)	II (%)	III (%)
Actual regime	45·8	33·0	21·2
Early ambulation	16·2	45·5	38·4
Traditional	55·7	31·0	13·3

The materials for the estimate in table IV are less abundant and conclusions must be accepted with caution. It appears, however, that with early ambulation the number of bedfast patients would be reduced to less than half the present figure and the number of fully ambulant patients would be nearly trebled. The increase in throughput might be nearly 15%.

In interpreting table V caution is again needed. It can, however, be stated that with early ambulation the reduction in bedfast patients would be considerable—the table suggests a reduction of three-quarters—while the number of fully ambulant patients would be nearly doubled. The corresponding increase in throughput would apparently be about 20%.

Statistical Fluctuation

It will be appreciated that the percentages shown in all the above tables are average values. Where they are based on reasonably large totals—say, 100 or more—they are of adequate reliability. But it should not be overlooked that even if the above percentages had absolute accuracy as averages, there would be considerable day-to-day variation in an actual ward—this variation being larger with smaller wards. In a small ward one must therefore be prepared for much larger fluctuations in the numbers of patients falling into the three main categories than would be the case for large wards.

TABLE IV—OBSTETRICS (ANTENATAL) 41 PATIENTS

Category	I (%)	II (%)	III (%)
Actual regime	47·3	35·6	17·1
Early ambulation	22·2	27·8	50·0
Traditional	65·2	19·6	15·2

TABLE V—OBSTETRICS (PUERPERAL) 50 PATIENTS

Category	I (%)	II (%)	III (%)
Actual regime	48·0	27·0	25·0
Early ambulation	11·9	38·1	50·0
Traditional	60·4	24·5	15·1

For a given size of ward it is possible, from the above data, to make estimates of the degree of variation to be expected. This may have considerable influence on the selection of a satisfactory ward-size.

Increase of Throughput

For various types of ward we estimate from the available data what proportion of patients would have been discharged under early ambulation. Suppose in a given case this is 20%. Then only 80% of the actual patients in the ward would remain, and it can be shown that, if early ambulation reduces the length of stay of all types of patient in the same ratio the relative change in throughput is given by 1/0 8 = 1 25 (i e., an increase of 25%). In practice it is unlikely that all lengths-of-stay would be reduced in the same ratio but without a detailed discussion of the distribution of length-of-stay and the differential effect of early ambulation on various types of patient it is impossible to say exactly what kind of modification is required. However, the simplifying assumption of *constant* reduction of length-of-stay adopted in this report is felt to give an important indication of the general order of improvement to be expected.

Discussion

During this survey of 836 patients in eight hospitals I had the opportunity of discussing early ambulation with the medical and nursing staffs, and as occasion arose with patients. Most of the doctors professed to believe in a modified form of early ambulation. In the same hospital there was often a considerable difference in the practice of ambulation in different wards. The opposition such as it was, came mainly from gynæcologists. There was a sharp difference of opinion as to whether a pelvic-floor repair should spend 21 days in complete bed rest or whether she might get out of bed within 3–4 days of operation. One gynæcologist assured me that the last thing she would allow her patients to do soon after operation was to stand by the bedside and cough.

Obstetricians on the whole were keen to have their cases out of bed early but emphasised the patients' need of rest before going home to perform household duties. Surgeons appeared to prescribe early ambulation more than any other class of doctor. Emphasis was laid on the necessity for first-class technique. I was told that early ambulation was not suitable for the less proficient surgeons and that good anæsthesia must accompany good surgical technique. It was also pointed out that physiotherapy and exercises in bed can in the opinion of some doctors, obviate the necessity for rising from bed in the first 24–48 hours. I was often told that if enough lavatories were provided close to the patients, far more of them would be allowed out of bed at an early stage.

Physicians on the whole tended to be more conservative. They had not the same enthusiasm for early length of stay of his hospital patients, and argues that the traditional physician or surgeon may not only keep his patients long in bed, but may also be compelled to keep them longer in hospital for repair of their wasted muscles and recovery from their general weakness On the other hand, many doctors who get their patients up early are reluctant to discharge them until they have had a period of convalescence in hospital This is particularly necessary in the case of obstetric patients, who on discharge tend at once to take up strenuous household duties

If there were a full positive correlation between ambulation and discharge, the policy adopted would clearly not affect the proportion of ambulant patients in hospital but would affect only the capacity of the hospital in terms of patients treated in a given time But there is not a full correlation between the two, as I shall show, and the effect of an early ambulation policy is therefore to increase the proportion of ambulant patients

The Present Survey

STANDARDS

In the present investigation the technique adopted was to examine patients actually in a number of hospital wards and to assess their capacity to get up and look after themselves In view of the controversy on the merits of early ambulation, it was decided that two assessments were necessary (*a*) from the standpoint of a doctor practising early ambulation, and (*b*) from the standpoint of a doctor of the traditional school

Patients were placed in three categories These are more or less arbitrary, but each has direct planning implications and corresponds with a distinct phase in the cycle of recovery

Category I —The bedfast (Patients who require intensive nursing and are unfit to get out of bed)

Category II —The partially ambulant (Patients able to leave their beds to wash and use the water closet, who do not normally require a bedpan. Meals are brought to them in bed The nursing attention which they require is not on the intensive scale of category I patients)

Category III —The fully ambulant (Patients able to get out of bed, normally unaided and generally up for hours at a time They still require nursing care but not as much as category II patients)

In the first attempt to assess patients in this way the staff of the Bristol Royal Infirmary generously cooperated The resident medical officer and the sister attached to each of 4 wards accompanied me round, and every patient was considered in turn by this panel of three Full details of the clinical condition of the patient were obtained, and assessment was made in full knowledge of any complications or deviations from normal displayed by him The assessment was made from the standpoints of the early ambulationist and of the traditionalist In this first study no record was taken of the actual ambulation status of the patients, this was later recognised as a serious omission, and in later surveys a record was made of the actual stage of ambulation which patients had attained at the time of the visit It also became apparent that a proportion of patients examined would already have been discharged under a régime of early ambulation Their inclusion under category III thus tends to exaggerate the proportion of ambulant patients It was therefore decided to include in future records a fourth category of " out "

In the main survey the original technique was followed and in all wards—except two in Edinburgh—I was accompanied by a doctor conversant with the condition of the patients and by the ward sister In most cases the doctor was a senior registrar but in some hospitals more senior members of the medical staff came round with me On the whole it appeared that the registrar had the merit of knowing the individual patients a also enough experience of his own specialty to app what alternatives in treatment and ambulation were feasible He was at the same time less than the senior man to have developed firm victions one way or the other on the merits o ambulation

After a little experience it was found not difficult to project one's mind into that of advoc the two schools of thought The three catego ambulation were also fairly straightforward to id although it was at times not easy to place m cases

TABLE I—GENERAL SURGERY 155 PATIENTS

Category	I Bedfast (%)	II Partially ambulant (%)	F am
Actual régime	50 3	20 0	
Early ambulation	16 4	35 0	
Traditional	66 7	17 3	

Some trouble was caused by the need to deci many patients would have been discharged u régime of early ambulation While it was poss determine with some confidence the number of p who on " medical grounds " could have been discl it was clear that external considerations—such a conditions—would have made some such dis impossible While allowance for external factors not in the circumstances be made for each ind patient, the reasons given for retaining in h some patients who could have been discharged the actual régime suggest that the crude figures b medical grounds alone would have to be hal practice

Conversely, some allowance in the " tradit assessment is necessary The discharge policy traditional régime would in nearly every case hav more cautious than that actually adopted, wi result that a ward run on traditional lines woul contained patients—normally in category III—wh in practice, been discharged If this fact were i the number of ambulant patients in a traditiona would be underestimated

In the whole survey, twenty nine wards, acc dating a total of 836 patients, were examined

TABLE II—GENERAL MEDICINE 167 PATIENTS

Category	I (%)	II (%)	(
Actual régime	53 3	24 6	
Early ambulation	25 7	28 3	
Traditional	61 1	13 9	

were divided into clinical departments as fo eight general surgical wards (230 patients), eight medical wards (237 patients), six gynæcological (185 patients), five obstetrical (antenatal and pue 147 patients), and two ear, nose, and throat (37 patients) These wards were in eight hospit which five were teaching and three non teaching of the hospitals were in Scotland All were of the general type with no special provision for long stay

RESULTS

The material collected in the early part of the s was later found to be incomplete, and was the rejected In most cases the different wards of a type were sufficiently alike for the data from them to be pooled The exceptions were the two E.N.T wards, which differed considerably—either in their practice or possibly in the type of patient admitted One general surgical ward appeared to practise a high degree of early ambulation compared with the other wards of the same type Leaving these exceptions on one side we were left with a sample of 522 patients drawn from twenty one wards, distributed as follows six general surgical wards (155 patients), six general medical wards (167 patients), four gynæcological wards (109 patients), six obstetrical wards (antenatal 41 patients, puerperal 50 patients) The estimates finally obtained, after adjustment, are set out in tables I–V

Table I shows that under early ambulation the number of bedfast patients in the general surgical wards would be reduced to less than a third of the present value, and the number of fully ambulant patients would be increased by about two thirds The data also suggest that the adoption of early ambulation would give an increase of about 10% over the current rate of throughput

Table II shows that under early ambulation the number of bedfast patients in the general medical wards would be reduced to rather less than half the present figure, and the number of fully ambulant patients would be more than doubled Here it seems that the adoption of early ambulation would give an increase of nearly 10% over the actual current rate of throughput

In the gynæcological wards (table III) the number of bedfast patients would be reduced under early ambulation to little more than a third of the present figure and the number of fully ambulant patients would be nearly doubled An increase of about 10% over the current rate of throughput could be expected

TABLE III—GYNÆCOLOGY 109 PATIENTS

Category	I (%)	II (%)	III (%)
Actual régime	46 8	33 0	20 2
Early ambulation	16 2	45 5	38 4
Traditional	55 7	31 0	13 3

The materials for the estimate in table IV are less abundant and conclusions must be accepted with caution It appears, however, that with early ambulation the number of bedfast patients would be reduced to less than half the present figure and the number of fully ambulant patients would be nearly trebled The increase in throughput might be nearly 15%

In interpreting table V caution is again needed It can, however, be stated that with early ambulation the reduction in bedfast patients would be considerable—the table suggests a reduction of three quarters—while the number of fully ambulant patients would be nearly doubled The corresponding increase in throughput would apparently be about 20%

Statistical Fluctuation

It will be appreciated that the percentages shown in all the above tables are average values Where they are based on reasonably large totals—say, 100 or more—they are of adequate reliability But it should not be overlooked that even if the above percentages had absolute accuracy as averages, there would be considerable day to day variation in an actual ward—this variation being larger with smaller wards In a small ward one must therefore be prepared for much larger fluctuations in the numbers of patients falling into the three main categories than would be the case for large wards

TABLE IV—OBSTETRICS (ANTENATAL) 41 PATIENTS

Category	I (%)	II (%)	III (%)
Actual régime	46 3	36-6	17 1
Early ambulation	22 2	27 8	50 0
Traditional	65 2	19 6	15 2

TABLE V—OBSTETRICS (PUERPERAL) 50 PATIENTS

Category	I (%)	II (%)	III (%)
Actual régime	48 0	26 0	26 0
Early ambulation	11 9	38 1	50 0
Traditional	60 4	24 5	15 1

For a given size of ward it is possible, from the above data, to make estimates of the degree of variation to be expected This may have considerable influence on the selection of a satisfactory ward size

Increase of Throughput

For various types of ward, we estimate from the available data what proportion of patients would have been discharged under early ambulation Suppose in a given case this is 20% Then only 80% of the actual patients in the ward would remain, and it can be shown that, if early ambulation reduces the length of stay of all types of patient in the same ratio, the relative change in throughput is given by 1/0 8 = 1 25 (i e, an increase of 25%) In practice it is unlikely that all lengths of-stay would be reduced in the same ratio, but without a detailed discussion of the distribution of length of-stay and the differential effect of early ambulation on various types of patient it is impossible to say exactly what kind of modification is required However, the simplifying assumption of *constant* reduction of length of-stay, adopted in this report, is felt to give an important indication of the general order of improvement to be expected

Discussion

During this survey of 836 patients in eight hospitals I had the opportunity of discussing early ambulation with the medical and nursing staffs, and as occasion arose with patients Most of the doctors professed to believe in a modified form of early ambulation In the same hospital there was often a considerable difference in the practice of ambulation in different wards. The opposition, such as it was, came mainly from gynæcologists There was a sharp difference of opinion as to whether a pelvic floor repair should spend 21 days in complete bed rest, or whether she might get out of bed within 3–4 days of operation One gynæcologist assured me that the last thing she would allow her patients to do soon after operation was to stand by the bedside and cough

Obstetricians on the whole were keen to have their cases out of bed early, but emphasised the patients' need of rest before going home to perform household duties Surgeons appeared to prescribe early ambulation more than any other class of doctor Emphasis was laid on the necessity for first class technique I was told that early ambulation was not suitable for the less proficient surgeons, and that good anæsthesia must accompany good surgical technique It was also pointed out that physiotherapy and exercises in bed can, in the opinion of some doctors, obviate the necessity for rising from bed in the first 24–48 hours I was often told that if enough lavatories were provided close to the patients, far more of them would be allowed out of bed at an early stage

Physicians on the whole tended to be more conservative They had not the same enthusiasm for early length of stay of his hospital patients, and argues that the traditional physician or surgeon may not only keep his patients long in bed, but may also be compelled to keep them longer in hospital for repair of their wasted muscles and recovery from their general weakness. On the other hand, many doctors who get their patients up early are reluctant to discharge them until they have had a period of convalescence in hospital. This is particularly necessary in the case of obstetric patients, who on discharge tend at once to take up strenuous household duties.

If there were a full positive correlation between ambulation and discharge, the policy adopted would clearly not affect the proportion of ambulant patients in hospital but would affect only the capacity of the hospital in terms of patients treated in a given time. But there is not a full correlation between the two, as I shall show, and the effect of an early ambulation policy is therefore to increase the proportion of ambulant patients.

The Present Survey

STANDARDS

In the present investigation the technique adopted was to examine patients actually in a number of hospital wards and to assess their capacity to get up and look after themselves. In view of the controversy on the merits of early ambulation, it was decided that two assessments were necessary: (*a*) from the standpoint of a doctor practising early ambulation, and (*b*) from the standpoint of a doctor of the traditional school.

Patients were placed in three categories. These are more or less arbitrary, but each has direct planning implications and corresponds with a distinct phase in the cycle of recovery.

Category I.—The bedfast. (Patients who require intensive nursing and are unfit to get out of bed.)

Category II.—The partially ambulant. (Patients able to leave their beds to wash and use the water closet who do not normally require a bedpan. Meals are brought to them in bed. The nursing attention which they require is not on the intensive scale of category I patients.)

Category III.—The fully ambulant. (Patients able to get out of bed, normally unaided and generally up for hours at a time. They still require nursing care but not as much as category II patients.)

In the first attempt to assess patients in this way the staff of the Bristol Royal Infirmary generously cooperated. The resident medical officer and the sister attached to each of 4 wards accompanied me round, and every patient was considered in turn by this panel of three. Full details of the clinical condition of the patient were obtained, and assessment was made in full knowledge of any complications or deviations from normal displayed by him. The assessment was made from the standpoints of the early ambulationist and of the traditionalist. In this first study no record was taken of the actual ambulation status of the patients; this was later recognised as a serious omission, and in later surveys a record was made of the actual stage of ambulation which patients had attained at the time of the visit. It also became apparent that a proportion of patients examined would already have been discharged under a régime of early ambulation. Their inclusion under category III thus tends to exaggerate the proportion of ambulant patients. It was therefore decided to include in future records a fourth category of "out."

In the main survey the original technique was followed, and in all wards—except two in Edinburgh—I was accompanied by a doctor conversant with the condition of the patients and by the ward sister. In most cases the doctor was a senior registrar, but in some hospitals more senior members of the medical staff came round with me. On the whole it appeared that the registrar had the merit of knowing the individual patients and had also enough experience of his own specialty to appreciate what alternatives in treatment and ambulation policy were feasible. He was at the same time less likely than the senior man to have developed firm convictions one way or the other on the merits of early ambulation.

After a little experience it was found not unduly difficult to project one's mind into that of advocates of the two schools of thought. The three categories of ambulation were also fairly straightforward to identify, although it was at times not easy to place marginal cases.

TABLE I—GENERAL SURGERY: 155 PATIENTS

Category	I Bedfast (%)	II Partially ambulant (%)	III Fully ambulant (%)
Actual régime	50·3	20·0	29·7
Early ambulation	16·4	35·0	48·6
Traditional	*66·7*	*17·3*	*16·0*

Some trouble was caused by the need to decide how many patients would have been discharged under a régime of early ambulation. While it was possible to determine with some confidence the number of patients who on "medical grounds" could have been discharged, it was clear that external considerations—such as home conditions—would have made some such discharges impossible. While allowance for external factors could not in the circumstances be made for each individual patient, the reasons given for retaining in hospital some patients who could have been discharged under the actual régime suggest that the crude figures based on medical grounds alone would have to be halved in practice.

Conversely, some allowance in the "traditional" assessment is necessary. The discharge policy of a traditional régime would in nearly every case have been more cautious than that actually adopted, with the result that a ward run on traditional lines would have contained patients—normally in category III—who had, in practice, been discharged. If this fact were ignored, the number of ambulant patients in a traditional ward would be underestimated.

In the whole survey, twenty-nine wards, accommodating a total of 836 patients, were examined. These were divided into clinical departments as follows: eight general surgical wards (230 patients); eight genera medical wards (237 patients); six gynæcological ward (185 patients); five obstetrical (antenatal and puerperal 147 patients); and two ear, nose, and throat ward (37 patients). These wards were in eight hospitals, o which five were teaching and three non-teaching. Tw of the hospitals were in Scotland. All were of the acut general type with no special provision for long-stay cases.

TABLE II—GENERAL MEDICINE: 167 PATIENTS

Category	I (%)	II (%)	III (%)
Actual régime	53·3	24·6	22·2
Early ambulation	25·7	28·3	46·1
Traditional	61·1	13·9	25·0

RESULTS

The material collected in the early part of the survey was later found to be incomplete, and was therefor rejected. In most cases the different wards of a given

NEW YEAR HONOURS

The list of honours published this week contains the names of the following members of the medical profession:

K.C.V.O.

Daniel Thomas Davies, C.V.O., M.D. Wales, F.R.C.P.
Physician to H.M. Household; physician to the Royal Free Hospital, London.

Francis Hugo Teale, C.V.O., M.D. Lond., F.R.C.P.
Formerly lecturer in bacteriology and immunotherapy, University College Hospital Medical School.

K.B.E.

Percy Selwyn Clarke, C.M.G., M.C., M.D. Lond., F.R.C.P.
Governor and commander-in-chief of the Seychelles.

K.B.E. (Honorary)

Francis Akanu Ibiam, O.B.E., M.B. St. And.
Member of the executive council, Nigeria.

Knights Bachelor

Kofoworola Adekunle Abayomi, M.D. Edin.
Member of the executive council, Nigeria.

Frank Macfarlane Burnet, M.D. Melb., SC.D. Camb., PH.D. Lond., F.R.A.C.P., F.R.S.
Director of the Walter and Eliza Hall Institute; professor of experimental medicine, University of Melbourne.

William Kelsey Fry, C.B.E., M.C., M.D.S. Durh., M.R.C.S., F.D.S. R.C.S.
Dean of the faculty of dental surgery, Royal College of Surgeons of England; consulting dental surgeon, Guy's Hospital, London.

Gordon Morgan Holmes, C.M.G., C.B.E., M.D., SC.D. Dubl., D.C.L. Durh., F.R.C.P., F.R.S.
Consulting physician, Charing Cross Hospital and National Hospital, Queen Square, London.

C.M.G.

Clifford Craig, M.D., M.S. Melb., F.R.A.C.S.
Surgeon superintendent, Launceston General Hospital, Tasmania.

C.V.O.

George Proctor Middleton, M.V.O., M.B. Aberd.
Surgeon apothecary to H.M. Household, Balmoral.

C.B. (Military)

Surgeon Rear-Admiral Kenneth Alexander Ingleby Mackenzie, B.M. Oxfd, K.H.P.

Major-General Thomas Young, O.B.E., M.B. Glasg., K.H.P., late R.A.M.C.

C.B.E. (Military)

Air Commodore Vyvian Stewart Ewing, M.B. St. And., R.A.F.

C.B.E. (Civil)

James Boyd, M.D. Belf., F.R.C.P.I.
Chief medical officer, ministry of health and local government, Northern Ireland.

Miss Lucy Meredith Bryce, M.B. Melb., F.R.A.C.P.
Hon. director, blood transfusion service, Victoria.

Joseph Stanley Hopwood, M.B. Lond.
Superintendent, Broadmoor Institution.

Peter James Kerley, M.D. N.U.I., F.R.C.P., F.F.R.
Director, radiological department, Westminster Hospital; adviser on mass radiography, Ministry of Health.

Geoffrey Marshall, O.B.E., M.D. Lond., F.R.C.P.
Principal medical referee, Civil Service Commission, consulting physician to Guy's Hospital, London.

Kamil Mohamed Ariff bin Kadir Mustan, L.M.S.
For public services in the Federation of Malaya.

Adam Rankine, M.C., M.B. Glasg., lately Colonial Medical Service.
Director of Medical Services, Mauritius.

Vincent Brian Wigglesworth, M.D. Camb., F.R.S.
Director of the unit of insect physiology, Agricultural Research Council.

O.B.E. (Military)

Lieut.-Colonel John Alistair Manifold, M.R.C.S., R.A.M.C.

Wing Commander Henry Lindsay Roxburgh, M.B. Edin., R.A.F.

O.B.E. (Civil)

James Fanstone, M.D. Lond.
Surgeon and founder, Hospital Evangelico Goiano, Anápolis, Brazil.

Thomas Gilray, M.B.
Medical practitioner at Napier, New Zealand.

John Alexander James, CH.M. Sydney, F.R.C.S., F.R.A.C.S.
Surgeon and physician, Australian Capital Territory.

Alexander Cameron McKillop, M.B. Edin.
Senior assistant physician, New Zealand State Asylum Service.

William Hugh Clifford Patrick, M.D. N.Z.
Regional medical officer, Ministry of Health.

Mohamed Ali Rana, M.B.E., M.R.C.S.
For public services in Kenya.

Andrew James Shinnie, M.D. Aberd.
M.O.H. for Westminster.

Don Sam de Simon, L.R.C.P.E.
Superintendent, Leprosy Hospital, Hendala, Ceylon.

Sinnatamby Subramaniam, L.R.C.P.E.
For medical and social services in Ceylon.

Allan Robert Stanley Vickers, CH.M. Sydney
For services to the Flying Doctor Service in Australia.

Leon James Williams, M.D.
For public services in Bermuda.

M.B.E. (Military)

Major Hamilton James Elverson, B.M. Oxfd, R.A.M.C.

Surgeon Lieut.-Commander William Boyd Jack, B.M. Oxfd, R.N.

Major Terence Richard Jansen, L.R.C.P.E., Ceylon Medical Corps.

Surgeon Lieutenant Trevor Stansfield Law, M.B. Lpool, R.N.

M.B.E. (Civil)

Arthur Griffiths Farr, M.B. Camb., Colonial Medical Service.
Acting senior medical officer, Tanganyika.

Samuel Ferguson Floyd, M.B. R.U.I.
General practitioner, co. Down.

Miss Agnes Grace Gillespie, M.B. Lpool.
Missionary, Mary Calvert Holdsworth Memorial Hospital, Mysore.

John James Sparks, M.D. McGill, F.A.C.P.
British vice-consul at Coatzacoalcos.

Francis Henry Whitehead, M.R.C.S.
Chairman, Wandsworth and Battersea war pensions committee.

Bar to A.F.C.

Wing Commander Hugh Patrick Ruffell Smith, A.F.C., M.B. Camb., R.A.F.

A.F.C.

Squadron Leader John Stafford Howitt, M.R.C.S., R.A.F.

Personal Papers

PATIENT'S PROGRESS

What are the functions of an almoner? I had been working as one for two weeks and I still wasn't sure, when one day in April, 1947, Peggy hobbled into my office on two sticks. Lank grey hair framed her colourless face. Her eyes peered owlishly from behind large round spectacles. She seemed highly nervous, rather dull, and rather deaf. She had very little to say for herself and she seemed very much under the influence of Mrs. Bullock * who accompanied her. Mrs. Bullock was a large, well-dressed, loud-voiced, overpowering woman, who, when asked if she was a relative or friend, announced that she was "one of the Good Samaritans of this world." So the Good Samaritan, protesting loudly, was asked to wait outside while I tried to sort out the difficulties that might arise when Peggy came into hospital for the cup arthroplasty to her hip. This is generally a two-year job, and at that time meant three months in hospital, several weeks wearing a walking iron, a long convalescence, and then a possible work readjustment. This programme often creates financial and domestic problems, and I wanted to talk to Peggy about her particular difficulties undisturbed. The interview was a complete failure. Peggy was too afraid to speak, and to my chagrin I had to ask the Good Samaritan to come back. She held forth at length about her own virtues, and implied that Peggy lived with her as a friend, for whom she was

---

* Names throughout this article are fictitious.

ambulation, and, perhaps because there is no starting point for treatment corresponding with an operation, the tendency was towards rest in bed while there was any doubt There were exceptions , thus, in the medical wards in two hospitals about half the patients were "up" in spite of the fact that the average ward age at the time of observation was less than for medical wards elsewhere In another hospital the practice of early ambulation and short stay appears to have been partly attributable to there being many consultants, each with only a few beds which he naturally tried to put to the fullest use In addition there were facilities for transfer of convalescent cases to other hospitals

The practice of early ambulation at first imposes a heavy strain on nurses, but later it eases the burden I have seen two nurses straining to keep a cholecystectomy patient upright on the edge of her bed She was of the 'fair, fat, fertile, and forty" type, weighing possibly 16 st , and as she swayed from side to side looking miserable it was all that they could do to prevent her from falling on the floor The initial effort to get a postoperative patient up is not always easy

Once early ambulation is established, the patient can take the responsibility for his intimate hygiene and so relieve the nurses of some of their work On the basis of the figures obtained in this survey, if we compare the number of patients actually bedfast with the number who would be bedfast under the practice of an early ambulationist, we find that on average about two thirds of those patients at present using bedpans in surgical wards would be liberated From my discussions, I am convinced that surgeons would welcome this, and very little objection from patients may be anticipated

Closely related to the problem of bedpans is the problem of bathing In the hospitals which I visited it was usual to find one bath for 20 patients or perhaps two for 30 I was assured in one hospital that every ambulant patient was expected to have a bath, which would be entered in the "bath book" As baths were only permitted on the ninth day in this maternity ward, the number of potential bathers was not very large In another ward even colostomy patients bathed themselves and the number of baths provided was considered inadequate It seems clear that at present there are not enough baths to meet the needs of patients, and that if early ambulation were to be practised more, the bathing facilities would have to be increased accordingly Perhaps because of the very inadequacy of bathing facilities in most existing wards the matter is given up as a bad job During this survey, in frequent visits to wards at all times I have never found an occupied bathroom

Summary and Conclusions

For more than fifty years early ambulation has been intermittently advocated by members of the medical profession During the war years expediency forced many doctors to adopt it in varying forms Around 1944 many papers on the merits of early ambulation were published in America , and in 1946 the appearance of Leithauser's book stimulated others to follow his example, though often they modified his technique

In the present survey 836 patients in eight acute general hospitals were assessed, mostly under three heads (*a*) their actual stage of treatment and ambulation, (*b*) the stage of treatment and ambulation which they would have reached under the care of a doctor practising early ambulation, (*c*) the stage of treatment and ambulation which they would have reached under the care of a doctor of the traditional school

In the wards studied, great variations were noted in the length of rest prescribed, and in the precipitancy with which patients were raised from their beds after operation, childbirth, or illness The practice of early ambulation in modified form was commonly observed. Reliance is often placed in physiotherapy and bed exercises, as a substitute for the early rising advocated by Leithauser

It was clear that many more patients would be permitted to "rise early" if the necessary facilities were provided Those partially ambulant would require more lavatories and bathrooms , and a full régime of early ambulation would call for increased sitting up space and dining facilities Moreover, early ambulation throws an initial strain on the nursing staff and for this reason some of the patients observed in the hospitals were not up as soon as the surgeon wished

From the results of this survey the following tentative conclusions are reached

1 A very strong case can be made for the practice of early ambulation, provided the necessary surgical and technical skill can be attained

2 In the great majority of wards studied, the normal practice still approximates much more closely to a traditional than to an early ambulation régime. Although the ambulation policy has affected surgical and gynæcological wards more than medical wards, the former still appear to offer a greater relative scope for its extension

3 It can be inferred from the figures that, if the practice of early ambulation prevailed, 70–90% of patients in the types of wards covered would require the use of basins and water-closets, and 40–55 % would require day space These percentages may be contrasted with the present 45–55% requiring the former and 15–30 % requiring the latter facilities It should be emphasised, however, that very few hospitals are equipped to provide for even these current percentages

4 An important secondary consequence of early ambulation is the increased effective capacity of the hospital resulting from reduction in the length of-stay necessary The data suggest an increase in the rate of throughput varying from about 10% in medical and gynæcological wards to 20% in obstetrical (*puerperal*) wards

I am very grateful to the late director of research, Mr John Madge M A , A.R I.B A , for assistance and advice Other team members, particularly Mr Norman T J Bailey, statistician to the department of human ecology, Cambridge University, and Dr Barbara Duncum, D PHIL. also gave me valuable help which I wish to acknowledge Permission for publication of this article has been granted by the Committee controlling the investigation

REFERENCES

Asher R A J (1944) *Brit med J* ii 967
Boldt H J (1907) *N Y med J* 85 145
British Medical Journal (1950) Editorial i 948
Bywaters E G L (1950) *Proc R. Soc. Med* 43, 199
Cullen B E (1947) *J Canad med Ass* 57 257
Cutler E C Hoerr S O (1942) *Proc int Postgr med Ass N Amer* p 232
de Soldenhoff R (1948) *Lancet* ii 961
Dunlop D M (1949) *Edinb med J* 56 146
Hartog C (1909) *Berl klin. Wschr* 46 402
Hunter W C Krygier I J Kennedy J C Sneedon V D (1945) *Surgery*, 17 178
Kummell H (1908) *Zbl Gynak* 32 1233
Lancet (1944) Editorial ii 790
— (1947) Editorial ii 427
Leithauser D J (1946) Early Ambulation and Related Procedures in Surgical Management Springfield Ill and Oxford
Nelson H (1944) *Arch Surg* 49 1
Ries E (1899) *J Amer med Ass* 33 454
Rotstein M L (1944) *Ibid* 125 838
Schafer P W Dragstedt L R (1945) *Surg Gynec Obstet* 81, 93
Steinhart P F (1946) *Ibid* 82 348
Swarbreck A B (1950) *Brit med J* i 936
Trice E T (1947) *Virginia med Mon* 74 103
Wood P (1950) *Proc R Soc Med* 43 195

Miss Meekins had been ill and had had an operation, and they had sent her to a convalescent home When she left she went to stay at a hostel and then, suddenly, all who knew her lost track of her

* * *

Six months later she walked into my office looking very smart and rather condescendingly told me that she had at long last contacted her long lost father, who was a retired estate agent in Philadelphia, and he was coming over to fetch her back to live with him I found that she was working as a housekeeper in Pimlico, having found the job herself She brought her father to see me when he arrived—a dapper little man in a panama hat I must confess I had wondered if there was anything phoney about this move, but the family likeness was too strong for there to be any doubt about his identity

So Miss Margaret Meekins, of independent means, sailed to the U S A , first class, on Aug 17, 1950

The Wider World

FIJI REVISITED

Sir Philip Manson-Bahr

C M G , D S O , M D Camb , F R C P

CONSULTING PHYSICIAN TO THE HOSPITAL FOR TROPICAL DISEASES, LONDON

I HAVE recently revisited the Fiji Islands after a lapse of forty years Naturally, there have been great changes A good road now encircles the main island of Viti Levu , large numbers of cars are to be seen in Suva, the capital , and everywhere the standard of living is high The Indians, who in 1910 were sugar plantation labourers, are now landowners on a considerable scale, and a great deal of the trade of the islands is in their hands Under a paternal government they enjoy full privileges, including free schooling and hospital treatment The Fijians, who in 1911 were a race only recently come under British rule, are now a civilised, highly organised community in whose ranks doctors, native medical practitioners, dentists, administrators, teachers, and all manner of technicians are to be found

Their very diseases have also changed Bacillary dysentery, which in 1910 I went out to investigate and which was then rampant, has practically disappeared I found at that time that Shiga's bacillus was spread mainly by the ubiquitous house flies ,[1] but now, probably owing to better sanitation and the application of D D T , the number of flies has greatly decreased and so has the incidence of bacillary dysentery Since 1943 a Mosquito Control Service, which was originally organised and directed by a remarkable layman, the late D W Amos, has been in operation in the islands The Fijians employed in this service acquire a specialised knowledge which enables them not only to recognise various species of mosquito but also to distinguish their larval characteristics So efficient has been their work that in the main island of Viti Levu filariasis has largely disappeared

In 1910 I was able to demonstrate[2] the transmission of the filaria of the Pacific, *Wuchereria bancrofti* var *pacifica*, by a new species of mosquito, now known as *Aëdes scutellaris* var *pseudoscutellaris* Theob —an insect which has peculiar breeding habits frequenting mostly small pools of water, discarded tins crab holes and coconut shells By eliminating these reservoirs the numbers of these mosquitoes in the vicinity of houses have been much reduced It has also been found that cutting the grass and clearing the bush around the native houses, or *buris*, interrupts the parasitic cycle by eliminating resting places of this mosquito after it has been engorged with human blood

In recent years a number of subvarieties of this main species have been separated in various islands of the Pacific, one of which—*A scutellaris* var *horrescens* Edw ,[3] a forest-frequenting form—has been recognised This variety breeds mostly in collections of water in the axils and branches of forest trees and in tree holes, whereas the first named is associated with cultivated areas and human habitations The larvæ of these two varieties are quite distinct, those of *horrescens* being covered with hairs and thereby easily recognised, though the adult females are identical

It appears probable, from what I was able to accomplish, that *horrescens* is incapable of transmitting the human filaria This is important, because any systematic measures against this forest loving species would be impossible to carry out Here then, is a pretty problem to be solved—namely, what is the substance or agency which endows a particular variety of mosquito with the property of transmitting the filaria worm ?

Unfortunately, there is much pulmonary tuberculosis among the Fijians, as has been made evident by mass radiography Tuberculosis, filariasis, yaws, typhoid, and paratyphoid are the chief scourges of these people, and probably any sanitary measures taken against one of them would have some effect against the others The rebuilding of native houses on modern lines and the provision of a good water supply and general sanitation are now being vigorously undertaken

Kwashiorkor, or malignant malnutrition, has lately been discovered in undernourished and neglected children in the back areas of the main island It is odd that these isolated cases have come to light when the general nutrition of the natives stands at a high level Undulant fever of the abortus type has also recently been discovered, and much more work requires to be done on fevers of short duration hitherto lumped together under the diagnosis of dengue

Many channels for research remain unexplored so far, for want of specially qualified doctors For instance, the bacteriological collection contains over 100 strains of the salmonella group waiting to be classified , and there are interesting possibilities for hæmatological research in a peculiar form of megalocytic anæmia which is prevalent among the island born Indian population and which appears to have a seasonal incidence In the wards of the Colonial War Memorial Hospital in Suva, medical practice is concerned with a medley of cases such as were seen in this country over a century ago Since systematic necropsies have been conducted, many hitherto unsuspected diseases, such as rheumatic carditis, have come to light

Dr J M Cruikshank, the principal medical officer, is a far seeing administrator who gives great encouragement to any of his officers who show an inclination for study outside the usual routine The Central Laboratory in Suva is a most efficient institution, and the technical ability of the Fijian and Indian assistants, under the able direction of Mr J E Pery Johnson, has to be seen to be believed

By some, Colonial officials are regarded as swathed with red tape , but as far as Fiji is concerned nothing could be further from the truth I know well that anyone with qualifications to undertake medical research work would be welcomed and would be given every assistance For those with the pioneering spirit and keen and inquiring minds the opportunities are great

The chance is not given to everyone to recommence a piece of work on which he was engaged so long ago, and I am grateful for being allowed to go to Fiji and once more work under my own steam so to speak During my four months stay many courtesies and privileges were afforded me by the Governor, Sir Brian Freeston, and by the Fiji government and its officers They gave me not only laboratory accommodation but every facility I needed for my research Everyone I might say, whether within the government or without joined in helping me accepting responsibility She avoided the question of whether the patient was an employee Peggy she said, had done a little work for her, but was not working for her now

---

[1] Bahr P H *Brit med J* 1914 i 294 Dysentery in Fiji during the Year 1910 Monograph 22 1912

[2] Bahr P H Filariasis and Elephantiasis in Fiji Monograph 29 1912

[3] Edwards F N *Bull ent Res* 1935 26 2

I was far from happy about the pair They didn't fit together, and the patient was so dreadfully nervous But the queue outside the door was long, and I knew I should have time to get to know Peggy when she came into the ward

Nearly two months later she came into the orthopædic ward and I saw her next day She still seemed too nervous to talk, but said she liked working for Mrs Bullock and would not change for anything in the world Her operation was postponed a week, which gave me a chance to make friends with her Finally she broke down and admitted she did not want ever to go back to Mrs Bullock

* * *

She could not remember her mother, but until she was 10 she lived with her father, two brothers, and a sister in Manchester When she was 10 her father went to America and she and her two brothers went to live at an orphanage When she was 16 she left and went to work for Mrs Bullock, whose household consisted of eight people Although her relatives tried to get in touch with her they were discouraged, and she was not allowed to see them or communicate with them

She was now 44 and for the last 30 years she had worked very hard Her hours were long and she had no life to call her own She had scarcely any time off When she did occasionally go to the cinema, her times of going out and coming in were strictly supervised She was paid 10*s* a week During the war her mistress was not allowed to keep two maids There was apparently another wretched downtrodden maid, so Peggy had to go out to work She was employed by two or three local women to do domestic work for a few hours a day, but she still had to work for Mrs Bullock before she went out and after she came in At one point she revolted and ran away to one of her other employers, but Mrs Bullock followed her and threatened the other employer to such an extent that Peggy returned For her outside work she was paid 30*s*, but Mrs Bullock deducted £1 and left her 10*s* out of which she had to pay her N H I, leaving about 7*s* for all her needs After all these years she had £10 in the bank and a few Savings Certificates While she was waiting to come in for her operation she was sent to spring clean the country cottage, and the day before her admission she washed blankets

* * *

This story seemed fantastic, but I contacted one of the women for whom Peggy had worked, and she confirmed it She too seemed a little frightened of Mrs Bullock, who had told her she was not to visit Peggy in hospital as anyone except Mrs Bullock upset the patient! Peggy's panel doctor, who had sent her to the hospital, said he believed my suspicions to be correct He had had to make special arrangements to see the patient when she was supposed to be out at work

The first thing to be done was to get Peggy to pluck up enough courage to decide not to go back to Mrs Bullock This was no easy task, as every time I got her to the point Mrs Bullock would visit her and play on her emotions to such an extent that she would weaken again Matters were finally brought to a head when I wrote to Mrs Bullock, asking her to see me to discuss certain difficulties and at the same time to let Peggy have her savings book, clothing coupons, &c Evidently realising that something was afoot, she did not reply Eventually, having laid in wait on visiting days for several weeks, I managed to meet her in the ward There was an unhappy scene, which was impossible to avoid, and Mrs. Bullock left threatening me with legal action for attempting to coerce Peggy to leave her However, she apparently thought this over and decided to throw in her hand She sent Peggy her belongings, which were not worth having, and we never heard of her again

Now that Peggy had had her pillar of strength removed she became very dependent on me, and my next big task was to give her a sense of independence I started by successfully tracing some of her family, and for weeks I would find odd people turning up at my office saying they were relations The effect on Peggy wa amazing and her delight was touching to see She bega to have faith, realised that she was not entirely friendles and started to build up hope for the future

She had only done domestic work and she had not th mental ability for anything more complicated It wa thought that she would be fit to go on with this kind o work eventually, so we promised to help to find her suitable residential post when she was fit She the decided she would like to work for the hospital—a sta which quite a lot of patients go through I did not thin it was a very good idea, for I was afraid she might remai too dependent on me , but I did not at that time want t rob her of her sense of security and thought she woul have plenty of time to change her mind An intervie was arranged with the domestic supervisor, who said sh would be able to find Peggy a suitable job when the tim came

By the end of September, 1948, Peggy could just wal with a walking iron At the beginning of October took her to a convalescent home where she could hav physiotherapy, and she stayed there several weeks. O her return she spent a weekend with one of her relative in London and came to the outpatient clinic for a check up Then she went to stay with relatives in Mancheste until after Christmas, when it was thought she would b ready to start work During her stay in Mancheste physiotherapy was arranged for her locally at a reduce fee, which the relatives were able to pay

* * *

It was a changed Miss Meekins who came to see m at the clinic at the end of January I hardly recognise the self assured vision with sparkling eyes She looke at least 20 years younger, her face generously made u and hair waved There was also a coy air about he which I found puzzling until in a rush of confidence sh confessed that she was now a betrothed woman abou to become a bride in March So that accounted for th strange letter I had received that morning asking me t give some unknown person a reference on her with a vie to a proposed engagement In my ignorance I ha interpreted the letter to mean that she had found a jo and that she would not need the post that was about t be offered to her at our Seaview convalescent home There are moments when it is difficult to contain one' curiosity, and by devious means I discovered that sh had met her fiancé by answering an advertisement in th *Evening News* He was a steady church going ma widower, and male nurse, at present out of work, bu approved by her relatives

I advised her to take the job at Seaview for the tim being, which she did Gradually she began to leave o her walking iron and have less treatment Although a first her letters were frequent and demanding, thes gradually lessened. The engagement fell through, an we had to deal with a broken heart , but it healed fairl quickly and I did not hear from her for long interval At one point there were suspicions that she was guilt of petty thefts, but she got over this too Two yea after I first met her I decided that she was thoroughl rehabilitated, for the only news I had was that she wa getting around well and I ought to see her running dow the drive to meet her latest boy friend I believe sh became engaged to a bus driver at Seaview at this tim

In October, 1949, Miss Meekins turned up again, havin got herself a job at a hospital as doctors' maid at a bette salary She was beginning to feel rather tucked away i such an out of the way place as Seaview Three month later, the almoner of that hospital rang to say tha

Letters to the Editor

CORONARY DISEASE AND MODERN STRESS

SIR,—Recovering from an acute respiratory infection has given me more leisure than usual to peruse your issue of Dec 23, and with it Dr Stewart's article This I much enjoyed, though more as an English essay than as a scientific paper I suppose one can enjoy an essay and still question some of the premisses and disagree with some of the conclusions of the essayist

Dr Stewart starts with a few dogmatic statements which are surely very controversial and goes on to a cautious and fairly critical examination of the evidence as to whether "modern stress" *has* caused an increase in coronary disease and finds that much of this evidence is inconclusive or conflicting He does, however seem convinced that "the better educated and those who work with their brains are more liable than their fellows to coronary disease" The only statistical evidence for this which Dr Stewart cites (and it is surely a question of statistics) is (1) Dublin et al,[1] that the mortality ratio of heart disease amongst doctors is 1 18 of the general male population of parallel age—not a very striking figure compared with influenza, for instance (*vide infra*)—and (2) the Registrar General s Decennial Supplement for 1931 (the last to be published) which shows that if the death rate from coronary disease in the general male population is 100, it is for

Agricultural workers	32
Coalminers below ground	40
Banking and insurance officials	183
Anglican clergy	218
Physicians and surgeons	368

Now I am very fond of the R G's Decennial Supplement and happen to have it in bed with me, but its accuracy depends, as I have pointed out before[2] upon the accuracy of the material from which it is compiled —namely death certificates The majority of persons do not die in modern well equipped hospitals, do not have post-mortem examinations, and are not seen by consulting physicians or cardiologists The death certificates from which these figures were compiled were from the years 1930–32 Levine's classical article on coronary thrombosis was published in 1929, and although the condition had been recognised before, and the association between coronary artery disease and angina pectoris had long been known, it is fair to say that coronary thrombosis as a cause of death was not commonly diagnosed even by experienced physicians until about 1930, amazing though it may seem The majority of such deaths would be certified as myocarditis and myocardial degeneration Diagram 3 (p 30) of the Decennial Supplement shows clearly that while "angina pectoris' increases as we go up the social scale myocardial disease does exactly the opposite, and the table on p 162 shows that the figures for myocardial disease ' are for banking officials, &c., 59, and for anglican clergy 57, whereas for cotton strippers and grinders (social class IV—surely not educated brain-workers) the figure is 213 Doctors show an excess in both categories

As the R G (or one of his henchmen) points out on p 60

> degenerative disease in the heart affects all classes of males to much the same extent but whereas amongst men whose social conditions are most favourable it tends to express itself as angina pectoris or coronary disease, at the other end of the scale it tends to take forms described on death certificates as myocarditis or myocardial or cardiovascular degeneration.'

This is surely a most important statement, without which most of the figures quoted by Dr Stewart are very nearly meaningless (He probably had not the benefit of a respiratory infection when compiling his paper)

I venture to suggest that the likelihood of persons dying in 1930–32 having seen a consulting physician or cardiologist might well be in the following order

Physicians and surgeons
Anglican clergy
Banking and insurance officials
Coalminers below ground
Agricultural workers

and that the chief difference is not one of disease but of nomenclature Perhaps the 1950–52 figures will show an equally nice social distinction between ' coronary thrombosis" and "myocardial infarction"

Despite this there is still a slight preponderance of deaths due to heart disease in males of social class I, and probably a considerable preponderance in doctors I am not trying to make out that it does not exist—merely that a great deal of it is illusory

Incidentally, if my present illness should require entry on a death certificate I feel sure that it will be described (probably erroneously) as "influenza," and I am sorry to note (Decennial Supplement, p 256) that the standardised mortality ratio for doctors of my age group is 133 (or 1 33 in the terminology of Dublin et al.), but the fact that the highest rate for influenza is amongst "makers of non metalliferous mine and quarry products" restores some of my hopes for the New Year As a bedside author I can recommend the R-G very highly

Department of Medicine
The University Manchester

ROBERT PLATT

USE OF BACTERIA TO CONTROL VIRUS DISEASES

SIR,—Two articles on bacteriophage in no 14 of *Science News*, by the late Prof F W Twort, F.R.S, and by the late Prof Felix d'Herelle, gave me what seems to be a novel idea for controlling virus diseases So little success has so far been achieved in this field that practical bacteriologists and pathologists might think the idea worth pursuing

Professor Twort writes (p 14)

> 'In test tube experiments it is easy to arrange conditions so that a bacteriophage will kill off its host the bacterium but it is equally easy to arrange another set of conditions in which the bacterium will kill or inhibit its invading bacteriophage '

Since there seems to be good evidence that some bacteriophages cure certain bacterial diseases, and that bacteriophages are viruses, one naturally asks whether the opposite process can occur Can virus diseases be controlled by suitable bacteria? Dialectically this seems to demand the answer Yes If some viruses exist at the expense of bacteria, it is surely probable that some bacteria normally exist at the expense of viruses

Where can one find such bacteria? Dr d'Herelle (p 47) points out that the bacteriophage that deals with dysentery and other intestinal infections may be found in the stools of convalescent patients This suggests that the search for suitable bacteria to counter a virus disease should begin in patients convalescent from that disease or perhaps in contacts who did not develop the disease d'Herelle is convinced that, in some bacterial infections, the patient's spontaneous recovery invariably coincides with the appearance of bacteriophage in the patient and is in fact attributable to the presence and activity of the bacteriophage. This raises the question whether recovery from virus infections is not dependent, in some cases at least, on the appearance of specific bacteria which attack the virus This may be the function of some of the benign bacteria harboured by the normal healthy body

---

[1] Dublin L I, Spiegelman M Leland, R G *Post-grad. med J* 1947 2 188

[2] *Brit med J* 1947 ii 77

In England Now

A Running Commentary by Peripatetic Correspondents

THEY do things in style north of the border On a recent visit to a Scottish university my fellow traveller and I (we wore blue, not red, ties) were invited, unexpectedly and in spite of our state of undress, to attend the biannual dinner of the Medical Faculty An impressive gathering of the professoriate, including at least two knights, bade us welcome, and dinner jackets were accompanied by boiled shirts and fly-away collars —none of your modern soft fronts and turn-me downs After the aperitifs we sat down to a traditional Scotch dinner, with the Dean, the essence of bonhomie, seated in his high chair in the centre First there was Scotch broth, with carrots intult and neeps intult and all the other "intults" that so intrigued Queen Victoria Then strange noises were heard from the kitchen, and presently a piper in full dress regalia swung into the dining hall, followed by the chef holding aloft a sonsy haggis, that chieftain of the puddin' race After the dish had been piped round the table and the chairman had stabbed it fiercely with a dirk, the piper was rewarded with his glass of whisky—it was a large whisky and he a young student, so he may be forgiven for not draining the glass at a gulp—and the company proceeded to wash down this tasty morsel with the same Highland dew With turkey and cranberry sauce we drank a fine claret, that Scottish symbol of the Auld Alliance Then came the plum pudding, followed by mince pies and then a mushroom savoury After the toast of the King, the vintage port was circulated (clockwise, of course), and its mellowing influence brought forth a succession of pawky stories, capped by one from the Dean about an Aberdeen plumber who, weary of life, decided to end it all, they found him in the kitchen with one end of a gas-pipe in his mouth and the other end fixed to the company's side of the gas-meter And so into the cold wintry night But one felt that in Scotland at any rate a professor still has some standing—and an appreciation of the good things of life

* * *

Among the more entertaining of our uninvited, though none the less welcome, guests at the clubhouse when we held our Christmas party was the resident engineer Dressed unobtrusively in a sports coat and grey bags he oozed inconspicuously into the bar at 8 30 P M and stayed there In my capacity as host I didn't really get around to him till about 12 50 A M., by which time he was feeling fine He began by offering me two or three pounds to pay for some of the whisky he had drunk. I liked the "some" "Don t like spending all time in bar," he explained, "rather dance but can t, knee trouble" I expressed sympathy "You're doctor," he went on, "understand these things, football," "Dangerous game," I agreed, "I gave it up when I was thirty-five" "Not just joint,' said the resident engineer, "it's carlidge, see? Semi semiloolar carlidge You're doctor Understand" I assured him I did and moved on Ten minutes later, with a young woman holding him up, he was steering an erratic course round the dance floor, semiloolar or no semiloolar In a dual sense he was out on his feet

* * *

My disability is cold feet—not the moral kind but the physical My feet used to get so cold on most winter evenings that it often took half an hour or more to get to sleep I tried and rejected (1) a hot-water bottle, which warms only the soles of one s feet, (2) bedsocks, which are a bit better but make the feet unbearably hot later in the night, (3) violent exercise shortly before bedtime, which is only partly effective and a nuisance to oneself and others, (4) warming the feet before a fire, which also deals only with one's soles and is of little use unless prolonged for about 20 minutes, and (5) soaking the feet in hot water, which is effective but laborious and time consuming A further objection to the last three methods is that they are difficult to practise away from home

The only treatment I have found at once simpl and effective is as follows (*a*) on arrival home in the evening, change into a dry pair of thick woollen socks. (*b*) Bedroom slippers need not be worn, but sit all evening with the feet on a cushion or hassock (*c*) Last thing before getting into bed, wrap a big woollen scarf tightly once round one foot and then round and round both feet together, and tuck in the end Within 2 minutes the f are perfectly warm and one should be fast asleep (*a*) and (*b*) are impracticable I can get to sleep in 5 minu on (*c*) alone, however cold my feet, and they do not too hot later, because the scarf slips off during the nig

Warning Be careful not to leave the scarf in b when away from home, it may be difficult to expl to your hostess why you declined a hot bottle

* * *

At this time of year I have to decide which of the not and entries in my 1950 pocket-diary deserve transplanti to the 1951 presentation model Addresses and telepho numbers are usually copied in year after year, but th time I shall use pencil for my Registrar friends and f my young sister who is training at a London teachi hospital and requires the Society column of the *Tim* to record her frequent transitions from the Londo nurses' home to the country branch and vice versa.

It is always amazing, on thumbing over the leaves, t come across entries which I have no recollection of makin Some at once recall a theatre date or a dinner wi Smith, but others are more obscure That name an address I came across in the July pages needed severa minutes' concentrated thought before it revived th memory of the charming Americans I met in the Tyrol promised to write to, and have till this moment shame fully forgotten Others are still more baffling—a compli cated list of groceries eventually reveals itself as a recip for Christmas pudding copied down for my mother fron a patient's dictation, and 'Phone Rodgers" on Sept 1 must have had some urgency at the time though nov I can remember no Rodgers in my life I hope remembered to phone him, anyhow

One year I found an old entry of "Constance White,' and the effort to recall this mystery woman cost m many sleepless hours before a friend, showing me roun his garden in the summer, asked casually if I had bough a rosebush of that name—he had seen me take the nam down in my diary the year before

* * *

Opening the Christmas mail is not without its profes sional hazards It was bad enough this year to open a 2½*d*.-stamped envelope and find it contained only a circular disguised as a Christmas card from Messrs Dru and Bottle, but my sister, a laywoman, who was helpin me sort the mail uttered a shrill yelp when she opened one envelope and, instead of robins and holly, found a realistic coloured illustration of a gastric ulcer in the early stages of healing "This is rather a nice one, don't you think?" I asked nonchalantly, a few minutes later, putting between her still tremulous fingers a cheery folder emblazoned with the motto "In cases of hæmorrhoids " and illustrated, again in colour, with a fine proctoscopic view "They must think you're a psycho analyst, dear," was her retort

* * *

In a Northern European capital, British anæsthesia was demonstrating its best to an assorted group drawn from every quarter of the Continent One drug after another had been injected into the vein, cunningly found in a difficult arm the endotracheal tube had been slipped into place with a facility that made the onlookers goggle, and the tubes and etceteras all fixed in place The patient lay corpse like and ready, and silence reigned except for the creaking of the breathing bag being nonchalantly squeezed The opening into the peritoneum appeared like a yawning crater, at the bottom of which could dimly be discerned some coils of gut Suddenly there was a clatter as the Professor threw down his instruments He glared at the top end 'I cannot work like this There is too much relaxation," he said, "too much relaxation"

In this country 20,000 people die every year from ulmonary tuberculosis, most have advanced disease hen the diagnosis is made All money spent on tempts to save these people has been wasted If ich takes one year to die in hospital then 20,000 in ospital for one year at £300 a year each = £6,000,000 This is the cost of running 1000 units, or twenty times he cost of the present mass radiography service)

What good are new quarters for the reception of those lready doomed by late diagnosis ? What good are more eds for the dying with more staff to attend their exitus ? Money spent on early diagnosis is money well spent

Mass X ray Service Grove Hospital
London S W 17

F A NASH

REGISTRARS

SIR,—In view of the new regulations regarding registrars, may I suggest that, out of fairness to applicants, every advertisement for a registrar appointment should clearly set out certain extracts of the conditions and terms of service

These extracts should explain that a registrar will be liable to dismissal after his first year of appointment, and that in any case his appointment will terminate after his second year He will be entitled to apply for a senior registrar post if he is permitted to proceed to this stage

It should be stated that if his application is successful and he obtains the position of senior registrar, he may be entitled to serve in this capacity for three years or in certain circumstances four years, and that his appointment as a senior registrar will then be terminated.

I feel, from personal experience of registrars, that future applicants may not be aware of the full nature of their contracts Attention should be drawn to the recurrent reviews and possibility of dismissal, and the ultimate termination of appointment

Friern Hospital
London N 11

F STEEL.

EFFECTS OF CORTISONE ON EARLY FIBROSIS OF THE LIVER IN RATS

SIR,—Dr Aterman's article of Nov 11 prompts us to record our results in similar experiments

Thirty male rats were treated in a glass topped chamber for 4 minutes daily with carbon tetrachloride inhalations One group of rats was used as controls and another group was injected subcutaneously with Cortisone (Ciba) 1 mg daily The animals were killed 20 and 45 days after the start of the experiment

Post-mortem examination of cortisone treated rats showed thymolymphatic and adrenal atrophy the splenic and hepatic hypertrophy, following the treatment with carbon tetrachloride was less severe in the rats treated with cortisone than in controls

Histological examination of the liver in the controls showed severe fatty degeneration as well as marked perilobular and intralobular reticulosis and fibrosis with consequent structural alteration of the lobules The growing reticular and collagenous tissue was found to be rich in acid mucopolysaccharides (Hotchkiss method) and alkaline phosphatase (Gomori method) Numerous mitotic, and sometimes atypical figures were present in the hepatic cells cells with giant nuclei were assembled in regeneration islets

The fatty degeneration in the livers of the cortisone-treated animals was practically of the same extent as in controls Glycogen was definitely increased A moderate increase of reticulum was observed in the portal spaces but collagen tissue was absent or very scanty The fundamental structure of the hepatic lobule was mostly preserved the new connective tissue was very poor in acid mucopolysaccharides, and practically no alkaline phosphatase was present The hepatic cells showed very few mitotic figures they were not assembled in regeneration islets nor did they contain giant nuclei

We may conclude that cortisone definitely modifies the evolution of carbon tetrachloride cirrhosis Fatty degeneration is not affected, but fibrosis, reticulosis, and parenchymal regeneration are greatly inhibited, such an effect is probably produced through a primary action on mesenchymal tissue and inhibition of cellular proliferation

Anatomo Pathological Institute,
University of Milan and
Farmitalia Research Laboratories Milan

C CAVALLERO
G SALA
A AMIRA
M BORASI.

ADJUVANTS TO STREPTOMYCIN

SIR,—The thorough and ingenious experimental studies upon which Dr Cathie and Dr MacFarlane based their use of streptokinase in the treatment of tuberculous meningitis gave good grounds for hope that this substance would be of value in the treatment of the disease, and their report (Dec 16) on a series of cases treated with it is of great interest

It is disappointing to note that when their cases are taken as a whole, including the relatively unsuccessful preliminary cases (as with the other quoted series in their table), the proportion of survivors is only 47% although two thirds of their patients were treated with streptokinase This is not very different from the results of others, and compares with 46% survivors in the group treated without streptokinase and reported by Dr Russell and myself[1] The cases that we reported are described by Cathie and MacFarlane as "selected" We would point out that the reason they were not successive admissions to the hospital was that in an undergraduate teaching hospital it is possible to set aside only a limited number of beds for this disease and many children admitted with tuberculous meningitis had to be sent elsewhere for treatment The selection was not made on clinical grounds but on the availability of a bed when each new case was admitted

The results obtained by Cathie and MacFarlane suggest that streptokinase may have some effect in reducing the incidence of serious sequelæ in patients who recover from tuberculous meningitis, but their evidence so far does not seem to indicate that it is capable significantly of increasing the proportion of survivors.

Royal Hospital for Sick Children
Glasgow

PATRICK MACARTHUR.

SIR —Dr Cathie and Dr MacFarlane have very ably described the methods of treating cases of tuberculous meningitis developing hydrocephalus and spinal block. We agree that ventricular drainage and administration by this route is necessary in the presence of raised intracranial pressure and hydrocephalus.

Changes in the flow of cerebrospinal fluid (C S.F) and even complete block may, however, be due to obstruction in the spinal canal rather than at the base of the brain Dr Cathie and Dr MacFarlane described such a case (no 37), which was admitted with a block in the dorsal region Surely it should be unnecessary to tap the ventricles in these cases if cisternal puncture is satisfactory ?

At present we have a patient, very similar to their case no 37, in which there was complete block of the spinal canal.

In this case tuberculous meningitis had been very satisfactorily treated with streptomycin given by repeated cisternal punctures The patient was given 100 mg of streptomycin in 5 ml of normal saline by cisternal puncture on alternate days for over three months Each injection was immediately followed by some vomiting but there were no other reactions This child previously had burr holes made in his skull The ventricles were not dilated and were tapped with difficulty each ventricular tap was followed by temporary but marked mental disturbance, and the taps were therefore abandoned after one week We now consider that ventricular puncture was unnecessary and probably harmful in this case polymorphonuclears, 19% lymphocytes 33% monocytes, 4% eosinophils, and 4% band cells Blood culture was negative, blood urea was 44 mg per 100 ml The urine contained nothing abnormal Radiography of the chest showed no abnormality Paul Bunnell test was negative Culture of the conjunctival sacs was sterile

---

[1] Russell S J M., MacArthur P *Lancet* 1950 i, 59

The clinical picture and investigations were typical of severe erythema multiforme

The patient was treated with aureomycin 250 mg 3 hourly by mouth for 8 days, and locally with lotio acid boric to the eyes and genitals Within 24 hours there was noticeable improvement in the condition of the eyes and mouth The speedy improvement was maintained, and he was discharged home 9 days after admission, showing only slight residual desquamation of the skin.

Although the patient was not severely ill his mucous membranes and skin were extensively involved, and he recovered in 9 days This compares with an average time of 3–4 weeks in other cases I have seen not treated with aureomycin

Rupert Hallam Department of
Dermatology Royal Infirmary Sheffield

I B SNEDDON

PROTHROMBIN CONSUMPTION DURING MENSES

SIR,—In your issue of Sept 30, Professor Baserga and his colleagues reported that in normal women with normal menses prothrombin consumption was constantly reduced during, and especially at the start of, the menstrual period In the course of a report[1] on the prothrombinopenic effect of penicillin, we recorded an increase in the prothrombin level during the premenstrual phase A systematic study of this problem has been planned

Beilinson Hospital Israel

Z LEWITUS

SALICYLATES IN ACUTE OSTEOMYELITIS

SIR,—The letter from Dr Kelemen and his colleagues (Sept 30) prompts us to mention some results we have reported[2]

Starting from the accepted principle that sodium salicylate inhibits hyaluronidase exclusively in vivo, one of us thought that such antidiffusive action might be promoted by liberation or production, under salicylate treatment, of anti hyaluronidase substances[3] The dramatic improvement in rheumatic diseases with 'Cortisone' and adrenocorticotropic hormone (A C T H), and the recognised remarkable antidiffusive activity of such hormones, caused us to investigate possible variations in the secretion of adrenal cortical hormones in patients under treatment with salicylates

We found that in guineapigs sodium salicylate in a daily dose of 0 075 g caused an increase of urinary output of 17 ketosteroids per day, the increase being maximal on the 3rd and 4th days and gradually decreasing with rather high levels on the 10th day After stopping the drug on the 20th day, the levels remained slightly raised With double dosage of sodium salicylate the effect was almost the same

Daily intramuscular administration of sodium gentisate in comparable doses evoked a slower and smaller increase in urinary output than that caused by sodium salicylate With both drugs we have observed a small but significant decrease in peripheral eosinophils and lymphocytes

These findings suggest the existence of a relation between salicylates and adrenal function These results should be considered together with those recently obtained by Shuman and Finestone,[4] who observed in man an increase of antidiffusive action during salicylate therapy, this they suggested was secondary to overactivity of the adrenal gland under adrenaline stress

F BERTOLANI
R LORENZINI
B BONATI

Institute of Pathology,
University of Modena

---

[1] Harefuah July 15 1948

[2] Bonati B Bertolani F Lorenzini R Atti LI Congresso Soc ital Med interna 1950

[3] Bertolani F Bergamini A *Rass Fisiopat clin Terap* 1950, 22 6

[4] Shuman C R Finestone R J *Proc Soc exp Biol* N Y 1950 73 248

MASS RADIOGRAPHY

SIR,—The facts given in Dr Hoffstaedt's art
Dec 9 will be familiar to most workers in mass
graphy, who will agree that, with limited resource
yield or "dangerous" groups should receive p
with special emphasis on patients referred by
practitioners Many units have been followin
policy since their inception

I should like to examine some of the stat
in your leading article of the same date, which
may cause misunderstanding The article say
"mass radiography, as used at present, is expe
This sentence is preceded by a statement that

> "the tuberculosis service needs much costly
> tion, it lacks new quarters and equipment
> dispensaries and chest clinics, more beds, more

and is followed by

> "some feel that we should not be spending s
> on finding new cases when we are not yet pr
> adequate treatment for those already found"

Presumably, it is to be understood that the
could be spent to greater advantage in another w
is not clear whether this refers to the £109 spent
the very early case in routine surveys, or to the £1
on the (somewhat more advanced) case referred
general practitioner Although we now know t
of finding an early active case of pulmonary tube
by mass radiography, no deductions can be mad
whether this represents good value for money
deductions cannot be made until we know wha
is likely to come from spending the money on any
proposed alternatives of "new quarters and equ
for the chest clinics, more beds, and more sta
seems unlikely that the expenditure of large s
money on new clinic buildings would save the
many patients

Large film radiographic apparatus is often wa
used in clinics Two types of cases referred at
commonly receive the same investigation,
discrimination These are (1) the ill, or cl
difficult, case, where a consultant's opinion is re
and (2) the not ill case, with minor respiratory o
symptoms, which the general practitioner sen
radiography to exclude pulmonary tuberculosis
on the first group that the consultant's skill a
expensive full routine investigation, including
films, sputum examination, blood sedimentatio
and blood counts, should be concentrated F
routine to be applied indiscriminately to the second
where all the doctor needs is a report on a 35 m
is a waste of public money This ritual not only
money but also costs lives, for general practi
well know that they must hesitate before re
"suspects" for radiography, because the syn
"indicating" the need for these investigations
common that if they did, the chest clinics wo
swamped with demands they could not mee
giving general practitioners access to mass radiog
reports, consultants would be freed to give
attention to the management of their tuberculou
and the investigation of clinical problems

On this service it costs £50 to find a case of
pulmonary tuberculosis Is this expensive? If w
by early diagnosis, shortened the stay in a sanat
at £8 per week, by only six weeks, the service ha
for itself Such cases can be prevented from bec
infectious, or can be sooner rendered non infec
and the patients can be restored to their jobs inst
becoming deteriorating invalids Often they c
treated effectively at home without recourse to
therapy in expensive institutional beds Early
can be treated in sanatoria with more patients per
than is possible with the later cases needing lon
in bed

mersion.' apparently the cubicle was only partly full water

The main interest of the report seems to centre on the ount of air-space unfilled by the water, and it would of some interest if this apparent discrepancy could be ared up

Hamcare. R W MONCRIEFF

PULMONARY HYPERTENSION IN MITRAL STENOSIS

SIR,—In their paper of Dec 30 Dr Bayliss and his lleagues confirm the finding of Hickam and Cargill[1] at in subjects with mitral stenosis the pulmonary terial pressure may rise with exercise without any crease in cardiac output They accept the argument the American workers that such rises cannot be tributed to the resistance offered by the mitral valve This argument overlooks the fact that since blood flows rough the valve only during diastole the effects of ear rate must be considered For example case 15 ad a resting rate of 58 per minute, and an exercise rate f 145 At rest the total diastolic time per minute would e about 36 seconds during exercise it could scarcely ave exceeded 12 seconds. Approximately the same uantity of blood was passed through the valve in both hese periods, and a higher pressure would be required to fect this in the shorter time.

The stenosed mitral valve causes turbulence, as evidenced by the diastolic murmur and is unlikely to act s a linear resistance. One would in fact expect the ressure-drop across the valve to be proportional to the quare of the flow rather than to the flow itself Thus n the case quoted the pressure across the valve during iastole might have increased some ninefold with exercise n spite of an unchanged cardiac output. It is clear that t cannot be assumed that the left auricular pressure emained unchanged.

I do not wish to deny that changes in pulmonary arteriolar tone may occur under the conditions of the experiments, but merely to point out that they cannot safely be inferred from the data

St Thomas's Hospital,
London S.E.1 A C DORNHORST.

ALARMING NAMES FOR HOSPITALS

SIR,—Your annotation last week on the need for a humane psychological approach to hospital names with regard to their repercussions, so often tragic, on the patients and their families and friends recalls a similar personal experience in relation to the old 'tuberculosis dispensaries.'

I had observed that the term was associated with great opprobrium by the ordinary patient whose dread of "consumption" frequently necessitated a more tactful explanation by the general practitioner, to persuade him to avail himself of the facilities provided by the dispensary In 1929 the local authority with which I have been associated fell in with my suggestion to replace this unfortunate designation by that of 'chest clinic,' and they have now the satisfaction of knowing that their pioneer change of title has been adopted throughout the tuberculosis service of the National Health Service by all regional boards

I have outlined in my book on Chest Disease in General Practice and, more recently in a paper on the Tuberculosis Service in the National Health Service[2] the machinery that exists and the wider objects visualised in relation to chest disease in general and to pulmonary tuberculosis in particular These embrace prevention, diagnosis treatment research, and undergraduate and postgraduate teaching

The radical change so far as the tuberculosis dispensary is concerned is now accepted, and the patient has been given peace of mind Undoubtedly the tuberculosis (chest) service leaves much to be desired but its potentialities for the future are unlimited.

On analogous lines, a more humane approach to the designation of hospitals with such alarming names as cancer and incurable should be possible Such a change need involve little inconvenience or financial difficulty and would no doubt contribute to greater coördination in the hospital service as a whole

London W 1 PHILIP ELLMAN

SIR,—From a long term viewpoint there is much to be said for explaining to the public the meaning of words like cancer and consumption But it will take very many years before the meanings are understood as we doctors understand them It is a matter of urgent simple thoughtfulness that alarming names should be abolished 'The Brompton' has given an excellent example by dropping the reference to consumption from its notice-board. It would be much easier for general practitioners to persuade patients needing special treatment to avail themselves of the special facilities without dangerous delay if the names were no longer alarming

It is to be hoped that the medical and lay members of the committees of hospitals with unfortunate inheritances in their names will read your annotation

Guy's Hospital,
London, S.E.1 RONALD MAC KEITH

HEPATITIS

SIR,—Your leading article of Dec. 30 and a paper by Ballard F Smith[1] of Buffalo, prompt me to address you

Dr Smith describes his experiences when dealing with cases of infective hepatitis among service personnel at Fort Clayton Hospital In July 1949 he noticed a high incidence in men who had been tattooed during the period usually accepted as the limit of incubation for homologous serum or syringe-borne hepatitis—40 to 160 days.

While serving on the staff of a large military hospital in Germany during the summer of 1947 it was pointed out to me while visiting one of the hepatitis wards, that amongst the patients admitted during the previous ten days no fewer than 6 had been tattooed on the same day and by the same artist rather less than four months before. Captain W T Hendry who had made the observation was encouraged to follow it up with the result that within a short space of time over 40 cases had been collected, all of which might well have been infected in this way As in Dr Smith's cases the disease differed in no way from other cases of infective hepatitis being treated in the hospital. In all cases syphilis and syringe episodes of all kinds were excluded

Captain Hendry visited the artist who had in every case been responsible for the decorations, and was fully satisfied that the technique used was such as to make easily possible the transfer from man to man of virus-infected blood I had considerable difficulty in restraining my colleague, who was anxious to submit his own epidermis to the artist's needle in his attempt to establish the relation between tattooing and hepatitis.

A more complete investigation was planned but difficulties arising from the constant release of patients at the end of their term of military service made this almost impossible. A number of recently tattooed men were, however, asked to write to Dr Hendry in the event of jaundice appearing and they were provided with special cards for this purpose I am not aware, however, whether there were any results from this

Our experience in 1947 would seem to support the opinion of Dr Ballard Smith—that in tattooing we have yet another way in which the infection of hepatitis can be, and I believe often has been spread.

Southampton. KENNETH M. ROBERTSON

---

[1] Hickam J B, Cargill W H J clin Invest 1945 27 10

[2] Postgrad med J 1945 21, 331

[1] Smith, B F J Amer med Ass. 1950 144 1074

We should therefore like to suggest that cisternal punctures should be tried before tapping the ventricles in cases where the flow of C S F from lumbar puncture is unsatisfactory This applies particularly to cases not showing signs of raised intracranial pressure

City General Hospital
Stoke on Trent

D C THURSBY-PELHAM
A McQUEEN ROBERTSON

STUDY OF DELINQUENCY

SIR,—I had not expected that my mild remonstrance (Dec 2), now described as a violent onslaught, would have made any dent in Dr Stott's stereotype of the psychiatrist as an old fashioned, incompetent, and pompous father figure But in face of the implied shortcomings of psychiatric practice described in Dr Stott's paper to the psychologists (Nov 25), I wanted to record my disagreement with his assertions

"" Cet animal est méchant—lorsqu'on l'attaque il se défend " Surely this is a simple enough explanation of the ' psychiatric onslaught " without the elaborate rationalisations of projected guilt feelings, scapegoating, Uncle Paul Reiwald, and all One wonders whether Dr Stott has even heard of child psychiatrists, or of the fellowship scheme of training in child psychiatry organised by the former Child Guidance Council and later by the National Association for Mental Health It would be difficult to imagine a more realistic training than that provided by the scheme, which incorporates the new techniques demanded by Dr Stott

Dr Stott omits from his list of social practitioners the school medical officer, it has been my experience, during 12 years of work in child guidance clinics, that the school medical officer is on his toes to "spot" the maladjusted child and is quick to refer him, and to demand priority for him, at the child guidance clinic As for psychiatric reports to the courts, Dr Stott must know quite well that, whatever the provocation, publication of these confidential reports would be impossible

His position to assess the validity of psychiatric judgments is perhaps not so unique, even I, as a psychiatrist responsible for treatment of delinquent boys in an approved school, have shared to some extent the facilities he has enjoyed of reading many psychiatric reports from a number of different sources And, Sir, I cannot confirm his general conclusions about the uselessness of these reports Taken as a whole, the reports have been extremely useful, fair assessments of the situation and sober forecasts of the boy's future, of course there have been the occasional exceptions, but I do not base my generalisations on the odd example

Bristol

FRANK BODMAN

SIR,—It is good of Dr Stott to admit (Dec 16, p 821) that the present revolution in clinical psychology was medically inspired I wonder what the academic psychologists were doing at the time Perhaps he should learn from this that the art of clinical medicine gives its votaries something more than technical knowledge, anatomical, psychological, or otherwise

A little psychology can be a dangerous thing I do not know that the crude mistakes made by bad psychiatrists are any worse than those made by bad psychologists We psychiatrists can be our own severest critics let Dr Stott leave them to us to speak to, and let him put his own house in order

I would accuse Dr Stott in his propagandist zeal of grossly over simplifying the problem of delinquency His remedy is far too easy From my experience let me repeat a word of advice Modern personality psychology may be perfectly straightforward in a study or an arm chair, but its practical application is a very different matter and needs something more than mere knowledge For example, his simple panacea of fitting people into a "belonging group" is very nice on paper, but let him try to put it into practice and he will find, as others have found, that it is not as easy as would appear In fact it is *because* they cannot feel secure and cannot find a satisfactory belonging group that so many cases need our help (I emphasise satisfactory, for some of the delinquent groups may make its members feel more secure but can hardly be tolerated by society)

Religious bodies have taught even more profound idealisms for many centuries, but have to admit that teaching, or preaching, alone is inadequate It is this something more which one gets from clinical experience with patients, and which is the great asset of a proper medical qualification One would hope that before long those who wish to be clinical psychologists will have to undergo something analogous in their training, this would make one more confident in handing over cases to their care

There is plenty of room for medical and non medical personnel in this field, and I am sure it would be happier if each of us could work for a better training of both each within his own branch of the profession

Leeds

H EDELSTON

ENDURANCE FEAT BY A YOGI PRIEST

SIR,—Dr Vakil has given a most interesting account (Dec 23) of the endurance of a Yogi priest sealed up in a 216 c ft concrete chamber Physiological considerations, however, do not explain away the mystery as easily as he supposes

It is not to be expected that a man sealed up in this way could use all the oxygen originally present Assuming a resting basal oxygen usage of 0 5 c ft an hour, or 0 236 litres a minute (a reasonable value for a normal man) and a respiratory quotient of 0 8, at the end of 56 hours in a gas tight cubicle of 216 c ft capacity, the atmosphere would contain only 7 8% of oxygen and 10 4% of carbon dioxide In this calculation no allowance has been made for the temperature, pressure or water vapour content of the gas in the chamber, because the data are not available, but probable values for these quantities would lead to the expectation of 6 6% of oxygen and 11 4% of carbon dioxide It would be a very extraordinary thing if a human being could be shown to survive for many hours in an atmosphere slowly approaching this composition Of course the Yogi priest may have had a lower metabolic rate than the 1700 calories per day which these figures assume, and there may have been a certain amount of gaseous diffusion through the walls of the chamber, or adsorption of carbon dioxide by the walls

When it comes to pouring water into the cubicle there seems to be a discrepancy in the figures, for 1400 gallons will not go into 216 c ft, and it is hardly credible that even a Yogi priest has a negative volume I suppose a good deal of the water soaked into the concrete walls

It is greatly to be hoped that Dr Vakil's article will stimulate others to investigate and report similar cases It would be very valuable indeed if an analysis could be made of the atmosphere in the chamber just before the release of the subject Until such figures are available we cannot be sure whether there is a real or only an apparent mystery

Department of Physiology,
The Queen s University of Belfast

A D M GREENFIELD

SIR,—I have read with considerable interest Dr Vakil's account, but its value as a scientific report is diminished by the inclusion of one or two inconsistencies, notably

1 The total air capacity of the cubicle 'worked out at 216 c ft Such a volume would hold 1346 gallons of water, whereas about 1400 gallons of water was introduced

2 Despite the apparent overfilling of the cubicle the priest is reported to have been in a state of almost complete

Misgiving centres chiefly on the salary of the assistant dical officer of health When taxation levels and the st of living are taken into account, a maximum salary £1150 in 1950 does not compare very favourably with maximum of £700 in 1929 Two other points of mparison are also available now which were not ailable then—namely, salaries in the hospital service d earnings in general practice The assistant medical ficer will undoubtedly look with some envy, as will the nior medical officer in charge of a school medical or aternity and child welfare department, at the current nancial status of his late colleague the chest physician e will also await with interest the promulgation of the lary scales for his colleague the public health dentist, ow under the consideration of another Whitley ommittee

Despite these doubts, the British Medical Association nd the Society of Medical Officers of Health are to be ongratulated on the skill and pertinacity with which ey pursued their claim The public health service, it has not gained all that was hoped, has nevertheless ained much by their efforts

---

Smallpox at Brighton

Up to 6 P M on Jan 1 there had been 11 cases of mallpox in Sussex, with 1 death Of these, 10 were Brighton residents and 1 belonged to the neighbouring urban district of Portslade Surviving cases are now at Long Reach Isolation Hospital, Dartford, where 4 were admitted on Dec 29, 2 on Dec 30, 3 on Dec 31, and 1 on Jan 1

The infection appears to have been brought into the country by an R A F officer, who reached Leuchars, Fife, by Service plane from Karachi, on Nov 27 On Nov 29 he travelled by train to Brighton and felt ill during the journey He went to bed on reaching his destination and later a sparse rash developed, which did not come under medical observation The minor nature of the complaint in this case is explained by the patient's high vaccination state, diagnosis in such a case is particularly difficult

This initial case passed on infection directly to a young woman and to a man, aged 53, in the house where the officer was residing in Brighton, the man died of hæmorrhagic smallpox on Dec 29 Indirectly, a woman and a man at Portslade were infected Unfortunately, the condition of the first woman patient, admitted to the Bevendean Infectious Disease Hospital, Brighton, on Dec. 18, was misdiagnosed until Dec 28 This delay allowed the dissemination of infection in the hospital, and 3 nurses there have now fallen victims Of these nurses, 2 had never been vaccinated, and the outlook in these cases is grave, the 3rd nurse was vaccinated only once, when a child The hospital has been in quarantine since Dec 31

The staff of a Brighton laundry is also involved, the officer's clothes were sent there on Dec 13 So far there have been 3 cases from this source 2 are women who dealt with the clothing at a receiving branch, and the 3rd is a sorter at the main laundry

It is difficult to forecast the likely extent of this outbreak because

1 The initial case was so modified that the patient was able to travel to and from Scotland in an infectious state

2 The second case remained in an ordinary infectious diseases hospital for 10 days during which no special precautions were taken The poor vaccination state of some members of the staff there aggravates the risk In this connection attention is drawn to the memorandum R.H.B (50)75 issued on Aug 17 1950

3 Infection in a laundry opens the way to further spread

To minimise these risks all possible action is being taken to trace and vaccinate all known contacts both in England and Wales and in Scotland Nevertheless special vigilance must be maintained throughout the country to detect the disease in casual contacts who have not come under surveillance Although there are possibilities of spread, so far secondary cases have occurred only in the direct line of contact No cases have been reported outside the Brighton area

Influenza

There has been a marked prevalence of influenza in Scandinavia, where a virus has been isolated that is not unlike the A prime strain which occurred in this country in 1949 The disease, which has been mild but with a high attack-rate, appeared first in Sweden and then in Denmark and Norway A high incidence of influenza has also been reported within recent weeks from certain parts of the U S.A, Northern Spain, Sardinia, Persia, and elsewhere

In the absence of notification of influenza the incidence of pneumonia cases and of deaths from pneumonia and influenza are used as a guide to the prevalence of the disease The following figures relate to the great towns of England and Wales

	Pneumonia (including primary and influenzal)		
Week ended Dec	*Cases*	*Deaths*	*Influenza deaths*
9	347	236	34
16	274	283	33
23	363	350	54

In England and Wales notifications of pneumonia numbered 573 in the week ended Dec 9, 684 in the week ended Dec 16, and 647 in the week ended Dec 23

These statistics afford no evidence of any serious influenza epidemic, but in the last week or more this disease has been very prevalent in the North-East, where a number of large towns have been hit, including Sunderland, Durham and Newcastle upon Tyne It seems likely that the disease has been introduced to this area from Scandinavia, and it may well be that laboratory studies, when completed will show the virus strain to be identical with that in Scandinavia The disease in the North East seems quite distinct from the so called influenza which is at present widespread in other parts of the country The infection may spread southwards in the next few weeks

Poliomyelitis

In England and Wales notifications of poliomyelitis in the week ending Dec. 23 were paralytic 38 (82), non-paralytic 15 (25) total 53 (107) The figures in parentheses are those for the previous week, compared with which there has been a decrease of 54 cases Uncorrected notifications for the corresponding week in 1947 and 1949 were 60 and 81

Total uncorrected notifications for 1950 up to and including the week under review are 8643 The corresponding figures for 1947, 1948, and 1949 were 9147, 2356, and 6791

Food-poisoning in Kendal

An outbreak of 124 notified cases of food-poisoning occurred in Kendal and south Westmorland during the three days before Christmas

The outbreak was due to staphylococcal infection of jellied brisket and jellied veal prepared on the premises of one pork-butcher in Kendal About 150 lb of these meats was sold, mostly in 1/4 lb and 1/2 lb orders, to several hundred customers The meats had been prepared on Dec 18 and 19, and sale was stopped on Dec 23

Clinically the features were onset 2–4 hours after ingestion, sharp abdominal pain, severe diarrhœa, and in most cases vomiting Usually there was no fever Although there was some initial collapse in elderly patients, recovery was complete within 24 hours 3 patients developed urticarial rashes, including a breast-fed baby whose mother had eaten the meat 1 asthmatic patient developed œdema of the feet and ankles

The first cases were notified on Dec 22, 85 patients and staff of the Westmorland Sanatorium, at Meathop, having fallen ill after an evening meal the previous day, in this institution about 55% of those at risk developed symptoms On Saturday, Dec. 23, notifications were received of wider spread to Kendal and the surrounding areas of south Westmorland, Windermere, and north Lancashire All patients had eaten jellied meats from the same shop in Kendal

An appeal for prompt notification of cases was broadcast by the B B C in the 1 P M news on Saturday,

Public Health

SALARIES IN THE PUBLIC-HEALTH SERVICE

BORN after a long gestation, not free from complications, Whitley Council Medical Committee "C" last spring began the reconsideration of public health medical salaries Some four months of negotiation brought out the differences, on matters of principle, between the staff side, ably represented by the British Medical Association, and the management (local authority) side of the council These differences proving irreconcilable, the dispute was referred to the Industrial Court, at whose hearings during four days in October both sides were represented by counsel The award of the court, which affects the salaries of 2000 local-authority medical officers, has now been published and was briefly noticed on p 918 of our last issue

The awards made operate from Oct 1, 1950 They replace the agreed scales formulated in 1929 by the committee presided over by Lord Askwith These awards had in the interval been modified, first by the inclusion of a war bonus of £60 in the lower salary ranges, and then in 1946 by the addition of 30%, 20%, and 10% to salaries whose minimum commencing points on the Askwith scale were respectively under £700, over £700, and over £1000 The final agreed revision took place in 1947, when the percentage additions to the basic Askwith minimum were increased respectively to 35%, 30%, and 25%

For assistant and senior medical officers the court has made the following awards, against which we show the claims of the staff side and the offer of the management side

	Staff side claim	*Management side offer*	*Industrial Court award*
Assistant medical officer	£960 × 50–1680	Grade I £750 × 50–950 Grade II £900 × 50–1100	£850 × 50–1150
Senior medical officer *	Minimum (depending on population) £1680 × 120–2160 Maximum £2040 × 120–2520	Grade I £1150 × 50–1350 Grade II £1300 × 50–1500 Grade III £1450 × 50–1650	£1250 × 50–1650

* *To be appointed only in areas where the population exceeds 250 000*

The awards for medical officers of health are set out in the accompanying table

The court has not fixed salary scales for deputy medical officers of health, divisional or area medical officers, or officers holding mixed appointments These are left for joint negotiation between the parties, with a right of reference, failing agreement, to the Industrial Court

Part time medical officers of health are to be paid in accordance with the Spens formula in respect of consultants Holders of combined appointments are to receive £100 per annum above the appropriate salary scale for the total population of the combined districts The method of assimilation to the new salary scale is laid down and will be readily accepted as fair A "no detriment" clause and sick pay scales are included, and discretion is given to count service with one authority on transferring in the same grade to that of another, in fixing the appropriate commencing salary The undertaking of teaching duties and the disposal of any fees therefore are within the discretion of the local authority

Under the Askwith agreement salaries could be exceeded in particular cases at the discretion of the employing authority In the case of assistant medical officers this was done by several authorities, notably (for different reasons) Lancashire and London. The only dictum of the new award on this point is as follows

> "In addition, if a local authority in the exercise of the discretion permitted under the Askwith agreement appointed a particular officer at a salary in excess of the minimum then current, the local authority shall in assimilating that officer to the scale now awarded fix his starting point at a similar amount above the new minimum, provided however that the maximum of the new scale shall not be exceeded in such cases except at the discretion of the local authority"

These words are important They offer a clear method of avoiding hardship to existing officers and allow progressive authorities and those in whose areas (as in London) the cost of living is high to continue their lead or to offer partial compensation for local circumstances What is not at present evident is whether this differential advantage may be applied to new appointments, but it is to be hoped that in this matter the authorities concerned will, with the agreement of Committee "C," maintain their enlightened policy

On the whole, the awards represent tangible salary gains to the public health service When compared with what the management side felt able to offer, they fully justify what was in effect an appeal to arbitration The medical officer of health may reasonably feel that his work is now to be remunerated on a basis which does represent his specialist qualifications and training and which does bear some relation to that of his clinical peer, the consultant On the other hand, the local authorities may also feel some satisfaction that (as the table shows) the maximum salaries of their chief officers are still closely related and that the team work so essential in local government will not, therefore, suffer from personal rivalries The varying scales of salary for populations of the same area will also help local authorities both to take account of local circumstances (as for instance in a county borough and an urban district) and to reward individual merit This principle is a new one in its application to public health salaries but there seems little reason to fear that local authorities will exploit it by always offering the lowest of the possible ranges

SALARIES OF MEDICAL OFFICERS OF HEALTH

Population not exceeding	Claim by staff side	Population not exceeding	* Offer of management side: Minimum of salary scale between	* Offer of management side: Increments	Award of Industrial Court: Minimum of salary scale between	Award of Industrial Court: Increments
50 000	1800 × 120 to 2280	75 000	1250 and 1650	4 of 50	1450 and 1650	4 of 50
100 000	1920 × 120 to 2400	100 000	1350 and 1850	5 of 50	1550 and 1850	5 of 50
200 000	2160 × 120 to 2640	150 000	1550 and 2050	5 of 50	1750 and 2050	5 of 50
300 000	2400 × 120 to 2880	250 000	1750 and 2250	2 of 100 1 of 50	1950 and 2250	2 of 100 1 of 50
500 000	2640 × 120 to 3120	400 000	2000 and 2500	2 of 100 1 of 50	2200 and 2500	2 of 100 1 of 50
750 000	2880 × 120 to 3360	600 000	2100 and 2700	3 of 100	2300 and 2700	3 of 100
750 000 +	3120 × 120 to 3600	} 600 000 +	At discretion		At discretion	

* This offer is the same as the scales agreed by the Joint Negotiating Committee for chief officers of local authorities It applies to accountants and treasurers engineers and surveyors chief education officers, and architects in charge of separate departments

orceful and pregnant minutes Everywhere he went he timulated interest and activity He created he improved he mprovised he did everything that was possible in war time o fill the existing gaps and to strengthen the weaker labora ories His efforts were crowned with success, and by the ime the regional hospital boards took over control the struc ure he had raised was ready to be incorporated as a permanent art of the National Health Service

Panton s contribution, however, was more than merely dding to the existing system He raised the whole tone of athology, and contributed substantially to the progressive ifferentiation that occurred during the war years between he curative and preventive sides of his subject Once it ecame clear that clinical pathology was to be organised under he new Act on a regional basis and public health bacteriology n a national basis, he insisted that the two groups of labora tories should work side by side complementing each other in the provision of a functionally unified pathological service Panton was simple direct, fearless unselfish, unassuming unpretentious, and absolutely loyal, he inspired affection and respect among both old and young and he probably contributed more than any one else to the present widespread dis tribution of pathological facilities that the country now enjoys

S C D also pays tribute to him as an administrator who never forgot he was dealing with people

"In the course of building up the Emergency Medical Service in hospital pathology Panton was called upon to deal with and to some extent to shape the destinies of many men and women He was an able organiser but his exceptional quality lay in that he never failed to remember that those whom he had to fit into his organisation were human beings all with their own personalities and each presenting a peculiar and unique case he was keenly interested in them all and to them always readily accessible all who approached him were sure of a sympathetic hearing and a careful consideration of their problems

Despite advancing years Panton never spared himself, and when in 1948 the change-over to the National Health Service took place, he was at the centre to facilitate the transition Only when this had been done did he retire, but, as events have proved, he had pushed himself so hard that he no longer had the health to enjoy the rest which he had earned so well

S P B, to whom we are indebted for much of this memoir, writes

'The account of his achievements shows a glimpse of his make up He was a man of great ability and excellent intel lect, yet he was not outstanding as a teacher, his lectures were interspersed with marvellous touches of humour but unfortunately these escaped all but the first few rows of his audience He did some good original work, notably on staphylococcal toxins and hæmatological problems—enough at any rate to show that given the opportunity he would have made valuable contributions to medical knowledge It could not be claimed however that he was a born investi gator, though his advice on a research problem could be of the greatest value and one always felt that something really useful would emerge from a discussion with him

'Until the war came with his appointment as consultant to the Ministry he was hardly known outside the London He was not a member of any of the societies which had to do with pathology and even towards the end, when he was at last appreciated at his full merit and he was offered honorary membership in the Association of Clinical Pathologists, he declined. Honours meant absolutely nothing to him and the one that came his way—a knighthood in 1945 for his services to pathology—he accepted because he thought the London Hospital would wish him to

'Prowess in athletics was not one of his achievements yet he delighted in the countryside enjoyed walking, and was or had been an enthusiastic fisherman. Above all he enjoyed his garden and he spent many a happy hour working in it though his botanical knowledge was defective and the methods he employed were sometimes unorthodox (On one occasion he transplanted a well grown apple tree in full bloom and what was the more surprising was that it survived the insult) None the less Otter s Pool was his chief relaxation and he looked forward to tending it in his retire ment and to receiving there the visits of all those pathologists for whom he had worked so hard It is sad to think that all that is no more

J J A. also writes of Panton's retirement, and tells how in the intervals of the landscape gardening he compiled reminiscences of medical life looking forward to seeing appear this sprin

When they do appear they will introduce a whimsical personality to the wider world outside fession and amplify and crystallise many memo who knew him in real life For Panton was such man once you got behind the barrier of his shyness a admitted to his friendship A tolerant twinkle in blue eyes betrayed the kindly observer of human wea and told of the quiet fun he got out of his freque apparently heated contests with authority For he individualist like his grandfather, William Frith the painter of *Derby Day* and he fought for what he considered right whenever he came up against authority—whether as a schoolboy at Harrow, an undergraduate at Cambridge a lecturer in London or an adviser at the Ministry of Health during the war

And a last tribute from F C O V runs

'Panton was undoubtedly conscious of his own great gifts in which strength of character was combined with an acute and wide understanding, but his essentially formidable personality was tempered in a most attractive way by a great sense of humour a very real sympathy and comprehension of those with whom he worked, and with a hatred of bombast in any form This last trait was presumably responsible his well known inaudibility at lectures which once reached me at lunch in ho was holding forth at a neighbouring tab think of something worth saying as loud was in fact a master of the spoken and a student he edited the hospital gazett writing most of it himself as he once told at a loss for the right word or phrase, a years he wrote stories for his grandchildr reminiscences This artistic facility, deriv his grandfather Frith, may have made impatient of the details inseparable from laboratory, though no one was more fertile i advice to others He was at his best by the investigation of a difficult case, and it was his of the needs of the clinician that led him to dev of organisation primarily to building up a routi service, first at the London and later throughout

divisi
late lectures
of the, at
Lan on
anc
gle
Lancet 1950
501
),
M
The Crichton Royal
ean of the medical
s Mr A J Heriot
tminster Hospital
P M Cases will
show progress
Copeman and
apeutic Effects
the seventh
July 15 to 21,
The central
grand
to the
of
of
jou
the ed
world

CYRIL HOCKEN TEWSLEY

C.M.G, M.A N.Z., M.D EDIN, F R C.P E, F R C
F.R A C P

THOUGH Dr Tewsley was born, received his early tion, and spent most of his professional life Zealand, he had, during his student days in Edinb and his war service, made many lasting ties with this country

The son of the late Henry Tewsley, he was born in 1878 in Dunedin From the local high school he went to Otago College, and he took his M.A. in 1901 before beginning his medical studies at Edinburgh He qualified in 1906 and after holding house-appointments at the North Riding Infirmary, Middlesbrough, took his F R C.S and his M D in 1909 before returning to New Zealand There he settled in general practice in Auckland, and in 1912 he was elected to the staff of the Auckland Hospital

[Alan Esdry

As soon as war broke out in 1914 he joined the New Zealand Medical Corps, and he left on active service with New Zealand s main body of troops He took part in the landing at Gallipoli, and he was later in charge of the convalescent hospital at Hornchurch Essex On demobilisation he settled once more in practice as a general and consulting physician in Auckland, where he was medical officer to the police force and prison, and chief of the medical staff of the St John Ambulance Association. Last August he was promoted to be a commander of the Order of St John in New Zealand. He was also a vice-president of the Royal Australasian College of Physicians and a past president of the Auckl and there was an immediate response The suspected food still unsold was surrendered by the manufacturer, and a warning not to eat jellied meat purchased from this shop since Dec 20 was broadcast by the B B C in the northern news on Saturday evening at 6 15 P M and repeated at 6 20 P M

The prompt publicity by the press and the B B C was undoubtedly the major factor in preventing the wider spread of the food-poisoning, for it was found that many people were keeping the meat for use over Christmas The Sunday newspapers repeated the warnings, and no onset later than Christmas Eve was reported It is expected that further cases with an earlier onset will be reported, and it is likely that a large number of cases will remain unnotified

Staphylococcus aureus was cultured from samples of the jellied meats sold and unsold, from the jelly stock prepared at a stage in manufacture before it is added to the brisket and veal, and from a skin lesion on the hand of a food-handler involved No presumptive connection can be made between this handler and the infected meat until the results of typing the organism are received from the Central Reference Laboratory All other samples of food and drink from patients w negative for food-poisoning organisms The gel powder used for thickening the meat stock was like negative Circumstantial evidence pointed to an dental infection of the jelly stock during the of preparation of the pressed brisket and veal, a the slow-cooling technique practised in manufac favoured active growth of the organisms, particu in the centre of each mould It is not yet possib assess the relative responsibility of toxin and li organisms in the production of the gastro-inte irritation, but it was felt that the toxin was the m likely factor

Routine cleansing and disinfection of the prem was carried out, and all utensils were steam steril Lectures on food-handling hygiene were given, a three film-strips of the Central Council for Hea Education were exhibited, to the management and st of the manufacturing firm, and several modifications the technique of manufacture were advised A ch of manufacturing methods of prepared meats in oth similar premises in the area is in progress, to minim the risk of such infections being repeated

---

Obituary

PHILIP NOEL PANTON

KT, MA, MB CAMB

ON Dec 27 Sir Philip Panton died at his home at Bourne End after a short illness, his retirement had lasted little more than a year Many will have heard this news with real sorrow, for, besides his colleagues and numerous generations of students at the London Hospital, he was held in high esteem and affection by hospital pathologists up and down the country, whose working conditions and status he had done so much to improve

Philip Noel Panton, son of the late James Panton, was born 73 years ago at Wareham in Dorset He was educated at Harrow and Trinity College, Cambridge, taking the natural sciences tripos in 1899 At St Thomas's Hospital, where he was contemporary with H R Dean and A E Boycott, he was grounded in pathology by Shattock and Dudgeon, and the inspiration given him by these two great teachers was largely responsible for his decision to specialise in this branch of medicine

[Walter Stoneman

Qualifying in 1903, he held house-appointments at Addenbrooke's Hospital, Cambridge, and then returned to St Thomas's to work with Dudgeon as a Louis Jenner research scholar Later with the Gilson research scholarship of the Society of Apothecaries he continued his specialist training, and when he was appointed assistant director of clinical laboratories at St Thomas's Hospital, his election to specialise in what, for want of a better term, is known as clinical pathology was made He held this post for only a short time, for in 1908 he went to the London Hospital as director of the clinical laboratory, a newly made post which he was to hold with distinction until 1946

This new department, started largely at the instigation of the late Mr Frank Kidd, began in a modest way, with one small room and a single technician Its exact relation to existing departments was not easily defined, but thanks to Panton's professional and statesmanlike qualities the early difficulties were overcome and it continued to develop and expand In 1934 he became director of laboratories in the hospital, which included the laboratories of the departments of chemical pathology and of bacteriology The creation of a division of pathology which would be a geographical whole readily available to the clinician, was one of his goals, and he lived to see its accomplishment Another objective which he set himself was to expand the research activiti the hospital laboratories The staff of the clin laboratory had not the leisure to use all the mater reaching them, and he realised that this could only done by the appointment of men with research abil freed from all routine duties Thanks to the generos of his friend the Rev M S Courtauld, this was accomplished in 1926 by the formation of two Freedom resear fellowships and a Freedom research studentship

If Panton had achieved no more than this he mi have been well content, but his major work was yet come With the outbreak of war in 1939 the Lon Hospital's laboratories were closed except for a sm clinical laboratory, and the staff and apparatus w sent to equip new laboratories in the two sectors pla under the hospital's ægis Panton was largely respons for planning this transfer, and he was instrumental having made a complete register of qualified patholog and laboratory technicians through the country At t outset he directed the laboratories of a sector, but it w early realised that the Ministry of Health needed adviser on hospital pathology and Panton was obvious choice

Of his work at the Ministry W J writes

> "More than anyone else, Panton established clin pathology as an integral part of our hospital service. consultant adviser to the Ministry of Health he saw to it the upgrading of hospitals in the Emergency Service incl adequate provision for laboratory work In coöperation w the medical branches of the fighting Services and the Med Research Council, he organised a scheme for the trainin pathologists and arranged for the posting of patholog where they were most needed He scrutinised every labora plan and visited regularly every laboratory centre in country Needless to say he knew personally every mem of the service During the war he travelled thousands of m on duty, often in great discomfort, for he always beli that he could accomplish much more by personal con than by writing letters from Whitehall He encour regional meetings of pathologists and arranged for re sentatives from the regions to meet him regularly in ministry for the discussion of matters of common inte At times he rebelled against the slowness of the departm machine but he had a great sense of humour and usually his own way in the end By laying the foundations of a sc laboratory service in the hospitals of this country Sir P Panton has provided his own permanent memorial"

From the first, Panton had the vision to see bey an emergency service Believing firmly that an essen to good medicine was good clinical pathology, he himself to create an adequate service of hospital pathol throughout the country G S W, who shared in arduous task, recalls how Panton performed it

> "He travelled round continually, observed the inadeq arrangements that so often existed for providing the clin with the laboratory help to which he was entitled, embodied his conclusions and recommendations in a serie

viding assessed values for each of the foodstuffs, selected om standard tables of analysis by an estimate of the optimum aily human requirement of each vitamin and mineral The harts in this way provide an immediate visual assessment of he value of the foods judged by human requirements The dea is ingenious, and will appeal to all who do not take kindly o large tables of figures

THE TROMBONIST'S A P

THE trombonist referred to by a Peripatetic Correspondent n Nov 11 (p 539) writes "Readers may like to know that my artificial pneumothorax causes no unusual sensations when play my trombone ' The word 'blowing" is a misnomer hen applied to playing a brass instrument The player merely projects a thin stream of air against his lip, which in urn vibrates the air column inside his instrument With orrect breathing the diaphragm takes the larger part of the train and the lung is not greatly overtaxed as was shown y my doctor s ingenious experiments In your next issue Nov 18, p 593) another correspondent suggests that the first rombonist has a more tiring part than his colleagues in the econd Symphony of Sibelius I cannot agree with this iew It is true that he has a short solo passage of three bars efore the coda but this is in the most comfortable compass f the instrument and is of equally comfortable dynamics he maximum effort called for in this work is undoubtedly n the solo commencing 18 bars from the end of the symphony, where all three trombones play the melody *fff* in unison his is one of the most exhausting passages in the symphonic epertoire

---

University of London

At recent examinations for the academic diploma in medical adiology the following were successful

M M Craig (diagnosis) Hussain Syed Ali, R J Dickson A W Reghers (therapy)

On Friday Jan 26, Prof A. W Downie will give a lecture at the London School of Hygiene Keppel Street, W C 1, on Infection and Immunity in Smallpox On Feb 7 and 8 at the School of Pharmacy, 17, Bloomsbury Square W C 1, Mr E Lester Smith, D SC, will speak on the Isolation, Properties and Functions of the Vitamins B_{12}

On Feb 26, at the London School of Hygiene Dr Engelbreth Holm professor of pathological anatomy in the University of Copenhagen, will lecture on Folic Acid and Growth of Tumours especially Rous Sarcoma All the lectures will be given at 5 30 P M.

The title of professor of clinical pathology has, as announced ast week, been conferred on Dr Montague Maizels reader n clinical pathology at University College Hospital medical school

Dr Maizels took the Conjoint qualification from Guy s Hospital n 1920 and his M B Lond two years later He acted as Anderson lemonstrator in clinical chemistry and medical registrar at Guy s before he was appointed pathologist to the Westminster Hospital During the late war he was director of the emergency blood transusion depot at Maidstone He has published papers on the anion and cation content of normal and anæmic blood and on cation control in human erythrocytes

University of Liverpool

At recent examinations the following were successful

M.D —J W L Edwards Elizabeth Rees

M Ch Orth —N J Blockey L Bonnin V K. Drennan, K S Fan Henry J H Hicks T McSweeney F Machanik, J B Maloney M. R. Reddy A M Sallam H O Williams

Final M B Ch.B —A B Anderson Dorothy F M Burnett R. W H Clarke F J Deakin C G H Hall J C Hinchliffe J A Howe D O Hughes P Hughes H G McDonald Roma MacDonald C McNamara Alice N O Brien Marianne A A Phillips J A Seddon V R Tindall A Unsworth T D Williams R. G B Willis D Winter M. C Winter (new regulations) B M Barnes Monica T Barry Winifred Billington Cynthia J Bladon Elizabeth J Coope H S Evans T K. Hardy, D H Jones Mary W Malone Eileen P O'Mahony C W R Pyne H Shecter Sheila M. Ward Marjorie J Williamson (old regulations)

Royal College of Surgeons of Edinburgh

At a meeting of the college held on Dec 20, with Mr W Quarry Wood, the president in the chair, the following were admitted to the fellowship

Sheroo Darabsha Bharucha R A. Bremner Leon Bryer, J C Campbell Mohendra Lal Chatterjee W Y Cornock Mohamed Fathi El Giziri, T G Evans R H Freeman D M. Hancock, W T Irvine, Gopal Krishna Robert Lipschitz Grant McIntosh J T Marcroft, A. R. Murison J R. Reid, Elia Gobrial Sarofim Aubrey Schiller B M. C Sedzimir T V Simpson, P C Steptoe A. E M. Stevenson, Frederick Viedge Thiagarajah Visvanathan C J Windsor

Royal College of Physicians of London

Dr H J Anderson will deliver the Goulstonian lectures on Tuesday and Thursday, Jan 9 and 11, at 5 P M., at the college, Pall Mall East, S W 1 He is to speak on Tuberculosis of the Pericardium

Faculty of Radiologists

The following candidates satisfied the board at the 1950 examination for the fellowship

A N Gaballa W S Holden G B Locke (radiodiagnosis), D G Bratherton B A Stoll R C Tudway (radiotherapy)

British Association of Plastic Surgeons

The following officers and members of council have been elected

President Mr A B Wallace (Edinburgh) vice-president, Mr R J V Battle (London), treasurer Mr R P Osborne (Liverpool) secretary Mr J P Reidy (London) editor Mr A B Wallace (Edinburgh) members of council Mr J N Barron (Salisbury) Mr G M FitzGibbon (Bristol) Prof T P Kilner (Oxford) Sir Archibald McIndoe (London) Mr J S Tough (Glasgow), and Mr Rainsford Mowlem (London) ex-officio as immediate past president.

Association of Psychiatrists of the Scottish Western Region

The following office bearers have been elected for 1950–51

Chairman Prof T Ferguson Rodger vice-chairman Dr A Dick, secretary Dr Hunter Gillies, treasurer Dr M. M Whittet Dr Gillies may be addressed at The Crichton Royal, Dumfries

King's College Hospital

Dr V F Hall has been appointed dean of the medical school in succession to Mr Harold Edwards Mr A. J Heriot succeeds Dr Hall as vice-dean.

Heberden Society

A clinical meeting will be held at the Westminster Hospital Medical School on Wednesday, Jan 24, at 4 P M Cases will include some demonstrated a year ago, to show progress Dr L E Glynn will show, for Dr W S C Copeman and Dr O A. Savage, a short film on the Therapeutic Effects of 'Cortisone'

International Hospital Congress

The International Hospital Federation is holding the seventh International Hospital Congress in Brussels from July 15 to 21, under the chairmanship of Dr René Sand The central theme will be the Care of the Chronic Sick and the Aged, and the speakers will include Dr E M Bluestone, director of the Montefiore Hospital New York, and Prof Pierre Delore, of the University of Lyons The federation may be addressed in this country at King Edward s Hospital Fund, 10, Old Jewry, London, E C 2

Blood Donors

In England and Wales gifts to the National Blood Transfusion Service in the quarter ended Sept 30 numbered 133 693, bringing the total for the first nine months of the year to 388,000—a new post-war record Over 31 000 volunteers joined the service in the September quarter This brings the total of donors to 398,000—a gain of nearly 10,000 in the quarter To keep ahead of the growing demand a further 190,000 donors are needed

Houses for Doctors

Housing authorities have been asked by the Minister of Health to help in securing houses for general practitioners In a circular the Minister expresses the hope that when a doctor s application to build his own house is supported by the executive council the local authority will consider the issue of a licence It would, furthermore, be helpful if in suitable cases local authorities "would be able to agree to provide a site by sale or lease It might be appropriate for the local authority to make a site available for the purpose on their larger estates Similarly, should a doctor apply to the local authority to rent one of their houses, the Minister trusts that the application will receive sympathetic consideration when it is supported by the Executive Council." When local authorities are considering the allocation of the tenancy of a house intended for occupation by a doctor, the executive council should be informed so that they can, if necessary, advertise the vacant practice It will be appreciated that the statutory functions of Executive Councils may be impaired unless there is the fullest possible co-operation between them and the local housing authorities " and on of the British Medical Association During the food'ar he served with the rank of colonel as A.D M S and ie northern military district in New Zealand th erly he became interested in the history of medicine, in he gave several pleasing addresses embodying his reanings

Dr Tewsley married a daughter of the late Dr P A Widsay, of Auckland His wife survives him with two ns and three daughters

TIMOTHY GERARD DEMPSEY

M B N U I

r T G Dempsey, who died in Dublin on Nov 25 he age of 34, qualified at the National University reland in 1941 Two years later he joined the staff he Grove Park Hospital in London, and here he ne interested in clinical research on tuberculosis as associated with the first clinical trials in Britain ra aminosalicylic acid, on which he published a paper in our columns in 1947 Later he visited ontinent, America, and India, where he lectured is experience with P A S In 1948 he joined the of the Mayday Hospital, Croydon, where he ituted a new régime of treatment

M K writes "Dempsey inspired his co-workers
an in their difficult task His charm
endeared him to his patients
red himself in his efforts
onstantly over-
on their behalf
, but during long
d his keen interest
aracteristic humour
was an inspiration
d two young children

remember a murmur for
spital when a visitor
le 'I wish I could-
ly as that let he
written word As
at St Thomas's,
me He was never
ad during his last
ren as well as his
ing possibly from
him somewhat
research in th
suggestion and
bedside in th
understanding
ote his power
ine laboratory
the country'

PI ARSONS

On Dec 27 S
Bourne End aft
lasted little mor
news with real
numerous gener
he was held i
pathologists u
conditions an
Philip Noe
was born 7

Parsons's life was like a race
stly, and modestly it went
e saw early that pædiatrics
utions to the teaching and
it was one of the bulwarks
inst sm, and he designed his career
those enus' In his rare but delightful moments
self confession he told me that it was on a return
rney from America, where he had learned so much,
t he saw how an English hospital might design its
rk to combine research, teaching, and practice in an
atmosphere of comradeship Those who worked with him in Birmingham will know best how quickly he made his hospital one of the most famous and happy pædiatric centres in the world But it was obvious to all of us who knew him that the success of his designs was achieved as much through the warmth of his charity as through the eagerness of his mind He was truly both a great physician and a beloved man In 25 years of ripening friendship I never heard him speak ill of any man nor any man say ill of him In these ways he went on gathering fame, and always a little surprised that it came as it did

"So many memories of Parsons crowd the mind that it is difficult to choose, but I shall cherish always the spontaneous kindness of his remarks to a younger man at the last meeting of the British Pædiatric Association In that frankness of discussion which has characterised the Windermere meetings, the young man had been somewhat roughly handled, and Parsons sprang to his defence with words of praise, advice, and encouragement that enriched the day He endured unfalteringly so that none of us could believe his age It was therefore fitting, though tragic, that his life should end suddenly on a Sunday morning when he came home from his chapel, warmed himself at the fire, and died"

Prof G R Girdlestone, surgeon to the Wingfield-Morris Orthopædic Hospital, Oxford, died on Dec 30, a e age of 69

Herbert French, consulting physician to Guy's and author of *Differential Diagnosis*, died on ge of 75

Notes and News

HELP YOURSELF SERVICE

On behalf of all the rest of us, the Ministry of Pensio look after the disabled of two world wars, and in *The Undefea* they give a good account of their stewardship In half hour this film contrives unobtrusively to give a gene picture of the scope of the Ministry s work while telling the simple yet moving story of Joe Anderson Joe is a glid pilot who loses both his legs and the power of speech wh he is shot down over Arnhem, and the Ministry's docto and welfare officers literally set him on his feet again T Ministry wisely believe that the best way of looking aft their charges is to teach them as far as possible to look aft themselves, and it is typical of this policy of self help th many of the parts in the film, including Joe Anderson, a admirably played by the disabled and the staff of the Ministr Not the least promising of these amateur starlets is t director of the Roehampton limb fitting service as himse The film is at present being shown at the Leicester Squa Theatre, London, W C 2

HOSPITAL SERVICE PLAN

The London Association for Hospital Services has soug to bring its hospital service plan into line with present-da charges and fees It has set up a scheme whereby the who of the maintenance charges and professional fees, at th statutory rates, will be refunded for a contributor, or any his dependants, treated in a fee-controlled bed in a Nation Health Service hospital The existing schemes have al been adjusted so as to give larger refunds in respect of mai tenance charges, and there is now cover for minor operatio in a surgeon s consulting room or the patient s own hom for consultations and investigations, and for home nursi If a contributor incurs any expenses related to a conditi for which he has treatment in a general ward, the associati is prepared to make a discretionary grant For medi cases whose stay in hospital is prolonged the six week lim in any one year for treatment qualifying for benefit has be removed, and benefit is now paid for conditions hither excluded—pulmonary tuberculosis, contagious or notifia infectious diseases, and mental deficiency and mental disea necessitating certification These improvements apply equa to the special scheme for doctors The association's offi are at Tavistock House South, London, W C 1

ŒSOPHAGEAL SPEECH

A film on Œsophageal Speech after Laryngectomy has be produced for the Department of Health for Scotland coöperation with the ear nose, and throat department the Victoria Infirmary, Glasgow The film, which runs 10 minutes, was made with the aid of Mr T O Howie, surge to the department, and has three purposes (1) to reassu patients about to undergo operation, (2) to train and real patients after operation and (3) to demonstrate the princip underlying the operation

BIBLIOGRAPHICAL INDEX

The committee of the London group of the university a research section of the Library Association, believing th a good deal of bibliographical material may not be com to the attention of those who might wish to use it has co municated with the editor of the *Bibliographic Index*, w has replied that she would welcome particulars of all speciali bibliographies for inclusion in the index The committ hopes that librarians and others will send details to Editor, Bibliographic Index, the H W Wilson Compa 950–972, University Avenue, New York 52, N Y

FOOD CHARTS

Messrs Vitamins Ltd have produced four food chart designed for use by dietitians catering officers, domest science teachers and others concerned in planning meals a in elementary teaching The nutritive value of the separ foods is expressed as the number of hours' supply of t various vitamins and minerals which is provided for an adu person by 1 oz. of foodstuff These figures are obtained

---

1 (1) The Vitamins and Minerals of Meat and Fish (2) The Vi mins and Minerals in Dairy Produce (3) The Vitamins a Minerals in Vegetables and Fruits (4) The Vitamins a Minerals in Cereal Foods From Vitamins Ltd. Upper Ma London W 6 6d each (8d post free)

APPLICATION OF PSYCHOLOGY TO DERMATOLOGY

R M B MacKenna
M.A , M.D Camb , F R C P
PHYSICIAN IN CHARGE OF THE DERMATOLOGICAL DEPARTMENT, ST BARTHOLOMEW'S HOSPITAL, LONDON

Ida Macalpine
M.D Erlangen L R C P E
ASSOCIATE CHIEF ASSISTANT IN THE DEPARTMENT

Six years ago one of us wrote a paper intended to focus attention on psychological factors in dermatology (MacKenna 1944) We now try to specify more precisely the psychological factors involved in the production and cure of skin diseases

Ideally, this psychological and dermatological approach to skin disease should be a double approach made by a single clinician For reasons of training this is hardly ever possible Hence it is necessary to establish fruitful coöperation between the dermatologist and the clinical psychologist This may seem a banal statement, but in reality there might easily enter into such common work a sense of rivalry concerning the scientific priority and validity of the two disciplines Since some of the differences between the two approaches are fundamental, they will be discussed first Secondly, the actual task of the clinical psychologist to a skin department will be dealt with Thirdly, some scientific methods suitable for such work will be examined

RELATION BETWEEN DERMATOLOGIST AND PSYCHOLOGIST

First, psychology and dermatology must be considered to be on equal footing Both sides must acquire a true conviction that psychology is a scientific discipline We say "a true conviction" advisedly There is a deep-seated tendency to consider the tangible and visible as more apparent, and hence more true, than the intangible, which is often considered for this very reason to be obscure A further reason is that psychology is still widely denied the status of a science, and the misuse of psychology and the disregard of its potentially scientific value by dermatologists and psychologists alike is calculated to perpetuate this attitude It cannot be too strongly emphasised that psychology should not be looked upon as a common-sense adjuvant to dermatologists, but rather as a scientific instrument in dermatological research If psychology is relegated to the position of "yet another test," no deeper understanding of a truly psychosomatic connection can ever be reached On the other hand it is important, not only that psychiatrists should apply basic scientific principles in the evaluation of their work, but that, particularly in dermatology, their investigations should be linked with physiological research

A deprecatory attitude to psychology is apt to have serious consequences The psychologist is likely to be consulted as a last resort when no physical treatment has proved to be of avail He will thus see only specially selected cases which tend to blur his view, and lead to lopsided conclusions The disease mechanisms he is trying to isolate will be obscured by superimposed habit formations accumulated during the long period which has elapsed since the onset of the disease This is the more unnecessary since an early psychological diagnosis can be made by a well trained psychologist or psychiatrist in much the same way as a dermatological diagnosis Quite often this can be done in a short interview, the margin of error in a psychological diagnosis being not necessarily any greater than that in medicine generally We have found that if the psychiatrist attends the outpatient department, and if necessary adds a few casual questions to those of the dermatologist, it is often possible to obtain essential information while the patient —not realising that this is also a psychological interview—has not yet mobilised his conscious or unconscious defences

If a competitive spirit is allowed to enter into, or even replace, the coöperation between dermatologist and psychologist, it usually ends in each specialist claiming that any benefit to the patient is due solely to his particular treatment The value of a psychological approach will then be measured by the results of treatment Actually the evaluation of therapeutic results is a formidable scientific task and in every branch of medicine has to be approached with extreme caution In dermatology it is particularly unwise—however tempting—to draw definite conclusions about the cause of the disease from the results of either physical or psychological treatment, whether they be positive or negative It is extremely doubtful whether satisfactory results of treatment will reveal the cause of the eruption first because psychological factors enter into every physical treatment to some extent (whether recognised as such or not), or in other words the doctor patient relationship may far outweigh the benefit of a prescribed ointment , secondly, during psychological investigation or treatment an eruption of cutaneous origin may undergo spontaneous involution because of unrecognised somatic influences Alternatively, psychological tensions other than those directly responsible for a skin symptom may have been lessened by psychotherapy, so that the total strain on the personality may have been eased and the stress which had found expression in the symptom can now be borne without leading to somatic disturbance

Similarly, negative therapeutic results cannot be taken to exclude either physical or psychological causation It is a truism to say that physical illness refractory to physical treatment is yet a physical illness Similarly, if a psychotic proves inaccessible to psychological treatment, one does not conclude that his condition is not psychological. In skin patients in particular, there is often a nice balance of somatic and psychological factors , a change in either of them may tip the balance towards symptom resolution It is not of course intended to suggest that results of treatment cannot be taken into account at all when assessing the cause of a disease But a premature *post hoc propter hoc* must studiously be avoided

PLACE OF THE PSYCHOLOGIST IN DERMATOLOGY

The psychologist invading a skin department has a double function first, with the means at his disposal to help as many patients as possible in as short a time as possible secondly, to make investigations exact enough to merit the name of "scientific research" These two tasks are not identical.

By its nature, short psychotherapy is a hit or-miss method But these short cases, too, could be exploited in the interest of deeper understanding It is not enough to be content with positive results. It is necessary to assess the various mechanisms which are operative in the treatment, and to distinguish in psychological terms what has brought about the improvement There are a variety of curative factors at work in short psychotherapy , for example, reassurance, catharsis, "confession," the alleviation of anxiety or guilt, or ordinary suggestive influence (intentional or unintentional) The time factor, or the duration of treatment, must also be taken into account This is particularly true in psychotherapy of long duration, as for instance in psychoanalysis proper, or in group therapy, which may last 12–18 months, sometimes much longer It may be argued that a given skin disease has a tendency to burn

Medico-Legal Society

The annual dinner of this society is being held at the Savoy Hotel, London, W C 2, on Thursday, Jan 11, at 7 45 P M Further particulars may be had from the hon secretary, 40, Carey Street, W C 2

Chemotherapy of Tuberculosis

The Medical Research Council of Ireland is holding a colloquium on this subject in Dublin from July 10 to 13 The speakers will include Dr Marc Daniels and Dr P D'Arcy Hart (London), Prof G Domagk (Wuppertal Elberfeld), Dr W H Feldman (Mayo Foundation), and Dr Edgar Lederer (Paris) Further particulars will be found in our advertisement columns

Compensation for Practices

Doctors in Northern Ireland who wish to claim compensation for their practices and who have not yet received a claim form should apply to the Ministry of Health and Local Government, Stormont, Belfast, or to the Northern Ireland General Health Services Board 27, Adelaide Street, Belfast Details of those who are eligible and further particulars will be found in our advertisement columns

Prescription of Spectacles

Under the National Health Service (Supplementary Ophthalmic Services) Amendment (no 2) Regulations, 1950, the Minister of Health has laid down that, from Feb 1, where an ophthalmic practitioner or ophthalmic optician has caused an excessive cost to the service by prescribing lenses or glasses beyond those necessarily required by the patient, the Minister may, after investigation, direct that a sum be deducted from the remuneration of the practitioner or optician

CORRIGENDUM *Primary Streptomycin resistant Tuberculosis* —In fig 4 of the paper by Dr Tinne and Dr Henderson (Dec 30, p 901) the resistant strain is above the control

Births, Marriages, and Deaths

BIRTHS

BRANCH —On Dec 22 the wife of Dr W E R Branch—a daughter

DICKINSON —On Dec 13, in London to Dr Barbara Dickinson (née Thomas) wife of Mr J R Dickinson F R C S —a son

GAIRDNER —On Dec 24 the wife of Dr Douglas Gairdner—a daughter

GRIMBLY —On Dec 12 in London to Dr Florence Chouler wife of Dr Alan Grimbly—a son

HAMILTON —On Dec 17 in New York the wife of Dr Leonard Hamilton—a daughter

HAVELOCK —On Dec 20 in Liverpool to Dr Joyce Havelock (née Buck) wife of Mr Brian Havelock—a son

HAWKSLEY —On Dec 29 in London, the wife of Dr J C Hawksley —a daughter

IMRIE —On Dec 24, at Guildford the wife of Dr D A Imrie —a daughter

JAMES —On Dec 28, in Birmingham, the wife of Dr Ronald James —a son

MACLEOD —On Dec 28, in London the wife of Dr W M Macleod —a son

PRANKERD —On Dec 23 in London, the wife of Dr T A J Prankerd—a son

RANDALL —On Dec 23 at Beckenham Kent the wife of Dr Keith Randall—a daughter

RIGDEN —On Dec 21, the wife of Dr B G Rigden—a son

SARGENT —On Dec 18 at Salisbury the wife of Dr David Sargent —a son

SLADEN —On Dec 28 at Clacton the wife of Dr F J Sladen —a daughter

MARRIAGES

CAMPBELL—POUND —On Dec 23, David George Robertson Campbell B M to Peggie Pound

WOLFF—KEENAN —On Nov 17 in London Frederick W Wolff, M B to Catherine Bernadette Keenan

DEATHS

ABERCROMBIE —On Dec 26 Robert Heron Abercrombie, M B Glasg aged 61

COOPER —On Dec 21 William Francis Cooper M B Camb

COUTTS —On Dec 19 at St Helier Jersey, Duncan Coutts M D Aberd F R C O G lieut -colonel I M S retd aged 68

GIRDLESTONE —On Dec 30 Gathorne Robert Girdlestone M A D M Oxfd F R C S aged 69

GULLY —On Dec 28 in London Robert Cullum Gully M D Lond

HARRIS —On Dec 26 in London Sampson George Victor Harris M D Durh D P H aged 85

HEATH —On Dec 23 at Barmouth John Rippiner Heath B A Camb M R C S aged 63

MARTIN —On Dec 27, at Exmouth Claude Buist Martin C M G M B Edin colonel R A M C retd aged 81

MITCHELL —On Dec 20 Albert Waldegrave Mitchell M R C S

PANTON —On Dec 27 at Bourne End Bucks Philip Noel Panton Kt M A M B Camb

THOMAS —On Dec 27 at Wembley Albert Edward Thomas M A D M Oxfd D P H Barrister at Law

WARRICK —On Dec 21 in London Robert Walter Warrick M B Lond

Diary of the Week

JAN 7 TO 13

Monday, 8th

INSTITUTE OF PSYCHIATRY, Maudsley Hospital Denmar S E 5
5 30 P M Dr E Stengel Lecture-demonstration
MEDICAL SOCIETY OF LONDON 11, Chandos Street, W 1
8 30 P M Dr Keith Simpson Mr Ivan Magill, D A Unex Death Following Operation

Tuesday, 9th

ROYAL COLLEGE OF PHYSICIANS Pall Mall East S W 1
5 P M Dr H J Anderson Tuberculosis of the Peric (First Goulstonian lecture)
INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle W C 2
5 P M Dr J O Oliver The Pyogenic Cocci in Dermatol
CHELSEA CLINICAL SOCIETY
7 P M (South Kensington Hotel 47 Queen s Gate Terrace, Mr Ebbe Munck Danish Exploration in N Greenland (Coloured cinematograph film)

Wednesday, 10th

INSTITUTE OF DERMATOLOGY
5 P M Dr C W McKenny X ray Technique
ROYAL FACULTY OF PHYSICIANS AND SURGEONS 242 St Street Glasgow
5 P M Sir John Parkinson Symptoms in Cardiac Diagn

Thursday, 11th

ROYAL COLLEGE OF PHYSICIANS
5 P M Dr Anderson Tuberculosis of the Pericardium Goulstonian lecture)
ST GEORGE S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner
4 30 P M Psychiatry lecture demonstration
ROYAL ARMY MEDICAL COLLEGE, John Islip Street S W 1
5 P M Sir Lionel Whitby Significance of Anæmia
INSTITUTE OF DERMATOLOGY
5 P M Dr J O Oliver Pathology
INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray s Inn W C 1
5 P M Air Commodore E D D Dickson Otitic Barotra
LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant Live
8 P M Dr O F Thomas Dr R M Todd Dr C A St Chemotherapy in Tuberculosis

Appointments

AINSLIE, DEREK, M A M B Camb F R C S D O M S asst. o mic surgeon (consultant) Middlesex Hospital London

BATEMAN D V M B Camb , D A anæsthetist He Hospital and Bishop s Stortford Hospital

BENSON R C S M B Lond M R C P general physician Green Hospital London

BEYNON D W M B Lond M R C P D C H pædiatrician t in areas of Bournemouth and East Dorset, West Dor Salisbury group of hospitals

CLANICK F E , M B St And , D A anæsthetist Bethna Hospital

DARKE, G H M B Lond , F R C S E senior surgical r Bristol clinical area

FISK G R M B Lond , F R C S , F R C S E orthopædic s St Margaret s Hospital Epping

FOXEN, F H M F R C S D L O ear, nose and throat s Enfield War Memorial Hospital

GRENVILLE HARRY M R C S D A anæsthetist, London Hospital and St Margaret s Hospital Epping

HALSTEAD JOAN M B Manc venereologist Croydon Hospital

HERBERT GLADYS M R C S D P H senior asst M O m and child welfare Newport Mon

HERINGTON GODFREY M B Lond D A anæsthetist, W Hospital

HUNTER W R CH M Lpool F R C S consultant general s Walton Hospital Liverpool

JACKSON H H W M B Lond F R C S senior surgical r South Somerset clinical area

KENTON BERNARD M R C S , D C H D A anæsthetist Green Hospital

KING TURNER C J M R C S appointed factory doctor I district Glos

LEWIS W J , M R C S D A anæsthetist (S H M O) Sou Hospital Bristol

McKELVIE I L M A Camb M R C S D M R radiologist District Hospital

MURRAY G H , M B Edin M R C P E consultant chest ph North Liverpool area

NELSON JONES ARCHIBALD M D Lond M R C P general ph Forest Hospital and Woodford Jubilee Hospital

READ A M M B Lond asst chest physician Portsmout

ROWLES AMELIA M B Wales D I H , asst M O H Walsall

SAINSBURY H S K M R C S asst M O H Herefordshire

SAVAGE T R M A B M Oxfd M R C P D C H pædia Oldchurch Hospital and Wanstead Hospital

SETH SMITH D W , M R C S D M R radiologist Norwo District Hospital

STEINGOLD LOUIS M B Glasg pathologist St Andrew s H Bow

SUTCLIFFE MARY M A M B Camb D P H deputy division and deputy M O H S 1 urban districts Surrey

SWINSON A E P M B Belf S H M O psychiatrist Hospital Wells

WAUCHOB D W M B Belf D P H deputy M O H Blackp

WICKES I G M A M B Camb M R C P D C H pædia South East Essex group of hospitals

APPLICATION OF PSYCHOLOGY TO DERMATOLOGY

R M B MacKenna
M A , M D Camb , F R C P
PHYSICIAN IN CHARGE OF THE DERMATOLOGICAL DEPARTMENT, ST BARTHOLOMEW'S HOSPITAL, LONDON

Ida Macalpine
M D Erlangen, L R C P E
ASSOCIATE CHIEF ASSISTANT IN THE DEPARTMENT

Six years ago one of us wrote a paper intended to focus attention on psychological factors in dermatology (MacKenna 1944) We now try to specify more precisely the psychological factors involved in the production and cure of skin diseases

Ideally, this psychological and dermatological approach *to skin disease should be a double approach* made by a single clinician For reasons of training this is hardly ever possible Hence it is necessary to establish fruitful coöperation between the dermatologist and the clinical psychologist This may seem a banal statement, but in reality there might easily enter into such common work a sense of rivalry concerning the scientific priority and validity of the two disciplines Since some of the differences between the two approaches are fundamental, they will be discussed first Secondly, the actual task of the clinical psychologist to a skin department will be dealt with *Thirdly*, some scientific methods suitable for such work will be examined

RELATION BETWEEN DERMATOLOGIST AND PSYCHOLOGIST

First, psychology and dermatology must be considered to be on equal footing Both sides must acquire a true conviction that psychology is a scientific discipline We say " a true conviction " advisedly There is a deep seated tendency to consider the tangible and visible as more apparent, and hence more true, than the intangible, which is often considered for this very reason to be obscure A further reason is that psychology is still widely denied the status of a science, and the misuse of psychology and the disregard of its potentially scientific value by dermatologists and psychologists alike is calculated to perpetuate this attitude It cannot be too strongly emphasised that psychology should not be looked upon as a common sense adjuvant to dermatologists, but rather as a scientific instrument in dermatological research If psychology is relegated to the position of " yet another test," no deeper understanding of a truly psychosomatic connection can ever be reached On the other hand it is important, not only that psychiatrists should apply basic scientific principles in the evaluation of their work, but that, *particularly in* dermatology, their investigations should be linked with physiological research

A deprecatory attitude to psychology is apt to have serious consequences The *psychologist* is likely to be consulted as a last resort when no physical treatment has *proved to be of avail He* will thus see only specially selected cases which tend to blur his view, and lead to lopsided conclusions The disease mechanisms he is trying to isolate will be obscured by superimposed habit formations accumulated during the long period which has elapsed since the onset of the disease This is the more unnecessary since an early psychological diagnosis can be made by a well trained psychologist or psychiatrist in much the same way as a dermatological diagnosis Quite often this can be done in a short interview, the margin of error in a psychological diagnosis being not necessarily any greater than that in medicine generally We have found that if the psychiatrist attends the outpatient department, and if necessary *adds a few* casual questions to those of the dermatologist, it is often possible to obtain essential information while the patient —not realising that this is also a psychological interview— has *not yet* mobilised his conscious or unconscious defences

If a competitive spirit is allowed to enter into, or even replace, the coöperation between dermatologist and psychologist, it usually ends in each specialist claiming that any benefit to the patient is due solely to his particular treatment The value of a psychological approach will then be measured by the results of treatment Actually the evaluation of therapeutic results is a formidable scientific task, and in every branch of medicine has to be approached with extreme caution In dermatology it is particularly unwise—however tempting—to draw definite conclusions about the cause of the disease from the results of either physical or psychological treatment, whether they be positive or negative It is extremely doubtful whether satisfactory results of treatment will reveal the cause of the eruption first, because psychological factors enter into every physical treatment to some extent (whether recognised as such or not), or in other words the doctor patient relationship may far outweigh the benefit of a prescribed ointment , secondly, during psychological investigation or treatment an eruption of cutaneous origin may undergo spontaneous involution because of unrecognised somatic influences *Alternatively*, psychological tensions other than those directly responsible for a skin symptom may have been lessened by psychotherapy, so that the total strain on the personality may have been eased and the stress which had found expression in the symptom can now be borne without leading to somatic disturbance

Similarly, negative therapeutic results cannot be taken to exclude either physical or psychological causation It is a truism *to say that physical illness refractory to* physical treatment is yet a physical illness Similarly, if a psychotic proves inaccessible to psychological treatment, one does not conclude that his condition is not psychological In skin patients in particular, there is often a nice balance of somatic and psychological factors , a change in either of them may tip the balance towards symptom resolution It is not of course intended to suggest that results of treatment cannot be taken into account at all when assessing the cause of a disease But a premature *post hoc propter hoc* must studiously be avoided

PLACE OF THE PSYCHOLOGIST IN DERMATOLOGY

The psychologist invading a skin department has a double function first, with the means at his disposal to help as many patients as possible in as short a time as possible secondly, to make investigations exact enough to merit the name of " scientific research " These two tasks are not identical

By its nature, short psychotherapy is a hit or-miss method But these short cases, too, could be exploited in the interest of deeper understanding It is not enough to be content with positive results It is necessary to assess the various mechanisms which are operative in the treatment, and to distinguish in psychological terms what has brought *about the improvement* There are a variety of curative factors at work in short psychotherapy , for example, reassurance, catharsis, " confession," the alleviation of anxiety or guilt, or ordinary *suggestive influence* (intentional or unintentional) The time factor, or the duration of treatment, must also be taken into account This is particularly true in psychotherapy of long duration, as for instance in psychoanalysis proper, or in group therapy, which may last 12–18 months, sometimes much longer It may be argued that a given skin disease has a tendency to burn

Medico-Legal Society

The annual dinner of this society is being held at the Savoy Hotel, London, W C 2 on Thursday, Jan 11, at 7 45 P M Further particulars may be had from the hon secretary, 40 Carey Street, W C 2

Chemotherapy of Tuberculosis

The Medical Research Council of Ireland is holding a colloquium on this subject in Dublin from July 10 to 13 The speakers will include Dr Marc Daniels and Dr P D'Arcy Hart (London), Prof G Domagk (Wuppertal Elberfeld), Dr W H Feldman (Mayo Foundation), and Dr Edgar Lederer (Paris) Further particulars will be found in our advertisement columns

Compensation for Practices

Doctors in Northern Ireland who wish to claim compensation for their practices and who have not yet received a claim form should apply to the Ministry of Health and Local Government Stormont, Belfast, or to the Northern Ireland General Health Services Board, 27, Adelaide Street, Belfast. Details of those who are eligible and further particulars will be found in our advertisement columns

Prescription of Spectacles

Under the National Health Service (Supplementary Ophthalmic Services) Amendment (no 2) Regulations, 1950, the Minister of Health has laid down that, from Feb 1, where an ophthalmic practitioner or ophthalmic optician has caused an excessive cost to the service by prescribing lenses or glasses beyond those necessarily required by the patient, the Minister may, after investigation, direct that a sum be deducted from the remuneration of the practitioner or optician

CORRIGENDUM *Primary Streptomycin resistant Tuberculosis* —In fig 4 of the paper by Dr Tinne and Dr Henderson (Dec 30, p 901) the resistant strain is above the control

Births, Marriages, and Deaths

BIRTHS

BRANCH —On Dec 22 the wife of Dr W E R Branch—a daughter

DICKINSON —On Dec 13, in London to Dr Barbara Dickinson (née Thomas) wife of Mr J R Dickinson F R C S —a son

GAIRDNER —On Dec 24 the wife of Dr Douglas Gairdner—a daughter

GRIMBLY —On Dec 12 in London to Dr Florence Chouler wife of Dr Alan Grimbly—a son

HAMILTON —On Dec 17 in New York the wife of Dr Leonard Hamilton—a daughter

HAVELOCK —On Dec 20 in Liverpool to Dr Joyce Havelock (née Buck) wife of Mr Brian Havelock—a son

HAWKSLEY —On Dec 29, in London the wife of Dr J C Hawksley —a daughter

IMRIE —On Dec 24, at Guildford the wife of Dr D A Imrie —a daughter

JAMES —On Dec 28 in Birmingham the wife of Dr Ronald James —a son

MACLEOD —On Dec 28 in London the wife of Dr W M Macleod —a son

PRANKERD —On Dec 23, in London the wife of Dr T A J Prankerd—a son

RANDALL —On Dec 23 at Beckenham, Kent, the wife of Dr Keith Randall—a daughter

RIGDEN —On Dec 21 the wife of Dr B G Rigden—a son

SARGENT —On Dec 18 at Salisbury the wife of Dr David Sargent —a son

SLADEN —On Dec. 28 at Clacton the wife of Dr F J Sladen —a daughter

MARRIAGES

CAMPBELL—POUND —On Dec 23 David George Robertson Campbell B M to Peggie Pound

WOLFF—KEENAN —On Nov 17 in London Frederick W Wolff, M B to Catherine Bernadette Keenan

DEATHS

ABERCROMBIE —On Dec 26 Robert Heron Abercrombie M B Glasg aged 61

COOPER —On Dec 21 William Francis Cooper M B Camb

COUTTS —On Dec 19, at St Helier Jersey Duncan Coutts M D Aberd F R C O G lieut -colonel I M S retd, aged 68

GIRDLESTONE —On Dec 30 Gathorne Robert Girdlestone M A D M Oxfd F R C S aged 69

GULLY —On Dec 28 in London Robert Cullum Gully M D Lond

HARRIS —On Dec 26 in London Sampson George Victor Harris M D Durh D P H aged 85

HEATH —On Dec 23 at Barmouth John Rippiner Heath B A Camb M R C S aged 63

MARTIN —On Dec 27 at Exmouth Claude Buist Martin C M G M B Edin colonel R A M C retd aged 81

MITCHELL —On Dec 20 Albert Waldegrave Mitchell M R C S

PANTON —On Dec 27 at Bourne End Bucks Philip Noel Panton Kt M A M B Camb

THOMAS —On Dec 27 at Wembley Albert Edward Thomas M A D M Oxfd D P H Barrister at Law

WARRICK —On Dec 21, in London Robert Walter Warrick M B Lond

Diary of the Week

JAN 7 TO 13

Monday, 8th

INSTITUTE OF PSYCHIATRY, Maudsley Hospital Denmark
S E 5
5 30 P M Dr E Stengel Lecture-demonstration

MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr Keith Simpson Mr Ivan Magill, D A. Unexp
Death Following Operation

Tuesday, 9th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East S W 1
5 P M Dr H J Anderson Tuberculosis of the Pe
(First Goulstonian lecture)

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle St
W C 2
5 P M Dr J O Oliver The Pyogenic Cocci in Dermatolog

CHELSEA CLINICAL SOCIETY
7 P.M (South Kensington Hotel, 47, Queen s Gate Terrace, S
Mr Ebbo Munck Danish Exploration in Nor
Greenland. (Coloured cinematograph film)

Wednesday, 10th

INSTITUTE OF DERMATOLOGY
5 P M Dr C W McKenny X ray Technique

ROYAL FACULTY OF PHYSICIANS AND SURGEONS 242 St Vi
Street Glasgow
5 P M Sir John Parkinson Symptoms in Cardiac Diagnos

Thursday, 11th

ROYAL COLLEGE OF PHYSICIANS
5 P M Dr Anderson Tuberculosis of the Pericardium (
Goulstonian lecture)

ST GEORGE S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S
4 30 P M Psychiatry lecture demonstration

ROYAL ARMY MEDICAL COLLEGE John Islip Street S W 1
5 P M Sir Lionel Whitby Significance of Anæmia

INSTITUTE OF DERMATOLOGY
5 P M Dr J O Oliver Pathology

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray s Inn R
W C 1
5 P M Air Commodore E D D Dickson Otitic Barotraum

LIVERPOOL MEDICAL INSTITUTION 114, Mount Pleasant, Liverp
8 P M. Dr O F Thomas Dr R M Todd, Dr C A St
Chemotherapy in Tuberculosis

Appointments

AINSLIE, DEREK M A M B Camb, F R C S D O M S asst oph mic surgeon (consultant) Middlesex Hospital London

BATEMAN D V M B Camb D A anæsthetist Hay Hospital and Bishop s Stortford Hospital

BENSON R C S M B Lond M R C P general physician Green Hospital London

BEYNON D W M B Lond M R C P, D C H pædiatrician to in areas of Bournemouth and East Dorset, West Dorset Salisbury group of hospitals

CLYNICK F E M B St And D A anæsthetist Bethnal Hospital

DARKE, G H M B Lond F R C S E senior surgical reg Bristol clinical area

FISK G R M B Lond, F R C S, F R C S E orthopædic sur St Margaret s Hospital Epping

FOXEN E H M F R C S, D L O ear nose and throat sur Enfield War Memorial Hospital

GRENVILLE HARRY M R C S D A anæsthetist London Hospital and St Margaret s Hospital, Epping

HALSTEAD JOAN M B Manc venereologist Croydon G Hospital

HERBERT GLADYS M R C S D P H senior asst M O, mat and child welfare Newport Mon

HERINGTON GODFREY, M B Lond D A anæsthetist, War Hospital

HUNTER W R CH M Lpool F R C S consultant general su Walton Hospital, Liverpool

JACKSON H H W M B Lond F R C S senior surgical reg South Somerset clinical area

KENTON BERNARD M R C S D C H D A anæsthetist B Green Hospital

KING TURNER C J M R C S appointed factory doctor Fa district Glos

LEWIS W J, M R C S D A anæsthetist (S H M O) South Hospital Bristol

MCKELVIE I L M A Camb M R C S D M R radiologist District Hospital

MURRAY G H M B Edin M R C P E consultant chest phys North Liverpool area

NELSON JONES ARCHIBALD M D Lond M R C P general phys Forest Hospital and Woodford Jubilee Hospital

READ A M M B Lond asst chest physician Portsmouth

ROWLES AMELIA M B Wales D P H asst M O H Walsall

SAINSBURY H S K M R C S asst M O H Herefordshire

SAVAGE T R M A B M Oxfd M R C P D C H pædiatr Oldchurch Hospital and Wanstead Hospital

SETH SMITH D W, M R C S D M R radiologist Norwood District Hospital

STEINGOLD LOUIS M B Glasg pathologist St Andrew s Hos Bow

SUTCLIFFE MARY M A M B Camb D P H deputy divisiona and deputy M O H S E urban districts Surrey

SWINSON A F P M B Belf S H M O psychiatrist M Hospital Wells

WAUCHOB D W M B Belf D P H deputy M O H Blackpo

WICKEN I G M A M B Camb M R C P D C H pædiatr South East Essex group of hospitals ppearance or formation of a symptom owes its existence the first place always to what is called the primary ain Primary gain is an attempt of the mental apparatus nder stress to secure or make possible the continued xistence of the personality as a whole Secondary gain of a minor order compared with primary gain, though one the less welcome when procurable The social ain in psychosomatic disease, in contradistinction to ysteria, can be expected to have much less importance, ven to be absent

If psychology is to make any fundamental contribution o dermatology it is essential to establish a clear differntial diagnosis between a psychoneurotic and a psycho omatic manifestation Psychoneurotic symptoms occur hen repression is faulty—i e , when repressed unconcious conflicts force a way through mental defences To apply the psycho analytic structure of the psychoeuroses to all skin manifestations will prove a stumbling lock to research into skin conditions It is at the same ime a doubtful service to psycho-analysis itself Somatic anifestations are more primitive, and their mechanism s simpler, than the elaborate mechanism of the psycho eurose Somatic manifestations such as skin disease re mostly "affect equivalents"—they may be a isguised discharge of anxiety, fear, rage, or any other imple affect They are due to a lack of discharge through conscious channels or to over-excitation and hence damming up It is well to admit, even to stress, that the detailed mechanism of such affect equivalents is not fully understood, and that much work will have to be done to explain in detail such " somatic behaviour " Research on these lines must include a study of emotional expressions and their disturbances, both from the psychological and physiological angle The following is an example of a simple affect equivalent

A woman of 45 had been suffering for 3 months from blepharitis, conjunctivitis and itching round the eyes She was for all practical purposes a well-adjusted woman—a wife a mother of two grown up children and doing a part-time clerical job She could not account for her symptoms, but on questioning it appeared that the trouble had started gradually about three weeks after the loss of her father, to whom she the eldest daughter, had been very much attached. Asked what the loss of her father meant to her she said that it had been a very great blow, and she volunteered the information that she had not shown much sorrow at the time of his death because she wanted to spare her mother s feelings She added that her own family had been surprised to find her so composed. Being given the opportunity "to let go during two therapeutic sessions her eye symptoms cleared up

The mechanism of the itching and inflammation round the patient's eyes may be looked upon as a "retention formation" in so far as an emotional response which had been denied an outlet at the proper time was later discharged in a less intense but more protracted and disguised form

Psycho analysis is the only method in which investigation and treatment coincide. The classical method cannot, for obvious reasons of time, be carried out in an outpatient department , but something approaching the classical method may be attempted in special cases What is often described as "short psycho analytic therapy" is fundamentally different (Macalpine 1950) Any therapy directed against a symptom is basically different from the classical method, in which the personality is allowed to unfold without any interference by the therapist or concentration on the symptom Not even in classical psycho analysis are all the therapeutic agents established beyond doubt It has to be admitted, therefore, that our methods of treatment need clarification, and their rationale more exact formulation

The type of treatment will eventually depend on forming an exact diagnosis if a symptom is psychoneurotic the classical method of psycho analysis is the ideal form of treatment , if however a psychosomatic symptom is—as we believe—of a different order, then other types of treatment are indicated

METHOD

Once sufficient knowledge has been assembled about the psychological aspect of a certain skin disease it may be possible to proceed to generalisations and eventually to establish certain reaction types , but it seems timely to warn against a too ready correlation of diseases with personality types In the literature skin patients are often referred to as " obsessionals " without any indication as to whether this is to be understood as a patient suffering from an obsessional neurosis or whether it is meant to describe with a convenient label a character make up within the normal range Even if it is ascertained that a person suffers from an obsessional neurosis, his skin symptom may yet be—and often is—a hysterical formation , or it may be superimposed and of different origin, and of an independent mechanism A depressed person may be easy to recognise , but from the standpoint of psychodynamics various forms of depression can be differentiated, reflecting disturbances at different levels, and having an entirely distinct significance If a skin patient is depressed the important question is whether the skin condition is a sequel to, the cause of, or coexistent with the depression Needless to say the patient's opinion cannot be taken as valid. Most skin patients insist that their depression is the consequence of an irritating, incapacitating, or disfiguring skin complaint But their depression often persists after the skin has cleared up

These considerations indicate that much must be done before we can hope to associate certain skin diseases with definite psychological constellations The urge to fasten certain skin diseases on to certain types is fraught with all the dangers of scientific short-cuts

Papers have been published in which, for instance, eczema is said to be due to aggressiveness or aggression This implies that one particular drive is considered the causative factor in the production of a skin disease But the aggressive drive is not only normal but a prerequisite of a normal personality, and it follows that no illness can be traced to it It is sometimes stated that a patient's aggression has reached abnormal heights To take an analogy from the physical side, this equals the statement that certain skin eruptions are due to, say, histamine Only through recognition of the vicissitudes aggression has undergone in the economic or dynamic household of the mental apparatus can we acquire deeper understanding of the part it plays in the formation of skin symptoms. If it were only a matter of an undue inborn pathological amount of aggression, one would more logically expect such a patient to become a violent criminal than a suffering skin patient If the dynamic principle of the mental apparatus is disregarded, we are thrown back once more into pre Freudian days of rigid syndromes and their description. So whether there is too much or too little aggressiveness (and the too little, although less often emphasised, may be the more serious and ominous of the two), an assessment of the quantitative factor alone will not better our understanding, but will eventually place us in a constitutional impasse It was precisely this constitutional impasse which so dissatisfied Freud that he started to work on dynamic lines In his early days hysteria was regarded as a constitutional degeneration. The pertinent question to be raised is why in any given case is there an insufficient outlet for or sublimation of, or mental defence against, aggression , or again, why has a skin patient so little tolerance to it that a pathological discharge into somatic channels takes place.

To give another illustration, it is often stated that skin patients have increased masochistic tendencies It itself out during such a period, irrespective of any other influence Evaluation of results, if they are to carry conviction, must therefore take this time factor into consideration

Other factors, too, deserve closer study We have found, for instance, that some skin conditions may disappear without any alteration in the personality A patient with pruritus may report as a first sign of improvement that his itch is no longer so severe, that the impulse to scratch is no longer so urgent or compulsive, or that it seems to come more from the surface than from inside the body In other patients, such as those with eczema of long standing, a personality change may be conspicuous before there is any symptomatic improvement Such patients report that their skin lesion is unchanged but that they feel happier in themselves and more capable of satisfactory adjustment, either in their work or in their social contacts The improvement of the skin disease lags behind a general improvement Some patients, on the other hand, relinquish their symptoms dramatically

A woman, aged 30, had suffered for 18 months from severe eczematous lesions, with an excruciating itch of both fore arms, wrists and neck, where she had extensive scratch marks After the third psychological interview—to the surprise of the therapist—she was clear of her eczema and free from itching, with only a few healing scratch marks left She had been violently opposed to psychological treatment

We agree warmly with Stokes and Beerman (1948) that clinical observation during the interview is a valuable aid to psychological diagnosis It can often be found that an itching skin complaint will behave like a sounding board when a certain topic is mentioned

In a woman with acute dermatitis of the whole neck the lesion became purple and started to exude profusely when she related humiliating situations to which she had been exposed, and to which she could not react at the time of their happening She was quite unaware of this "organ language", in fact she excused herself for rubbing and wiping her neck during the interview by explaining that "for no reason what ever" these bouts of itching and weeping of her neck would suddenly occur

In another case of acute generalised eczema, a woman of 21 started to scratch frantically whenever her relationship to her father was discussed

Thus even from "short-treatment" cases considerable insight can be gained, but deeper understanding can be reached from those patients who can be studied over a long period

As stressed above, results of treatment have unjustifiably been taken as methods of investigation Not only have they been unduly used to explain the cause of a skin disease, but a further error in method has crept into some of these investigations the literature shows that therapists are inclined to conclude that what has cured the patient is the particular brand of psychology in which they themselves are trained and naturally believe These disputes between psychologists of various schools have the more prejudicial effect on psychosomatic research in that they tend to focus attention too exclusively on mental conflicts and their psychic resolution The illness, its symptoms, and its solution or cure are regarded as occurring in the psychological sphere According to this view, a mental conflict can be expressed in words, it has a meaning and it is easily understandable, when somatic disturbances appear they serve to express or dramatise mental conflict For instance, a patient may have a skin rash on his hands, his symptom represents symbolically, in the form of a compromise, a conflict between wishing to do and defending against doing a forbidden deed Such would be the underlying dynamics of the hysterical symptom formation according to Freud As in the case of a phobia, the symptom represents a compromise between two opposing tendencies, and, of course, somatic manifestations such as skin disease may have such a conflict meaning

A man, aged 35, was seen with a circumscribed eczematous lesion without scratch marks over the knuckles of the first and second digits of his hands He described the sensation of this lesion as irritating, not violently nor constantly, but occurring in bouts,-particularly at periods when he was idle. To relieve this itching sensation he said he never scratched violently at any time, but "I put my hands into my trouser pockets so far that the lesion rubs gently against the seam and," he continued, "I have to rub it against something which is soft and firm at the same time" His marital relations had been severely curtailed (coinciding with the lesion on the hand) because of a protracted illness on the part of his wife Owing to a frustration of his hetero sexual life the temptation arose to revert to the forbidden masturbatory practices of adolescence His skin rash represented both a gratification and the defence against it, he was altogether unaware of the symbolism of rubbing against something 'firm and yet soft" The eczema on his hands cleared up completely after six sessions

Such cases follow the classical symptom formation which Freud has described for the psychoneuroses Because the symbolism of such psychoneurotic symptoms can relatively easily be discerned, there is a tendency among workers in this field to read such a symbolic content into all skin manifestations This has led many to assume tacitly that all psychosomatic illnesses can somehow or other be considered as psychoneuroses But somatic manifestations are by no means always, or even predominantly, psychoneurotic (Glover 1949) In contradistinction to psychoneurotic symptoms they have no meaning, no psychic content, and their formation does not follow the classical pattern indicated by Freud for the psychoneuroses Indeed, it is well to remember that the incidence of psychosomatic disease is far higher than the incidence of the psychoneuroses

The neglect of purely clinical and physiological data when skin disease is looked upon as of the same order as the psychoneuroses may be illustrated in this way

Some writers describe adult endogenous eczema as being based on certain conflict patterns of an adult preconscious type—for instance, over-dependence'independence Certain types of infantile eczema (of the eczema-asthma-hay-fever type) cannot be accounted for by the same mechanism unless of course the observer assumes that in the case of infantile eczema a mental apparatus of such maturity exists that mental conflicts of an adult preconscious order can occur Yet infantile and adult eczema seem to constitute a nosological entity, and no theory which does not embrace both types can be considered complete or valid The mental complexity of the adult observer may easily mislead him into reading his own complicated mental structure into the simpler mental structure of the infant This tendency has led some psycho-analysts *into assuming adult functioning* in the infantile body/mind unit But this attitude seems to brush aside the basic fact that an immature structure cannot be taken to have adult function Form and function are but two aspects of the same thing, they are intimately linked up together A baby in arms cannot conceivably experience conflicts of the same order as the adult The carrying back of adult conception into the first year of life (as is necessary if adult and infantile eczema are to be correlated on a conflict interpretation) furthermore makes nonsense of dynamic developmental approach in psychology

Moreover, if a skin symptom is always considered to be psychoneurotic, the social gain of such a symptom (i e, the quest for sympathy, commiseration, love, and attention, or the infliction of punishment or revenge on the environment) is often overemphasised by the observer It has even led to skin disease being explained *solely* on the grounds of social gain This "secondary gain" does of course exist, it is, in fact a regular occurrence of some importance in hysteria But even in hysteria the secondary gain is, after all only secondary The

RECENT HISTORY OF CORONARY DISEASE[1]

J N MORRIS
M A Glasg, M R C P, D P H
From the Social Medicine Research Unit, Medical Research Council

(*Concluded from p 7*)

Questions Arising

The volume of evidence that can be presented from his single study is small in relation to the size of the problem and its complexity. And the present findings may be disqualified by the limitations previously mentioned (or by others that have been overlooked entirely). Nevertheless questions must be put about the bearing of these seemingly paradoxical findings on the current picture of the pathogenesis of coronary heart disease, and the suggestion that coronary atheroma has decreased must be explored.

NATURAL HISTORY OF CORONARY HEART DISEASE

According to the current view there are, locally, three main interacting elements in ischæmic heart disease (Blumgart 1943, Blumgart et al 1940, Friedberg 1949, Horn and Finkelstein 1940, Leary 1934, Parsons Smith 1950, Saphir et al. 1935, Welch 1920, Winternitz et al. 1933). These are

1. Atheroma, with narrowing of the coronary arteries, vascularisation of the intima, necrosis, and hæmorrhage,
2. Recent and old occlusion of the arteries,
3. The collateral circulation,

and their interaction is modified by conditions affecting the cardiac output and the demands on it.

Of these three, occlusion is crucial in determining the transition from the merely pathological to the clinical, for the production of the heart disease here considered. The occlusion, in turn, whether or not it can result from sclerotic narrowing alone (and this may have been absolutely commoner and relatively more important forty years ago), is due more often to coronary thrombosis, variously produced, and the first line of speculation must be based on the proposition that the central cause of ischæmic heart disease and of its increase lies in coronary thrombosis and the occlusion it causes.

The thrombosis and the atheroma are obviously related and are usually regarded as the "acute" and "chronic" phases of one "disease"—whence the notion (if only implicit) of "arteriosclerotic" heart disease. The atheroma is the basis of the clotting, which is a complication of the degeneration in the vessel, the more the atheroma the greater is the likelihood of thrombosis and occlusion, and the heart disease is thus the inevitable end result of the advancing degeneration. The present observations, however, raise the question whether this notion is any longer particularly useful. If there has been an increase in the heart disease, if the atheroma of the victims of the heart-disease is not qualitatively different from the atheroma of the rest of the population, and if the trends shown in tables II and III are generally confirmed—even if only to the extent of showing that there has been no increase of atheroma—then the notion of arteriosclerotic heart disease would be of historical interest only. The character of the disease has changed, it seems, the two phases have become dissociated. Indeed, with fewer eligible for the heart-disease—i e, fewer with advanced atheroma—more seem to suffer from it. This would be a general proposition. Even if the dissociation has occurred in not more than one population (which has nevertheless shared in the general increase of the heart disease), it must still be considered whether the notion was not too simple in the first place. Finally, there are many who remain unconvinced that there has been any increase of ischæmic heart disease during this century. But there is no suggestion that it is in fact becoming more rare. On this basis alone the possibility of a decrease in coronary atheroma must raise questions on the meaningfulness of many of today's assumptions about the pathogenesis of the heart disease. More cogent reasons for doubt than anything said here are provided by the common observations that only a fraction of those with severe coronary atheroma have the heart disease (Blumgart 1943, White et al 1950, Wyn Jones 1931), and that those who do have the heart disease may have only moderately severe atheroma (not to mention the unfortunates with a solitary plaque), whereas many with very severe degeneration escape. Explanation of such phenomena in terms of a particularly effective anastomotic circulation may partly be begging the question, because it may only be with repeated occlusion that the question commonly arises. Moreover the thrombosis and the heart disease seem to be increasing as much at earlier ages as in later life, when there is manifestly more degeneration, and perhaps more in the middle aged than in the very old.

What then is the relation of coronary thrombosis and heart disease to coronary atheroma? Perhaps advanced atheroma provides the basis, is the predisposing factor, but what will precipitate the heart disease, who of the many so predisposed will develop the thrombosis/occlusion, and when, may not be a function simply and directly of the atheroma or of its severity. There may be a necessary and critical level of atheroma (Leary 1934, Saphir et al 1935) that is the *condition* of the heart-disease, but beyond that other factors are possibly more important as *causes* of it. The indication may therefore be to pay less attention to the atheroma which predisposes, and more to the thrombosis which precipitates, the heart disease.

There are two main aspects of this thrombosis: the coagulating blood and the local disturbances of the degenerate vessel that provide the setting and opportunity for the clotting. Fundamental questions of constitution and personality, nutrition, hæmodynamics, and endocrine responses are involved in these processes, and more specific ones. Is there any evidence, for instance, of changing frequency in intravascular thrombosis at other sites? Pulmonary embolism might be so investigated, though this would be very difficult (Strom 1950). Are sufferers from coronary thrombosis prone to clotting elsewhere? (Meakins and Eakin 1932). How are intimal necrosis or mural hæmorrhage, the rupture of atheromatous "abscesses," or the separation of plaques related to changes of heart beat and blood pressure, to dilatation and spasm of the coronary arteries? (Blumgart 1943, East and Oram 1948, Friedberg 1949, Horn and Finkelstein 1940, Master et al 1939, Paterson 1938, Winternitz et al 1933). And what of the relations of habits of life and psychological forces to the neural and humoral mechanisms of these? (Bülbring et al 1949, Proceedings of the First National Conference on Cardiovascular Disease 1950, *Psychosomatic Medicine 1945*, Registrar General's Occupational Mortality Supplement 1938, Wolff 1950).

As yet there is little warrant for this shift of interest from the chronic events of coronary heart disease to the acute, either in the clinical history of victims (where the frequency of silent thrombosis and infarction is only one of the difficulties) or in studies of their blood coagulation (Boyer 1946, Friedberg 1949, Mintz and Katz 1947, will be realised that the skin is the predominant seat of masochism, hence this statement gets no further than its starting point, and leads to a stalemate It is again only the study of the underlying dynamics which will yield an answer to the question why does one patient show more masochism than another? It is in any case necessary to distinguish between primary (mostly constitutional) and secondary (developmental) masochism It is undisputed that women have by nature stronger masochistic (passive) tendencies than men, and one might accordingly expect to find that severely itching forms of endogenous dermatoses would be more prevalent among the female than the male population Common experience suggests, however, that there is no great preponderance of female cases This seems to point to the fact that primary masochism is not responsible for the formation of the skin complaint, hence it is doubly necessary to differentiate between primary and secondary masochism Secondary masochism comes into operation when aggression can no longer be turned outward, either against people or in a sublimated form to attack tasks and problems of daily life One has to find the cause for this incapacity to show or tolerate aggression and to the subsequent "turning in on the self" of aggressive drives Many factors may make the normal display of aggression impossible for a person—among them guilt feelings, anxiety, or fear of injuring or destroying a love object

---

[1] "Coronary disease" is taken here to include (1) coronary atheroma (atherosclerosis) and (2) coronary, ischæmic (arteriosclerotic) heart-disease, particularly the syndrome of thrombosis, occlusion, and infarction and its variants. "Ischæmic" heart-disease is the most accurate term, but "coronary" heart-disease is convenient and in too common use to be discarded.

Another example of the pitfalls of neglecting the dynamic approach can be found in the evaluation of "precipitating factors" These are often considered to be obvious inasmuch as they have a certain reality value But this view is highly misleading The precipitating cause of a skin disease is only very exceptionally known to the patient, and even if it is known its unconscious meaning is not understood Quite commonly the patient will present the psychologist with what one might term a "cover cause"

A woman of 48 suffered from intermittent attacks of urticaria She related that she had noticed her outbreaks occurring after eating fish on Fridays She had lost her only son during the late war and was preoccupied with guilt feelings towards him She had wanted to give him a good education and had saved up to give it him on his return When these problems were worked through with her, the outbreaks of urticaria stopped Her son had been killed on a Friday

The reality value of these precipitating factors is much smaller than is usually assumed The great adversities of life—as for instance the loss of dear ones—are astonishingly rarely followed by the outbreak of a skin disease Further, reference is often made to precipitating factors without due regard to the period intervening between the impact of these and the onset of the disease This period might be compared to the incubation period of infectious diseases and certainly merits closer attention not only as to duration but also to inter current developments in the psychic apparatus—a point which had already been noticed by Freud in 1895 The term "trigger reaction" which has found its way into psychological writings must be viewed with some suspicion Trigger reactions are not standard behaviour patterns of fixed value The psychologist is concerned rather with the cartridge which the trigger fires he must discover how it got there and how it is that certain psychic constellations act as an explosive agent

CONCLUSIONS

The psychologist approaching skin disease should have an open mind with as little bias as possible in regard to method A sound training both in psychology and psychiatry is necessary The clinical psychologist should keep in touch with the clinical and physiological aspects of his work Both aspects of the problem should constantly be correlated

We would like to single out at random three problems where such correlation of approach is likely to be fruitful The first is an attempt to evaluate the factors that determine whether a skin disease will take an acute subacute, chronic, recurrent, or intermittent course. The second concerns abnormal skin sensibility the hyperæsthesia and hyperalgesia which may be demonstrated by a physiologist who investigates many itching skin diseases seems to us closely related to the increased skin libidinisation of the psycho analyst Thirdly, the phenomenon of itching with its attendant rubbing and scratching seems to present a vast field for investigation from both the physiological and psychological angle. Itching, although one of the commonest symptoms, has not as yet received the detailed and all round investigation it deserves

Reviewing some of the present trends in psychological investigation of skin disease, we have pointed out blind alleys, and errors and pitfalls in method, for it is often an advance in research to do no more than to specify problems more accurately and to re examine fundamental issues

Attention has been drawn to the common mistake of classifying certain skin patients as psychoneurotics. Whereas the structure and the dynamics of the psycho neuroses are well established, in Freudian theory, the separate mechanisms governing psychosomatic behaviour have yet to be worked out Freud (1929) himself insisted that psycho analysis which had uncovered the structure of the psychoneuroses (the "transference neuroses" proper) "had but little to add to the clarification of the common neuroses (the "actual neuroses"), this task, he maintained, had to be left to biological and medical research

It has been suggested that a study of emotional expression both physiologically and pathologically is essential to accurate understanding Such an approach would not only correlate physiological with psychological data, but would conceivably throw light on some pathological aspects of the dermatoses As Erasmus Wilson said as long ago as 1870 "The limits between the physiological and pathological are barely discernable The blush of emotion is scarcely to be distinguished from the blush of transient erythema or urticaria, and the too frequent repetition and the permanence of the blush become a confirmed erythema, as in gutta rosea" (rosacea)

As some of the opinions submitted in this paper may not be accepted by all psycho analysts, or for that matter by all non analytical students in this field, we wish to state that we have expressed only our personal views

REFERENCES

Freud S (1900) Selected Papers on Hysteria and other Psycho Neuroses New York

— (1929) Introductory Lectures on Psycho analysis London chapter 24

Glover E (1949) Psycho analysis London chapter 11

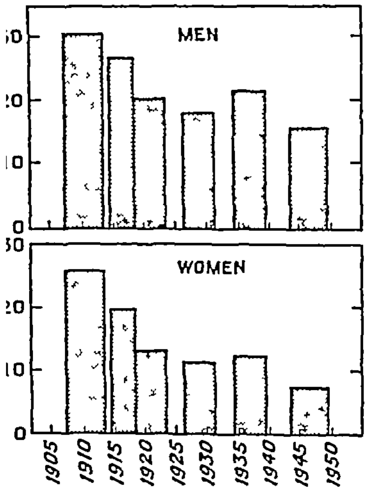
Macalpine I (1950) *Psychoanalytic Quart* (in the press)

MacKenna R M B (1944) *Lancet* ii 679

Stokes J H Beerman H (1948) in Modern Trends in Dermatology edited by R M B MacKenna London chapter 1

Wilson E (1870) *Lectures on Ekzema* London

' So long as a variety of hospitals remained under the direct control of the department, a great deal could be done to assist families by arranging for the removal to hospital of patients suffering from various sorts of illness, but especially of patients suffering from chronic sickness and even of old people who were feeble enough to require treatment as patients it would be of great help to the department and to the people if it had control of the use of at least a certain number of beds, and was thereby able promptly to admit a patient after consideration of the medical certificate and of the social conditions of that patient in relation to those of others recommended for admission —Dr W L BURGESS, M O H for Dundee in his report for 1949 ring forty years is associated with nutrition, with anges in the national diet A clue to the answer may provided by a more detailed study of the behaviour of atheroma in this London Hospital series The condition of the coronary arteries in 1915–39 was therefore investigated with the material and methods already described The 1915–18 to 1927–31 figures include all the available reports, those for 1935–39 include only the reports of Dr Woods and Professor Russell, so as to permit more direct comparison with the figures given previously for 1944–49



4—Prevalence of advanced coronary heroma at the age of 50–70 in men and in omen (data from necropsies at the London ospital) each hatched column shows erage percentage for the years included, nd the percentages are standardised on e age-distribution of the population of ngland and Wales in 1947

Fig 4, which ates the data of tables IV and V to those of les II and III, shows the same broad tendency in th sexes, and it may be summarised as follows decrease between 1908–13 and 1919–23, then small anges till 1935–39, and a further decrease in 1944–49 is interesting that decreases occurred during both oning periods (Aschoff 1924, Beveridge 1928, Ministry Food 1949, Vartiainen and Kanerva 1947), and this cords with many views on intake of animal fat, the od lipids, and atheroma The nutritional relations of heroma are now being unravelled, and not only is ere promise, with the application of physical chemistry well as biochemistry, that the rôle of the lipids, luding cholesterol, will be clarified, but it may soon so become possible to consider other possible connec ons between atheroma and diet Questions already ise about the extraction rate of flour, the vitamin B mplex, and intermediate cholesterol metabolism, out choline, other lipotropic factors, and the fatty position, and about the intake of antithyroid sub ances (*Annals of Internal Medicine* 1950, Cowdry 1933, Ministry of Food 1949, Gofman et al 1950, Hueper 1944–45, 1949, Steiner 1950) The calcification, as distinct from the fatty stage, might have been mainly decreased —which recalls one feature of the nutritional history of the first world war (Drummond and Wilbraham 1939) Other changes, however, should also be remembered, there was, for instance, a steep decline in the consumption of alcohol during the first war, and there may have been something of this among civilians in the second Moreover, it is no longer altogether fanciful to think of diet in relation to hypertension Such a coincidence of decrease in atheroma with food rationing suggests that the present findings are not due to special causes operating locally in this particular population, but may be of more general significance There is insufficient evidence on which to discuss other possible factors in the decrease, such as changes in the water supply and cooking habits

As interesting as these reductions is the modest recovery during the inter war period which left the level at its close (1935–39) about the same as at its beginning (1919–23) This was not the case with diabetes and gall bladder mortality—also possibly related to fat intake—which fell in both wars and rose between them Perhaps such increase in fat consumption as occurred in this section of the population during the inter war years was adequately covered, vis à vis atheroma, by other simultaneous improvements in the diet, but there is no basis for such speculation Possibly the suggestion of an increase in coronary atheroma in the relatively prosperous years of 1935–39 may be significant Possibly there is here a combination of "generation" and contemporaneous effects on the cohort exposed during the first world war Possibly the small response during 1919–39 merely reflects technical flaws and inadequacies of the present approach to the problem

I do not feel competent to discuss the relevance of these findings to the various theories of the pathogenesis of atheroma other than nutritional (Duguid 1949, White and Ferrero 1949) Nor can the relevance of animal experimentation on atheroma to the human problem be considered here I have dealt only with the coronary arteries, but may be able to report later on the abdominal aorta The question of the special localisation of atheroma would be most usefully discussed in the present connection, when comparative evidence on the historical trends of atheroma in different arteries is available

BLE IV—PREVALENCE OF ADVANCED CORONARY ATHEROMA MALES AGED 50–70 AT NECROPSIES IN THE LONDON HOSPITAL

Age group (yr)	No of cases							
	In 1915–18		In 1919–23		In 1927–31		In 1935–39	
	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma
0–54	123	12%	139	14%	169	8%	62	13%
5–59	107	24%	140	18%	183	16%	84	17%
0–64	94	30%	109	21%	143	17%	62	26%
5–69	62	50%	63	33%	89	38%	54	37%
Total	386	St rate 50–69 27 0%	451	St rate 50–69 20 4%	584	St. rate 50–69 18 2%	262	St rate 50–69 21 7%

These cases form group C Deaths from coronary heart disease, om hypertensive disease from arteriosclerosis in other sites and ith diabetes are not included.

St rate = standardised rate

TABLE V—PREVALENCE OF ADVANCED CORONARY ATHEROMA IN FEMALES AGED 50–70 AT NECROPSIES IN THE LONDON HOSPITAL

Age group (yr)	No of cases							
	In 1915–18		In 1919–23		In 1927–31		In 1935–39	
	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma	Total	Proportion with advanced atheroma
50–54	43	5%	67	4%	90	7%	34	6%
55–59	44	18%	63	6%	79	8%	40	8%
60–64	37	27%	49	14%	63	10%	33	15%
65–69	40	35%	30	33%	47	26%	16	25%
Total	164	St rate 50–69 19 8%	199	St rate 50–69 13 1%	279	St. rate 50–69 11 5%	123	St rate 50–69 12 4%

See footnote to table IV

Indicator of Atheroma Further Validation

Tables IV and V again show fairly regular patterns with age and sex. An attempt was now also made to compare in finer detail the findings for 1935–39 with those for 1944–49, as the reports of Dr Woods and Professor Russell alone were analysed for these years In this period the reduction in

Peters et al 1946), though emphasis on the thrombosis has in a different way improved the possibilities of treatment

Decrease of Atheroma and Increase of Heart disease

Another question must be put Is the decrease of atheroma suggested by tables II and III unrelated to the increase of heart disease shown by table I, having merely coincided in time, or are the two processes in some part cause and effect ? How sensible this question is depends primarily on whether the decrease is general, granted that the increase has been observed in many populations Two obvious mechanisms whereby a decrease of atheroma might so operate suggest themselves If calcification is a method of healing of atheromatous lesions, and during the process mural capillaries are obstructed (Winternitz et al 1933) and atrophy, a decrease in calcification may favour an increase of subintimal hæmorrhage (Buck et al 1950, Cowdry 1933) Spasmodic contraction, too, may be commoner in vessels not so calcareous More generally, a decrease of the atheroma might promote the development of the heart disease because with less narrowing of the arteries there may be less stimulation to open up the intercoronary vessels This might be of particular moment if acute thrombotic occlusive lesions were increasing for other reasons, and if emergency responses of the anastomotic circulation were not fully effective But these are not problems that can be investigated from the present material Nor is it possible to do more than put the cognate question—whether ischæmic heart disease is occurring more commonly in persons with less severe atheroma, whether (as it were) there has been a lowering of the critical level of coronary atheroma This last proposition would, of course, go further than that previously put forward, which merely suggested that the heart disease *is increasing* despite the decrease of severe atheroma—without implication about the degree of atheroma necessary in the individual case The nature of the present material cannot permit of an estimate even of the amount of calcification in the coronary arteries of those dying from coronary heart disease

Increase in Heart-disease, and its Prevention

If the present observations are sound, explanation of the increase of coronary heart disease by an increase of the predisposing atheroma becomes unconvincing The mechanism of the increase may be an increase of the thrombosis that is the precipitating cause, and—possibly serious in relation to the collateral circulation—this may be occurring at younger ages than formerly In turn this increase in thrombotic accidents or incidents may be due to changes in the coagulability of the blood or to an increase of disorders in the vessel wall that promote coagulation No clue to the causes of the increase of the heart disease has emerged, except for the suggestion of a qualitative change in its incidence about the close of the first world war This, if confirmed, would indicate study of changing modes of life and the changing environment, the epidemic constitution, of those years

Two possible approaches are indicated to the prevention of coronary heart disease Control may be achieved through reduction of the predisposing atheroma But if the heart disease is increasing because the precipitating thrombosis is increasing, the reduction might have to be very radical to show results The indications are that even now only a small minority of those " eligible " in terms of coronary atheroma do actually have the heart disease, at any rate in the ages considered If there has been anything like the decrease of advanced atheroma shown by tables II and III, and nevertheless the net result has been the recent increase of the heart disease, it would obviously need a tremendous further decrease of atheroma to annul the effects of the increase in thrombosis—indeed the decrease would have to be as steep as the increase Alternatively, prevention may become possible through control of the intravascular thrombosis A fortiori, these considerations would apply in populations where coronary atheroma has not decreased and there are greater numbers eligible, unless it can be shown that there is an aggravating factor associated with the decrease itself In that event the problem would become even greater—so to control the atheroma that the lesions did not sufficiently mature to form the basis of thrombosis and not only to reduce the volume of severe atheroma

Occlusion without Thrombosis

This " thinking aloud " started from the proposition that coronary thrombosis is the central problem But what of the many cases where no recent thrombus is found ? Should it be a common fact that occlusion can be produced by sclerosis alone, and infarction merely by stenosis, it must make nonsense of much that has just been written If coronary heart disease has increased and *the sufficient cause in a large group* is severe atheroma, *the main finding of the present investigation* becomes suspect on that account alone Theoretically it is possible that the atheroma decreased in the vast majority of the population but increased in a special minority To this *it may be objected that* severe coronary atheroma, as severe as in these cases *with* the heart disease, occurs so often in those *without* it—an observation that demands a search for additional causes Perhaps some of the explanation lies not in the diseased vessels but in what is required of them

The question arises, however, whether these facts can be accepted They are often not at all clear (and, in passing, one who works much in the " inexact " sciences cannot but be impressed by the differences of opinion among the experts in a field such as this—consider the variation in the reports of mural hæmorrhage alone, for example) Not only may it be very difficult to be sure *whether previous thrombosis has* participated in an occlusion that appears at present to be merely sclerotic, but it may also be impossible to assess the contribution of old thromboses to the present failure in coronary function Moreover, where arteries appear only to be narrowed, the problem may have to be reconsidered in the light of the work on fibrinolysin and the possibility that thrombus has been dissolved (Macfarlane and Biggs 1949) *This aspect of the matter must so unsatisfactorily* be left

DECREASE OF CORONARY ATHEROMA

The possibility of a decrease in coronary atheroma between 1908–13 and 1944–49 is interesting from two *points of view The first has just been considered*—the thinking it may provoke on ischæmic heart disease But the proposition has been advanced that tables II and III are to some extent typical of the general population, or the " hospital class " of it, and the question of a decrease in the atheroma has therefore an intrinsic significance There may be important constitutional elements in coronary atheroma, and there is little doubt that the " population " of 1908–13 was more homogeneous than that of 1944–49 , but there is no useful approach along these lines Heredity apart, there are three main *sets of conditions associated* with the degeneration There is more coronary atheroma among males, and the incidence increases with age, with hypertension (and in hearts of above average weight), with obesity, and in certain metabolic disorders (Friedberg 1949, Wilens 1947) Research today is concerned mainly with the last and, particularly, with the nutritional components The present evidence suggests that there has been a decrease of coronary atheroma in both sexes, at age 35– or 45–69, in those with and without hypertension The question next arises whether this over all decrease e abdominal aorta, for instance Nor has any attempt ot been made to relate this fundamental pathology of geing to the recent remarkable decline in the death tes of older people (British Medical Association 1950) here seems no reason, perfectionism apart, why it ould not be possible in ten years' time, and again in venty, to provide a comprehensive account of atheroma, oth the degenerative lesions and the occlusive, with uch finer criteria than was possible in this retrospective udy If a sufficient number of morbid anatomists oöperated, it may be possible to make such judgments y sex and age, by economic status and nature of occupa on, by social and medical history, and even inter-ationally Such an approach is well established in other elds, and valuable knowledge has already been gained om necropsy material about pulmonary tuberculosis nd peptic ulcer Meanwhile the 1944–49 parts of ables II and III provide a limited estimate (because of the estricted sample and the simplicity of the classification) nd a conservative one (because severe hypertension and oronary heart-disease are deficient in the sample) of he prevalence of coronary atheroma in the population oday

Summary

The recent history of coronary disease has been onsidered

Clinical experience and the Registrar General's tables uggest that coronary heart disease has increased, ndependent of the ageing of the population and improved iagnosis

A sample study of coroners' records suggests that spontaneous rupture of a cardiac ventricle in the elderly is similarly occurring more often

An analysis was made of the necropsy records of the London Hospital, where the coronary arteries as well as the myocardium have been routinely examined since 1907–08 Some 6000 reports from these years to 1949 were studied, relating to both sexes and to ages 30/35–69 inclusive

These reports show about a sevenfold increase from 1907–14 to 1944–49 in the number of cases of coronary heart-disease They suggest that coronary thrombosis and myocardial infarction were rare before the first world war and have since become common—i e, that as a common disease they are new and not merely newly recognised The initial and biggest increase in this series took place towards the close of, and in the early years after, the first world war

An attempt was next made to estimate the prevalence of coronary atheroma in the population from these records They showed a substantial decrease of advanced coronary atheroma, as defined mainly by the report of calcified lesions in the arteries, between 1908–13 and 1944–49 The decrease was seen in all the relevant sex, age, and pathological categories (including hypertensive) studied. It occurred in two phases that seemed to be connected with the two world wars

Some implications of these contrasting trends are discussed—e g, that coronary thrombosis and heart-disease may not be simple and direct functions of the atheroma Possible nutritional relations of the decrease of the atheroma are considered, together with their relevance to the health of an ageing population

With new problems of community health, new indicators of what is happening are needed This exercise in documentary research illustrates one kind of contribution that social medicine, on its epidemiological side, may be able to make

I am grateful to many people for their help in the course of this investigation. Prof D S Russell, director of the Bernhard Baron Institute of Pathology granted me free access to the reports and she and Dr W W Woods gave me much valuable advice and criticism. I am also indebted to other members of the staff of the London Hospital, to teachers, friends, and colleagues, and particularly to my statistical colleague, Mr J A Heady, for greatly appreciated suggestions and practical assistance The following kindly gave me information or permission to examine their material Dr E Geiringer, Prof C Polson, Dr C K. Simpson, Dr D Teare, the Registrar General, the Records Officer of the London County Council, and the coroners and their officers for Cardiff, Cardigan District, Devon Barnstaple, Essex North, Gloucester Tewkesbury, Hampshire Fordingbridge Hundred, Leeds, Liverpool, London East and West, Manchester, Middlesex East and West, Oxfordshire West, Salford, Surrey East and West, and Sussex East

REFERENCES

Annals of Internal Medicine (1950) 33 250
Aschoff K. A L (1924) Lectures on Pathology New York.
Bedford T H B (1933) *J Path Bact* 36 333
Beveridge W H (1928) British Food Control London
Bjernsson J (1941) Arteriosclerosis Copenhagen
Blumgart H L (1943) In Pain Baltimore
— Schlesinger M. J, Davis D (1940) *Amer Heart J* 19 1
Boyer N H (1946) *Med Clin N Amer* 30 1060
British Medical Association (1950) Report of the Committee on Nutrition London p 96
Brooks H (1906) *N Y med J* 84 825
Buck R C Paterson J C Rossiter R J (1950) *Lancet* i 830
Bülbring E Burn J H Walker J M. (1949) *Quart J Med* 18 73
Cassidy M (1946) *Lancet* ii 587
Closs K. Dedichen J (1949) *Ibid* ii, 1242
Cowdry E V (1933) Arteriosclerosis London
Drummond J C Wilbraham A (1939) The Englishman s Food London
Duguid J B (1949) *Lancet* ii 925
East T Oram S (1948) *Brit Heart J* 10 263
Friedberg C K. (1949) Diseases of the Heart London
Gofman J W et al (1950) *Circulation* 2 161
Gordon W H Bland E F White P D (1939) *Amer Heart J* 17 10
Harrison C V Wood P (1949) *Brit Heart J* 11 205
Hedley O F (1939) *Ann intern Med* 13 598
Herrick J B (1912) *J Amer med Ass* 59 2015
— (1919) *Ibid* 72 387
— (1942) A Short History of Cardiology Springfield Ill
Horn H Finkelstein L E (1940) *Amer Heart J* 19 655
Hueper W C (1944–45) *Arch Path* 38 162 243 350, 39 51 117 187
— (1949) *Med Clin N Amer* 33 773
Hutchison R (1950) *Brit med J* i 72
Johnston C (1936) *Amer Heart J* 12 162
Krumbhaar E B Crowell, C (1925) *Amer J med Sci* 170 828
Leary T (1934) *Arch Path* 17 453
Levy R L Bruenn H G, Kurtz D (1934) *Amer J med Sci* 187 376
Lindgren I (1950) Angina Pectoris Stockholm
Macfarlane R G Biggs R (1949) G R Minot Symposium on Hæmatology New York.
Mackenzie J (1914) Diseases of the Heart 3rd ed. London
Master A. M. Dack S Jaffe H L (1939) *Amer Heart J* 18 434
McNee J W (1926) *Quart J Med* 19 44
Meakins J C Eakin W W (1932) *Canad med Ass J* 26 18
Ministry of Food (1949) Food Consumption Levels in United Kingdom London
Mintz S S Katz L N (1947) *Arch intern Med* 80 205
Norris G W (1911) Studies in Cardiac Pathology London
Parkinson J Bedford, D E (1928) *Lancet* i 4
Parsons Smith, B T (1950) *Ibid* i 889 943
Paterson, J C (1938) *Arch Path* 25 474
Perring R J (1949) *Lancet* ii 1163
Peters H R. Guyther, J R. Brambel C E (1946) *J Amer med. Ass* 130 398
Proceedings of the First National Conference on Cardiovascular Disease (1950) New York.
Psychosomatic Medicine (1945) 7 206
Registrar-General (1931–48) Annual Statistical Review of England and Wales Tables Part I Medical
— (1938) Occupational Mortality Supplement
— Census of England and Wales 1911 1921 1931
— Estimates of the Civilian Population at Dec 31 1947 and of the Population at June 30 1949
Ryle J A Russell W T (1949) *Brit Heart J* 11 370
Saphir O Priest, W S Hamburger W W Katz L N (1935) *Amer Heart J* 10, 567
Simpson K. C (1947) *Lancet* ii 745
— (1950) Personal communication
Steiner A. (1950) *Med Clin N Amer* 34 673
Steiner P E (1946) *Arch Path* 42 359
Stocks P (1949) Sickness in the Population of England and Wales in 1944–1947
Strom A (1950) Personal communication. See also *Lancet* 1949 ii 1242
Turnbull H M. (1915) *Quart J Med* 8 201
Vartiainen I Kanerva K. (1947) cited in 1948 Year Book of General Medicine Chicago p 514
Welch W H (1920) Papers and Addresses Baltimore vol I p 116
White N K. Edwards J E Dry T J (1950) *Circulation* 1 645
White P D Ferrero C (1949) *Ann intern Med* 31 33
Wilens S L (1947) *Arch intern Med* 79 129
Willius F A. Dry T J (1948) A History of the Heart and Circulation London
— Smith H L Sprague P H (1933) *Proc Mayo Clin* 8 140
Winternitz, M C Thomas R M. LeCompte P M. (1933) The Biology of Arteriosclerosis Springfield, Ill
Wolff H G (1950) *Circulation* 1 187
Wyn Jones E (1931) *Quart J Med* 24 199
Yater W M. et al (1948) *Amer Heart J* 36 334 481 683

calcified lesions, which is primarily indicated by fig 4, may have been accompanied by some reduction in the degree and extent of the fatty lesions "numerous" or "large" or "confluent" fatty lesions were more commonly reported in 1935-39 than in 1944-49, and minor fatty lesions more commonly in 1944-49 than in 1935-39[12] But the categories used are not precise enough to show whether there was a disproportionate decrease of the calcified lesions among all the lesions sufficiently mature to form a potential basis for local thrombosis And, in general, such estimates approximate to the "qualitative" category that has hitherto been avoided in this investigation As regards the main trend of the investigation, the internal consistency of the findings is reassuring in view of the several changes in staff and the gradual amplification of the reports none of the 39 separate sex age groups based on 2535 observations from 1919-23 to 1944-49 exceeded in advanced atheroma the corresponding groups of 1908-13

Recalling the possibility of a "seesaw" effect, it can again readily be shown that improvement in the diagnosis of coronary thrombosis, &c, will not explain away the main trend reported Simple "book keeping," and the addition of all the cases of table I to the figures of tables IV and V, will not make good the substantial and particularly interesting decline of atheroma noticed in 1919-23, for instance But there is a limit to the value of such largely circumstantial evidence, as of the internal consistency of the material, or the logical consistency of the various arguments, and what is needed is further *independent* data

Public-health Aspects

Three plagues seem to have visited the middle aged men of this century peptic ulcer, cancer of the bronchus, and coronary thrombosis There is little as yet to relate them but tobacco, and this is still of doubtful importance in two Coronary thrombosis is the most lethal of the three, and, with hypertension, may possibly be the leading cause of death today The ageing of the community partly explains its greater frequency, but too much is often made of this In the past forty years the numbers eligible by age for angina pectoris, for instance, have little more than doubled Over the same period the number of doctors has increased almost as much Speaking broadly, therefore, each doctor should be seeing on an average about the same number of cases as forty years ago—the problem of recognition apart This is not borne out by general experience Of course it may be that those now living to middle age are qualitatively different, they have survived, or been preserved through, hazards that would previously have been mortal Consequently they may be in some way constitutionally more liable than their coevals of forty years ago to succumb to diseases that are prevalent, including coronary heart disease The fall which is occurring in death rates at all ages might be partly due to the fact that fewer diseases are prevalent As yet there are no satisfactory methods of investigating this kind of problem

A main task of public health is to reduce coronary heart disease and other disorders, and its policies must be based on available knowledge of the causes Today the only hopeful approach to prevention is by controlling the main predisposing condition, coronary atheroma, and this may need to be radical if it is to achieve its object Public health has some experience with this kind of problem, or at any rate with its nutritional aspects There is evidence of geographical, and possibly also of ethnic and class, variations in the incidence of atheroma (Bjornsson 1941, Cowdry 1933, Gordon et al 1939, *Psychosomatic Medicine* 1945, Steiner 1940) I recent years a varied group of nutritional disorders ha become less common for various periods—e.g , go cirrhosis of the liver, diabetes, gall bladder disea vesical calculus, chlorosis, and rickets It has becom possible to frame national food policies, though lit is yet solved of the problems of health education in subject like obesity At the least, the possibility o such a decrease as fig 4 illustrates, reinforces curren scepticism about the importance of heredity and "bio logical" ageing in determining the severity of atheroma and suggests that there may be an opportunity f rational preventive medicine in this central healt problem of an ageing population

Disease, however, is commonly the product of man contributory biological and social factors, as well as o its more immediate conditions and causes, and the factors must also be known This is a main area o epidemiology, the study of disease as a group phenomen in the community, and of its preference for particula ages, occupations, economic classes, and environmental situations Knowledge of such factors may point to more proximate ones, whether predisposing or precipitating, but even basic facts of the prevalence of coronary thrombosis are lacking (Cassidy 1946, Hedley 1939, Johnston 1936, Proceedings of the First National Conference on Cardiovascular Disease 1950, White and Ferrero 1949, Yater et al 1948) Moreover with new health problems now indicators of what is happening in the community are needed The time is probably ripe for the experimental application of the tried techniques of public health to this kind of problem Coronary heart disease could, for example, be "notified" to some public health departments, and, in conjunction with sociomedical surveys, this procedure might be valuable in following up "hunches" about ætiology that are now popular At present the main source of information must be the mortality rates, and cardiovascular disease of middle and old age is, unfortunately one of the darkest areas of vital statistics (The currently certified death rates from hypertension in particular reflect little credit on our medical schools) There is already a case for field inquiry into the meaning and quality of the certification of these conditions, as a preliminary to an educational campaign, though it may be worth waiting to see what new information comes from the introduction of the latest International List It is only possible to speculate now about the significance of the slowing up of the increase in the mortality in England and Wales during the recent war (fig 1), a movement noticed also in Scandinavia and Germany (Lindgren 1950, Strom 1950, Closs and Dedichen 1949) Hospital statistics for this period are more than usually obscure There may well be a clue here to the nutritional relations of coronary thrombosis (and/or hypertension) or to the part played by psychological influences

The present study suggests also that greater use could be made of necropsy material in epidemiological study In the case of coronary heart disease it would be relatively simple to organise some system of ascertainment of spontaneous rupture of a ventricle in the elderly This might be a useful indicator (and it might also have the advantage of bringing forensic medicine closer to the rest of medicine) More obviously, measurements o the prevalence of coronary atheroma in the populatio are needed, and the investigation now reported wa undertaken primarily in an attempt to demonstrat their feasibility At least it has yielded a provocativ picture of changing prevalence over the years It seem a pity that the consequences of the epochal "experimen of opportunity" carried out by war and post war foo policy have not yet been assessed on an adequate scal in terms of arteriosclerosis, of cerebral and coronar atheroma, or, more precisely, as the amount of lipoid i

---

[12] Standardised rates of "early" atheroma at the age of 50-69

	1935-39	*1944-49*
Major fatty lesions		
Male	35.2%	31.0%
Female	25.1%	23.4%
Minor fatty lesions		
Male	40.9%	49.5%
Female	60.8%	65.1%

"Not stated" cases were ignored The few with no coronary atheroma were included in the minor fatty lesions

2 The operation carries a serious risk of injury to the adder and ureters

3 The whole object of the operation may be nullified by jury to the peritoneum

4. The operation opens up the extraperitoneal tissues, which e supposed to have less resistance to infection than the ritoneum.

he first two objections have no real substance, since it not intended that the occasional surgeon should tackle ese difficult obstetric problems to the experienced elvic surgeon the operation is one of ease—indeed a ource of pleasure

Any gross invasion of the peritoneal cavity during the peration should be readily avoided, but it must be dmitted that, from time to time, close inspection of the eritoneal flap will reveal minute perforations These ust be closed by simple ligation before opening the terine cavity, so that the full benefits of the procedure y be retained

The last objection must have been raised under a ious misapprehension, the Waters (1940) operation erely involves fascial planes that are of necessity ened up during the course of the commoner transperi neal lower uterine-segment operation and therefore it ould not involve any more risks

TECHNIQUE

Various techniques have been devised Thomas 870), of New York, was the first to perform the opera on, and he recorded (Thomas 1878) 5 cases, with 2 aternal deaths and the loss of 1 fœtus Latzko (1908, 909) devised an improvement that remained the ethod of choice until recently, this gave a rather adequate exposure of the lower uterine segment and as technically difficult if the child was large

A very great advance was made when Waters (1940) nd Ricci (1940) introduced their modification of the d Physick-Sellheim technique Waters's operation ves an excellent exposure of the lower uterine segment, ut his method of dissecting the fascial peritoneal flap om the superior bladder wall can prove both difficult nd tedious By modifying the Latzko operation, orton (1946) obtained a better exposure with less risk f injuring the peritoneum Bourgeois and Phaneuf 1949) advise a bilateral paravesical approach to the wer uterine segment, this modification makes it easier nd quicker to dissect up the peritoneo fascial flap from he bladder, while retaining the advantage of the wide xposure of the lower uterine segment provided by the aters method

We now use the technique of Bourgeois and Phaneuf o attempt will be made to detail the method, but xperience has warned us of certain dangers and difficulties that may be readily avoided Brief mention of hese points may help others to avoid the errors we made

In opening the abdomen great care must be exercised, or it is very easy to open the peritoneal cavity inadvertently, particularly at the upper end of the incision The nterior rectus sheath should be incised at the lower ngle of the wound, and the peritoneum and extra eritoneal fatty tissues should be stripped back with he fingers as the sheath is laid open with scissors The ladder is emptied before the operation, and nothing is gained by filling it with fluid, coloured or otherwise

If the surgeon stands on the patient's right side, a transverse incision through the transversalis fascia over the bladder is made and extended laterally to the left as the assistant retracts the left rectus abdominis muscle This leads directly to the paravesical triangle, which is bounded above by the peritoneal reflexion, internally by the obliterated hypogastric artery running along the side of the bladder and externally by the left uterine artery The floor of the triangle is covered by the so-called "chicken fat," and, when this is wiped away, the prececervical fascia is exposed Division of this fascia allows the bladder to be rapidly mobilised from the uterine wall, and leads on to the dissection of the peritoneo fascial flap from the superior bladder wall. This is easy if the dissection is carried out with a sharp scalpel while the tissues are kept under tension, the urachus will have to be divided between clamps close to the bladder

The peritoneal flap is inspected for perforations at this point in the operation These are readily detected by the leakage of intraperitoneal fluid, and are easily and safely closed by simple ligation (no purse string sutures) The bladder should then be examined and any weak points in its wall oversewn with catgut

At this stage of the operation the freely mobilised bladder is pushed down behind the symphysis pubis out of harm's way, thus exposing the lower uterine segment and cervix in readiness for the usual "trapdoor" uterine incision

The delivery of the fœtal head out of the pelvis may be difficult, but this momentary embarrassment may be obviated by the use of the Trendelenburg position

The uterine incision is sutured in the usual manner with no 5 monofilament 'Nylon,' and the same material is used in closing the abdominal wall The retrovesical area is treated with proflavine (1%) and sulphathiazole (99%) powder, and the space is drained for forty-eight hours

The premedication given to the mother has been atropine gr $^{1}/_{100}$ Spinal analgesia induced with heavy 'Nupercaine' $^{1}/_{200}$ in 6% glucose has been the anæsthetic procedure of choice in 47 out of the 52 cases

TYPE OF CASE CHOSEN

The modern operation of lower uterine segment cæsarean section is safe for the mother in cases of election and also when performed early in labour These favourable results are not obtained in the infected or potentially infected patient For this reason Dieckmann (1946) laid down certain criteria by which the dangerous case could be recognised. He advises either vaginal delivery or cæsarean hysterectomy for such patients His contraindications to transperitoneal cæsarean section are as follows

1 Labour over twenty four hours
2 Membranes ruptured over twenty four hours
3 Attempts at delivery by forceps or by version
4 Induction of labour by bag, bougie, or pack.
5 Evidence of uterine infection
6 More than six vaginal examinations
7 More than twelve rectal examinations
8 Dead or damaged fœtus

We have chosen extraperitoneal cæsarean section as the preferable mode of delivery when faced with these examples of dystocia

The cases in the present series fall into two main groups (1) those in which uterine inertia had persisted so long as to render the patient potentially or frankly infected, the cervix had not yet reached the stage of full dilatation, and the possibility of a successful vaginal delivery of a living infant had become remote, and (2) those in which cephalopelvic disproportion or malpresentation precluded the vaginal delivery of a living child, whether or no the stage of full cervical dilatation had been reached, and in which outside interference had rendered any form of transperitoneal cæsarean section dangerous

Of the 52 cases 42 (80%) were primigravidæ and 10 (20%) multiparæ Of the 10 multiparæ only 3 had living children, pregnancy having ended in stillbirth after difficult forceps delivery in 3 cases and in abortion in the remaining 4 Ages ranged from 19 to 43, average 29 8, 26 women (50%) were aged over 30

In 10 cases definite pyrexia was noted on admission to hospital. One of these women had an intra uterine

AN ASSESSMENT OF EXTRAPERITONEAL CÆSAREAN SECTION

F R STANSFIELD
M D Lond , F R C S , F R C O G
VISITING GYNÆCOLOGIST
L W D DRABBLE
M R C S , M R C O G
REGISTRAR, OBSTETRIC AND GYNÆCOLOGICAL DEPARTMENT
IPSWICH GROUP OF HOSPITALS

INTRA-PARTUM intra uterine infection is not so common today as it was twenty years ago Nevertheless a steady stream of patients either frankly or potentially infected as a result of either protracted labour or interference under adverse conditions still continues to flow into the obstetric beds of the specialist hospitals

Our improved methods of antenatal care and our better understanding of the mechanics of labour have undoubtedly reduced the number of such cases , but the problem of how to treat them remains as difficult as ever, and the outcome for the mother and child leaves much to be desired.

Chemotherapeutic agents and antibiotics have undoubtedly improved the immediate results so far as the mother is concerned, but they have not reduced the number of stillbirths It is far too early for us to assess how the long term results due to infection subsequent to trauma inflicted during a difficult vaginal delivery have been affected by these agents

A search, among the possible alternative methods of treatment of the difficult obstetric case of this type, for a means whereby the maternal mortality and morbidity, together with the total fœtal loss, could be reduced led one of us (F R S) in 1940 to embark on a series of extraperitoneal cæsarean sections This series has now reached a total of 52 cases and, although this is a small number (the incidence has been only 1 per 1000 deliveries), the results have been extremely encouraging

ALTERNATIVE METHODS OF TREATMENT

Sedation

Sedation is the generally accepted routine method of treating uterine inertia, and it is usually effective Nevertheless there remain cases in which no response is obtained, uterine motility is persistently sluggish, the risk of infection steadily increases, and all too often the fœtus dies before delivery by the vaginal route is possible Sedatives were given in the early stages of labour in most of the present series

Oxytocics

Œstrogens, vitamin B_1, and calcium may all improve uterine contractions, provided there is no cephalopelvic disproportion, but their action is uncertain Reid (1946) has studied the use of dilute solutions of ‘ Pituitrin ’ in an attempt to improve the strength of uterine contractions and expedite delivery In cases in which labour had lasted more than twenty hours before treatment was started only 8 6% had normal deliveries and 12 9% required a cæsarean section Reid does not mention any maternal mortality and cites only a corrected fœtal mortality of 116 5 per 1000 In a similar series (Stone 1950) 13 labours of over twenty hours' duration were treated in a like manner with 1 fœtal death and no maternal fatality There were but 2 spontaneous deliveries, 10 required operative vaginal delivery, and 1 a cæsarean section

Bradford et al (1949) concur in this and state that after thirty hours' labour there is a rapidly diminishing likelihood of spontaneous delivery, 48% requiring major operative delivery Obviously oxytocics do not yet provide a solution to our problem

Cervical Incisions

The incision of an incompletely dilated cervix, followed by forceps delivery, is a mutilating operation in which severe trauma is blindly inflicted on the woman, who runs the immediate risks of shock, hæmorrhage, and acute infection, and, all too often, becomes in later life the victim of chronic gynæcological disabilities. The injury inflicted on the cervix must also be held responsible, at least in part, for the secondary sterility so commonly found among patients thus operated on. The risks incurred by the fœtus during this operation are not negligible Douglass and Graves (1948) report in their cases a maternal mortality of 1 9% and a gross fœtal loss of 24%

Craniotomy

Craniotomy will continue to be the elective method of treatment in those cases in which the fœtus has already died and can be delivered per vaginam without undue injury to the mother What of the case in which the fœtus is still alive, a vaginal delivery without some form of destructive operation is impossible, and the risks of peritonitis resulting from a transperitoneal cæsarean section are too great for it to be undertaken? Must the fœtus be sacrificed ?

There is the further problem of the case in which the child is already dead, a vaginal delivery is impracticable without unwarranted injury, and early delivery is necessary because of the mother's condition

Embryotomy does not solve these problems. Baird (1936) reported a maternal mortality of 7 2% as a sequel to these procedures

Transperitoneal Cæsarean Section

The classical operation need not be considered in these days , it already stands condemned It remains only to report the results of the transperitoneal lower uterine-segment operation Marshall (1949) reports that cases in labour for over forty eight hours without interference carry a maternal mortality of 2 49% , interference raised this figure to 4 54%, with a gross fœtal loss of 160 per 1000

Cæsarean Hysterectomy

Cæsarean hysterectomy entails much the same risks as a transperitoneal cæsarean section and, as a further disadvantage, robs the survivors of future childbearing —an important point, since most of them are primigravidæ Dieckmann (1948) reports that he performed this operation in 33 cases in which infection was suspected there were 6 cases of peritonitis, with 1 death

Extraperitoneal Cæsarean Section

A consideration of the above methods shows that none provides a satisfactory answer to our problem, and naturally one seeks a happier solution In this spirit we will analyse the possible advantages and drawbacks of extraperitoneal cæsarean section

This is a lower uterine segment operation and therefore has all the advantages attached to such a procedure It has yet further advantages there is no intraperitoneal spill of infected liquor, and any risk of postoperative seepage through a peritoneal suture line is eliminated the likelihood of postoperative ileus is reduced , and there should be no trouble from postoperative adhesions The operation area can readily be treated with sulphonamides and antibiotics and it is easily drained

This operation is better than a difficult vaginal procedure It provides easy access to the uterus, with a clear view of the operation field permitting adequate hæmostasis and accurate coaptation of the edges of the uterine wound In discussing the merits of this operation one must not overlook the much improved fœtal salvage (see below)

Various objections have been raised to the procedure

1 The technique is difficult

THE OXYGEN PARADOX

EXPERIMENTS ON THE EFFECTS OF OXYGEN IN HUMAN ANOXIA

F LATHAM
M.D , B Sc Manc
SQUADRON LEADER, ROYAL AIR FORCE

THE giving of oxygen in anoxic states has sometimes had adverse effects, especially in the treatment of chronic cor pulmonale Also Comroe and Schmidt (1938) found that, after emergency tracheotomy for obstruction of airways, symptoms appeared which seemed to be attributable to the temporary cessation of cerebral circulation following sudden reoxygenation of the arterial blood

The mechanism of these disturbances differs in certain ways from that of the true paradox phenomenon The latter name was first applied by Ruff and Strughold (1939), and before this the condition had mostly passed unrecognised Briefly, when a person is anoxic and is suddenly supplied with an abundance of oxygen, his condition may rapidly worsen, and in severe cases there may be clonic muscular spasms or unconsciousness for up to 30 seconds Quite often the condition is more transient and it may pass unnoticed unless brought to light by special tests

The incidence of this paradox reaction in aviation has been emphasised by Schwarz and Malikiosis (1939), who described the case of a pilot who, having interrupted his supply of artificial oxygen to attend to a mechanical defect at 20,000 ft , collapsed unconscious when he began to breathe oxygen again Noell and Roeder (1943) demonstrated the reaction in decompression-chamber tests with Lottig's writing test They noted in several cases a striking deterioration in muscular co-ordination and mental faculties on breathing oxygen again after experimental anoxia The general deterioration ensued just after the circulation time would have indicated full arterial reoxygenation, and symptoms could still be detected up to 40 seconds later Noell et al (1943) obtained an electro encephalogram in a typical case

Baxter et al (1943), studying syncopal reactions in anoxia and their relation to epilepsy, found that some persons lost consciousness 30 seconds after breathing oxygen again, but later they assumed that these persons would have collapsed in any case if the anoxia had been allowed to continue longer Stavraky (1944) attributed this collapse to the direct depressing effect of oxygen on the central nervous system and to sudden constriction of cerebral blood-vessels caused by inhalation of oxygen in acapnic states

The physiology of this crucial postanoxic recovery stage has been inadequately covered, and the transient nature of the phenomenon has only served to increase the difficulties of investigation The paradox reaction is more easily demonstrated in normal healthy people, and is of particular interest in relation to the use of oxygen by aircrew, since several cases have been described recently which resulted from resumption of the oxygen supply after sudden anoxia due to very rapid decompression to high altitudes

The symptoms seem to be entirely due to a profound disturbance in the central nervous system The ensuing cardiovascular collapse may mask many of the primary nervous symptoms, which in mild cases consist of slight tremblings, clonic muscle cramps, malformation of letters in writing tests, and deterioration of logical thinking The onset of symptoms coincides with a change in facial colour following peripheral dilatation Noell (1947) states that in severer cases, leading to convulsions and unconsciousness, the convulsion may be a manifestation of latent epilepsy and he localises the symptoms to the extrapyramidal system and the hypothalamus

Before investigating this reaction it was necessary to assess quantitatively its true relation to the return of oxygen into the circulation A modified form of writing test, which gave a continuous indication of physical and mental integrity or impairment, was applied to a group of healthy people, and the results were correlated with the cardiovascular and blood pH changes found in succeeding experiments

WRITING TEST

It was considered necessary to use a technique which would detect immediately any sudden mental or neuromuscular change, and a modified form of Lottig's writing test appeared satisfactory Sixty anoxia tests were carried out on 52 persons, mostly healthy young aircrew and members of the laboratory staff The experiment was divided into two parts The first group of 30 persons were anoxic for 4 minutes in a large decompression chamber at a simulated altitude of 20,000 ft , and the second group, consisting of 8 of the first group and 22 other persons, for 5 minutes at the same height Standard drill was adhered to for the decompression chamber runs, several minutes being allowed at altitude on pure oxygen before the anoxia test was started As soon as the subject's oxygen tube was disconnected and his oxygen supply was turned off he was instructed to

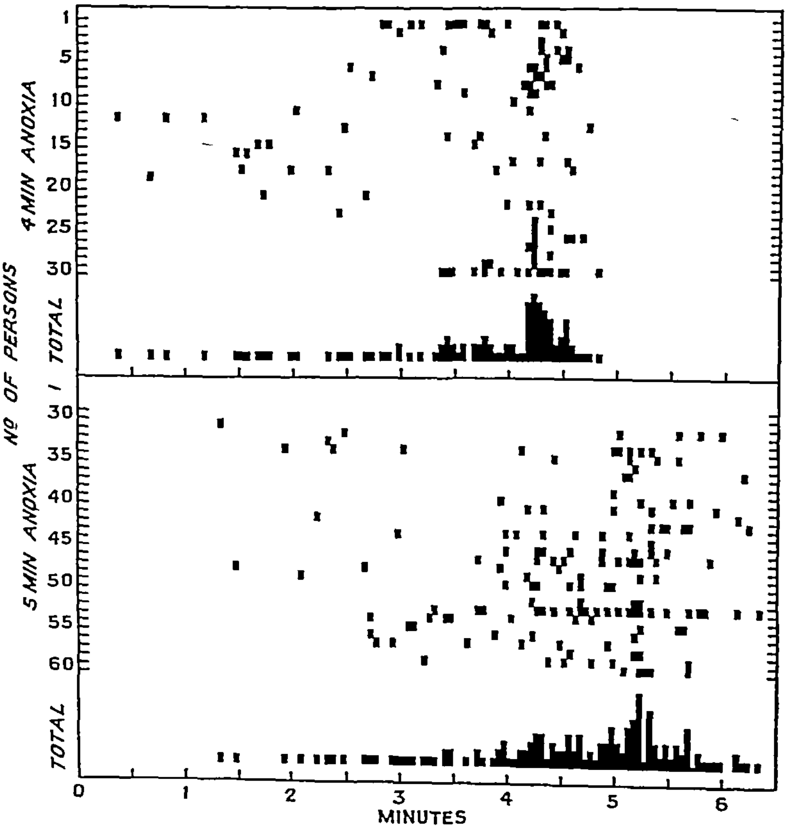


Fig 1—Errors made in 3-second periods in writing test by two groups of persons subjected to anoxia and then reoxygenated

Clostridium welchii infection, and yet was delivered of a living child

Uterine inertia was the main indication for operation in the greater part of the series, labour having been in progress for over forty eight hours in 33 cases (63%) and for over thirty six hours in 44 cases (85%) Fœtal distress was established in 34 cases (65%)

Of the fœtuses, 47 presented by the vertex and, as might be expected, there was a high incidence of occipito posterior positions The breech presented in 2 cases, the face in 1, the brow in 1, and there was 1 transverse lie Definite cephalopelvic disproportion was present in 4 cases, one of which was further complicated by prolapse of the umbilical cord

In 9 cases (17%) there had been operative interference per vaginam before section was undertaken , yet in only 1 case—that in which the face presented and attempts to correct a mentoposterior position had failed—was the cervix fully dilated

RESULTS

Maternal

There were no maternal deaths, and no patient developed peritonitis *At operation the peritoneum* had been buttonholed in 2 cases, and the bladder opened in 1 None of these cases presented undue difficulty during the puerperium

Puerperal pyrexia of notifiable degree developed in 9 patients (17%) in 6 of these it was due to an intra uterine infection, in 2 to a *Bact coli* urinary infection, and in 1 to an enteritis caused by *Salmonella aertrycke*

There was a high incidence (46%) of minor urinary infections, which, however, did not give rise to notifiable pyrexia and rapidly settled on treatment One patient developed an internal saphenous thrombophlebitis, and mild wound sepsis delayed healing of the abdominal incision in 2 cases

Fœtal

The number of children lost was 4 (7 6%) There was 1 stillbirth, the mother being an elderly primigravida whose pregnancy was complicated by essential hypertension Of the 3 neonatal deaths the first was due to atelectasis in a baby weighing 7 lb 13 oz whose mother had had pre eclampsia and accidental hæmorrhage , the second was in an infant weighing 3 lb whose mother had cholelithiasis and acute cholecystitis , and the third was in a child weighing 5 lb 8 oz who died on the seventh day from a non traumatic cerebral hæmorrhage, and whose mother had had nephrolithiasis with renal failure at the time of delivery

Well marked fœtal distress had been noted before operation in the case of the stillbirth and the death from atelectasis

Remote Sequelæ

No urinary fistulæ or any persistent disturbance of bladder function resulted from the operation Mangone (1948) made similar findings

There were no chronic wound sinuses, but 2 patients later developed incisional herniæ

Subsequent Obstetric History

Up to the time of writing, 17 patients have, between them, gone through 22 further pregnancies after the operation Of these pregnancies 16 ended in spontaneous delivery of living infants and 6 were submitted to further cæsarean section In no case was a further cæsarean section undertaken because of doubts about the security of the uterine scar, and all the scars seen at a subsequent operation were found to be sound

CONCLUSIONS

The objective of every obstetrician is to conduct the woman safely through her pregnancy and labour without damage to herself or to the baby Unfortunately, in a small proportion of cases difficulties arise that make t ideal hard to attain, and, in the past, hazardous vag deliveries have been undertaken, with disastrous re to the child and permanent injury to the mother

We consider that many of these failures can be eli nated by the use of extraperitoneal cæsarean section, a we are fortified in our belief by the results we ha obtained Similar good results have been reported several American workers (see table)

RESULTS OF EXTRAPERITONEAL CÆSAREAN SECTION I INFECTED OR POTENTIALLY INFECTED PATIENTS

Reference	No of cases	Maternal mortality	Fœtal mortality	
			Stillbirths	Neona deaths
Keettel and Randall (1949)	26	0	1	[illegible]
Levine and Weiner (1947)	25	1	2	0
McCall (1949)	18	0	4	1
Daichman and Pomerance (1944)	76	0	2	[illegible]
Norton (1946)	53	0	4	
Present series	52	0	1	[illegible]
Total	260	1 (*0 4%*)	14 (*5 6%*)	6 ([illegible]

McCall s 18 patients were all grossly infected We have had to reject many reported series of cases of extraperitoneal cæsarean section because the operation had been done on patients who did not fulfil Dieckmann s criteria of potential infection In yet other reports the information was too scanty for us to form a opinion

There is a definite trend nowadays towards a broad ening of the range of indications for cæsarean section and this change of attitude has been justified by th results The extraperitoneal approach to the uter permits a further justifiable extension of the indication already accepted for cæsarean section, and at the sam time leads to a reduction in the total incidence of th operation, because the surgeon may safely allow a tri of labour to proceed far longer than is the present custo

SUMMARY

The alternative methods of handling the labour women who are potentially or actually infected a reviewed, and the advantages and disadvantages of extr peritoneal cæsarean section are discussed The operati technique is outlined

52 mothers were operated on without fatality The was 1 stillbirth and 3 neonatal deaths

The results obtained warrant the inclusion of th operation in the armamentarium of every obstetrician.

ADDENDUM

Since writing this article we have performed the operati on 6 further occasions, the indication in all cases w prolonged labour, with fœtal distress in 3 There was maternal death and no case of puerperal pyrexia All th babies survived

REFERENCES

Baird D (1930) *Lancet* i 295

Bourgeois, G A Phaneuf, L E (1949) *Amer J Obstet Gyn* 57, 237

Bradford W Z , Woltz J H E Bradford W B (1949) *Ibid*, 1093

Daichmann I , Pomerance W (1944) *Ibid* 47 678

Dieckmann, W J (1946) *Ibid* 52, 244

— Bjork F J Aragon, G T (1948) *J Amer med Ass* 1 1017

Douglass, L H Graves J H (1948) *Amer J Obstet Gynec* 55 6

Keettel W C , Randall J H (1949) *Ibid* 58, 510

Latzko, W (1908) *Wien klin Wschr* 21, 737

— (1909) *Ibid* 22, 477

Levine, W Weiner S (1947) *Amer J Obstet Gynec* 54 1013

McCall M. L (1949) *Ibid* 57, 620

Mangone E K (1948) *Ibid*, 56 1138

Marshall C Mc1 (1949) Proc British Congress Obstet Gyn London

Norton J F (1946) *Amer J Obstet Gynec* 51 519

Reid D E (1946) *Ibid* 52 719

Ricci J V (1940) *Amer J Surg* 47 33

Stone M L (1950) *Amer J Obstet Gynec* 59 49

Thomas, G (1870) *Ibid*, 3 125

— (1878) *Ibid* 11 225

Waters E G (1940) *Ibid* 39 423

o the back of his chair so that the observer could connect nd disconnect the oxygen without the subject's know-edge The blood pressure recorder was attached to the subject's right arm, and the blood flow recorder to his left The heart-rate could be obtained from either of these recordings also At the end of each period of anoxia each subject was given 100% oxygen

Method—The blood pressure was recorded continuously by a modification of a principle first described by Doupe et al (1939) It consisted of a sphygmomanometer arm-cuff automatically blown up by an electrically operated solenoid valve actuated by signals generated from a photo electric cell placed on a finger distal to the cuff The cuff pressure followed the systolic blood pressure and in this way continuous recordings were obtained The apparatus was switched off at intervals to avoid discomfort to the subject Forearm blood flows were recorded again automatically at a rate of 6 a minute by intermittent venous occlusion plethysmography This apparatus was designed by Kerslake (1949)

Results—Blood-pressure and heart rate seemed to begin to change before symptoms referable to the central nervous system could be detected The classical blood-pressure rise of 15–20 mm Hg during anoxia was followed by a fall to normal levels in every case, beginning within 2–4 seconds after the return of oxygen This could not possibly have been a cerebral effect In three persons the blood pressure subsequently fell to subnormal levels (about 105 mm Hg) and since it was associated in these cases with a considerable rise in peripheral blood flow it was sufficient to produce faintness, dizziness, and reddening of the vision In no case did the pulse rate fall below the average resting level The greatest fall in blood pressure always established itself by the 35th second and only appeared to be significant when associated with a coincident increase in peripheral blood-flow None of the 8 persons lost consciousness The most interesting case is shown in fig 3 This subject had felt faint and confused also during a writing test Fig 4 shows the average blood pressure and peripheral blood flow in all the subjects except this one Blood flow showed no significant change during anoxia lasting 4 or 5 minutes, and a significant increase did not begin until 15 seconds after the return of oxygen, the peak appearing at the 30th second

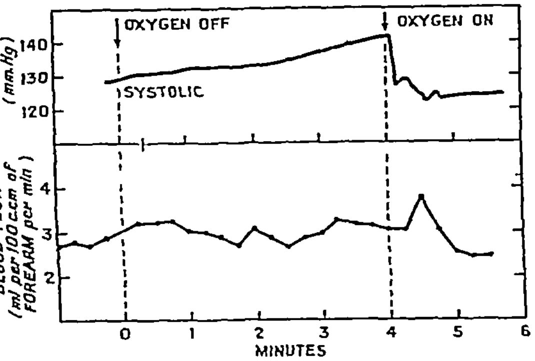


Fig 4—Average blood-pressure and peripheral blood-flow in 7 persons during recovery from 4 minutes anoxia (excluding case shown in fig 3)

BLOOD pH

It was thought that a sudden change in pH of the arterial blood brought about by sudden reoxygenation under these conditions, if coinciding with the nervous phenomena, might be the initiating factor It has also been well established that changes in the excitability of various portions of the reflex arc bear a direct relation to blood pH The magnitude of the pH change in susceptible cases was not known, so 8 persons were investigated

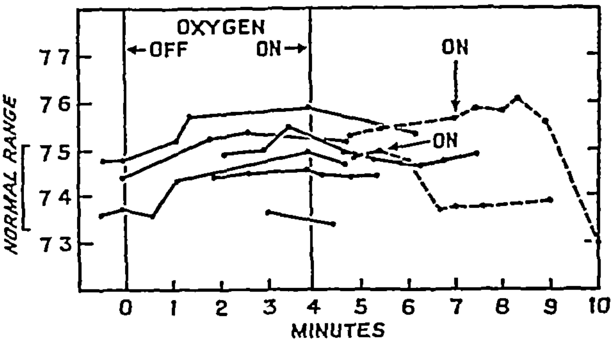


Fig 5—Changes in blood pH of 8 persons recovering from anoxia at a simulated altitude of 20,000 ft. Interrupted lines show results obtained with 5½ and 7 minutes anoxia in 2 persons The other 6 persons underwent 4 minutes anoxia.

Method—Arterial blood samples were withdrawn anærobically at short intervals, and their pH was determined during and after anoxia at a simulated altitude of 20,000 ft The successive blood samples were immediately sealed off on removal and cooled to 0°C, and the measurements were made at 38°C within an hour of removal in a new type of miniature glass electrode cell with a capacity of 0 3 c cm The accuracy of the glass electrode was shown to be ± 0 01

Results—The outcome of the experiment suggested that the pH of the blood decreased relatively slowly after sudden reoxygenation by not more than 0 04 in the first minute of recovery (fig 5) The initial rise at the start of anoxia was not linear and seemed to follow closely the expected changes in tension of arterial carbon dioxide Of the 8 persons 2 showed premonitory signs of fainting, but their blood-pH curves did not differ from those who had no symptoms The well marked pH changes found in the person subjected to 7 minutes' anoxia (fig 5) were not shown by those subjected to 4 minutes' anoxia, and it is surprising that they were tolerated without symptoms So this person was tested again to determine the pH changes following alterations in alveolar carbon dioxide tension at ground level Fig 6 shows that, in this test, hyperventilation caused the alveolar partial pressure of carbon dioxide to decrease by at least 10 mm Hg, and the pH of the blood to increase by about 0 23, within 12 seconds The initial fall in blood pH is difficult to explain, but might have followed a short period of apnœa after the third alveolar

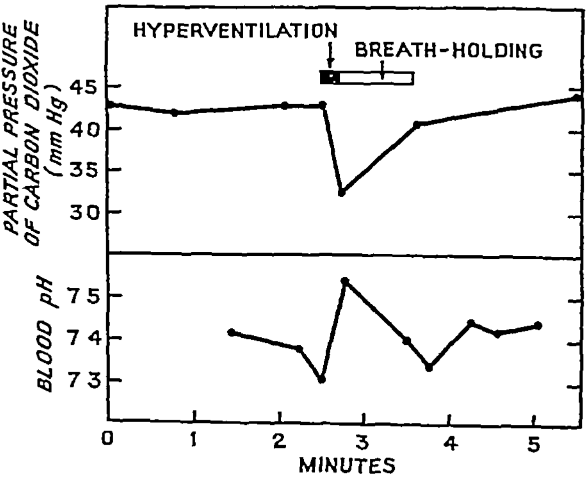


Fig 6—Changes in blood pH and carbon-dioxide tension at ground level after hyperventilation and breath-holding in the person who had undergone 7 minutes anoxia (see fig 5)

start writing Full chamber ventilation was used, and the observer maintained strict silence so that the subject's attention should not be diverted At the end of the anoxia period the subject's oxygen tube was reconnected without his knowledge At the end of the experiments the individual errors were plotted on a time scale, and the incidence of errors in each group was compared At the same time any subjective symptoms were noted by the observer, but these were not taken into account in preparing the final graph (figs 1 and 2)

Errors

This method of recording reactions did not give a complete picture of the changes taking place when the oxygen supply was resumed Subjective symptoms could not be recorded on the graph, and for this reason it is difficult to assess the number of persons showing an unmistakable paradox reaction The subjects fell broadly into four categories during the recovery stage -

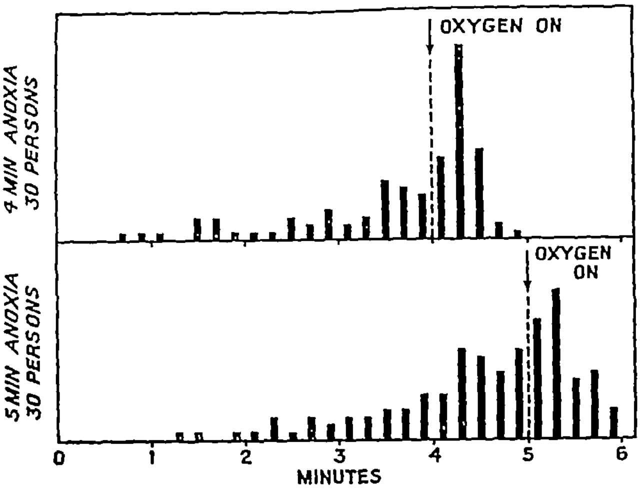


Fig 2—Errors made in 12 second periods in writing test

1 Those showing both errors and symptoms (5) See table

2 Those showing symptoms alone (3) See table

3 Those showing errors alone (5)

4 Those showing gradual recovery from anoxia without any detectable paradox reaction (39)

Categories 3 and 4 overlap and cannot be easily differentiated unless the errors show grouping during the recovery period If it is assumed that three consecutive errors after the 9th second of the recovery stage, without previous gross errors, are an adequate demonstration of the paradox reaction, at least 13 persons, including those with symptoms also, showed a paradox reaction after either 4 minutes' or 5 minutes' anoxia

If all the errors made by the 4-minute anoxia group are totalled over 3 second (fig 1) or 12 second (fig 2) periods, there seems to be a considerable increase in their incidence from the 9th to the 18th second after the oxygen was turned on This is more obvious when the graph is compared with the errors of the second group, where the anoxia was allowed to continue to the end of the 5th minute, by which time practically all of the second group were making errors The peak during their subsequent recovery stage was not so obvious, since reactors and non reactors were not adequately differentiated

To examine whether these results provide statistical proof of the paradox reaction, the sets of frequencies of errors in different time intervals may be compared as wholes The comparisons will be between the 4 minute and 5 minute anoxia groups Figs 1 and 2 show that the number of errors increased during a short interval after resumption of the oxygen supply It may be presumed that, if oxygen had not been given, the frequency of errors for the 4 minute group would have been about the same as that for the 5 minute group, since the trends for the two when both were anoxic—i e , up to 4 minutes—are very similar The mean numbers of errors for the two groups of 30 persons each from 4 minutes 9 seconds to 4 minutes 24 seconds were 1 10 for the first group and 0 47 for the second. The probability that the difference 0 63 was due to chance is shown by the *t* test to be less than 0 01 This can be accepted as good evidence that the increased number of errors following the resumption of the oxygen supply was not due to chance fluctuations.

SYMPTOMS AND ERRORS ON RESTORATION OF OXYGEN AFTER ANOXIA

Subject no	Symptoms	Time of onset after return of oxygen (sec.)	Errors
1	Faintness	30	+ -
2	Felt faint and dizzy	20	None
3	Confusion and ‘ alcoholic glow ’	20	+
4	Faintness ‘ queer	20	+
5	Faintness	18	None
6	Orange visual aura	30	+ -
7	Dizziness	16	None
8	Complete confusion lasting 17 seconds	15	+

Symptoms

Of the 52 persons tested 8 had sensations varying from simple confusion to impending collapse No person became unconscious The accompanying table gives a summary of the cases

In most cases there was also a perceptible change in the handwriting after the 9th second of recovery Writing speed increased above normal and letter formation deteriorated Irregularly shaped numerals indicated tremors and loss of control of fine movements

CARDIOVASCULAR CHANGES

8 persons were subjected to anoxia at a simulated altitude of 20,000 ft , and their blood pressure and peripheral blood flow were simultaneously recorded during the progress of the anoxia and the subsequent recovery 3 of these persons repeated the experiments later, and 2 also underwent 10 minutes' anoxia at the same altitude

In each experiment the subject was seated in an arm chair, and the lead from his oxygen mask was attached

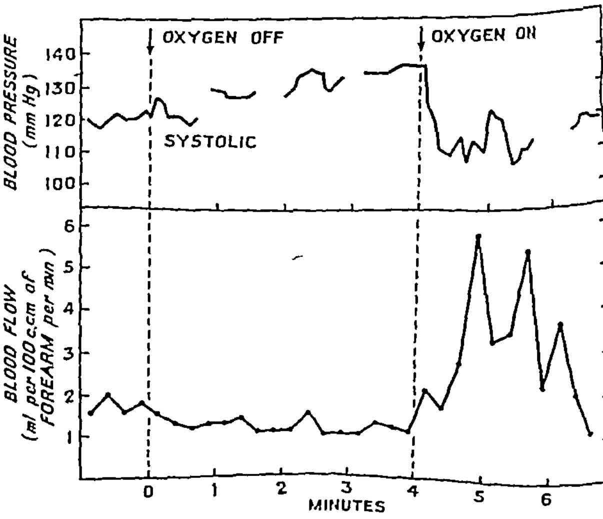


Fig 3—Cardiovascular changes during recovery from 4 minutes anoxia

9th and 12th seconds of the recovery stage from anoxia Initially it is a disturbance of the central nervous system, as manifested by an increase in writing test errors, which reaches its peak during the 12th second of recovery A slight secondary rise in the incidence of errors seems to coincide with the cardiovascular changes, which are most pronounced at about the 30th second of the recovery stage These tests have also demonstrated the onset of muscular incoördination and mental confusion developing during this period When the duration of the anoxia is increased, paradoxical symptoms in the form of faintness also increase, but the efficiency of the writing test deteriorates when the anoxia is severe

The late symptoms are those of a cardiovascular collapse associated with a fall in blood pressure and an increase in peripheral blood-flow The sequence of events is best described as follows

Systolic Blood pressure

(1) With the sudden return of oxygen there is an initial rapid fall within 2-4 seconds, which is most probably due to a rapid increase in the pulmonary vascular bed impairing cardiac filling

(2) The greatest fall in blood pressure coincided with the greatest increase in peripheral blood flow at about the 30th second

(3) Restoration to normal was usually completed within 1 minute after the return of oxygen.

Forearm Blood flow

(1) There was no significant change during the course of the 4-minute anoxia.

(2) The average curve showed a significant increase beginning *9 or 10 seconds after the return of oxygen,* and this coincided with the onset of the maximum of errors

(3) Blood flow returned to previous normal levels within 60 seconds

Blood pH

Blood pH changes followed rapidly the alveolar partial pressure of carbon dioxide The average increase in pH at the end of 4 minutes anoxia amounted to 0 09 Return to normal levels was a gradual process, which in some persons took up to 4 minutes There did not seem to be any correlation between the pH changes in the arterial blood and the production of a paradoxical reaction

It is considered probable that the neurological manifestations of the paradox reaction follow a sudden impairment of cerebral circulation due to a rapid fall in systolic blood pressure when the breathing of oxygen is started again A constitutional element is important in deciding whether the phenomenon is terminated by a cardiovascular collapse about 15 seconds after the initial onset of nervous symptoms The risk of a paradox reaction is entirely eliminated if oxygen is readministered slowly

Acknowledgment is made to the Director General of Medical Services, Royal Air Force, for permission to publish this article

REFERENCES

Baxter N E White C S Watts D T (1943) Annual Report of the Altitude Training Unit Alameda California
Bouckaert J J Heymans C (1935) *J Physiol* 84 367
Comroe J H. jun. Schmidt C F (1938) *Amer J Physiol* 121 75
Doupe J Newman H W Wilkins R W (1939) *J Physiol* 95 239
Gellhorn E Steck I E (1938) *Amer J Physiol* 124 735
Grandpierre P Franck C (1945) *Rev Corps Santé milit* 1 226
Kerslake D (1949) *J Physiol* 108 398
McMichael M. (1943) Unpublished report for National Research Council, Canada.
Noell W (1947) U.S.A.F Proj no 497 Rep no 1
— Kornmueller A. E Gremmler J (1945) *Arch Psychiat Nervenkr* 116 394
— Roeder W (1943) *Luftfahrtmed* 8 339
— Schneider M (1941) *Ibid* 5 234
Palme F., Kornmueller A. E Strughold H (1941) *Ibid* p 161
Ranke, O F (1936) *Ibid* 1 120
Ruff, S., Strughold H. (1939) Grundriss der Luftfahrtmedizin Leipzig
Schwarz W Malikiosis X (1939) *Luftfahrtmed.* 3 244
Stavraky G W (1944) Unpublished report for National Research Council, Canada.
von Euler U S, Liljestrand, G (1946) *Acta physiol scand* 12 301

A METHOD OF ESTIMATING THE COLLATERAL RESISTANCE DURING OBSTRUCTION OF THE MAIN ARTERY TO A LIMB

A C DORNHORST
M D Lond, M.R C P
READER IN MEDICINE

E P SHARPEY-SCHAFER
F P C P
PROFESSOR OF MEDICINE

IN THE UNIVERSITY OF LONDON

From the Department of Medicine, St Thomas's Hospital Medical School

THE blood flow through any limb segment depends on the local arterial pressure and the resistance offered by the peripheral vessels In normal limbs the local blood-pressure does not differ appreciably from the central pressure, but in a segment distal to an obstruction of a main artery this is not so, since the blood must traverse collateral vessels which may present a resistance comparable to that in the periphery In these circumstances the flow will be equal to the central pressure divided by the sum of the collateral and peripheral resistances Since the presence of this collateral resistance is the essential functional disability in such limbs, it is desirable to be able to estimate its magnitude In practice, as the main arterial tree becomes obstructed the peripheral resistance tends to decrease, so that measurement of the blood-flow does not allow an estimate of collateral resistance By simultaneous measurements of flow and pressures, however, such an estimate can be made

To illustrate the method a special set of circumstances was chosen where it was probable that collateral resistance was different in two limbs of one patient It has been shown that cases of osteitis deformans have a greatly increased blood-flow in the affected region (Edholm et al. 1945) and that there is an increase in the size, and possibly in the number, of arteries present (Edholm and Howarth, personal communication) A patient with osteitis deformans of the right humerus, without involvement of the left humerus or of either forearm, afforded an opportunity of studying a pair of limbs in which the arterial supply was different when the main arteries were temporarily occluded

METHOD

The method of study is shown in fig 1 A forearm and hand were enclosed in an air filled plethysmograph

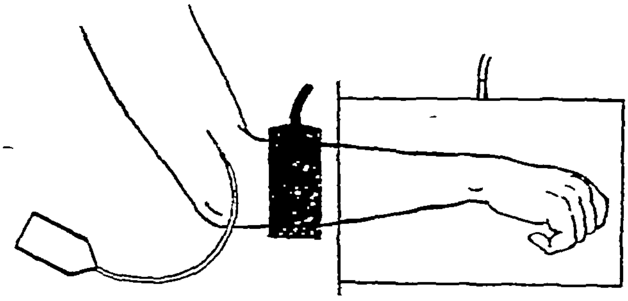


Fig 1—Plethysmograph on forearm and hand cuff on upper forearm, and needle inserted into brachial artery

A narrow cuff was placed immediately proximal to the plethysmograph just below the elbow A needle was inserted into the brachial artery at the bend of the elbow, and the pressure recorded with a condenser manometer (Hansen 1949) The brachial artery was occluded digitally about the middle of the humerus

PROCEDURE AND RESULTS

The experiment was designed to record the blood flow and blood-pressure in each arm in their normal state and sample was taken In conclusion it can be stated that the blood pH changes during the recovery stage from anoxia do not seem to bear any direct relationship to the oxygen paradox , reactors and non reactors gave similar results

DISCUSSION

The first objective change in a person suddenly reoxygenised after anoxia appears between the 9th and 12th seconds, and is predominantly a disturbance of the central nervous system, as manifested by deterioration of logical thinking, confusion, and muscular incoordination Any classical cardiovascular collapse which may develop, however, does not become established until much later, at about the 30th second of the recovery stage, and such symptoms again come under the heading of the paradox reaction, even in the absence of any preliminary detectable disturbance of the central nervous system The paradox reaction can be manifested by either or both of these distinct changes

The neurological symptoms can be explained in several ways The return of oxygen leads in every case to an immediate fall in the blood pressure, which fall impairs the cerebral circulation and consequently increases the cerebral anoxia for a while before the brain cells fully recover from their previous state The symptoms also appear at the same time that oxygenated blood first reaches the brain The possibility that a Bohr effect may lead to a temporary further increase in cerebral anoxia is not supported by the findings in the last series of experiments, which indicate that the production of a paradox reaction does not bear any relationship either to the blood-pH change due to sudden reoxygenation of the arterial blood or to the change brought about by hyperventilation during the anoxia The only other possibility is an entirely local metabolic disturbance confined to the brain cells

The rapid fall in blood pressure on reoxygenation after anoxia has been demonstrated independently on animals by many workers Grandpierre and Franck (1945) demonstrated this fall in anoxic dogs 3 or 4 seconds after the return of oxygen Similarly, von Euler and Liljestrand (1946), studying the control of the pulmonary arterial blood pressure in chloralosed cats, showed that with the return of oxygen the fall in pulmonary arterial pressure was almost immediate and was followed about 2 seconds later by a similar fall in systemic blood pressure These changes were present after extirpation of the stellate ganglion and vagotomy—i e , they were a direct effect on the lung vessels These workers also showed that, when the lung flow was doubled, there was only a 20% increase in pulmonary arterial blood pressure, demonstrating the great distensibility of the pulmonary vascular bed After reoxygenation, therefore, the high oxygen and low carbon dioxide tensions exert a local dilating effect on the pulmonary vessels This in itself would cause a sudden temporary decrease in cardiac output and fall in systemic blood pressure, and at the same time a high partial pressure of oxygen and low partial pressure of carbon dioxide in the arterial blood would cause a similar fall in blood pressure by its action on the aortic and carotid chemoreceptors This change, however, would take longer to develop and would entail peripheral blood flow changes of an equal intensity unless it was brought about by a sudden decrease in cardiac output Such a decrease in cardiac output, from a purely dynamic aspect, could only take place if there were a coincident and temporary increase in the pulmonary vascular bed and a fall in pulse rate as demonstrated It may be noted that, according to Bouckaert and Heymans (1935), carotid sinus reflexes do not affect the cerebral vasomotor tone in any active way It seems that the blood pressure changes are only significant contributory factors towards a fainting type of reaction when they are associated with a later increase in peripheral blood flow There are many factors which could give rise to the increase in blood flow observed during the recovery, and it is difficult to determine which predominates It is unfortunate that the subjects of the experiments were unable to perform the writing test simultaneously with the blood pressure and blood flow recordings during all the experiments An accurate timing of these reactions is important in referring to work carried out by Noell and Schneider (1941), who measured femoral blood flow and blood pressure in anæsthetised dogs and found a decrease in femoral blood flow with return of oxygen in anoxic animals, which was greatest after 15–20 seconds These findings are in accordance with those of Ranke (1936), Gellhorn and Steck (1938), and McMichael (1943)

The possibility of a sudden cerebral ischæmia due to local vasoconstriction appears at first sight to be sound enough Although Noell and Schneider (1941) state that cerebral blood flow only follows the systemic arterial blood pressure during anoxia, there is other evidence that high oxygen tensions in the presence of low carbon dioxide tensions cause active vasoconstriction of cerebral vessels The electro encephalograms obtained during the recovery stage from anoxia do not entirely support this theory Palme et al (1941) showed that the bioelectric changes typical of cerebral anoxia had disappeared by the end of 10 seconds after the return of oxygen If the recovery period were associated with a cerebral vasoconstriction sufficient to cause enduring cerebral anoxia, one would expect the bioelectric manifestations of anoxia to be continued long into the recovery stage, certainly over the crucial interval from the 9th to the 15th second in the paradox reaction Noell, Kornmueller, and Gremmler (1945) also found that the abnormal electro encephalographic waves typical of convulsive states only appeared after the classical picture of cerebral anoxia had disappeared

It is obvious that many factors contribute to the final outcome, and a constitutional element is important in determining whether or not the nervous manifestations of the paradoxical reaction are further complicated by circulatory collapse It seems that a person does not always produce a paradox reaction even if he has been shown to be a good reactor on a previous occasion In the light of past experience it has been found that, providing the oxygen is turned on slowly, in all cases the risk of a paradox reaction is eliminated No untoward effects in aircrew have been noted when this rule has been applied

SUMMARY AND CONCLUSIONS

60 anoxia tests were carried out on 52 people at a simulated altitude of 20,000 ft The subjects were divided into two groups, the first being anoxic for 4 minutes, and the second for 5 minutes During the performance of a modified Lottig's writing test the incidence of errors during the recovery stages was calculated and compared

Further experiments were made on 8 of these subjects to determine the precise cardiovascular changes during the recovery stage from anoxia For this purpose blood pressure, peripheral blood flow, and pulse rate were recorded with apparatus specially designed to give automatic and continuous records

A further nine experiments were made to determine the blood pH fluctuations during the course of the paradoxical reaction The measurements were made with a new micro pH cell on intermittent arterial blood samples

A paradox reaction to oxygen was demonstrated in 13 of the 52 subjects and seemed to begin between the nor Rs changed during the experiment If these assumptions are justified, the experimental points will lie on the intersections of the lines It will be seen that this requirement is approximately fulfilled

Calculation gives a value of Rc on the left some five times that on the right The difference in pressures when the cuff is inflated so as to obstruct all flow is less striking than might be expected, because the flow through the part of the arm between obstruction and cuff is greater on the diseased side Indeed Rs on the right is about a third of that on the left

The method may be applied to cases of occlusive disease of the main artery, if the artery can be entered with a needle distal to the block

SUMMARY

Blood flow and blood pressure were measured in the forearm and hand, with the main artery open and occluded, in a resting state and during reactive hyperæmia

The data allowed the calculation of the resistance of the collateral vessels with the artery occluded

An example is given of a patient with osteitis deformans of one humerus in whom collateral resistance was found to be five times greater on the normal than on the affected side

The method can be used for the study of limbs with occlusive arterial disease, provided local arterial pressure can be measured

We are indebted to R W Halls for technical assistance and Miss C J Dewe for the drawings

REFERENCES

Edholm O G Howarth S McMichael J (1945) *Clin Sci* 5 249
Hansen T (1949) Pressure measurement in the human organism Copenhagen

TREATMENT OF EARLY SYPHILIS

WITH PENICILLIN, NEOARSPHENAMINE, AND BISMUTH, AND WITH PENICILLIN AND BISMUTH ALONE

F J G JEFFERISS
M.R C S
ASSISTANT DIRECTOR

R R WILLCOX
M.D Lond
SENIOR ASSISTANT

G L M McELLICOTT
M R C S
DIRECTOR

VENEREAL DISEASES DEPARTMENT, ST MARY'S HOSPITAL, LONDON

Two years ago, McElligott et al (1948) reviewed 275 cases of early syphilis treated with penicillin and a course of neoarsphenamine and bismuth lasting from six to ten weeks The total dose of penicillin ranged from 2 4 to 4 million units in 7½–12½ days Two thirds of the male patients and half the females were treated as outpatients with penicillin in oil beeswax mixtures, the remainder being admitted to hospital and given 40,000–75,000 units of amorphous penicillin three hourly or four hourly Contrary to expectation, more failures were noted in the smaller number of patients receiving aqueous penicillin at short intervals than among those given daily injections of oil-beeswax mixtures At the time of review 54% of the total had been followed from twelve to eighteen months, 70 2% nine months or more, and 78 1% six months or more Eleven patients in this series were treated again, four of these showing recent genital lesions, and all of them positive serum reactions The possibility of reinfection rather than relapse could not be dismissed in any of the four clinical failures

To these cases we now add 286 cases treated on similar lines, and report on the follow up of the whole 561 patients and on the results of treating 183 primary and secondary cases with penicillin and bismuth alone

The comparatively high incidence of toxic effects in the previous series, and the improved quality of the available penicillins, with their very high crystalline II (G) content, encouraged us to abandon arsenicals in the treatment of early syphilis in the autumn of 1947, and up to now we have had no cause to regret our decision

Bismuth is relatively harmless and, though there is no certain evidence that a true synergism exists between it and penicillin in the treatment of early syphilis in man, the poor results of intensive and semi intensive arseno therapy without added bismuth suggest that a more slowly acting drug may be necessary to aid the immune processes in "mopping up" any straggling spirochætes We still feel that the prolongation of the total treatment time may possibly have lowered the incidence of infectious relapse, and that, in some cases, it has perhaps prevented reinfection among married couples or other regular consorts Be that as it may, the inevitable high absentee rate during the period of surveillance is probably lowered if the treatment time is not so curtailed as to bring it into contempt

Since the publication of our first paper few further attempts have been made to assess the results of combined antibiotic and metal syphilotherapy

Eames and Miller (1949) reported the results of treating 1022 Army patients with 4 000,000 units of penicillin combined with a ten week course of neoarsphenamine and bismuth Owing to demobilisation there were many defaulters from subsequent surveillance but an actuarial assessment disclosed a failure rate of 15% at eighteen months

Marin et al (1949) combined 2 400 000 units of penicillin with arsphenoxide four times weekly for five weeks and bismuth twice weekly over the same period, and of 230 patients treated 185 were followed from six to thirty months The results in 36 seronegative cases were adjudged 100% satisfactory, in 55 seropositive primaries 90% satisfactory and in 94 secondary cases 86% satisfactory

Pardo Castello and Pardo (1950) treated 47 patients with early syphilis with twenty daily injections of 500,000 units of penicillin in aqueous solution with from ten to twenty biweekly injections of subsalicylate of bismuth Of 41 patients observed from three to fifteen months 26 attained or maintained seronegativity, the remaining 15 showing no signs of relapse with a declining serological titre

O'Malley (1950) reports 365 cases of early syphilis treated with various doses of penicillin plus three or four injections of arsphenoxide and bismuth Of 86 followed for a year 4 were seroresistant and 8 showed serological relapse, 1 of which had mucocutaneous lesions in addition The failure rate was assessed at 13 95%

In both of our series we have tried to classify the known failures as relapses or reinfections after critical examination of each case In coming to a decision we have been guided by the following principles

(1) A slowly declining serological titre, even up to twelve months or longer, is no evidence of failure of treatment

(2) A continued rising serological titre after treatment is always evidence of failure, and static positive findings, in both complement fixation and precipitation tests, are most likely to be so if they persist for six months or longer

(3) A solitary genital mucocutaneous lesion on a new site with negative or declining serum reactions is probable evidence of reinfection more especially if it follows exposure with a known infectious consort A mucocutaneous relapse is almost invariably preceded by a rising titre in the serum test

PENICILLIN, NEOARSPHENAMINE, AND BISMUTH

Patients	*Men*	*Women*	*Total*
No treated	336	225	561
Stage of disease			
Primary	269	75	344
Secondary	67	150	217
Dark field			
Positive	298	163	461
Negative	38	62	100
Serum tests			
Positive	215	201	416
Negative	121	24	145

in reactive hyperæmia, first with the main artery open, and secondly with the artery occluded

Identical observations were made on each arm, and the results are shown in fig 2 Resting blood flow and blood pressure were first recorded and found to be the same in both arms Blood flow and blood pressure were again recorded immediately after releasing the cuff inflated to 300 mm Hg for thirty seconds The brachial artery was then occluded, and about ten seconds later, when the blood pressure had fallen to a stable figure, the blood flow was again measured and was found to be 5 ml a minute in the normal arm and 12 ml a minute in the affected arm The blood pressure in the affected arm was higher, and greater pulsations were recorded than on the normal side After twenty seconds the forearm cuff was inflated to about 300 mm Hg This caused a rise in blood-pressure and an increase in pulsations on both sides, the rise in blood pressure being relatively greater in the normal limb During this period there was, of course, no blood-flow in the forearm and hand After thirty seconds the cuff pressure was dropped suddenly to less than 30 mm Hg, and the blood flow and blood pressure were recorded The blood flow increased, and the blood pressure decreased, on both sides The blood flow was less and the blood pressure lower in the normal limb

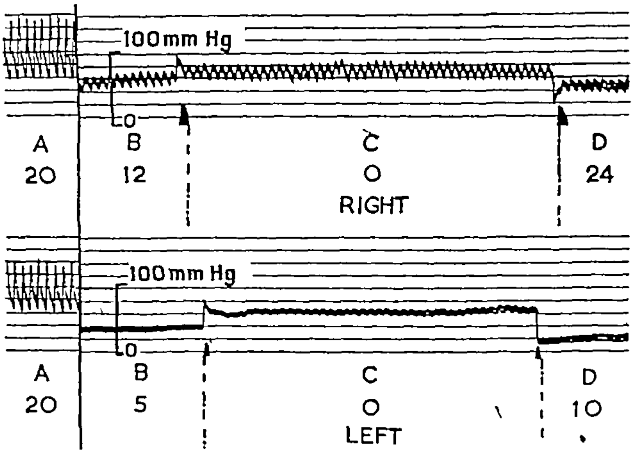


Fig 2—Upper record pressure in right brachial artery (affected limb) Lower record : pressure in left brachial artery The arteries are unobstructed during A and obstructed in the mid brachial region during B, C, and D During C the cuff was inflated to about 300 mm Hg The figures are the respective measured flows in ml per min

ANALYSIS OF RESULTS

The drop in pressure across an ideal resistance is, with appropriate units, equal to the product of the resistance and flow through it Thus, the difference between the local and central blood pressures in our experiment is equal to the value of the collateral resistance multiplied by the total blood flow in the limb distal to the obstruction We have measured the pressures, and if the flow is known the resistance can be immediately calculated In fact we have not measured the total flow through the resistance but only a part of it, since there was about 10 cm of arm between the obstruction to the brachial artery and the collecting cuff However, from the data it is still possible to calculate the resistance if certain assumptions are made The design of the experiment allows a check on the validity of these assumptions

Consider the situation when, while the artery is occluded, the cuff is inflated to a high pressure Although no blood-flow is recorded the local blood pressure is still less than the central, because some tissue above the cuff is supplied through the collaterals If the vascular resistance of these tissues is Rs, then

$$Rs = \frac{p}{P - p}\ Rc$$

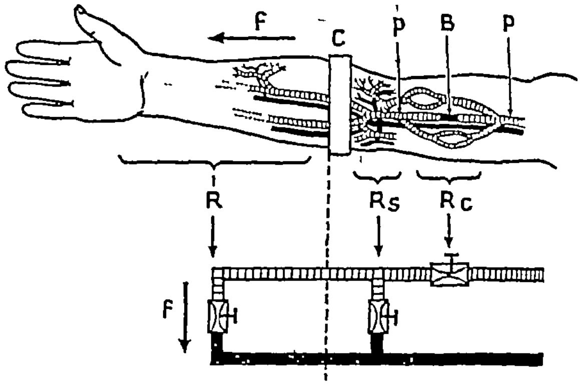


Fig 3—Diagrammatic representation of the conditions during the experiment : P, central pressure p, local pressure ; Rc, collateral resistance Rs, shunt resistance R, peripheral resistance f, measured flow B block in main artery , C, cuff

where P=the central pressure, p the local pressure under these conditions, and Rc the collateral resistance (see fig 3) If at other times a flow (f) is occurring through the part of the limb distal to the cuff, then, if Rc and Rs do not change and the local pressure is p′,

$$Rc\left(f + \frac{p'}{Rs}\right) = P - p'$$

Substituting for Rs as above, and solving for Rc, gives

$$Rc = \frac{P}{p}\ \frac{p - p'}{f}$$

In our experiment, besides measuring P and p, we have for each side two sets of values of p′ and f, since the flow is increased after the period of total ischæmia Hence two estimations of Rc can be made on each side In fig 4 all values for flows and pressures are plotted together with the values for either limb with the main artery unobstructed The graph may be interpreted as follows line A corresponds to the flow pressure relation in the periphery of either limb under normal conditions—i e , it represents peripheral resistance—line B represents the resistance lowered during reactive hyperæmia after thirty seconds' complete ischæmia , and lines C and D represent the pressure drop resulting in either arm by flow through the collaterals when the main artery is occluded Our assumptions are (1) that the peripheral vessels were in a similar state in both arms and reacted in the same way to thirty seconds' ischæmia , (2) that the pressure flow relationship was substantially linear over the experimental range , and (3) that neither Rc

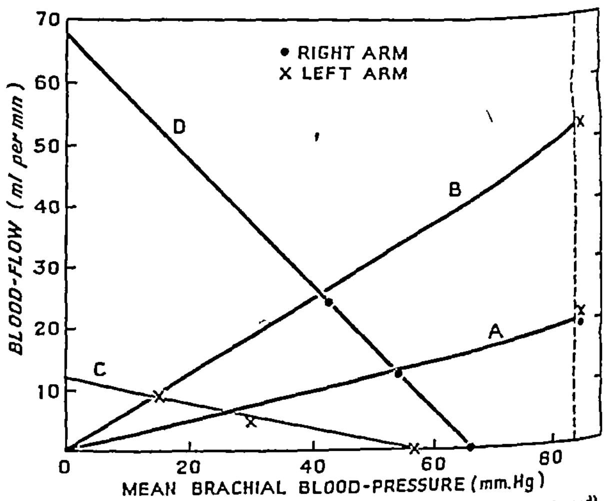


Fig 4—Pressure-flow relationship in both arms : ●, right (affected) arm ; X left (normal) arm Points on interrupted line are with artery unobstructed other points are with artery obstructed. See text.

eclamptic shortly before term, was delivered by cæsarean section of a macerated fœtus not thought to be syphilitic

Potential Failures

The 17 secondary syphilitics (14 men and 3 women) who defaulted before a decline in titre could be noted have already been mentioned and it is impossible to guess how many, if any, ultimate failures these will produce

The remaining 7 potential failures are as follows

(1) Three secondary syphilitics defaulting between four and nine months after treatment with declining serum titres

(2) One late secondary case (*T pallidum* not isolated) defaulting at eight months with a strongly positive serum titre

(3) One patient, diagnosed on clinical and historical grounds as a seropositive cervical chancre (*T pallidum* not isolated) whose serum titre had only partially declined up to the fourth month and had remained static for a further six months

(4) Two secondary syphilitics whose Wassermann reactions became negative within four months but Kahn tests were weakly positive at eighteen months Further treatment was withheld for it is our experience that such cases ultimately become completely negative

Known Failures

Two have returned nine and fifteen months after treatment with penile chancres (*T pallidum* present) but with negative serum reactions Both of these admitted re exposure from three to six weeks previously and are classed as *reinfections*

Three men whose serum tests had become negative returned nine and twelve months after treatment with dark-field positive genital lesions and positive serum reactions Although re-exposure was admitted they are classed as *relapses*

CONCLUSIONS

Patients —744 cases of early syphilis treated at St Mary's Hospital in 1946–48 are reviewed men 459 women 285, primary stage 427, secondary stage 317, dark-field positive 597, dark-field negative 147, seronegative 179, seropositive 565

Treatment —All patients had an eight-day course of penicillin, 561 receiving neoarsphenamine and bismuth in addition, and 183 added bismuth only

Toxic Effects —The only significant side-effects were those attendant on intravenous arsenotherapy

Cerebrospinal Fluid —Diagnostic lumbar punctures on 160 patients disclosed two instances of abnormality

Surveillance

229	patients were followed for	24 months or more
298	„ „	18
383	„	12
443	„	9
501	„	6
579		3
165		Less than 3

Results —The fact that 56 patients (7 5% of the total) defaulted while still seropositive, most of them immediately after treatment, and that only a little more than half the total have been observed for twelve months or more, deters us from attempting to calculate a percentage failure rate We are therefore content to enumerate the known failures as follows

Known reinfections	12
Known relapses	13
Weakly positive precipitation tests persisting for over nine months	3
Possible neuro-failures	2
Total	30

These figures support our opinion that eight daily injections of 500,000–600,000 units of penicillin in oil-beeswax suspension, followed by a short course of neoarsphenamine and bismuth, or of bismuth alone, is likely to be equally good treatment for early syphilis, and the fact that the early and later failure-rates do not seem to be worsening with the lapse of time is partially due to a diminishing reservoir of infectious syphilis from which reinfections could be acquired and to a steady improvement in the treponemicidal power of available penicillin preparations

Though the C S F is almost invariably normal a year or more after apparently successful treatment, 2 of 160 specimens of C S F tested showed some abnormality in seronegative patients It thus seems advisable to continue the practice of diagnostic lumbar puncture until cure is presumed

We are becoming increasingly convinced that, provided penicillin resistant strains of treponemata do not appear—and there is no evidence that they are likely to do so—the end of the arsenical era is probably at hand, and that the best treatment of syphilis in the future will be effected without the aid of these powerful albeit toxic drugs

Our thanks are due to our serologist Dr R H Gorrill and to Dr G W Csonka and the staff of the department for their help in this study

ADDENDUM

Since the submission of this article 2 further serological relapses have occurred, one twenty-four months and the other thirty-nine months after treatment The first patient a man with secondary syphilis, had received eight daily injections of 600,000 units of penicillin in oil beeswax followed by twelve of bismuth (0 2 g) at four day intervals The cerebrospinal fluid was normal at the time of relapse The second a woman with secondary syphilis, had received eight daily injections of 500 000 units of penicillin in oil beeswax followed by 4 3 g of neoarsphenamine and 3 4 g of bismuth given in twelve injections at four-day intervals Serum tests remained continually negative for thirty-four months and the C S F was normal at the time of relapse In both cases serological reversal has rapidly followed retreatment

REFERENCES

Eames J W Miller D H (1949) *Brit med J* ii 672
McElligott G L M. Jefferiss F J G Willcox, R R. (1948) *Brit J vener Dis* 25 45
Marin A Boulais F L Lambert A Foley J P Leclerc G (1949) *Ann Derm. Syph Paris* 9 23
O'Malley C K (1950) *S Afr med J* 24 127
Pardo-Castello V Pardo O A (1950) *Arch Derm Syph Chicago* 61 196

STREPTOMYCIN IN LATENT GENITAL TUBERCULOSIS IN WOMEN

I Halbrecht
M.D Strasbourg
From the Maternity Hospital, Hadera Israel

In the past eight years the importance of genital tuberculosis in the pathogenesis of sterility in women has been firmly established [1–7] The so-called "latent" form is much the commonest, and, in contrast to the exudative form, the prognosis is almost always good On the other hand the latent form almost always gives rise to sterility which is unresponsive to treatment

The sterility in these women seems to be caused, not by the tuberculous infection of the endometrium but by partial or total occlusion of the fallopian tubes, or it may be due to the extensive changes from the early tuberculous process in the endosalpinx and the perisalpinx. Most investigators take the view that the infection is not primarily of the reproductive organs, but that these

Treatment

The total dosage of penicillin varied between 2 4 and 5 million units in eight days, the great majority receiving 500,000–600,000 units in an oil wax medium daily for eight days This was followed by an average of 4 0–4 5 g of neoarsphenamine (0 45 g every four days) and an average of about 2 0 g of bismuth (0 2 g of the oxychloride simultaneously with the arsenic)

Toxic Effects

No toxic effects of bismuth were noted, those of the penicillin were trivial, being limited to a few cases of urticaria, which were controlled with anti histamine drugs Those due to arsenic were comparatively numerous

	Men	*Women*
Toxicodermal		
Ninth day erythema	19	18
Dermatitis	8	5
Pruritus	1	2
Herpes zoster	1	1
Gastro intestinal		
Hepatitis accompanying ninth day erythema	1	0
Icterus	17	1
Urobilinogen in urine	2	2
Nausea and vomiting	2	9
Miscellaneous		
Nitritoid crises	2	0
Granulocytopenia	2	1
Anæmia	0	1
Pyrexia	1	1
Headache	1	2
Pains in joints	2	1
Œdema	0	1
Numbness of extremities	0	1
Total	59	46

Total toxic effects 105

The incidence of jaundice in men was high and, although syringes and needles were boiled for fifteen minutes before use, this was attributed to the virus of homologous serum jaundice It is of interest, however, that 6 of these patients had previously had severe ninth day reactions

Surveillance

As was to be expected in a large metropolitan clinic with many of the patients foreigners and others casually employed, the default rate during post treatment observation was high, and 34 seropositive patients defaulted shortly after completion of treatment, and 5 others disappeared within six months and before becoming seronegative However, apart from these and the failures which are noted, all but 26 became seronegative within six months, and all of these achieved sero negativity within a year, 14 of them within nine months The surveillance periods were as follows

Men	*Women*	*Total*	*Follow up (months)*
32	26	58	36 or more
74	50	124	30 ,, ,,
127	88	215	24 ,, ,,
142	112	254	18 ,,
179	128	307	12 ,,
207	141	348	9
232	162	394	6 ,,
265	186	451	3 ,,
63	47	110	Less than 3

Failures

Of the 22 failures noted to date 10 have been classified as reinfections, 4 of the others relapsing with muco cutaneous lesions and the remaining 6 serologically There are also in addition 2 doubtful neuro failures Diagnostic lumbar punctures have so far been done on 146 patients, with completely normal results except in the following 2 cases

The cerebrospinal fluid (C S F) of a woman examined thirty two months after treatment showed 6 lymphocytes per c mm and a doubtful increase of globulin, all other findings including the Wassermann reaction, being negative This patient unfortunately defaulted immediately afterwards

A second woman, examined at twenty nine months, showed a paretic Lange curve, with all other findings negative In this case no treatment was given until the C S F had been twice rechecked at thirty one and forty months with similar results The patient was then treated again with 4,800,000 units of penicillin in oil beeswax in eight days, and on lumbar puncture at forty six months the C S F was normal

The significance, if any, of these two questionable recurrences of neurosyphilis is doubtful, especially in view of their negative serology, but they are both included among the failures Our known failures therefore may be classified as reinfections 10, relapses 10, and recurrences of neurosyphilis 2

PENICILLIN AND BISMUTH ONLY

Patients

	Men	*Women*	*Total*
No treated	123	60	183
Stage of disease			
Primary	78	5	83
Secondary	45	55	100
Dark field			
Positive	98	38	136
Negative	25	22	47
Serum tests			
Positive	91	58	149
Negative	32	2	34
Penicillin (4 8 mega)			
Oil beeswax	123	49	172
Aqueous	—	11	11
Bismuth			
1 5–2 5 g	109	42	151
Less than 1 5 g	14	18	32

Treatment

All patients received 4,800,000 units of penicillin in eight days and, except 11 cases in which two hourly injections of aqueous solutions were given, this was administered in eight daily injections of 600,000 units in an oil-wax mixture In all cases this was followed by weekly or occasionally bi weekly injections of 0 2 g of bismuth oxychloride, 151 patients being given doses of 1 5–2 5 g, and 32 less than 1 5 g Except for a few cases of urticaria, none of which, with the help of antihistaminics, was severe enough to interfere with treatment, no adverse side effects were noted

Surveillance

Men	*Women*	*Total*	*Follow up (months)*
12	2	14	24 or more
33	11	44	18 ,,
54	22	76	12
60	35	95	9
69	38	107	6
86	42	128	3 ,,
36	19	55	Less than 3

Up to February, 1950, 76 patients have been followed for a year or more, and over half of the total for nine months *The 55 patients* who have been followed for less than three months include 17 secondary syphilitics who defaulted before any significant decline in serum titre could be recorded, but, apart from this, all but 11 patients have become seronegative within three months and 9 of these within nine months and 2 within a year It is now our practice to postpone examination of the C S F until the second year of post treatment observation, provided that the serological response has been satisfactory, and of the specimens of C S F so far examined all have been found normal

Three women were given "insurance" treatment with eight daily injections of 600,000 units of procaine penicillin G because of a subsequent pregnancy The offspring of 2 of these were clinically and serologically normal at six months after birth, and the third patient, becoming pre-

BACTERIOLOGICAL CONTROL OF AUREOMYCIN THERAPY

ELIZABETH TOPLEY
M.D Lond

E J L LOWBURY
M.A, B.M Oxfd

L HURST
A I M L T

OF THE MEDICAL RESEARCH COUNCIL BURNS UNIT, BIRMINGHAM ACCIDENT HOSPITAL

IT is now recognised that 'Aureomycin' rapidly becomes inactive in nutrient media at a temperature of 37°C and at pH levels above 6 0, also that the bacteriostatic titre is considerably higher than the bactericidal titre and is markedly affected by the size of the original inoculum and the stage of growth of the culture used (Paine et al 1948) With these considerations in mind we have developed a disc assay method for detecting aureomycin in burn exudates and a ditch plate technique for testing the sensitivity of *Staphylococcus aureus*[1] to aureomycin These methods are briefly described here because they may be useful in controlling aureomycin treatment of staphylococcal and other infections Further experimental details will be reported elsewhere

DISC ASSAY METHOD FOR DETECTING AUREOMYCIN

Minimal quantities of aureomycin were detected by using Evans peptone agar at the lowest pH (5 6) and the lowest incubation temperature (25°C) which together allowed adequate growth of the indicator organism Fig 1 demonstrates the value of this low temperature and pH In laboratories without a 25°C incubator moderately satisfactory results can be obtained by using a heavy inoculum of a quickly growing indicator organism (*Bacillus cereus*),[2] incubating at 37°C, and reading the results in four hours To obtain the widest zones of inhibition, however, the lower temperature is important

With these modifications, the standard procedure of disc assay (Heatley 1949) was adopted The organism should be sensitive, as judged by the tube dilution method described below, to 0 04 µg of aureomycin per ml Many strains of *Staph aureus* and the only strain of *B cereus* that we tested are of this order of sensitivity Each organism has minor practical advantages over the other, and both are at present being used in this laboratory The stage of growth of the organism does not seem to be important, but smaller inocula have been shown to produce larger zones of inhibition around aureomycin discs A 1 in 1000 dilution of a 24 hour culture is the highest dilution that, after 24 hours' incubation on media of pH 5 6 at 25°C, gives clearly definable zones In these tests we used a phthalate acid buffer at pH 3 as solvent and diluent for aureomycin (Randall et al 1949)

Detection of Aureomycin in Burn Exudates

Discs 9 mm in diameter were cut with a cork borer from thick fluffless blotting paper dry sterilised in a hot-air oven, and stored in small petri dishes Each disc soaked up about 0 02 ml of fluid In the assay of dilutions of aureomycin this quantity was delivered from a '50 dropper' pipette immediately before assay To collect samples of exudate the discs were placed with sterile forceps on the burnt area where, within 10 seconds they soaked up exudate or blood from the raw surfaces They were also used for sampling exudate left on dressings or neighbouring skin and at necropsy for taking multiple samples from tissues and fluids —e g, bone marrow, cerebrospinal fluid, and intestinal contents

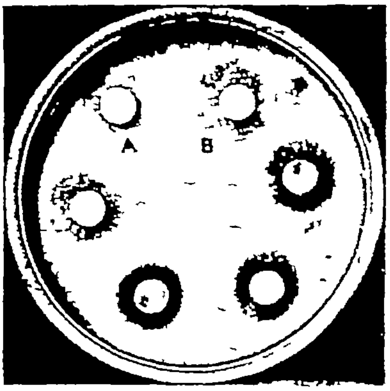


Fig 2—Detection of aureomycin in burn exudate. An undiluted 24-hr broth culture of *B cereus* was the test organism on a plate at pH 5 6 incubated for 18 hr at 25 C. Discs A and B contained 0·02 ml of aureomycin solution 1 µg and 5 µg per ml respectively the other discs had received exudate from four different burned areas on a patient treated with aureomycin 250 mg six hourly by mouth.

These discs have been assayed on plates together with discs containing known amounts of aureomycin So far, on the assumption that each disc absorbs about 0 02 ml of exudate, zones of inhibition equivalent to between 1 µg and more than 10 µg per ml have been obtained on every occasion from the 6 patients whose burn exudates were sampled while they were receiving aureomycin (at least 250 mg six hourly, see fig 2) and never from patients not receiving aureomycin

It is too early to say whether aureomycin in exudates can be assayed with any precision The experimental error of the assay method has yet to be defined, and we do not know whether the curve of zone diameter and log concentration for aureomycin in exudate is a straight line and whether it parallels that for aureomycin in phthalate buffer (Knudsen and Randall 1945)

The heat lability of aureomycin can be used to differentiate zones of inhibition produced by aureomycin from those produced by other constituents of the exudate Zones produced by aureomycin on pH 5 6 plates seeded with *Staph aureus* and incubated at 25°C become much smaller and are often eliminated if they are incubated for a further day at 37°C This reduction in size does not occur if the bactericidal agent in the exudate is, for example, a compound applied locally, such as dibromopropamidine, or the product of bacteria, such as *Pseudomonas pyocyanea*, colonising a burn For this reason it is recommended that assay plates, after incubation at

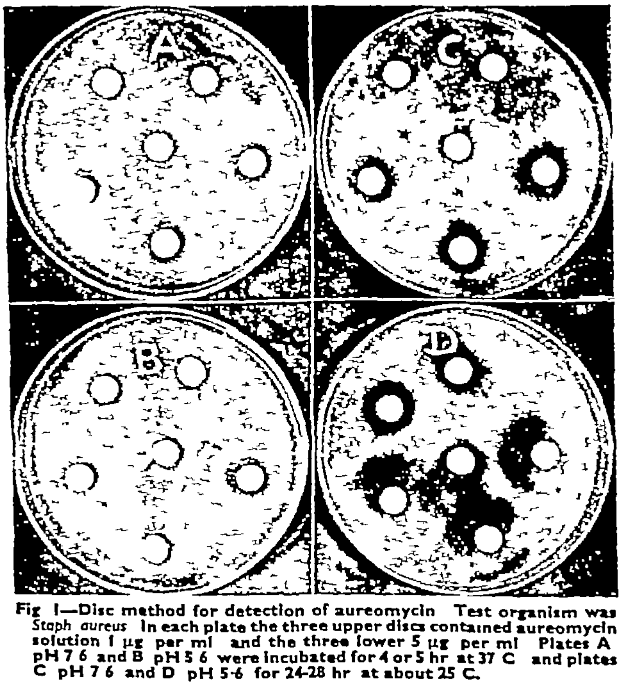


Fig 1—Disc method for detection of aureomycin Test organism was *Staph aureus* In each plate the three upper discs contained aureomycin solution 1 µg per ml and the three lower 5 µg per ml Plates A pH 7 6 and B pH 5 6 were incubated for 4 or 5 hr at 37 C and plates C pH 7 6 and D pH 5·6 for 24-28 hr at about 25 C.

---

[1] The name *Staph aureus* is used to designate any coagulase positive gram positive coccus

[2] The strain of *B cereus* (no 5) was supplied by the Lederle Laboratories Division of the American Cyanamid Company New York

are involved in a descending process from the mesenteric glands and other neighbouring organs This process attacks first the tubes and, much later, the endometrium, and it causes no symptoms Thus, when endometrial tuberculosis is discovered accidentally the anatomical changes in the tubes may be so far advanced that conception is out of the question, and in these circumstances the prospect of curing the sterility is very poor even if the tuberculous process can be arrested Nevertheless, bearing in mind the possible extension of infection to adjoining organs, one is justified in making every effort to treat the condition conservatively, however poor the prognosis for conception

MATERIAL AND METHOD

In evaluating any treatment of endometrial tuberculosis, it has to be remembered that this disease is almost always associated with endosalpingitis and/or perisalpingitis This report, however, is concerned with the treatment of endometrial tuberculosis only, and not of genital tuberculosis in general, because our methods of confirming therapeutic success or failure are limited to endometrial biopsy and to cultures from menstrual discharge

Genital tuberculosis, and particularly endometrial tuberculosis, may clear up spontaneously, so this account deals only with cases recently diagnosed and treated After treatment the result of a single endometrial biopsy is unreliable; for in serial biopsies one may be positive and the next, without further treatment, negative These negative results can only be regarded as accidental, and for this reason we have based the evaluation results not on endometrial biopsies alone but also on cultures of menstrual discharge, of which we have made as many as possible both before and after treatment

Five sterile women in whom endometrial tuberculosis was diagnosed by biopsy, and one woman whose menstrual discharge showed *Mycobacterium tuberculosis* on culture, were treated with streptomycin We made every effort to treat these cases of latent genital tuberculosis with the minimal effective doses, in order to prevent side effects Three patients received 1 g daily in two doses of 0 5 g, the other three received 1 g daily for eight days only, followed by 0 5 g daily in two doses during the rest of the course The total amount of streptomycin received by each of five out of the six cases was 40–45 g

CASE REPORTS

Case 1—Aged 20 Married 5 years, no pregnancy Bimanual examination of uterus and adnexa was negative Insufflation on Oct 7, 1947, showed the tubes to be patent Endometrial biopsy on March 27, 1948, showed normal endometrium First curettage, on June 26, revealed endometrial tuberculosis, as did a second on Oct 13 Endometrial biopsy on March 16, 1949, also gave positive proof of tuberculosis and cultures of menstrual discharges of two menses produced growth of *Myco tuberculosis*

The patient received 1 g of streptomycin daily for 75 days Endometrial biopsy on Oct 2 showed no endometrial tuberculosis, and three cultures of menstrual discharge after treatment were negative

Case 2—Aged 32 Married 10 years, sterile No history of tuberculosis Bimanual examination revealed a tumour of the left adnexa the size of an average apple Suspicion of tuberculosis was confirmed by endometrial biopsy, and two of six cultures from menstrual discharges were positive

The patient received 45 g of streptomycin spread over 45 days Thereafter endometrial biopsy showed a normal endometrium, and four cultures were negative

Case 3—Aged 30 years Married 4 years, no pregnancy At the age of 20 the patient had had pleurisy with effusion Pelvic examination showed no pathological change in uterus or adnexa Biopsy in July, 1948, showed tuberculosis of the endometrium, and of eight cultures of menstrual discharges, five showed numerous colonies of *Myco tuberculosis* The patient received altogether 45 g of streptomycin of which 8 g was given during the first 8 days and the remainder in doses of 0 5 g daily Biopsy performed after treatment was completed indicated that the endometrium was normal and five cultures were all negative

Case 4—Aged 40 years Married 10 years, no pregnancy No history of tuberculosis Genitalia normal In 1947 salpingography showed occlusion of the right tube, endometrial biopsy at this time revealed severe tuberculosis of the endometrium

This patient received 45 g of streptomycin, 20 g during the first 20 days, and the remainder in 50 days After the treatment a biopsy showed normal endometrium

Case 5—Aged 35 years Married 10 years, sterile Biopsy in 1946 showed tuberculosis of the endometrium Pelvic examination revealed nothing abnormal except for sinistroposition of the uterus Seven cultures of the menstrual discharges between January and July, 1949, gave two positive results

This patient received 42 g of streptomycin between Sept 15 and Nov 6, 1949 Biopsy on Dec 20 revealed normal endometrium Six cultures since the end of the treatment have all been negative for tuberculosis

Case 6—Aged 39 years Married 8 years, sterile Sinistroposition of the uterus, which was otherwise normal Three insufflations showed that the tubes were patent, and this was confirmed by salpingography Biopsy revealed normal endometrium, but three cultures of the menstrual discharges were positive for *Myco tuberculosis*

This patient received 40 g of streptomycin in 40 days and biopsy immediately after the treatment revealed endometrial tuberculosis

SUMMARY AND CONCLUSIONS

Of six confirmed cases of latent genital tuberculosis treated with streptomycin, five responded

The total dosage was 40–45 g in five cases, and 75 g in one case. The daily dosage was 1 g, but in two cases it was only 0 5 g for part of the course

These results encourage us to believe that streptomycin, even in the fairly low total dosage of 40–45 g, is effective in cases of latent genital tuberculosis The failure in one case (case 6) may have been due to insufficient dosage One advantage of this treatment is that the endometrium is preserved, and so the remote chance of subsequent pregnancy is not finally removed

The histological studies were made at the central pathological institute of the Kupath Holim, and the bacteriological studies at the central laboratories of the Kupath Holim in Tel Aviv and Haifa Special thanks are due to the directors of these institutes Dr J Casper, Dr E Bregman, and Dr L Hirsch

ADDENDUM

Since this report was completed we have successfully treated with streptomycin six further cases of latent genital tuberculosis in women, bringing the total number of cases treated to twelve

REFERENCES

1 Halbrecht, I (1946a) *Schweiz med Wschr* 76, 708
2 — (1946b) *Lancet*, i 235
3 Rabau, E, Halbrecht, I, Casper, J (1943) *J Amer med Ass* 122 801
4 Sharman A (1944) *J Obstet Gynæc* 51 85
5 Shaup K L jun (1949) *West J Surg* 57 221
6 Shockeart, J M, Ferin, J (1939) *Bull Soc R belge Gynéc Obstet* 15 467
7 Sutherland A M (1943) *J Obstet Gynæc* 50, 101

"There is, incidentally, an extraordinary disinclination to regard tuberculosis as an infectious disease, as it is, amenable to the same principles of control and prevention as other infections This attitude, despite the clear evidence of the last fifty years and the experience of other countries, is likely to prove disastrous for Scotland where tuberculosis is getting beyond control The position is far too serious to permit of tentative measures by those who have little experience of the problem "—Dr J R W HAY, medical officer of health for Kirkcaldy, in his report for 1949 consuming tube dilution technique for organisms producing zones of inhibition more than 1 mm shorter than the Oxford staphylococcus

It is not known how infection with these slightly more resistant strains (sensitive to aureomycin 0 16 µg per ml) would respond to aureomycin therapy, but the difference in their sensitivity from that of most strains may well be of no clinical significance The observation that a blood agar ditch plate technique can detect so small a difference in sensitivity indicates its presumptive value for the detection of organisms whose resistance is clinically significant The method is being used in this Unit to detect minor variations in the sensitivity of *Staph aureus* isolated from patients before, during, and after aureomycin therapy

SUMMARY

The detection of aureomycin in burn exudates by a blotting paper disc plate assay method is described The sensitivity of this test was enhanced by using agar plates at pH 5 6 and incubating the test plates at 25°C The method has the advantage of being applicable to 0 02 ml quantities of contaminated fluids

For testing the sensitivity of *Staph aureus* to aureomycin, inoculation across a blood agar plate with a ditch containing 10 µg of aureomycin per ml of agar at pH 5 6 is recommended This method detects organisms resistant to 0 04 µg of aureomycin per ml

Thanks are due to Mrs F E Brand and Mr H Lilly for technical assistance Aureomycin hydrochloride capsules (Lederle) were kindly provided by the Antibiotics Clinical Trials Committee of the Medical Research Council

REFERENCES

Heatley N G (1949) in H W Florey et al Antibiotics London chapter 3
Knudsen L F Randall W A (1945) *J Bact* 50 187
Koelzer P P Giesen J (1949) *Med Klin* 45 1442
Paine T F jun Collins H S Finland M (1948) *J Bact* 56 489
Randall W A Kirshbaum A Nielson J K Wintermere D (1949) *J clin Invest* 28 940

TEMPORAL ARTERITIS

TWO CASES TREATED WITH AUREOMYCIN

J M Rice Oxley
D M Oxfd, M R C P
SENIOR MEDICAL REGISTRAR

A M Cooke
D M Oxfd, F R C P
PHYSICIAN

RADCLIFFE INFIRMARY, OXFORD

Since first described by Horton, Magath, and Brown (1932), the syndrome of temporal arteritis has become a well recognised entity It occurs in elderly patients, over 55 years of age, and is characterised by an inflammatory reaction in the temporal arteries, with headache and signs of constitutional disturbance including fever, sweats, anorexia, and loss of weight The temporal arteries are thickened and tortuous, and the overlying skin is often reddened In some cases the disease spreads to the retinal vessels and causes disturbances of vision The white cell count may be normal or show a leucocytosis, and the erythrocyte sedimentation rate (E S R) is almost constantly raised

The ætiology remains obscure, but in view of the inflammatory changes in the walls of the affected vessels, and the fever, infection seems to be the most likely cause We have so far seen no reports of the response of temporal arteritis to any of the known chemotherapeutic or antibiotic agents The two cases described here were treated with ' Aureomycin '

CASE RECORDS

Case 1 —A clergyman, aged 65, was admitted to the Radcliffe Infirmary on Aug 17, 1950 Three weeks earlier he had begun to get severe headaches affecting the whole of the right side of the head and face The pain was most severe in the right temporal and right occipital regions The right side of the head and face felt abnormally sensitive When the headaches started, he began to feel ill in himself, he went off his food and sweated at night Ten days before admission he had had some carious teeth removed from his right upper jaw, but the pain had remained

Past History —? Paratyphoid fever, 1919 Cholecystectomy, 1923 In October, 1949, he attended the outpatient department because of epigastric pain Barium meal and barium-enema examinations gave normal results, but he was found to have a large calcified cyst in the liver This finding, however, was thought to be unrelated to the pain He was discharged from outpatients in March, 1950, and had no recurrence of epigastric pain afterwards

On examination he looked ill, with a pale face and haggard expression, and complained of constant severe headache Temperature 102°F, pulse rate 90, respirations 20 per min Both temporal arteries were thickened, the right more than the left The skin was reddened over the frontal branch of the right temporal artery The arteries were not very tender No other abnormality was found

Investigations —Hæmoglobin 80% white blood-cells 10,000 per c mm , E S R 85 mm in 1 hour Blood culture sterile Blood urea 27 mg per 100 ml Plasma protein 6 3 g per 100 ml (albumin 3 1 g) Agglutination of salmonella and brucella negative Cerebrospinal fluid and urine normal On radiography of the chest no lesion was seen Biopsy of a section of the right temporal artery showed inflammation of the inner zone of the media and the intima There were several small foci of necrosis with giant cells closely applied to them , surrounding these were proliferating fibroblasts, occasional lymphocytes, and moderate numbers of eosinophils The adventitia showed proliferation of fibrous tissue, which seemed to vary in proportion to the severity of the medial changes

Progress —For the first week after admission the patient continued to have severe headaches and a temperature of 101° or 102°F every night The biopsy done on his seventh day in hospital was followed by an immediate and dramatic improvement in the pain His temperature after the biopsy also fell slightly, but he continued to feel ill and his appetite did not return On the twelfth day after admission treatment with aureomycin 0 5 g six hourly was begun He became afebrile in twenty four hours, but his temperature rose to 99 8°F the next night After this there was a steady improvement his appetite returned, he began to feel well, and after he had been on aureomycin for two weeks he was getting up and was symptom free His temporal arteries appeared normal, and he was afebrile except for an occasional rise of temperature to 99°F After the aureomycin was stopped, he remained well and was discharged home on Sept 13

Case 2 —A children s nurse, aged 66, unmarried, was admitted to an Oxford nursing home on June 13, 1950 Two weeks previously she had begun to feel unwell and was found to have a temperature of 100°F She stayed in bed, but there were no further symptoms Eight days before admission she had been admitted to Moreton in Marsh Hospital, where she had irregular fever up to 102°F There were then no abnormal physical signs except tenderness in the left lower quadrant of the abdomen She continued to have fever and was transferred to Oxford

On examination she had a pale complexion but did not look ill Temperature 100 6°F, pulse rate 84, respirations 20 per min Blood pressure 140/74 mm Hg No other abnormal physical findings

Investigations —Hb 66% white cells 8000 per c.mm E.S R 125 mm in 1 hour Chest radiography normal

Progress —Three days after admission she began to complain of " painful spots " on the forehead worse on the left than on the right Examination showed a striking enlargement of the temporal arteries with a nodular irregularity of outline and slight reddening of the skin over the vessels There was little tenderness The diameter of the vessels appeared to be about $^{1}/_{4}$ in The condition was more severe on the left side Other superficial vessels and the optic fundi appeared normal She remained febrile and looked progressively more ill

On June 27, two weeks after admission the temporal arteries were still enlarged and painful and treatment with aureomycin 0 5 g six hourly was started Within twenty-four hours her temperature fell and she looked better, but she began to complain of nausea Six days after the start of treatment with aureomycin the temporal arteries looked

25°C for 24 hours, should be incubated for a further day at 37°C If the zones of inhibition remain unaltered they are almost certainly produced, at least in part, by some agent other than aureomycin

The method can be made more specific for aureomycin by choosing an indicator organism that is resistant to the commonly used chemotherapeutic agents We therefore recommend the use of a penicillinase producing *Staph aureus* rather than the Oxford staphylococcus

The disc assay method is simple to use and has the advantage over dilution methods in being applicable to 0 02 ml quantities of contaminated fluid The method should be suitable not only for burn exudates but also for wound exudates, capillary blood, and other body-fluids The disc technique for sampling body fluids has been described by Koelzer and Giesen (1949), working on the assay of streptomycin, and the general conception of assaying exudates has been discussed by E J Pulaski (personal communication)

DITCH PLATE TEST FOR AUREOMYCIN SENSITIVITY

Various agar ditch and filter paper strip techniques for testing sensitivity to aureomycin have been tried With a given concentration of aureomycin (10 µg per ml), filter paper strips gave much more variable and smaller zones of inhibition than an agar ditch Incubation at 37°C was found to be better than at 25°C because, although the zone of inhibition was smaller, the result could be read with precision after 18 hours' incubation, a point of considerable practical importance It was unnecessary to adjust the whole plate to an acid reaction provided the aureomycin agar ditch was prepared with Evans peptone agar at pH 5 6 The ditches were therefore made in 10% horse blood Hedley Wright agar layered plates at pH 7 6 It was found convenient to test penicillin sensitivity on the same plate as that used for aureomycin sensitivity

Segments of blood agar are removed on opposite sides of the plate with a sterile scalpel then one ditch is filled with pH 5 6 Evans peptone agar containing 10 units of penicillin per ml. while the other is filled with the same agar containing 10 µg of aureomycin per ml The plate should be used on the day it is prepared, for otherwise the zones of inhibition may spread too far across the plate A loopful of a 24 hour broth culture of the *Staph aureus* to be tested is placed equidistant from the two ditches and spread first across one ditch and then across the other, one side of the loop being used for one ditch only In our present inquiry each plate received parallel inocula of 5 strains of *Staph aureus* and a control (the Oxford staphylococcus, which was sensitive to 0 02–0·04 µg of aureomycin per ml by the tube-dilution method) In reading the results the important measurement is the relative lengths of the zones produced by the Oxford staphylococcus and by the test strain As described below, organisms producing zones more than 1 mm shorter than that of the Oxford staphylococcus should be further tested by a tube dilution method

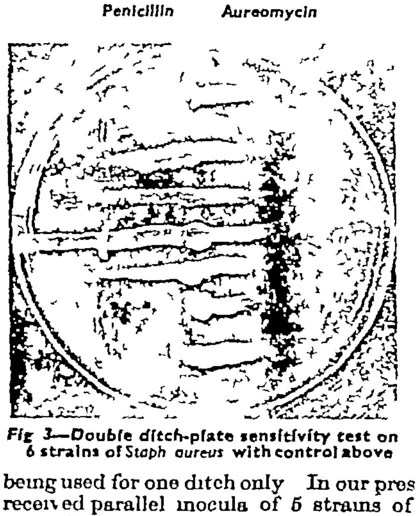


Fig 3—Double ditch-plate sensitivity test on 6 strains of Staph aureus with control above

In fig 3, from above downwards, strains 1, 6, and 7 are sensitive and 2–5 resistant to penicillin Strains 1–3 and 5–7 are sensitive to aureomycin, strain 4 gives a zone more than 1 mm shorter than the Oxford staphylococcus (strain 1,) and should be re tested by the tube dilution method

Reliability —The ditch-plate method has been used in parallel with a tube dilution method in which 0 5 ml quantities of doubling dilutions of aureomycin in pH 5 6 Evans peptone water were inoculated with 0 02 ml quantities of a 1 in 1000 dilution of the same 24 hour broth culture as was used for the plate test The tubes were incubated at 25°C for 24 hour, the end point was taken as the highest dilution with no turbidity

The accompanying table compares the results obtained with 152 strains of *Staph aureus* tested by the two methods in parallel These were the 28 available bacteriophage types [3] and 124 strains recently isolated from burns under treatment in this Unit When a strain has been tested more than once, the first result only is included Of the 152 strains tested, 140 (92%) produced zones on the ditch plate not more than 1 mm shorter than the Oxford staphylococcus and were sensitive to 0 04 µg per ml in the tube All the 28 bacteriophage types fell into this category Among the burns strains there were 7 [4] which were resistant to 0 04 µg per ml in the tube, and all of them had produced zones of inhibition on the ditch plate at least 2 mm shorter than the Oxford staphylococcus, so their resistance would have been detected if this had been the only routine sensitivity test applied But there were 5 other strains of *Staph aureus* which were sensitive to 0 04 µg of aureomycin per ml but which also produced zones 2 mm shorter than the Oxford staphylococcus This discrepancy indicates the desirability of testing such strains by the tube dilution method as well as the ditch plate

COMPARISON OF BLOOD AGAR DITCH PLATE AND TUBE DILUTION METHODS FOR TESTING SENSITIVITY OF *Staph aureus* TO AUREOMYCIN

Difference in length of zones on ditch plate* (mm)	No of strains sensitive to various tube dilutions of aureomycin (µg /ml)					Total strains
	0 01	0 02	0 04	0 08	> 0 08	
+3			2			2
+2	1	3	6			10
+1	3	12	5			20
None	8	70	12			90
−1	2	11	5			18
−2	1	3		1	1	6
−3			1		2	3
−4				1	2	3
Total strains	15	99	31	2	5	152

The dotted lines divide the 12 more resistant strains from the remaining 140

* i e, length of zone of inhibition produced by test strain on blood agar ditch plate minus length of zone produced by Oxford staphylococcus

To determine the consistency of the results on individual strains all staphylococci found to be relatively resistant by the ditch plate or tube test have been retested one or more times by both techniques By the tube dilution method in every instance the strains previously sensitive to 0 04 µg per ml were again sensitive to this strength and the strains previously resistant to 0 04 µg per ml were again resistant to it, but, so far, all strains tested have been sensitive to 0 16 µg per ml By the blood agar ditch method all strains resistant to 0 04 µg per ml in the tube have, on being retested, again produced zones of clearing 2 or more mm shorter than the Oxford staphylococcus

It seems from these results that a satisfactory routine would be to test all staphylococci in the first instance by the ditch plate method, and to reserve the more time a tentative diagnosis of leptospirosis was made. The patient had worked in the cellar of his house about a week before feeling ill; he did not know whether the place was rat infested. A course of penicillin 100 000 units three hourly was begun on Dec. 27 and continued for ten days. The agglutination test became positive (1/300) on Dec. 29. Within twenty four hours of the first injection the patient felt very much better and his temperature became normal, but jaundice and hæmaturia lasted eight days. He was discharged on Jan. 12, 1949, completely cured.

---

[3] These were bacteriophage propagating strains kindly supplied by the Staphylococcal Reference Laboratory Colindale Their bacteriophage types were 3A, 3B 3C 6/53a, 7 29 29A, 31/44 42B/47C 42C 42D 42E 44A, 47 47A 47B 51 52 52A 31A 53 54 55 57 69 70 71 and 47D

[4] Of these 7 relatively resistant strains 4 were of bacteriophage types 47, 47/53 47/53 and 53 and 3 could not be typed with the available unconcentrated phages

Case 3 (under the care of Dr E. Sanders).—A sewage worker, aged 40, reported ill on April 1, 1949. That day he had a rigor followed by fever, headache, and myalgia in arms and legs. He came into hospital on April 7, being then very ill, with temperature 99.2°F, suffusion of eyes, asthenia, jaundice, and albuminuria.

The diagnosis of Weil's disease was evident and a course of intramuscular penicillin 100 000 units three hourly was started at once and continued for ten days. On admission the blood urea level had been 125 mg per 100 ml but on the fifth day of treatment it fell to 44 mg per 100 ml. On April 12 the serum showed agglutination of *L. icterohæmorrhagiæ* in dilution up to 1/3000 with a trace at 1/10,000. The patient made rapid progress, and his temperature was normal from the second day onward. Jaundice cleared after a few days and the blood urea level was normal on April 21. Liver function tests were normal on admission, but unfortunately they were not repeated during the later stages of the illness. He returned home on May 3, 1949.

Case 4.—An electrical engineer aged 26 became suddenly ill on April 27, 1949, with severe frontal headache and generalised muscular pains. About ten days before the onset he had gone swimming in the river Thames near Teddington Lock (rather flooded at the time). On April 30 (the day of admission to hospital) he vomited once and his temperature rose to 101°F. When first seen he was irritable and fatigued, with a dry coated tongue, nausea, and injected conjunctivæ and scleræ. On May 2 albuminuria was found and a questionable icteric tinge of the scleræ. A course of penicillin 100 000 units four hourly was given for eight days. The first agglutination test was positive (1/3000) on May 4. Ten days later the titre rose to 1/10 000, with a trace of agglutination at 1/100 000. Within twelve hours of the first injection the patient became afebrile and he remained so throughout the rest of the illness. Clinical improvement was most striking in this case, symptoms having disappeared within twenty four hours except for headache which persisted for several days longer; jaundice and albuminuria disappeared by the end of the penicillin course. Red blood cells were seen in the urine for the last time on May 12. He was discharged from hospital on May 21, 1949.

Case 5.—A man, aged 35, employed in a live sewer called in his doctor because of the sudden onset of rigor, backache, headache, and myalgia in his arms. Next day he complained of anorexia, constipation, and epigastric pain. Albuminuria was found by the patient's doctor, who sent him into hospital three days later with a provisional diagnosis of Weil's disease. At examination on June 13, 1949, the most noticeable features were the sallow complexion, dry coated tongue, slight suffusion of eyes, pyrexia, and profound prostration. Intramuscular penicillin was started soon after admission and continued for fifteen days (100,000 units three hourly for forty-eight hours and thereafter four hourly). On the second day of treatment jaundice and frank hæmaturia appeared; symptoms of uræmia, especially lethargy, became pronounced. However, the clinical picture soon changed for the better and on the eighth day of treatment icterus and nephritis were on the wane. On July 1 the patient was normal in all respects; his erythrocyte sedimentation rate (E.S.R.) was normal. The agglutination test did not become positive till June 27, 1949 (1/300). He was sent home on July 18.

Case 6.—A plumber aged 47 employed on repairs of outside drains was admitted to hospital on Nov. 11, 1949, with four days' history of asthenia, pains in the legs and headache ushered in by a rigor, vomiting, abdominal pain, and headache. Thirty six hours before admission jaundice had appeared, the urine had become a deep amber colour, and he had been pyrexial. He was very ill, with temperature 97.4°F, moderate icterus, and a dry tongue covered with brown fur; he was perspiring freely and his liver was slightly enlarged and tender on palpation. His blood pressure was 110/70 mm Hg. He was drowsy and complained of fatigue, aching in the legs, and constipation. Since no urine had been passed in the past thirty six hours, the bladder was catheterised; this produced a few ounces of bile stained turbid urine in which urobilin could not be detected. Albuminuria was present.

A course of penicillin was started immediately, an initial dose of 500,000 units being followed by doses of 100 000 four hourly. On Nov. 14 the dosage was increased to 500,000 units four hourly till Nov. 29. Four hours after the first dose of penicillin the patient had a rigor with deterioration in his general condition, and his temperature rose to 100.4°F one and a half hours after the rigor began. Next day no urine was passed, but the anuria was short lived and twenty four hours later urinary secretion started; on Nov. 15 the output measured 110 oz. The improvement in the renal condition could also be seen in the return to normal values of the blood urea, which had been 220 mg per 100 ml on admission and was only 38 mg on Nov. 24. Icterus, however, continued to deepen until the patient's skin and mucosæ were deep golden orange. It was obvious that treatment had not arrested the progress of hepatic lesions. Thus, the colloidal gold reaction, negative on the day of admission, became positive (+ + + 3) on Nov. 21 and the thymol turbidity test increased from 2 units (normal 0–4) to 7 units. There was a febrile period (Nov. 18–24) with the temperature varying from 99.6° to 101°F and signs in the chest suggesting left basal pneumonia. No special treatment was given. On Nov. 29 penicillin was discontinued.

The serological diagnosis remained uncertain until Nov. 21, when the patient's serum showed agglutination of *L. icterohæmorrhagiæ* in dilutions up to 1/1000; before that day the result was doubtful, with agglutination in a dilution of 1/30 on Nov. 16. On Dec. 5 renal and liver function tests were repeated and found normal; the blood urea level was 32 mg per 100 ml, and a blood count was normal in all respects. The patient was discharged on Dec. 20.

DISCUSSION

The beneficial effect of penicillin given early in Weil's disease is shown by the rapid fall of the temperature and by disappearance of such symptoms as headache, myalgia, epigastric pain, and apathy; urine output, blood-urea level, white cell count, and E.S.R. return to normal quicker than in untreated patients. No leptospira can be found in the urine twenty four hours after the first dose of penicillin.

According to published reports febrile relapses do not occur in penicillin treated cases, but the febrile period in case 6 suggests that this is not always so. Another interesting point in case 6 is the reaction seen a few hours after the administration of penicillin. Clinically it resembled the Jarisch-Herxheimer reaction occurring in primary and secondary syphilis treated with penicillin, but no description of such reactions in Weil's disease has been published.

Though penicillin does not seem to have any effect on the course of established hepatitis, it probably protects the liver as well as the kidneys from further assaults by leptospira which might be alive and multiplying were it not for penicillin's growth inhibiting powers. It has been conclusively shown, both in laboratory animals and in man, that penicillin has no inhibitory action on the formation of leptospiral antibodies in the penicillin treated infection, and thus does not interfere with the agglutination of *L. icterohæmorrhagiæ* by the patient's serum.

Another antibiotic effective in leptospirosis icterohæmorrhagica is 'Aureomycin,' which will probably take the place of penicillin as the drug of choice because of its efficacy when taken by mouth. Heilman (1948) has reported that aureomycin is about twice as effective as penicillin in protecting hamsters from a fatal leptospiral infection.

SUMMARY

An account is given of six cases of Weil's disease treated at an early stage with parenteral penicillin normal, but nausea and sometimes vomiting became so severe that it became doubtful whether she could continue with the treatment She was therefore given 'Aludrox' 1 drachm before each dose of aureomycin This controlled the nausea but it is now known that aludrox seriously interferes with the efficacy of aureomycin treatment Four days later, after a total of ten days, the aureomycin was stopped Within forty eight hours the headache recurred, with enlargement and tenderness of the temporal arteries, and the temperature which had been about 99°F, rose to 100°F

During the next two weeks there was a gradual improvement in her condition and by July 17 the temporal arteries had once more become normal On this day the patient complained for the first time of defective vision in the right eye and was found to have a visual defect of about one third of the right half of the right visual field The left visual field was normal, and no ophthalmoscopic changes were seen For the next two weeks there was a further improvement in her general condition, and during this period since her hæmoglobin had remained at 66% and she had been unable to tolerate ferrous sulphate tablets, she was transfused with two bottles of group A blood By Aug 9 she was getting up, and expressed herself as feeling perfectly well There was no fever, little headache, and the temporal arteries were normal She was discharged on Aug 17 symptom free

DISCUSSION

There can be no doubt about the diagnosis of temporal arteritis in either of the two cases described In the first case confirmation was obtained by biopsy, and in the second case, although no biopsy was done, the clinical manifestations were conclusive In case 1 the patient improved steadily while he was on aureomycin, and the difference in his whole appearance before and after starting the drug was remarkable After two weeks he was afebrile and symptom free In case 2 the drug was badly tolerated, and its effect was less conclusive However, the fall of temperature and return to normal of the temporal arteries soon after starting treatment with aureomycin, and the relapse forty eight hours after it had to be stopped, indicated a definite influence of the drug on the disease

The disease untreated is self limited and its duration variable Horton and Magath (1937) found that in their cases the illness lasted four to six months, but Cooke et al (1946), who reviewed all the previously published reports, considered that the average duration of the disease was much longer than this The total duration of the disease in case 1 was only seven weeks, and in case 2 only eleven weeks (nine weeks from the onset of the changes in the temporal arteries) This short duration seems to be further evidence of the beneficial effect of aureomycin therapy

Although it is not claimed that the result of treatment in two cases is in any way conclusive, it is felt that the response to aureomycin was sufficiently encouraging for this remedy to be tried by other workers

SUMMARY

Two cases of temporal arteritis are described

Both patients were treated with aureomycin In one case there was a steady improvement in the patient's condition during treatment After two weeks' treatment with 0 5 g six hourly he was symptom free, and he has remained well since In the other case the aureomycin was badly tolerated and had to be withdrawn before a complete course could be given However, the patient showed considerable improvement while under treatment, and she relapsed within forty eight hours of its withdrawal

Aureomycin seems to deserve further trial in temporal arteritis

REFERENCES

Cooke W T Cloake P C P Govan A D T Colbeck J C (1946) *Quart J Med* 39 47

Horton B T Magath T B (1937) *Proc Mayo Clin* 12 548

— — Brown, G E (1932) *Ibid* 7 700

PENICILLIN IN WEIL'S DISEASE

A I Suchett Kaye

M D Paris, M R C P

SENIOR MEDICAL REGISTRAR, ST CHARLES' HOSPITAL, LONDON

Weil's disease (*Leptospirosis icterohæmorrhagica*) carries a mortality of about 20% in patients in whom liver and kidneys are seriously affected Milder cases, especially anicteric, recover spontaneously , but there is no means of foretelling early in the illness how severe the course will be Hence active treatment, with penicillin, is always indicated

Heilman and Herrell (1944) have demonstrated the curative action of penicillin in experimental leptospiral infection, and Alston and Broom (1944) its lethal effect on leptospira in vitro Chang's (1946) experimental results have, in the main, confirmed these findings and, on the basis of experiments with leptospirosis in guineapigs, he advocated for human leptospirosis a daily dosage of 250,000–300,000 units of sodium penicillin Hart (1944), Carragher (1945), Bulmer (1945), and Patterson (1947) have commented favourably on the clinical use of parenteral penicillin in Weil's disease, they have noticed rapid disappearance of leptospira from the urine and an absence of febrile relapses, but no apparent effect on the jaundice and nephritis

Experimental observation as well as clinical experience has provided ample evidence of the necessity of giving penicillin at the earliest stage of the infection The ideal would be antibiotic treatment in the preicteric phase Unfortunately the diagnosis is not then easy, especially as facilities for the rapid demonstration of leptospira are not always available The fact that the infection may occur often in people whose occupations carry no professional hazards of leptospirosis adds to the difficulties of early diagnosis Patterson (1947) wrote " The average patient [with leptospirosis icterohæmorrhagica] presents a picture of moderately severe influenza with decided conjunctival and scleral engorgement If the clinician remembers just this much he will usually make the correct diagnosis " The urine should be examined in every case of suspected Weil's disease, the finding of albuminuria strongly supports the diagnosis

The six cases of Weil's disease described here were treated with penicillin The course of penicillin was started before the seventh day of the illness—i e , before agglutination tests had become positive According to Bulmer (1945), the true value of penicillin in Weil's disease can be ascertained only by observing its effect during the preicteric phase Such observations are scanty, and the timing and results of treatment in cases 1, 2, 4, and 5 are, in this respect, of some interest.

CASE RECORDS

Case 1—A business man, aged 27, became ill on Oct. 27, 1946, the onset being marked by rigor, generalised pains, pyrexia, and dry cough Three days later he was admitted to hospital with a temperature of 103°F He was then seriously ill , he was apathetic, with a dry coated tongue, and complained of influenza like symptoms , albuminuria was present Penicillin was given in an initial dose of 60 000 units and *continued in doses of 30,000 units three hourly* for seven days On Nov 1 jaundice appeared and blood was found in the urine These findings supported the diagnosis of Weil's disease, though the circumstances in which the infection could have occurred remained a mystery The patient's serum did not show agglutination of *L icterohæmorrhagiæ* (1/1000) till Nov 6 His temperature became normal twelve hours after starting penicillin therapy Jaundice and microscopical hæmaturia persisted for about three weeks He was discharged fit on Dec 10, 1946

Case 2—A salesman, aged 27, fell ill on Dec 22, 1948, with fever, abdominal pain, constipation, hæmaturia, lumbago, and headache He was admitted to hospital on Dec 25 with a provisional diagnosis of acute nephritis Two days later a slight icteric tinge of scleræ was observed and soreness, dysuria, or bleeding, and whether there has been venereal contact The source of the discharge must be located, the urine tested, and threadworms and piles excluded The macroscopic appearance of the discharge is often characteristic To examine the discharge microscopically a specimen should be collected from the fornices with a long handled 'Bakelite' spoon, and a wet film should be made Elaborate methods of illumination or staining are not usually essential unless venereal disease is suspected The trichomonas is almost invariably associated with a grade 3 flora, and the monilia with a grade-1 or grade-2 flora

Treatment must be appropriate to the cause that of trichomonas and monilia being sometimes tedious Life is too short to carry out repeated vaginal paintings, and the more that treatment can be made self applicable the better Dr Jackson advocated ringing the changes on two or more methods of treatment in cases of trichomonas infestation—e g, 'Picragol' powder, 'S V C' tablets, or carbarsone suppositories, combined with douching with 'Milton' (as in veterinary practice) or with lactic acid, and, in cases where the mucosa is thin, œstrogens locally or orally Where the husband is also infected with trichomonas the wife is constantly subject to reinfection, but the treatment of the male is extremely difficult About 50% of a series of 468 women attending the Whitechapel clinic were found to be infested with trichomonas Of those thus infected, 130 had no evidence of gonorrhœa and 102 had In a series of infertile women attending the Exeter and District Women's Welfare Association clinic, the incidence of trichomonas was 15%, while in a birth control series at the same clinic it was only 5% This lends support to the view that chemical contraceptives have a deterrent effect on trichomonas

For monilia Dr Jackson recommended alkaline douches and a gentian violet, glycerin, and borax suppository For vaginitis in the very young œstrogens by mouth or locally are undoubtedly of value Non specific cervical discharges yield dramatically to treatment with the electric cautery, together with sulpha drugs by mouth or penicillin by injection

Reviews of Books

Textbook of Physiology and Biochemistry

GEORGE H BELL, B SC, M D, F R F P S G, professor of physiology, University of St Andrews, at University College, Dundee, J NORMAN DAVIDSON, M D, D SC, F R F P S G, Gardiner professor of physiological chemistry, University of Glasgow, HAROLD SCARBOROUGH, F R C P E professor of medicine, Welsh National School of Medicine Edinburgh E & S Livingstone 1950 Pp 918 45s

NOWADAYS the major techniques in clinical research are physiological, and the medical student reading physiology should grasp certain principles as a preliminary to his clinical work He should learn the way in which physiological knowledge is collected, and have some appreciation of the difficulties of biological measurement From this he should understand the arduous labour required to build up knowledge, and the tenuous and evanescent character of many of our working hypotheses, and should learn to value the open mind Selection from the vast subject is necessary in a textbook, and the facts chosen should be strictly accurate Thus the student will realise that physiology not only serves medicine but often leads the way, and that it is one of the great scientific foundations on which practice should be built

This new textbook has been compounded by an excellent team consisting of biochemist, general physiologist, and clinician all of high academic standing Those who turn to it merely for an account of modern applied physiology may at first feel disappointed For example, the chemical data are a little too isolated from discussion of the living processes, in the section on protein needs mention might have been made of Borst's finding that tissue breakdown is greatly reduced by adequate provision of calories in fat and carbohydrate, and electrocardiography is too sketchily outlined to give a solid basis for modern practice in this subject Again, Prinzmetal's recent work suggests that the importance of circus movement in auricular fibrillation and flutter has been overstressed The section on pulmonary circulation is hardly adequate, and Starling's law of the heart is erroneously stated, in a table, to be concerned somehow with changes in heart rate The mechanism of swallowing is poorly described, little reference being made to reflexes from the palate and pharynx which can be abolished in man by local anæsthesia while the motor pathway which may be involved in many diseases affecting the medulla is not given enough emphasis Some of the illustrations—such as the clinical photographs of scurvy—are not good enough to help the inexperienced reader But it is easy to pick such faults by looking for them, and all these are minor blemishes As a whole the book is sound and well up to date It gives good references particularly to human physiology, and the sections on the circulation, vitamins, and endocrinology are all satisfying It may well become the standard physiological manual for British students But if the student is really to appreciate the live character of physiology, a brief section on the limitation of many present day methods and the necessity for statistical study would be a salutary addition

Regional Dermatologic Diagnosis

ERVIN EPSTEIN, M D, consultant in dermatology and syphilology to the Oakland Area Veterans' Hospital and Mt Zion Hospital, Oakland, California London Henry Kimpton 1950 Pp 328 42s

EACH chapter deals with skin diseases that may affect a part of the body—e g, the nose, lips, or hands—and at the end of each chapter the diseases are tabulated On the title-page Dr Epstein admits that his book is not intended for specialists, and, so far as it is possible to deal with the diagnostic problems of dermatology in this way, the idea has been well carried out The value of such a work is a little doubtful, especially now that more and more so called skin diseases are proving to be symptoms of more general disorder of bodily and mental health. The dermatologist of today must be a highly trained general physician with special knowledge in his own branch, and it would be wrong to encourage students to tackle dermatology from the regional standpoint Nevertheless the harassed practitioner may find this book useful, for not only is the text lucid but the illustrations are excellent and there is much valuable information on treatment

Surgery of the Shoulder

A F DEPALMA, M D, professor of orthopædic surgery, Jefferson Medical College, Philadelphia London: J B Lippincott 1950 Pp 438 £7

ANY book dealing with disabilities of the shoulder inevitably provokes comparison with Codman's masterpiece Though Professor DePalma's work is less strictly personal, since it includes opinions and techniques from many sources, it nevertheless emerges bravely from the comparison Beautifully produced, it has first-class diagrams and X ray reproductions

The normal pathology of senescence as it affects the shoulder has been studied in a large number of subjects, and correlated with the symptoms—or lack of them—during life Gross tears of the rotator cuff and other degenerative lesions commonly found are compatible with normal function, which raises the question whether operation is not performed too often for traumatic ruptures There is an obvious difference, as Professor DePalma notes, between the slowly developing degenerative lesion and the sudden disruption which allows no time for compensating adjustments, but, he says even fresh traumatic lesions pointing to rupture of the cuff do not demand immediate exploration Many individuals so affected regain complete usefulness of the arm if the tear is not too severe" More important than the size of any tear in determining weakness in abduction is disproportion between the power of the deltoid and of the short rotators Gross lesions of the cuff may not impair function in the aged, where the deltoid is already correspondingly weak But cuff pathology is in advance of true senescence, and even a small tear in a middle aged labourer

There is ample experimental and clinical evidence of the curative value of penicillin if administered early in the disease Our aim should be to make the diagnosis on clinical grounds and start antibiotic treatment in the preicteric phase, and to confirm the diagnosis by agglutination tests later

I wish to thank Dr Thomas Hunt for his kind interest and help in the preparation of this paper

REFERENCES

Alston J M Broom J C (1944) *Brit med J* ii, 718
Bulmer E (1945) *Ibid* i 113
Carragher, A E (1945) *Ibid* p 119
Chang S L (1946) *J clin Invest* 25 752
Hart V L (1944) *Brit med J* ii 720
Hellman F R (1948) *Proc Mayo Clin* 23, 569
— Herrell W E (1944) *Ibid*, 19 89
Patterson, H M (1947) *J Amer med Ass* **134**, 1077

PARATYPHOID URINARY CARRIER TREATED WITH CHLORAMPHENICOL

J M KENNEDY
M B Belf, D P H.
MEDICAL SUPERINTENDENT, LODGE MOOR HOSPITAL, SHEFFIELD, LECTURER ON INFECTIOUS DISEASES IN THE UNIVERSITY OF SHEFFIELD

E L M MILLAR
M D, M Sc Sheff, D.P H.
DEPUTY MEDICAL OFFICER OF HEALTH, SHEFFIELD

THE treatment of carriers of typhoid or of paratyphoid bacteria in the fæces with chloramphenicol has so far produced little improvement, but the result achieved in the following case of a carrier of *S paratyphi B* in the urine is encouraging

A *S paratyphi B* infection broke out in Sheffield in the autumn of 1946, and one of the patients, a boy aged 8 years, was transferred from the City General Hospital to Lodge Moor Hospital on Dec 12, 1946, convalescing from paratyphoid fever *S paratyphi B*, Vi phage type 2, which was the type responsible for the epidemic, was continuously present in his urine The following treatments had no effect

March 1947 sulphaguanidine 6 g daily for seven days (total 42 g)
April 1947 sulphadiazine 6 g daily for seven days (total 42 g)
May, 1947 sulphadimidine 6 g daily for seven days (total 42 g)
June 1947 intramuscular penicillin 20 000 units three hourly for ten days (total 1 6 mega units)
July 1947 'Mandelix' 1 drachm thrice daily for fourteen days

On Sept 15, 1947, the patient was discharged home as a persistent urinary carrier of *S paratyphi B*, and the public health department of the city was notified During the next sixteen months nine urinary specimens were examined, all gave moderate or heavy growths of *S paratyphi B* and some pus cells were also present There were no red cells or casts

In August, 1948, serum agglutination with *S paratyphi-B* antigens gave the following results Vi, 1 5 +, O, 1 100 +, H (type aggn), 1 500 +, (group aggn), 1 200 +

On Jan 13, 1949, the patient was readmitted to Lodge Moor Hospital for streptomycin therapy *S paratyphi B* was isolated from the urine and examined for sensitivity, with the following results penicillin, resistant, sulphathiazole and sulphadiazine, slight inhibition, sulphadimidine, no inhibition and streptomycin, moderate inhibition

From Jan 20 to Feb 8, 1949, intramuscular streptomycin 0 5 g was given six hourly for 21 days (42 g)

On Feb 12, 1949, *S paratyphi B* was still present in the urine

From March 3 to March 23, 1949, intramuscular streptomycin 0 5 g was given six hourly for 21 days (42 g)

On March 24, 1949, *S paratyphi B* was still present in the urine and the organism now resisted more than 50 units of streptomycin, whereas originally it was inhibited by 4 units

On April 2, 1949, the boy was discharged home again as a persistent urinary carrier After his discharge from hospital specimens of urine taken at three-week intervals persistently showed *S paratyphi B* in large numbers

On March 23, 1950, the patient was readmitted t hospital for chloramphenicol therapy From April to April 10 he was given chloramphenicol 1 g thric daily His urine, examined on April 12, 17, 21, and 2 showed neither *S paratyphi-B* nor *Bact coli*

On May 1 the boy was discharged home Since the he has been under our observation, and fæcal specimen have been examined but *S paratyphi B* has never bee found Specimens of urine were examined on May *17, 24*, and *31*, and June 15, none of these grew *S para typhi B*, but *Bact coli* was grown from the specimens May 24 and 31, and a light growth of *Strep fæcalis* wa obtained from the specimen of May 17 The boy is no permitted to attend school after an absence of almo four years

Further investigation will be required before we ca safely claim to have established the powerful disinfecta qualities of chloramphenicol in urinary infection

We are deeply indebted to Dr L G Cook, directo of pathology, City General Hospital, Sheffield, for th bacteriological examinations

---

Medical Societies

DEVON AND EXETER MEDICO-CHIRURGICA SOCIETY

Vaginal Discharge

AT a meeting on Dec 21 Dr MARGARET HADLE JACKSON spoke on vaginal discharge Some degree discharge, she said, is physiological, though the charact of the normal vaginal content varies according to t age of the woman Thus, microscopically, there a recognisable an infantile, a mature, and a postmenopaus (senile) type of discharge In the mature type thr distinct grades can be distinguished by their chara teristic flora, and the grade tends to remain fair constant in any particular individual

In a case of vaginal discharge it is useful to attem to classify it as (*a*) physiological, (*b*) due to hormon imbalance, or (*c*) pathological Physiological discharg are mere exaggerations of the normal secretory desquam tive processes they occur commonly in young unmarri women and demand no treatment except reassuran and occasionally a warm water or bicarbonate douch Cases due to hormonal imbalance may present with, f example, a profuse mucoid discharge with a grade flora often associated with a follicular cyst, or, if d to ovarian deficiency, with a thin discharge, a grade flora, and many squames of the basal type In t pathological group special importance attaches the age of the patient Among the infantile, where t mucosa is thin, the commonest cause of discharge vaginitis, either traumatic from foreign bodies or mastu bation, or infective, due to the gonococcus or oth organisms In the mature, other traumatic causes ha to be borne in mind—e g, rings, menstrual tampon buried sutures in a healing perineum, and fistulæ in bladder or rectum In addition one has to consider t possibility of allergic reactions to contraceptives, infestations with trichomonas, monilia, or yeasts (t last two particularly common in pregnancy and diabetes mellitus), of venereal disease, and of cervic and uterine lesions In the postmenopausal, where t mucosa has again become thin, apart from discharg due to polyps or malignant disease, one encounte atrophic vaginitis, often characterised by a profu and offensive discharge which only very rarely contai trichomonas or monilia

In investigating a case of vaginal discharge the histor is of first importance whether there is irritatio

THE LANCET

LONDON SATURDAY, JAN 13, 1951

Early Movement, Early Rising, and Early Discharge

WHEN a method has been practised for over fifty years, it can scarcely be considered new and revolutionary But the number of surgeons who favoured early ambulation has until lately been small—too small Only gradually have we returned from post-Listerian complacency to physiological sanity LISTER's followers, reared on the teaching of bacteriology and immunity, seemed to look on Nature as an amiable half wit who must be prevented from running their operations It took the impact of a world war on a generation not yet steeped in orthodoxy to bring back the outlook of HUNTER, and indeed of LISTER himself, that Nature's methods, perfected over millions of centuries, are always purposeful and nearly always right

For the past thirty years at any rate most surgeons have believed that the less an operation is allowed to interfere with the normal tenor of a patient's life the quicker and the more complete will be his recovery Those who pass from belief to action—and it is a big step—permit their patients after operation to assume any attitude in bed they prefer, make them breathe deeply and move their arms and legs as soon as they are conscious, encourage them to sit on the edge of the bed to urinate and on a commode to defæcate, and urge them to get out of bed when the spirit moves them, the sooner the better But this advance in practice, like all advances not conducted on the parade ground, has been on an uneven front Some run ahead, perhaps too far In 1946 LEITHAUSER, whose early experience seems to have been among colleagues somewhat behind the times, suddenly saw the light, and, like many repentant converts, rushed ahead of the preacher Not merely did he push patients out of bed as soon as they were conscious, he pushed them out of hospital as soon as they could totter Others still lag behind One surprising fact emerging from the papers we published last week by Dr GOODALL and by Dr PAYLING WRIGHT and her colleagues, is the extent to which conservative practices still linger Dr GOODALL states that " in the great majority of wards studied, the normal practice still approximates much more closely to a traditional than to an early ambulation regime " Taking an average of 155 patients in general surgical wards, he found that only about 30% were fully ambulant in contrast to nearly 50% who might have been Dr WRIGHT's paper deals largely with gynæcological cases, but it is interesting to note that in 3 of the 4 gastrectomies and all the 3 hernia operations included in her series the patients were still in bed after ten days

When should a surgical patient become ambulant —i e, walk round the ward ? Surely not as soon as he recovers from the anæsthetic He can be hustled out of bed at this stage by the taunts, exhortations, and hot-gospelling of house officers, sisters, and physiotherapists, but how he hates it! Natural desires are a sure guide to procedure in most things —certainly in the selection of diet and the choice between activity and rest The chief need in the immediate postoperative period is that the process of healing in recently divided and resutured tissues shall not be prejudiced The arrest of capillary hæmorrhage, the sealing of spaces, the knitting of gaps by fibroblasts, and the bridging of incisions by epithelial cells—all these require rest, complete and uninterrupted, to the injured part, though to that part alone This can be attained only by rest in bed, while deep breathing and leg exercises are carried out under the supervision of the physiotherapist After four days the wound is safe against lesser strains, and it will be protected from major ones by nociceptive reflexes that do not reach the level of conscious pain The worst strains to which a recently repaired surgical wound can be subjected are those of coughing and the use of the bedpan On the fourth day the sensible and cooperative patient welcomes the first steps to a chair, and Dr WRIGHT shows that it is physiologically wise for him to do so, since he has arrived at the point where further recumbency would lead to venous stasis The main danger of the postoperative period is venous thrombosis, of which venous stasis is undoubtedly a major cause, and the infarction and embolism that may follow Of interest in this connection is Dr WRIGHT's observation that whereas the average rate of flow in the veins of arms and legs, as measured by the transit of radioactive saline solution, was accelerated in both her groups during the first four days, it was considerably slowed after that time in the non ambulant group and did not return to normal till after three weeks, whereas in the ambulant group it was above the preoperative rate during the whole of this period

Dr GOODALL points out that a policy of early ambulation, adopted universally, would add 10–20% to the effective capacity of a hospital and would reduce greatly the call on nurses' time, though it would also necessitate an increase in basins, water closets, and day space But he does not suggest, as does LEITHAUSER who records an average stay of 1 9 days in hospital following interval appendicectomy, that patients, having been got up, should be got out It is essential to good surgery that a patient should remain under constant skilled supervision until the chance of any systemic or local complication is well past—i e, for a minimum period of ten days in almost any surgical condition serious enough to demand hospital treatment A visit to a clinic where early discharge is the rule quickly reveals that it leads to greater waste of beds, for the second and subsequent admissions take more bed days and involve more paper work than retention till the patient is well Hasty discharge also leads to increased morbidity, and often to a lamentable end-result

Laboratory Study of Starvation in Volunteers

IN the last decade the reappearance of famine on a grand scale in many parts of the world has provided all too much material for studying the reactions of man to gradual starvation But because famine conditions are never ideal for accurate observations, such first-hand descriptions often lack scientific precision. These considerations led Prof. ANCEL KEYS and his colleagues of the University of Minnesota to study semi starvation in volunteers under laboratory with a powerful deltoid may lead to incapacity because the humeral head can no longer be steadied against the glenoid before abduction begins

The interrelated syndromes of frozen shoulder, bicipital tenosynovitis, and calcifying degeneration of the cuff are well covered, with a proper emphasis on the importance of lesions of the long biceps tendon derived from the recent work of Hitchcock and Bechtol Of recurrent dislocation, Professor DePalma says that any operation which restricts external rotation will be curative, but he reminds us that spontaneous cure with age is the rule

The chapter on fractures and fracture dislocations of the upper end of the humerus is full of common sense The patient is more important than the local lesion, perfect anatomical reduction is not essential to rapid functional recovery, and the attempt to achieve the first may prejudice the second In much comminuted fracture dislocations the *author is prepared to excise all the head fragments and anchor* the musculotendinous cuff to the upper humeral shaft

There are sound chapters on tumours of the region, and on shoulder pain of neurogenic origin The final chapter on operative techniques is particularly helpful on arthrodesis

The book has the welcome virtue of keeping a proper balance between conservative and operative management

Asthma

CLEMENT FRANCIS, M B, surgeon and i/c of allergy clinic, Metropolitan Ear, Nose, and Throat Hospital London Heinemann Medical Books 1950 Pp 50 5*s*

THERE is a lot of interest in this miniature manual on asthma From a wide experience Dr Francis makes many wise and practical remarks about the use of drugs and anæsthetics, the indications for operation on the upper respiratory tract, and the value of skin-testing and physiotherapy He finds that the difficult cases are the aged, the aspirin-sensitive (4 6% in 1357 cases), the inhaler addicts, and those with advanced bronchitis and emphysema To learn from the author it is not necessary to accept his conception of vasomotor instability as the main mechanism in asthma, nor does his claim for the value of nasal cauterisation rest on its alleged effect in increasing that stability An empirical treatment or one whose action is misunderstood can still be valuable The late Alexander Francis first treated asthma by cauterisation of the nasal septum in 1896 Why have not more doctors tried it? Is it prejudice or distrust of a treatment that has many of the characteristics of a ritual? Or is it that they are not convinced by the figures and the arguments? When Dr Francis claims that 76% of cases achieve complete relief or 50% improvement, the figures have a familiar ring for asthmatics Many physicians achieve results as good without the cautery, as possibly would Dr Francis if he denied this part of his treatment to a group of controls

Die Leptospirose

Eine kurze Darstellung für Ärzte, Tierärzte, und Gesundheitsbehörden W RIMPAU Munich and Berlin Urban & Schwarzenberg 1950 Pp 157 D M 10

Professor Rimpau, who was director of the State Bacteriological Research Institute at Munich until he retired in 1948, is an acknowledged authority on leptospirosis and has himself contributed much to our knowledge of the subject In this comprehensive and well-balanced review he presents detailed information on the laboratory, clinical, and epidemiological aspects of this group of diseases as they affect man

After describing the morphology of leptospires and methods of cultivation he summarises different views about the viability or otherwise of the granules seen in old cultures, which some workers believe to be a resting phase Unfortunately he does not state his own opinion Details are given of the serological techniques used in the study of leptospires in the laboratory and of the methods employed in carrying out surveys to determine the infection rate in rodent carriers Professor Rimpau assesses the value of the different tests and the significance to be attached to their results, and deals shortly with the morbid anatomy and histology of Weil's disease While rats infected with *Leptospira icterohæmorrhagiæ* remain carriers for life field mice carry *L grippotyphosa* for a few months only, and the infection rate varies greatly from year to year Evidence is accumulating that suggests the survival of the organisms in damp soil throughout the winter

In the clinical section the author differs in one important respect from most other writers The genus Leptospira contains a number of species, and it has been customary to give a distinctive name to the disease caused by each species—such as Weil's disease and canicola fever—and to group these into "severe" and "benign" forms, depending on the presence or absence of jaundice, and on the mortality-rate Professor Rimpau prefers to emphasise the essential similarities which are found in all forms of leptospirosis, pointing out that, in every case, leptospires first circulate in the blood, and then settle in the liver, kidney, and central nervous system—tissues for which they have a special affinity During the early stages there are no distinctive symptoms only thereafter do individual differences among species and strains give rise to different clinical pictures, and though some symptoms, such as jaundice or meningitis, are more commonly caused by certain species, the species of the infecting organism cannot be diagnosed on clinical evidence alone For this reason he uses the term "leptospirosis" instead of "the leptospiroses," and describes the different symptom complexes as variations on a single theme, without reference to the species involved Much can be said in favour of this viewpoint, and if, as seems possible, streptomycin or 'Aureomycin' supersedes specific antiserum as the most effective treatment, identification of the organism becomes unnecessary On the other hand, prophylaxis depends either on the use of specific vaccines, or on measures directed against the carrier hosts, and for these purposes accurate information about the species implicated is essential In stressing the unity of the symptomatology, therefore, care must be taken not to lose sight of the wide diversity of the methods of infection and hence of the means of prevention

---

An Introduction to Medical Photography (London Staples Press 1950 Pp 240 30*s*)—Miss Josephine Hunt, S R.N, medical photographer at the Royal Cancer Hospital, summarises the type of work undertaken by a hospital photographic department and the equipment used Her book i not complete enough for reference purposes, but those wh want to know what sort of work is involved will find it helpful The sections dealing with the responsibilities of the photographer to his patient on the one hand, and to the medical staff of the hospital on the other, are particularly to b commended

Digitalis and other Cardiotonic Drugs (2nd ed New York and London Oxford University Press 1949 Pp 245 45*s*)—Dr E R Movitt brings his review up to date wit information about preparations of *Digitalis lanata*, thevetin and new as well as older preparations of *D purpurea* Squi receives a whole chapter to itself which seems hardly deserved The pharmacological action of digitalis, on which there ha been important work in the past few years, is considered i detail Here as on other topics the author withholds hi own opinions, though many would welcome an attempt t integrate differing views on theory and practice The style is discursive, but the bibliography is comprehensive, and th cardiologist will find good use for the book as a work o reference

Les Symptômes de la tuberculose pulmonaire et se **complications** (2nd ed Paris Masson 1949 Pp 983 Fr 1800)—This latest edition of Prof Edouard Rist's book o the symptoms and signs of pulmonary tuberculosis can b confidently recommended to those whose interests lie in th field It is beautifully written at a tempo one can only cal old fashioned in comparison with so many modern text whose authors apparently think it enough to convey fac without amenities of style That facts are here in abundanc can be judged from the sections on amyloidosis (25 pages on pains in the chest (23 pages), and on striæ occurring in th skin of the thorax (10 pages) The book shows evidence o wide personal experience and wide reading, and of dee thought on both It is not a students' textbook, but i contains a vast amount of information, and should tak its place on the reference shelf beside *The Pathogenesis o Tuberculosis* The footnotes are not the least of its felicities that their entry is effected by an invasive property inherent in the cells themselves, and colour is lent to this hypothesis by the identification of hyaluronidase in some mammalian tumours and one fowl tumour,[8] and of collagenase in many[9] It remains to be seen, however whether one or both of these enzymes are always produced by invasive growths, and whether they are always absent from benign growths Secretion of enzymes of the mucinase class might account for extravascular infiltration of collagen and other connective tissues, as well as for breaches in vessel walls, and the possibility that these enzymes are present in actively invasive tumours cannot be lightly dismissed

Whether enzymes destructive of connective tissue exist in tumours or not, there can be little doubt that ruptures and defects in vessel walls aid the entry of all types of embolic cell. By means of models, **Young** and **Griffith**[10] have studied the physical conditions that allow entry by cells lacking invasive power Their model presupposed that capillaries (represented by a thin-walled collapsible tube filled with circulating fluid) lie freely in a fluid medium (represented by a box reservoir containing the same fluid and polystyrene beads to mimic cells) Beads passed through holes into the tube only when the external pressure exceeded the pressure within the tube In this experiment an unstable equilibrium existed for a time, during which the terminal segment of the tube oscillated, alternately closing and opening as the internal pressure fell below and rose above the external pressure In living tissues, however, interstices between fibrils of connective tissue are normally filled, not with fluid, but with a jelly-like substance which liquefies locally in inflammation and œdema, and **Young** and **Griffith** went on to investigate what happens when the collapsible tube is surrounded by a continuous glycerin jelly With increased pressure in the tube the alkaline fluid contained in it was forced through a preformed hole into the jelly, which eventually broke up as the pressure increased When the pressure in the tube was again reduced below that in the gel (which was impregnated with phenolphthalein) masses of broken up jelly passed into the tube The model suffered from one serious limitation, of which **Young** and **Griffith** are aware the tube representing a capillary vessel was not, in their own words, "braced and guyed by strands of reticulin and collagen" When extravascular pressure rises, these external attachments make all the difference to the lumen of thin-walled vessels, instead of closing, as **Ribbert** supposed and the model shows, the walls of the vessels are pulled apart by the fibrils This opening mechanism was first suggested by **Gaskell**,[11] and its existence has been confirmed by **Pullinger** and **Florey**[12] Thus the conditions that co exist in life—rise of extravascular pressure with patent blood and lymph capillaries—are those shown by **Young** and **Griffith** to favour cell embolism

By measuring the pressure inside intratesticular grafts of Brown Pearce carcinomata and comparing it with the pressure in normal ungrafted testes of the same rabbits, **Young** and his colleagues[13] have established that the pressure in the tumour, measured as tissue resistance to injected saline, rises during the healthy growth of grafts, whereas in a normal testis the pressure remains remarkably constant, and this implies that pressure in the tumour rises relatively to intracapillary pressure, which is assumed to be the same in both testes Only a breach in the vessel wall is then necessary for forced entry by embolic tumour cells Holes or ruptures are obviously made by hæmorrhages and by the defects often found in sinusoidal vessels of rapidly growing tumours. **Young** and his co workers suggest that hæmorrhages may be due to a temporary rise in intravascular pressure, which causes the endothelial walls to burst mechanically It is more likely, however, that blood leaks, or is forced, out of the growing tips of the capillaries that form continuously in response to the stimulus of the ever-growing tumour, and that tumour cells enter these same tips as well as the defectively lined sinusoids Hæmorrhages in their van are a feature of growing capillaries, and the added volume of blood increases tissue pressure and stretches open neighbouring lengths of vessel These are widened also by products of inflammation—œdema fluid and plasma, and possibly fluid exuded from vessels made hyperæmic by X irradiation **Young** and his associates draw attention to many conditions likely to increase pressure inside tumours further growth and rise of pressure as time passes, aspiration biopsies and other factors causing hæmorrhage, local anæsthetics adding fluid under tension and palpation entailing compression from without

Though none of these mechanisms can be confidently blamed for any particular metastasis in man or in animals—so capricious are the ways of tumour cells—nevertheless their capacity for harm warns us to avoid them

Danger in the Home

On Dec 14 the *Radio Times* published a sketch to illustrate the Postmaster General's annual injunction to "post early for Christmas" It represented a little girl in a nightdress leaning across an unguarded open fire towards a Christmas stocking hanging from the mantelpiece An innocent, sentimental drawing, yet hundreds of little girls in this country are burned every year, many of them fatally, in doing just this kind of thing A document recently issued by the Ministry of Works[14] shows that in 51 out of 306 accidents to children which were studied in detail the cause was lack of a fire guard, and in a further 14 the fire guard provided was either too wide in the mesh or so flimsy that any child could knock it over Of nearly 7000 fatal accidents in the homes of England and Wales every year, about a fifth are due to burns and scalds, and of course children are the chief victims

The report is issued for the benefit of research workers and "not for general publication', but its findings should have headlines in every popular newspaper The sources of information cover a wide area and their volume should in itself lend weight to the results of the investigation For fatal accidents the figures supplied by the Registrar-General and the conditions General summaries of their observations, which were made in 1943–44, will be found in two papers[1] and in their recent book, *The Biology of Human Starvation*[2]

---

[8] Pirie A *Ibid* 1942 23 277
[9] Gersch I Catchpole H R *Amer J Anat* 1949 85 457
[10] Young J S Griffith M D *J Path Bact* 1950 62 293
[11] Gaskell W H *Arb physiol. Inst Leipzig* 1877 11 143
[12] Pullinger B D Florey W H *Brit J exp Path* 1935 16 49
[13] Young J S Lumsden C E. Stalker A. L *J Path Bact* 1950 62 313
[14] Ministry of Works Chief Scientific Adviser s Division An Inquiry into Accidents in the Home

The subjects of the study were 32 conscientious objectors who lived in the laboratory for a year For a control period of 3 months the men were given a diet supplying 3492 calories daily, and on this they maintained their normal health and weight Then for 6 months the calorie value was reduced to 1570 daily, in the form of potatoes, cabbage, turnips, and cereals, with only a few grammes of animal protein per week —the kind of diet that people in northern Europe consume in famines On this they lost an average of 24% of their body weight and developed the classical signs and symptoms of famine victims By the end of 6 months, however, through a remarkable series of adjustments, most of the subjects were no longer losing weight Basal metabolism now accounted for only 962 calories a day, compared with the initial 1576 calories Two thirds of this fall was attributable to the reduced mass of their metabolising tissues and the remaining third to less intense tissue metabolism A more significant fall was in the calories used up in their daily activities—from 1567 to 451 per day No change was detected in the metabolic efficiency of carrying out such standard tasks as walking on a treadmill (after the necessary corrections for loss of weight), so this last fall must be ascribed to voluntary curtailment of physical activity The men moved slowly and cautiously, climbed stairs one at a time, and eliminated all unnecessary movements—means which closely resemble those observed by LEYTON[3] in prisoners of war At the same time there were profound personality changes All the men became apathetic, depressed, and introverted, avoiding social contacts so far as possible Most of them were more emotionally irritable than before, though their overwhelming physical lethargy usually prevented any aggressive behaviour Their aversion to intellectual effort made them seem stupid, but psychological tests revealed no impairment of memory, reasoning power, or verbal and arithmetical facility

In the last 3 months of the experiment various methods of rehabilitation were compared Recovery was slow but ultimately complete When they left the institute the volunteers were normal in most of their functions, but it was another 9 months before they regained full normality They seemed to recover best on a good mixed diet of about 3500 calories daily, with light exercise Additional calories, protein supplements, and special vitamin preparations had no apparent effect on the pace of recovery

Among the more detailed observations published separately were some important ones on the tissue fluids[4] and the circulatory system[5] Nearly all the subjects developed famine œdema During semi-starvation the absolute plasma volume increased only slightly, and the total amount of extracellular fluid (thiocyanate space) was substantially unchanged But owing to the great reduction in cellular mass there was a *relative* increase in both extracellular fluid and plasma volume Throughout the experiment there was a close correlation between the volumes, expressed in ml per kg body-weight, of plasma and of extravascular fluid The observations support the view that famine œdema is a reflection of a simple disproportion between the losses of extracellular fluid and of cell mass following a defective supply of calories In the present case œdema appeared without any reduction in plasma proteins The main cardiac finding in the experiment was well-marked atrophy of the heart muscle, radiological measurements indicating an average reduction of 17% in heart volume , a similar atrophy has been noted in necropsies of famine victims The average pulse rate became progressively slower for the first 8 weeks, when the basic rate was 35 per minute, but thereafter it remained about the same The bradycardia was not an indication of heart block Electrocardiograms showed reduced voltages of deflections but no important changes in rhythm Both systolic and diastolic blood pressures fell, and, in contrast with the pulse rate, the pressures went on falling to the end of the experiment, the maximum reductions being 30 mm Hg in systolic and slightly less in diastolic These changes were completely reversed on rehabilitation, and after 32 weeks most of the cardiovascular measurements were normal Cardiac function, on the other hand, recovered more slowly, which confirms the empirical finding that famine victims need long and careful convalescence All the volunteers became slightly anæmic, with an average fall in hæmoglobin level from 15 1 to 11 7 g per 100 ml in 24 weeks The causes of this anæmia are uncertain , but it is agreed that severe anæmia in famine victims is not simply a consequence of lack of calories or animal protein, so a search must be made for infections or other factors adversely affecting the bone marrow

The results of this experiment—skilfully conceived and faultlessly executed—will be of great practical value to administrators planning relief measures as well as to doctors working in future famines And unless means are quickly found to increase the world's food supplies and distribute them more equitably,[6] periodic famines seem to be an inescapable prospect

Cell Embolism and Metastasis

THE pathways and propulsion of cells in and out of blood and lymphatic channels remain subjects for fresh inquiry, though they are as old as cellular pathology itself It appears from the work of MILES and NIVEN[7] that the passage of polymorphonuclear leucocytes outwards through capillary walls is not due simply to their motility and to physical changes of the endothelium in inflammation for such passage to take place the intravascular pressure must probably exceed that in shock, where leucocytes are not found outside capillaries in infected foci Likewise the entry of fixed cells into blood and lymphatic capillaries requires both a breach in the vessel wall and a force that detaches the cells and drives them in The trauma of bone fractures or blast will make a breach for fat emboli , but such trauma does not account for the emulsification or entry of the fat With regard to tumour cells, there is a tacit assumption of these already had diffuse peritonitis or localised abscess The urgency of early operation is further underlined by the observation that of 480 patients with a history of less than twenty four hours 46 had peritonitis in the flank or pelvis, 25 generalised peritonitis, and 9 a localised abscess It says much for the training of our younger surgeons that of the 1074 patients in this low mortality series all but 46 were operated on by registrars and house surgeons

---

[1] Keys A *J Amer med Ass* 1948 138 500 Taylor H L Keys A *Science* 1950 112 215

[2] Keys A Brozek J Henschel A , Mickelsen O Taylor H L Biology of Human Starvation Minneapolis University of Minnesota Press London Oxford University Press 1950 Two vols Pp 1385 £6 10s

[3] Leyton G B *Lancet* 1946 ii 73

[4] Henschel A Mickelsen O Taylor H L Keys A *Amer J Physiol* 1947, 150 170

[5] Keys A Henschel, A , Taylor H L *Ibid* p 153

[6] Leading article *Lancet*, 1950 ii 446

[7] Miles A A Niven J S F *Brit J exp Path* 1950, 31 73

Operative technique in this series followed the usual practice Preference was given to incisions over the site of the disease The cæcum was inturned after removal of the appendix, and in 4 cases, where this was impossible because of thick infiltration of the cæcal wall, a drainage tube was inserted through the aperture into the cæcum In a few instances the appendix could not be removed Drainage was used very sparingly Even localised abscesses were closed, and indeed abscesses gave more trouble when drained than when they were sewn up If the abscess is opened, debris is removed, and a chemotherapeutic agent is introduced, prompt healing may fairly be expected without drainage However, Moloney and his colleagues think that drainage is indicated when surgical intervention has left raw bleeding areas (the older surgeons also took this view) or when a well localised abscess has thick walls Cultures revealed most commonly *Bacterium coli*, which was sometimes the only organism isolated *Streptococcus fæcalis* and anaerobic streptococci were the next most common organisms, *Clostridium welchii* was less often found Actinomycotic filaments were not unusual in smears These organisms have varying sensitivity to chemotherapeutic agents, and so logically both the sulphonamides and antibiotics may be used at the same time Sepsis in the wounds was less when ‘Nylon’ was used for sewing up than when catgut was employed, and late discharge of sutures was much more common with catgut than with nylon Lung complications were very rare Only 1 patient died of pneumonia, and this was an infant who had this disease on admission There was 1 death from pulmonary embolism, 1 other patient had hæmoptysis from this cause Femoral thrombosis occurred in only 6 cases Mechanical obstruction developed in 6 patients, of whom 3 died despite further operation In view of the extensive use nowadays of intravenous infusion therapy, it is interesting to note that only 35 of 98 cases of diffuse peritonitis were deemed to need this treatment It was found that, in the absence of paralytic ileus, patients would absorb by mouth or rectum as much liquid as they required

The majority of patients had left the hospital by the twelfth day, but of the 98 patients with diffuse peritonitis 38 were kept longer than eighteen days Clearly remarkable progress has been made in the treatment of acute appendicitis

RUBELLIN A NEW CARDIAC GLYCOSIDE

IN the 175 years since Withering first exploited the beneficial action of the foxglove in congestive heart-failure, the galenical preparation of digitalis, with its uncertain constitution, has successfully withstood the challenge of crystalline strophanthin and is only slowly giving ground to its more serious rival, digoxin Time will show whether rubellin, a newly isolated glycoside reported by Isaacson [1] from South Africa, should be ranked as a clinical competitor, which will bear comparison with digoxin

Rubellin has nothing to do with german measles, it is obtained from the plant *Urginea rubella*, a member of the natural order Liliaceæ The digitalis like action of this highly soluble crystalline glycoside has been demonstrated by Sapeika [2] Using ouabain as a standard, he showed that the relative potencies of the cardiac glycosides are, in descending order rubellin 121, ouabain (international anhydrous) 100, prorubellin (a sugar free glycoside obtained by acid hydrolysis of rubellin) 50 5, strophanthin 44, lanatoside C 31, digoxin 19, and digitoxin 3 6 In a concentration of 10^{-6}, rubellin had the typical digitalis effect on the isolated frog's heart, as well as on the isolated mammalian (cat and rabbit) heart and on the heart and blood pressure in the intact animal Observations in man showed that the effective dose was 0 003 mg per kg of body weight intravenously Rubellin need not be assayed biologically It was effective in patients with heart disease with either normal or abnormal rhythm, acting best in cases of auricular fibrillation and congestive failure When administered intravenously it alleviated all the urgent symptoms in 2 hours, when its full action became evident It seems to be useful in cases where, owing to vomiting or unconsciousness, it is impossible to give digitalis by mouth, and where immediate treatment of congestive cardiac failure is imperative, provided that no other digitalis drug has been given within the previous ten days, digitalis may, however, be given by mouth at the same time as intravenous rubellin

VIRUSES AND GENETICS

VARIATION among the viruses has attracted much attention in the past not only because of its theoretical interest but also because of its practical usefulness Thus rabies, as Gordon [1] reminds us, affords the classical example of virus modification in the laboratory put to good purpose But known types of virus variants are not always characterised by simple loss of pathogenicity on transfer from one host to another Indeed there seem to be three sorts of variants Firstly, there are those with modification of pathogenicity without alteration of antigenic characters the classical 17D strain of yellow-fever virus has for instance lost its pathogenicity in tissue culture without losing its antigenic potency, and this has made it a useful immunising agent in man Secondly, there are antigenic modifications without change in pathogenicity, as suggested by the observations of Hammon and his associates [2] on the encephalitic agent recovered from mites This, when passaged in mice, possessed the St Louis encephalitis virus antigen, yet on egg cultivation the antigen characteristic of Western equine encephalitis virus emerged Thirdly, there are alterations both of pathogenic properties and of antigenicity Such have been exemplified by variant influenza virus strains, as shown by Hirst,[3] who passaged virus direct from human material in eggs and showed the strain to be different from that derived by ferret and then mouse adaptation

The influenza viruses, as Gordon remarks, excel in their “mutability,” and all the three types of variation mentioned above have been encountered in laboratory work, in addition to the O–D variation in hæmagglutinin shown by recently isolated strains of virus A The observations of Isaacs and Edney [4] on the Melbourne virus A strain make it hard to believe any longer in the “purity” of any stock virus The difficulty pointed out by Gordon in the analysis of virus genetics has lain in the past in the fact that pure clones of particles derived from a single parent particle have not been available. This difficulty was overcome by Isaacs and Edney when they passaged virus in eggs at high dilutions whereby less than half of inoculated eggs yielded virus growth At such limiting dilutions, egg fluids were either non infective, or contained virus with properties resembling the parent, or else yielded a variant strain with new records kindly provided by the coroners for North London and Liverpool have been freely used, and they tell a consistent story Of late years public attention has largely focused on road accidents, and it is harder to classify home accidents so as to make a comparison, but the following figures (for years before the derationing of petrol) are not far from the mark as representing deaths

---

[1] Isaacson B *S Afr med J* 1950 24 901
[2] Sapeika, N *Ibid* p 912

[1] Gordon F B *Ann Rev Microbiol* 1950 4 151
[2] Hammon W M, Reeves W C Cunha R Espana C Sather G *Science*, 1948 107 92
[3] Hirst G K *J exp Med* 1947 86 357
[4] Isaacs A, Edney, M *Brit J exp Path* 1950 31 209

—	On the road	In the home
1945	4005	5996
1946	4161	6287
1947	4187	6835

When the years 1943, 1944, and 1945 were studied in detail by the Domestic Accidents Panel of the Ministry of Works, it was found that just under half the deaths were due to falling, and nearly a fifth to burns and scalds In an analysis of children's deaths following accidents in the home a total of 2348 boys and 1791 girls under fifteen was recorded As might be expected, there was among boys a preponderance of "hazardous" accidents, such as falls, electric shock, and explosions, but girls showed a sad superiority in burns, especially by clothing catching fire between one and fifteen years the figures were boys 96, and girls 301 As a cause of death for children under one year, suffocation was an overwhelming cause—1026 boys and 702 girls out of totals of 1181 and 814 At other ages the noteworthy figures are the high percentage of fatal falls in women over sixty five, and of course the high rates for women between twenty and sixty five, compared with men of the same age

In the study of mainly non fatal accidents valuable information was received from a wide variety of sources, including the Birmingham Accident Hospital, the almoners of a number of London hospitals, the Edinburgh city police, and health visitors on the staffs of medical officers of health In the Birmingham Accident Hospital about 5000 domestic "accidents" patients are treated each year As the sample for examination[15] the investigator chose just under 3000 cases of accident within the home which had been treated in eight months of the year, two months being taken from each quarter It is interesting to note that falls and cuts and bumps were most frequent in the summer months, and burns and scalds in November–December The latter causes take the highest place among children under two years, but give place to other injuries when the boys begin to knock around When the proportion of accidents in a given age group was related to the proportion of the population in that age group, the following ratios were obtained

Age	0–4	5–14	15–64	65+
All accidents	2 8	1 1	0 8	1 1
Falls	2 6	0 9	0 7	1 9
Burns and scalds	4 9	1 1	0 6	0 5
Falling on fire	8 9	0 8	0 3	—
Catching clothing on fire	3 4	0 6	0 8	1 1
Pulling over hot liquids	11 3	0 2	0 1	—

One of the striking features of this analysis is the high ratio in children under four years, and it is easy to see how important and necessary it is to protect young children, especially against burns and scalds The Birmingham study also showed that in 1946 40% of the patients were children under ten years of age—double their proportion in the population—and that 4% of the people living within easy reach of the hospital received treatment for home accident. The reports from other sources—the Edinburgh Royal Infirmary, the London hospitals, and the health visitors—tell much the same tale Personal rather than structural factors are the main cause of accident, but it is clear that there are most injuries where housewives live in overcrowded and ill equipped homes they are distracted by the difficulties of keeping an eye on the children while trying to get through the day's work without confusion and disorder A long story of fighting against the heavy odds of environment often lies behind such expressions as thoughtlessness, carelessness, or negligence

The prevention of accidents in the home involves many factors, including personal instruction, propaganda, and attention to safety in construction—especially of stairs and passages, because falls are the commonest cause of injury The fact that faulty equipment is not a frequent cause of accident is no excuse for permitting dangerous things to be made and sold We know how to make gas and electric fires safe by placing guards at a proper distance from the source of heat, yet so far hardly any manufacturer has taken advantage of that knowledge We know too how the dangers of the open fire can be minimised by insisting on the legal requirements about fireguards and making sure that only approved patterns are sold Every fireplace could easily be provided with sockets to take a standard type of guard Yet we continue, year by year, to tolerate hundreds of quite unnecessary tragedies

Annotations

GENERAL PRACTICE

We cordially welcome the Central Health Services Council's appointment of a committee on general practice (see p 104) Much ground must now have been cleared by the English and Scottish councils' committees on cooperation between general practitioner and other services, and by the B M A 's general practice review committee—not to mention the reports on the subject already published We trust therefore that conclusions will be reached, and advice offered, within the period of six months that has been mentioned in the press

APPENDICITIS

The mortality of appendicitis, though it has fallen steadily since 1920, is still considerable in this country more than 1500 people died from it in 1946 A survey of 1074 cases of acute appendicitis treated at the Radcliffe Infirmary, Oxford, during the period 1925–48 goes some way towards explaining the reasons In this review Moloney and his associates[1] remark that the dangerous ages at which to suffer from appendicitis are 5–14 and after 55, and the death rate for females is 40% less than that for males One curious feature is that as the social scale is descended the number of deaths falls off Possibly some difference in the habits of the upper classes—it may be dietetic—renders them more susceptible The general mortality in the whole Oxford series was 1 4%, and, as would be expected, it was highest (6 2%) in the cases with diffuse peritonitis Of all the patients 83% were in the surgeon's hands within forty eight hours of the onset of the attack, yet 25%

---

[15] See Castle O M *Lancet* 1950 i 315

[1] Moloney G E Russell W T, Wilson, D C *Brit J Surg* 1950 38 52

(18)

Special Articles

THE MEDICAL CARE OF THE ELDERLY

T N Rudd
M.D Lond, M R C P
PHYSICIAN, THE BELMONT HOSPITAL, TIVERTON, DEVON

No one who reads the medical papers can fail to be impressed by the number of careful reports on conditions of the elderly, sick and healthy, in hospitals and in their own homes, throughout the country

Excellent surveys have been made by British Medical Association special committee (1947) and by Sheldon (1948) on field conditions in large centres, while the treatment and care of the chronic elderly sick in hospitals have been the subject of painstaking surveys by Thomson (1949) and many others All these authors stress, with almost monotonous regularity the rising proportion of elderly to younger members of the community to be expected as a result of increased longevity and a falling birth rate Conditions of neglect under which the aged live have been noted in this country and in the United States of America (Thewlis 1946) In support of the youngers, on whom the care of the elderly falls, Sheldon (1950) has made it clear that the wage earning community is probably bearing as heavy a burden of old age as it can tolerate

The attitude of neglect towards old age and its problems has had many causes some old people are inarticulate, and unduly passive towards their disabilities, while others are querulous and difficult, all are of diminishing significance in the community, and as such, their complaints can be more easily disregarded, furthermore, some are unpleasant in their habits While our well developed moral sense quite properly prevents us from feeling any desire to apply euthanasia to the aged sick, it is seldom strong enough to make us give human sympathy or unselfish help in their needs They are thus in some respects the counterpart of the sacred cow of the Hindus

Another cause of neglect of the old is ignorance—a failure to understand how very real their needs are A new attitude is however steadily arising, and much practical sympathy is being shown, though this is at present incoordinate Hospital inpatient and outpatient services the Red Cross, the W V S ("meals on wheels"), county council welfare organisations, and private charities are all trying to do something—in many areas with no coordinating committee

Some charities are still working on an outdated system of relief Thus some almshouse trusts give help in money, rather than in goods or service we then find old people living in almshouses in a state of neglect, and in certain areas the neglected poor may even be found inside and not outside the almshouses A capable and vigorous middle aged woman, appointed as warden, will often make a remarkable improvement in the standard of living Without having to give too much help herself she will know where to get the help needed to keep the old people well cared for

The aged poor of any neighbourhood derive help from many organisations Medical care comes from the State doctor and the district nurse, upkeep from the State (old age pensions) and from private charity (almshouses and trusts), as well as from local government sources (county council hostels and "outdoor relief"), at Christmas, gifts from private charities are added Day to day help is given by "meals on wheels," provided either by the W V S or the local authority, and by the local authority "home helps" scheme, but in some areas these two services are given only to those who are medically certified as being "sick" Old age pensioners associations help to supervise the needs of the old, to represent their interests, and provide them with social and club facilities When an old person becomes seriously ill, he is—or should be—moved to hospital, but the hospital service (which should be merely ancillary to the greater problem of care of the aged) is quite unable to cope with the calls made on it

COORDINATION OF EFFORT

A State sponsored committee should be set up in each administrative area to promote the welfare of the aged, survey the various organisations already promoting their welfare, and assess what is needed to *provide a comprehensive scheme* A Government body (local or central) should be approved to receive the recommendations of these committees, and to afford them help which is beyond their own power to obtain Organisations which would be represented on the committee would include

House committees of local hospitals
Red Cross and St John organisation
W V S
Old age Pensioners' Association
Charitable trusts
Clergy
Committees of old people s homes, hostels, or clubs
Geriatric social workers
District nurses
General practitioners
County council welfare department

A careful report made by such a committee, after six months' work, would awake much public interest in the area, and this might lead each community to take a pride in its record for care of the elderly, as it does in the achievements of its football team

CLINICAL GERIATRIC PROBLEMS

The ultimate problems for scientists are the reasons for ageing, and its prevention These may never be solved, but we can at least learn more of the variations of disease in old age Important changes of attitude are now becoming general (Rudd 1950) rehabilitation, especially, has come right to the fore, but it can only be successful if based on a sound and complete diagnosis of the case—a task for experienced geriatric clinicians These need greater opportunity for investigating disease, the support of a more comprehensive specialist service in the various departments of medicine and surgery, and more knowledge of necropsy results confirming or disproving clinical findings Conferences, too, are needed on geriatric clinical problems for those practising this branch of medicine, and postgraduate courses for general practitioners anxious to apply new knowledge Family doctors should have an increased capitation-rate for this time consuming branch of their work Those with a large list of old people are hard pressed to give weekly injections of mercurial diuretics if they have a correspondingly long list of wage earners and children The general practitioner's need for increased diagnostic facilities cannot usually be met by the general hospital outpatient department geriatric outpatient departments will be required, preferably in geriatric hospitals The detailed lay-out of such a department is beyond the scope of this paper, but the principle may be outlined

Aims maintenance of health and independence of the elderly diagnosis of disease, treatment of major and minor defects

Staffing geriatric physician, geriatric nurses, physiotherapist, occupational therapist, social workers (and possibly geriatric district nurses)

Special facilities pathological examinations (a postal service would be adequate), radiology for bone and chest conditions (cases requiring more elaborate investigations could be referred to a general hospital)

In hospitals which have no physiotherapy departments, the geriatric outpatient department should be linked up with an outside physiotherapy clinic, but preferably massage should be given by personnel on the geriatric staff whose methods are geared down to the properties which thereafter bred true This technique was later used by Burnet and Lind [5] in their work on the neurotropic W S influenza virus which produces encephalitis in mice The strain was coupled up with one of several other strains which would not give rise to encephalitis and which had antigens distinct from W S The progeny of the " marriage " induced encephalitis but exhibited the antigen of the second parent, and passage at limiting dilution provided no evidence that the phenomenon was due to simple mixture An example of such a new strain was obtained by using neurotropic W S and swine influenza virus and thereafter demonstrating a neurotropic virus possessing the swine antigen Genetic recombination has, of course, already been shown in the case of the *Bacterium coli* T bacteriophages [6 7], but the demonstration of a similar phenomenon in an animal virus is new and confirmation will be eagerly awaited It seems that mutation is not the only way in which virus variants arise, and one begins to wonder how Nature, or man himself, ever manages to keep a virus unchanged in character

BRISTOL'S PROBLEM FAMILIES

" HE just lets time roll by," used to be the burden of a comic song, and in some families its underlying principle is the accepted design for living The wonder is, perhaps, not that there are such families but that there are not more of them Luckily for the rest of us they seem to be on the wane Fifty years ago Charles Booth wrote of a submerged tenth today Dr R C Wofinden [8] thinks the fraction much smaller, "probably less even than a submerged hundredth "—which goes far to allay the fear that these highly prolific, mainly unproductive, sometimes delinquent, yet often contented people are on the increase Dr Wofinden has just completed, on behalf of the Problem Families Committee of the Eugenics Society, a pilot inquiry in Bristol, and four others are planned for Luton, Rotherham, the West Riding, and Kensington, with the object of standardising a suitable method of investigation which might prove useful later to other committees, and possibly even to an interdepartmental committee interested in this subject

Though the method chosen at Bristol proved to have drawbacks, the inquiry confirmed some known facts and brought others to light Local authority officers and many voluntary agencies collaborated, and a field worker visited the 155 families studied More than half of them were housed on corporation housing estates, and some had been, or were about to be, evicted from such estates because of failure to pay the rent This seems at first glance to justify the old cry of " once a slum dweller always a slum dweller ", but Dr Wofinden is at pains to remind us that this is untrue He quotes an unpublished study of 50 rehoused families made by Dr I G Davies, who traced back the history both of the successful tenants and the failures Both groups, he found, had come from the same slum conditions, but in the failures personal characteristics outweighed the influence of improved conditions In general the standard of intelligence among them was low, and they could not plan their domestic life with any system " there was a ' hand to mouth ' flavour in all their actions " He concluded that they would need training in domestic methods and regular supervision if they were to become good tenants, and Dr Wofinden thinks there is much to be said for rehousing families of this kind in a ' half way house "—a reconditioned older property—and promoting them to a corporation house only when they have learned to live in a decently hygienic fashion In Bristol there was little overcrowding, in the official sense, despite the fact that the problem families were often large the average number of children was 5 8 per family But they were sociable, and apt to crowd into one or two rooms—the more readily since there was seldom much in the way of furniture to attract them into the others The children, nearly all of them dirty, verminous, ill clad, and ill shod, were almost uniformly—and somewhat disconcertingly—happy The Curtis Committee laid much stress on the importance of family life, especially happy family life, so the problem becomes, as Dr Wofinden says, how to reclaim the family without breaking it up

Of the fathers, mainly unskilled and semi skilled workers, less than half were in steady employment, and the rest took what casual employment they could get, or did not care for any work Rather more than half were mentally subnormal, and about a quarter had a weak moral record in which such things as chronic alcoholism, imprisonment, bigamy, and incest figured Others had psychological or physical defects More than half the mothers appeared to be in poor health, and three quarters of them were mentally subnormal No less than 101 of the 882 children of these 155 families are in mental defective institutions, approved schools, special schools, or residential children's homes, or boarded out with foster parents Thus 11 4% have become a direct charge on the State The rates of juvenile delinquency and of illegitimacy were high Other studies have revealed a high infant mortality rate in such families as these, but in Bristol the rate was not significantly higher among them than among other families in the city

Dr Wofinden suggests that the welfare services departments of the local authorities should be made responsible for problem families in their areas, and that they should work in close touch with the health department A small committee of officers might be set up, representing the health, housing, welfare, education, and children's departments, and with some coopted representatives of voluntary bodies, to confer on the needs of these families He also considers that convalescent care should be available for ailing mothers, and that social reablement centres should be set up where mothers can be admitted for a time, with their families, and given some training in their job Home advisers, who will go into the homes and actually help with the housework while they teach, have proved their value, and should be more widely used. Where furniture is needed he thinks the local authority should be able to give or lend it He believes that these measures, with a realistic rehousing policy based on the " half way house," would go far towards reducing the submerged hundredth to a still smaller fraction

EGYPTIAN SILVER JUBILEE

THE 25th anniversary of the foundation of the Fuad I University, Cairo, was celebrated on Dec 27 in the presence of H M King Farouk Addresses of congratulation were presented by the vice chancellors of the universities of Oxford and Cambridge, the president of the Royal College of Physicians, the junior vice president of the Royal College of Surgeons, and the president of the Royal College of Obstetricians and Gynæcologists The honorary degree of doctor of medicine was conferred on Dr Russell Brain, that of master of surgery on Sir Cecil Wakeley (in absentia) and Mr Philip Mitchiner, and that of master of gynæcology on Prof Hilda Lloyd The new graduates were invested by Dr Mooro Pasha, dean of the faculty of medicine

---

DR GEORGE CATHCART, consulting surgeon to the Throat Hospital, Golden Square, London, died in Edinburgh, on Jan 4, at the age of 90

---

[5] Burnet F M Lind P E *Aust J Sci* 1949 12 109
[6] Delbrück M *Colloq int Centre Natl Recherche sci* 1949 8 91
[7] Hershey A D Rotman R *Genetics* 1949, 34 44
[8] Problem Families in Bristol London Eugenics Society and Cassell & Co 1950 Pp 60 2*s* 6*d*

Visit of H M Queen Mary

usually on some subject suggested by one or other of the boys, prayers follow. Letters from boys who have left the school show how often some point or other in the little homily goes home, at all events this family gathering in the evenings is remembered by many with serious affection as the centre point of life in the school.

But moral standards have to be acquired at many levels. The newcomer to the school sees no harm in pinching cigarettes or fruit, so the first simple device is to ensure that he finds it does not pay. The boy who takes twenty cigarettes is made to pay back thirty, the boy who steals fruit is compelled to pay for it at retail price, though by honest trading he could have it at the wholesale rate. But while he is learning, at this level, that by cheating he only robs himself, he is also beginning to find how pleasant it is to be trusted and praised, and self-interest as an incentive is gradually displaced by self-respect. Senior boys can become prefects (though without powers to inflict punishment accorded to prefects in public schools), and those who are due for discharge in a few months time graduate into the "discharge house," where they have their own dormitory and sitting-room, wear long grey flannels and marvellous "discharge" ties, and need no resident master to supervise them.

PENALTIES

Human nature is not amenable to pure reason. Before any of us gives up the egoism with which he was born, and consents to live socially, he must concede that there is "no future" (as the Cotswold schoolboys say) in crime, or even in antisocial behaviour. Mr Joyce has found that, with some boys, penalties can be used constructively to teach this elementary fact. Feeding penalties are now forbidden (as indeed they should be for growing children) but he does make use of detention for the determined rebels. The boy who defiantly refuses to do his work goes into confinement—in the visitors' room. Here he gets a comfortable bed with a pink eiderdown, pictures on the walls, plenty of books, the wireless, a private garden with an aviary, and three good meals a day, but no society other than that of the master whom he can summon by bell to attend to his needs. After twenty-four hours in these surroundings—scornfully dubbed "sissy" by the school at large—he is usually ready to come out and join in. And if he wants freedom on these terms he has only to ring the bell, as a notice on the wall informs him. Nor does he get shut up without plenty of warning. The headmaster explains quite clearly in advance that if he chooses to do his share like the rest he is entitled to their privileges, if he chooses not to, then he chooses the penalty as well and he, nobody else, has imposed it. Incidentally, Mr Joyce believes that official penalties, however modified, should not be abolished entirely. If there are no official penalties, he finds, you get unofficial punishments creeping in.

THE FOUNDATIONS OF SOCIAL BEHAVIOUR

The school has good games teams and plays other schools at times. Some boys who had just returned from playing a public school spoke hotly of the miserable discomfort in which their friendly hosts were living. "No chairs or backs to the seats—just forms—and no separate tables in the dining room. Nothing like as good as our place!"

Is it justifiable to place the delinquent in more agreeable surroundings than the well-behaved sons of the rich? It depends what the school can bring to the characters of the boys in it. As a rule the public school boy has behind him a secure home, and parents who have good moral standards and are capable of showing steady affection and giving sound guidance, at home he may even live a little "soft." For him school is, and probably should be, a toughening experience. Most delinquent boys have no such background of security; they come from broken homes, from scenes of family discord, or from no home at all. They have had little training in self-control, and have acquired few liberal principles. For them the school must provide the stable background which they never found at home; it must not toughen the little tough still further. While there is no "soft" living at the Cotswold school (the equipment is strong and plain as it usually needs to be in any strictly male society, whether juvenile or adult) the surroundings are beautiful, and the approach friendly. Those who do not respond to the new chance it offers them are few.

Perhaps the best tribute to the work of the school is to be found in the fact that many of the boys like to revisit it, recently five old boys came down to stay for the inter-house dramatic competition, and one even brought his wife for part of the honeymoon.

needs of the elderly A hospital car service would be needed to collect each morning's patients The department would also be a coördinating centre for the many organisations interested in the welfare of old people, and the moderate expense of setting such departments up would be offset by the advantages they offer

The prime need of old people, however, is social care medical attention takes only second place The social worker is thus a necessity in any geriatric organisation, and she can learn far more of the real needs of the person visited than the busy doctor is able to do She will also find out whether the doctor's recommendations are being carried out, and what social factors are frustrating his efforts The geriatric district nurse might also enter the picture, to carry out continuation treatment under the doctor's instruction This would ensure that the enormous numbers of elderly cardiac patients requiring mersalyl injections were given their weekly dose with the regularity which their condition demands

RECOMMENDATIONS

1 Wider knowledge of clinical geriatrics is urgently required, and this calls for more intensive practice of medicine among the aged, more careful investigation of their ailments, and more necropsy studies

2 Regional postgraduate courses in geriatrics are needed

3 An increased capitation fee should be given for patients in this age group, to compensate the general practitioner for the time spent on them, and to encourage him in the practice of geriatrics

4 Geriatric outpatient departments should be set up

5 There should be a closer liaison between general practitioner and social workers

REFERENCES

British Medical Association (1947) Care and Treatment of the Elderly Infirm London
Rudd T N (1950) *Practitioner* 164, 549
Sheldon J H (1948) Social Medicine of Old Age London
— (1950) *Brit med J* i 319
Thewlis M W (1948) Care of the Aged London
Thomson A P (1949) *Brit med J* ii, 243, 300

A SCHOOL WITH A VIEW

THE forerunner of the modern approved school was the reformatory, often a forbidding place, in which work, discipline, and moral training were applied as the official remedies for badness in boys The pioneers were not far out in their ingredients these three go to the making of all good citizens, both in and out of approved schools But in the hundred years since the reformatories were started we have begun to find that the remedies are more effective, and the results more lasting, if the moral training is accepted and assimilated into the character, the discipline imposed from within, and the work done with a sense of personal achievement

The boys who arrive at the Cotswold School,[1] aged anything between thirteen and sixteen, have seldom had much moral training, and such discipline as they have known has been erratic and arbitrary Many of them don't care for work Yet over the past nine years 77% of those leaving the school have proved to be responsible people, never coming again into the hands of the police A further 10% have been brought into court for minor offences (such as riding a bicycle without a rear lamp), and only 13% have got into serious trouble Considering how late (speaking in terms of development) they come, and how short a time some of them stay, these results are surely remarkable

THE APPROACH

The change from a restless rebellious child to a reasonable and mannerly young person with a sense of responsibility is not achieved in a moment, but quite probably it begins from the moment the delinquent boy sees the school "Is this where we're going to have lunch?" one asked, as he saw what he took for a hotel lying hospitably open to the world no barbed wire, no men with guns to *gratify a film fed imagination*, but spacious grey buildings, some old some new, lying among gardens lawns, and playing fields in a Cotswold valley He must have felt at that moment, however obscurely, that his fellow countrymen hardly regarded him as an outcast or an enemy

There are three houses in the school, all good but all as different—Mr C A Joyce, the headmaster, finds—as the personalities of the masters in charge of them In one there is almost military precision, the boys being required to do things to time and keep strictly to the house-rules In the second they are expected to take more responsibility for their own behaviour and to work to a much less rigid time table In the third there is almost a random atmosphere, but everybody seems to be happy and at home in it The headmaster asks every new boy whether he thinks the stricter house would suit him best or one of the others, and takes his answer into account when placing him It is quite common, he finds, for a boy in one house to ask to be transferred to another

Another subject always comes up in that first conversation with the headmaster

"Oh, and by the way," he says as the boy is leaving, "if you think of running away at any time, just come and have a word with me first, will you? What are you grinning at?"

"Because you wouldn't let me go," comes the invariable reply

"I would, I couldn't stop you, anyway But if you'll come to me first I'll explain exactly what you'll be losing by it You see, you get fourteen days' holiday, but if you're away for three days without leave, you lose three of them "

This is the standard teaching about penalties "You don't *have* to have them, you bring them on yourself"

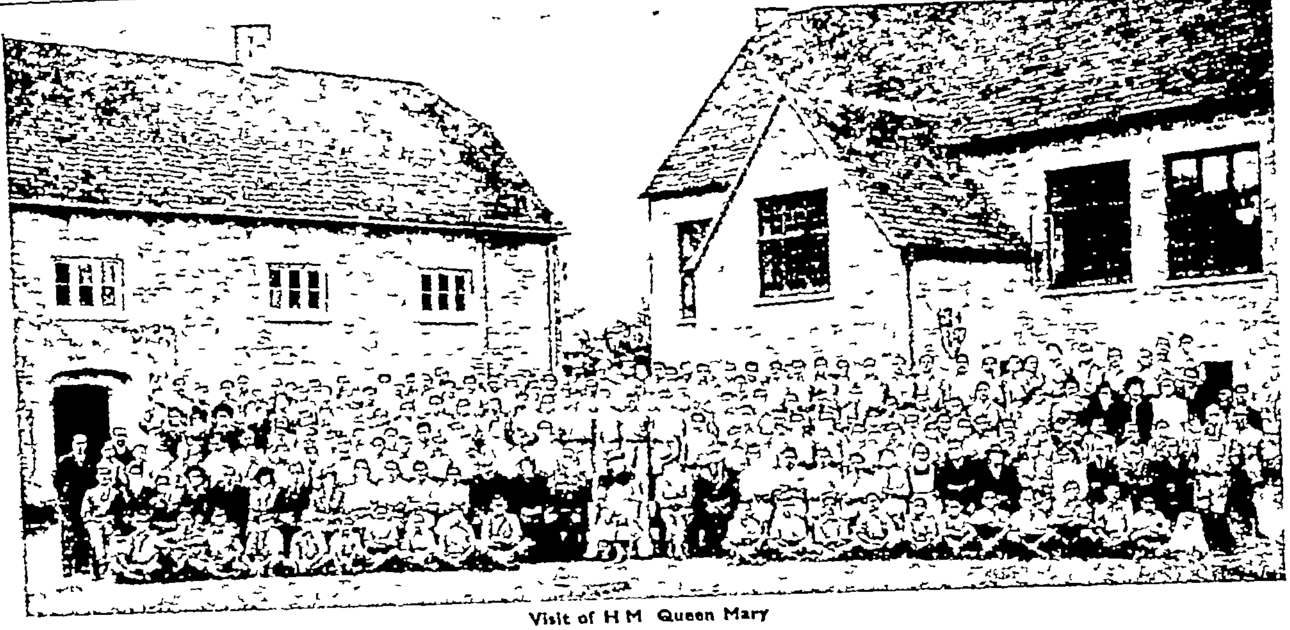
THE WAY IT IS DONE

Boys under fifteen get ordinary schooling, but with the addition of regular classes in suitable ethics ("based on Aristotle, but I don't tell them that") The older boys can learn many different trades and occupations The home farm gives them experience in milking and the care of farm animals, and there are plenty of rabbits and birds and other pets to look after Gardening is taught by a Scottish master, *a personality*, who puts up outspoken weekly reports on their work and character on a public board, and is both enjoyed and respected There are carpentry and engineering shops, classes in shoemaking, and a building and decorating department The teachers take pleasure and pride in their crafts, and that attitude is catching

Manners are friendly and good Boys passing each other or crossing the path of a visitor pass the time of day, and they notice and comment on any failure in manners among members of visiting schools Through the whole curriculum runs moral training, implicit and explicit The religious background is important, in the headmaster's view The boys take a large share in the services in the school chapel, and though only one service in the week is compulsory more than half the boys come to the three other services at which attendance is voluntary On weekdays evening prayers are held in the school hall When the school bell rings, at eight o'clock, there is a minute of silence, boys wherever they are in the school pause in what they are doing and stand, to observe it Afterwards they and the masters gather in the school hall, and there is a short talk, lasting three or four minutes, from the headmaster,

---

[1] Managed by the London Police Court Mission



Visit of H M Queen Mary

usually on some subject suggested by one or other of the boys , prayers follow Letters from boys who have left the school show how often some point or other in the little homily goes home , at all events this family gathering in the evenings is remembered by many with serious affection as the centre point of life in the school

But moral standards have to be acquired at many levels The newcomer to the school sees no harm in pinching cigarettes or fruit , so the first simple device is to ensure that he finds it does not pay The boy who takes twenty cigarettes is made to pay back thirty , the boy who steals fruit is compelled to pay for it at retail price, though by honest trading he could have it at the wholesale rate But while he is learning, at this level, that by cheating he only robs himself, he is also beginning to find how pleasant it is to be trusted and praised , and self interest as an incentive is gradually displaced by self respect Senior boys can become prefects (though without powers to inflict punishment accorded to prefects in public schools) , and those who are due for discharge in a few months' time graduate into the "discharge house," where they have their own dormitory and sitting room, wear long grey flannels and marvellous "discharge" ties, and need no resident master to supervise them

PENALTIES

Human nature is not amenable to pure reason Before any of us gives up the egoism with which he was born, and consents to live socially, he must concede that there is "no future" (as the Cotswold schoolboys say) in crime, or even in antisocial behaviour Mr Joyce has found that, with some boys, penalties can be used constructively to teach this elementary fact Feeding penalties are now forbidden (as indeed they should be for growing children) but he does make use of detention for the determined rebels The boy who defiantly refuses to do his work goes into confinement—in the visitors' room Here he gets a comfortable bed with a pink eiderdown, pictures on the walls, plenty of books, the wireless, a private garden with an aviary, and three good meals a day , but no society other than that of the master whom he can summon by bell to attend to his needs After twenty four hours in these surroundings—scornfully dubbed "sissy" by the school at large—he is usually ready to come out and join in And if he wants freedom on these terms he has only to ring the bell, as a notice on the wall informs him Nor does he get shut up without plenty of warning The headmaster explains quite clearly in advance that if he chooses to do his share like the rest he is entitled to their privileges , if he chooses not to, then he chooses the penalty as well and he, nobody else, has imposed it Incidentally, Mr Joyce believes that official penalties, however modified, should not be abolished entirely If there are no official penalties, he finds, you get unofficial punishments creeping in

THE FOUNDATIONS OF SOCIAL BEHAVIOUR

The school has good games teams and plays other schools at times Some boys who had just returned from playing a public school spoke hotly of the miserable discomfort in which their friendly hosts were living "No chairs or backs to the seats—just forms—and no separate tables in the dining room Nothing like as good as our place!"

Is it justifiable to place the delinquent in more agreeable surroundings than the well behaved sons of the rich ? It depends what the school can bring to the characters of the boys in it As a rule the public school boy has behind him a secure home, and parents who have good moral standards and are capable of showing steady affection and giving sound guidance , at home he may even live a little "soft" For him school is, and probably should be, a toughening experience Most delinquent boys have no such background of security they come from broken homes, from scenes of family discord, or from no home at all They have had little training in self control, and have acquired few liberal principles For them the school must provide the stable background which they never found at home it *must not* toughen the little tough still further While there is no "soft" living at the Cotswold school (the equipment is strong and plain as it usually needs to be in any strictly male society, whether juvenile or adult) the surroundings are beautiful, and the approach friendly Those who do not respond to the new chance it offers them are few

Perhaps the best tribute to the work of the school is to be found in the fact that many of the boys like to revisit it , recently five old boys came down to stay for the inter-house dramatic competition, and one even brought his wife for part of the honeymoon

CENTRAL HEALTH SERVICES COUNCIL

THE Central Health Services Council has appointed a committee to consider "whether the existing arrangements for engaging in general practice under the National Health Service are such as to enable general medical practitioners to provide the best possible standard of service and, in particular, to advise upon (i) the range of work and standards of practice which should be expected from the general practitioner by the public and medical profession, (ii) types of general practice, (iii) mode of entry into general practice, (iv) non medical help, (v) equipment and environment, (vi) method of remuneration, (vii) liaison with hospital and specialist services, (viii) liaison with local authority services"

The members are Sir HENRY COHEN, F R C P (Liverpool) (chairman), Dr G O BARBER (Dunmow), Dr S C BARNES (Wirral), Mr N F BAYLIS (clerk, Nottingham County and City Executive Council), Dr W RUSSELL BRAIN, P R C P, Dr J A BROWN (Birmingham), Dr B CARDEW (general secretary, Medical Practitioners Union) Dr H G DAIN (Birmingham), Sir ALLEN DALEY, F R C P (M O H, County of London), Dr E A GREGG (chairman of council, British Medical Association), Dr W V HOWELLS (Swansea), Dr ENID HUGHES (Ruthin), Alderman Mrs V F KING (chairman, Southampton Executive Council), Prof HILDA LLOYD, P R C O G, Dr W N PICKLES (Aysgarth), Dr A TALBOT ROGERS (Bromley Kent) Mr E W SCORER (member of Sheffield Regional Hospital Board), Dr STEPHEN TAYLOR (London) Dr J S THOMAS (Manor Park London), Mr H P TRAVIS (secretary, Bolton Hospital Management Committee) Sir CECIL WAKELEY, P.R C S, and Dr C W WALKER (Cambridge)

The secretary is Mr H N Roffey of the Ministry of Health Any person or body wishing to submit evidence the committee should in the first place give notice to Secretary, Room 358, Ministry of Health, Caxton , Tothill Street, S W 1

DINNER TO LORD HORDER

LAST Saturday over 150 members of the Fellowship for Freedom in Medicine and their wives or husbands assembled at the Park Lane Hotel to pay tribute to Lord Horder on the eve of his 80th birthday The company included members who had come from all parts of England and Sir Henry Dale, F R S, read telegrams from a number of well wishers who were unable to be present Sir Henry said that, as one who was some years younger than the chief guest, and as one of his pupils, he was proud to be present on this very special occasion

Proposing the toast of the evening, "Lord Horder, good luck to him and to the Fellowship for Freedom in Medicine," Dr R Hale-White expressed the belief that however great Lord Horder's service may have been to profession and public as a consulting physician he was rendering a greater service now in his stand against the barbaric attack on Medicine When the Act became law many were horrified, some said so, a few said What can we do?, but nobody did anything much except Lord Horder Dr Hale White went on to pay tribute to the enormous amount of work that Lord Horder had done for the Fellowship, and how his wisdom had guided it Turning to the guest of the evening he said You tell me that you are 80 tomorrow In age it is not the number of years that counts, but the man. You combine the wisdom and the experience of age with a love of fun and a zest for life that many leave behind them in their teens I say you are the man, more than any other, that doctors up and down the country look to to show them a way out of the mess, and that goes for the public too It is due to the steadfastness of your actions, and to the fact that you will not tolerate any division of the profession into specialists and G P s, those inside the Act and those outside physicians and surgeons, the senior and the junior, or even the profession and the public'

Lord Horder's speech in reply was characteristic in its telling phrases and witty asides He was greatly moved by his reception

Public Health

DOES VACCINATION HELP TO SPREAD SMALLPOX?

C KILLICK MILLARD

M D, D Sc Edin

MEDICAL OFFICER OF HEALTH FOR LEICESTER, 1901–35

IF I were asked in what principal respect my position as regards the vaccination question differed from orthodoxy, I think I would say In making a distinction between the effect of vaccination upon the individual and its effect upon the community When I first pointed out this distinction many years ago it was rather scoffed at The community, it was said, was made up of individuals, therefore if vaccination benefited the individual by protecting him from smallpox, it must necessarily benefit the community Nevertheless it is quite conceivable that a thing may be beneficial to the individual and yet detrimental to the community Take the analogous case of smallpox inoculation When this was introduced into this country in the 18th century, it was certainly beneficial to the individual, in that it reduced the risk of his dying from smallpox Like vaccination, it gave him a mild attack of disease in order to prevent a more severe attack later on At first it was believed to be a very real blessing, but after a time it was discovered that inoculation had a very serious drawback from the point of view of the community—it tended to spread smallpox, and often smallpox of a virulent type Ultimately it was made illegal

Now I submit that vaccination, like inoculation, has a definite tendency to spread smallpox, and (what is most important) smallpox often of a virulent type. It does this because, after its full protective effect has worn off, it mitigates an attack and is thus very apt to mask the true nature of the disease, and the modern methods of controlling smallpox (chiefly isolation and close surveillance of contacts), depend entirely for their efficacy upon prompt recognition of each case

OPINIONS FROM THE PAST

The part played by mild modified cases of smallpox which have escaped recognition—"missed" cases—has of course been long admitted Here are some expressions of opinion from medical officers of health (now deceased) who had practical experience of fighting smallpox

Dr J NIVEN, M O H., Manchester "It is not too much to say that by far the most important factor in the spread of smallpox in Manchester has been the over looking of cases The attack as a rule was so mild that no medical advice was sought or it was not recognised as smallpox by the medical attendant' In fact this matter is of so much importance that it is not too much to say that if there had been no case over looked there would have been practically no smallpox outbreak in Manchester' (Health Reports, 1902 and 1903)

Dr A K CHALMERS, M O H, Glasgow "As in past outbreaks we are again finding that one of the greatest obstacles to effectively coping with the disease is the occurrence of an extremely mild and modified form which escapes recognition until as a result secondary cases of a graver nature arise' (Smallpox Report, 1903)

Dr W E ARMSTRONG, M O H, Newcastle upon Tyne 'With respect to the more positive means by which the spread of smallpox has been favoured, probably the failure to recognise the disease in its mildest forms is entitled to first place A large number of localised outbreaks have been traced back to such mild unsuspected cases, where persons affected had for weeks been going about in a highly infectious state" (Smallpox Report, 1903)

It will be noted that in none of these utterances is it suggested that these mild cases, the cause of all the rouble, were difficult to recognise *just because they had een vaccinated some years before* Very often the fact f their having been so vaccinated is not even mentioned , ut at the time of which we are writing it was major mallpox which had to be dealt with, and in major mallpox mild modified cases such as we are considering ere almost unknown except in vaccinated subjects ometimes indeed the effect of vaccination in mitigating mallpox in these cases—so detrimental to the community -was actually hailed as a boon, as of course it was rom the point of view of the individual Thus the o.H for Carlisle wrote

> "In several instances the disease was so little marked as to escape recognition until a late period of convalescence when, as the result of the examination of all the inmates of infected houses the cases were detected Such cases were invariably associated with efficient vaccination in the persons in whom they occurred thus bearing impressive evidence of the power of vaccination in mitigating the severity of smallpox ' (Annual Report 1903)

Some medical officers did indeed recognise and admit his drawback to vaccination, but they regarded it as n argument for more rather than for less vaccination , nd there was a definite movement at that time in favour f making revaccination as well as infant vaccination ompulsory Today of course any question of compulsory evaccination has long since passed so what we have o consider now is how far this undoubted drawback to accination outweighs any advantage it may have in rotecting the community By " vaccination " is implied accination of the general population not the vaccination nd revaccination, as often as may be necessary of a andful of officials who may have to handle smallpox whenever a case may occur

And here I would give credit to Dr J H C Dalton or being the first, so far as I know to draw attention o this aspect of the vaccination question In 1893 in the *Medical Chronicle*, he wrote

> "That the community are benefited however, is a much more doubtful point It may even be urged that infant vaccination may promote rather than arrest an epidemic
>
> It has often been observed that the origin of an epidemic has been in two or three vaccinated persons who had the disease in such a mild form that it was not recognised until late Now vaccination undoubtedly causes the disease to be mild if vaccination had not been systematically performed prompt means of isolation could have been at once taken and possibly the epidemic could have been stamped out For these reasons I am inclined to doubt whether infant vaccination is such an unmixed blessing to the community that the State should enforce it with legal penalties "

Of course antivaccinists have repeatedly drawn attention to the frequency with which outbreaks of smallpox have been started by vaccinated persons, but as they have been unwilling to admit the mitigating effect of vaccination, they were unable to make use of what is, as I submit, one of the strongest of all arguments against universal vaccination of the general population

EXAMPLES

A striking example of the mischief which may be done by an unrecognised case of smallpox occurring in a vaccinated subject was the outbreak in the East End of London in 1911

Annie Levy , aged 12, *vaccinated in infancy,* living in Stepney, was taken ill with a modified attack of smallpox She went as an outpatient to the London Hospital where the case was diagnosed as chickenpox and she was sent away with a bottle of medicine Later she was admitted to the Mile End Poor Law Infirmary and placed in a ward with some 60 women and children She was seen by the medical superintendent but he too failed to recognise the real nature of the case The girl was sufficiently ill to be placed on the visiting list and was visited by her relatives and friends , also a large number of the public visited the ward and were allowed inside on visiting days

The consequences of this error in diagnosis were about as serious as they could have been 26 other inmates of the institution contracted the disease and 8 of these died , 5 nurses were attacked and 1 of these died , a scrubber who lived out and 4 of Annie Levy's brothers and sisters were also attacked In addition there were a large number of cases in persons who had visited the institution Altogether there were some 70 cases (10 fatal) directly or indirectly traceable to Annie Levy before the outbreak was stamped out As was said at the time, if we had wanted a prize method for spreading the disease and starting a widespread epidemic we could hardly have devised a better one !

Although there had been a good deal of vaccination default in the East End, the great majority of the cases which occurred in this outbreak were in vaccinated persons Thus out of the first 54 affected no less than 41 were vaccinated, 3 being in children under five years Yet the provaccinist press did not hesitate to attribute the outbreak to the neglect of vaccination Here is a sample of what one influential paper, circulating among the *intelligentsia*, wrote

> The feeling has of late been gaining ground in well informed circles that the anti vaccination campaign, and the deplorable effect it has had upon legislation, would before long lead to the re appearance of the hideous disease which vaccination had practically stamped out For years the Mile End Guardians have been anti vaccinators, discouraging vaccination in every direction The result has been that a large unprotected population has grown up and the soil has been only waiting for the seed The agitation against vaccination is one of the most idiotic things which even our sentimentalists in their record of imbecility have ever carried on

At the time this was written there had been 25 cases in the outbreak but only 2 of the patients were unvaccinated, one of these being a baby only a month old It was this sort of travesty of the truth, not at all unusual at the period of which we are writing, which made antivaccinists ' see red " , and, looking back, one can hardly be surprised that it did so

Here are some further examples

Newhaven, 1912 " This small outbreak of 26 cases originated with a seaman This man who had come back to England was attacked a week after his arrival by a mild illness with skin eruption for which no medical advice was sought Eleven out of twelve inmates of the house were attacked by smallpox, and seven other cases occurred in neighbouring dwellings whose infection could be referred to the household primarily affected Four other cases occurred later in two other households which were probably related, and four other cases in neighbouring districts which could be directly traced Of these 26 cases five proved fatal including three unvaccinated children in one household

Croydon 1918 ' A 'de mobbed' soldier, W , returned to his home from Macedonia During his journey home another soldier, supposed to be suffering from chickenpox, was removed from the truck in which W was travelling W was kept in quarantine for two weeks before being allowed to go home He did not admit to having had any symptoms But after reaching home he infected his wife and she infected their four children Five other cases were infected from these '

New Forest R D 1921 ' The infection was introduced by a seaman who returned to his home from a voyage to the East suffering from a mild and unrecognised attack of smallpox Of the nine persons in the household all with the exception of one well vaccinated child, contracted the malady and a direct contact was also infected "

In none of these reports is there any reference to the vaccinal condition of the original overlooked case which caused the outbreak , but I think we may safely assume that they had all been vaccinated and quite possibly revaccinated Revaccination is no guarantee against the occurrence of unrecognised cases

UNRECOGNISED CASES OF SMALLPOX IN THE UNVACCINATED

It may be argued that unrecognised cases of smallpox may occur in persons who have never been vaccinated, and this is true Such cases fall into two quite different categories (1) mild and trifling cases, and (2) very severe cases The mild and trifling cases very rarely occur when we are dealing with true major smallpox but only when we have to do with a mild strain of the disease, and, when this is so, *the mildness tends to breed true* Here is an example taken from my own experience in Leicester

Elizabeth C, aged 18, unvaccinated, was taken ill with a mild attack of discrete smallpox the source of which was never discovered She consulted a doctor, but he mistook the case for one of chickenpox and no precautions were taken The result was that she infected all the 9 members of her household, 6 employees at the factory where she worked, and 4 persons outside, also one of her sisters carried the infection to her Sunday school where a teacher and 5 scholars were attacked 25 persons in all But *only 1* of the 25 cases proved fatal How different would have been the result if the mild infecting case, Elizabeth C, had been suffering from a severe strain of smallpox made artificially mild by vaccination!

In the second category of unrecognised cases in unvaccinated subjects, the disease is of a very severe type, and the illness may be mistaken for measles or other zymotic, purpura, or some form of toxæmia Dr C O Stallybrass in the *Medical Officer*, of July 29 last, mentions for example the *Tuscania* outbreak of 1929, with 35 cases and 11 deaths, in which the unrecognised case was ascribed to "purpura" Of this the Chief Medical Officer to the Ministry of Health, in his annual report for 1929, wrote

> These cases presented an entirely different clinical picture from that to which the public has lately been accustomed They are marked by profound prostration, hæmorrhage into the skin and a confluent eruption The disease is so severe from the outset that medical aid is at once sought the patient is confined to bed and thereby the number of contacts is reduced to a minimum "

Dr Stallybrass thinks that the danger of spread from unrecognised cases in unvaccinated subjects counterbalances my argument as to the danger of spread from unrecognised cases in the vaccinated I am sorry I cannot agree But Dr Stallybrass has had such a great experience in dealing with smallpox that his opinion must necessarily command great respect I can only leave it therefore for others to decide I would merely point out that the outbreaks he quotes are very exceptional (he includes one from Canada), that the patients are not ambulant or only ambulant for a very short time, that they are so ill that a doctor must necessarily be called in, and that they have generally been persons recently arrived home from the East It ought not to be too much to expect of doctors that in such cases resembling measles, purpura, or toxæmia, with the patient seriously ill, they should bear in mind the possibility of malignant smallpox

Incidentally I am all in favour of every one who visits the East being efficiently protected by recent vaccination, just as I am in favour of their being inoculated against other Oriental diseases, but I do not think it necessary that we at home should all be inoculated against those diseases

WHAT TYPE OF CASE IS MOST INFECTIOUS

It is often supposed that a severe case, seriously ill, with a profuse eruption fully developed, must give off more "infectious material" than a slight trivial case, hardly ill at all, and with only a very sparse eruption I am not aware, however, that there is any very definite evidence to support this view The fact is we have little knowledge of the conditions under which infection is given off from one individual or is transmitted to another Often when we expect the disease to spread it does not do so, and vice versa We are quite in the dark as to why this should be Let me give one of several examples from my own experience where much greater spread might have been expected

R W, a tailor by trade, tramped from London and took lodgings in Leicester He was taken ill the day after his arrival Three days later the eruption appeared and he then went as an outpatient to the Royal Infirmary sitting in the waiting room amongst a number of other patients Unfortunately the nature of his illness was not recognised The same afternoon he visited one of the most frequented drinking bars in the town The following day (Sunday) he stayed in all day but the next day he again visited a public house The man was now so ill and the eruption so obvious that the publican's suspicions were aroused and he sent word to the Health Office Meanwhile, however, the occupier of the house where he was lodging had also become suspicious and called in a doctor who at once reported the case and he was then removed to hospital The attack proved to be a very severe one, of the hæmorrhagic type, which proved fatal three days after admission Here again we naturally expected that further cases would arise, but not a single further case resulted

As a contrast let us consider the comparatively recent outbreak of virulent smallpox at Glasgow Here, an Asian seaman, Moosa Ali, "well vaccinated," recently arrived in this country from the Far East, developed an attack of smallpox As the event proved it was major smallpox, but so mild and modified by his previous "good" vaccination that the experts decided, after careful consideration, that it was chickenpox and no proper precautions were taken The result was most disastrous During the short time he was in hospital he infected no less than 18 other persons in, or in connection with, the institution, and 6 of these died This case, in spite of being clinically so slight, must indeed have been highly infectious

THE ROYAL COMMISSION ON VACCINATION

The most authoritative and exhaustive inquiry ever made into vaccination was the Royal Commission, and by the very first term of their reference it was instructed to inquire and report as to (1) "the effect of vaccination in reducing the prevalence of and mortality from smallpox,"—in other words, the effect of vaccination in protecting the community Yet after seven years' deliberation the commissioners never answered this question at all What they did was to express their opinion as to the effect of vaccination *upon the individual* nothing whatever is said as to its effect upon the community—i e, in reducing the prevalence of and mortality from smallpox In view of all the claims, so often and so confidently made, as to the great reduction in smallpox prevalence and mortality which vaccination was supposed to have effected since its introduction at the beginning of the 19th century, this omission is certainly most surprising

The fact is of course that it is in its effect in protecting the community that the case for vaccination is weakest, and it is here that the antivaccinists have, in my opinion, much the best of the argument and have scored their strongest points As regards the effect upon the individual the provaccinist case is almost impregnable—except that the duration and extent of the protection conferred has been greatly overestimated—and it is because the antivaccinists refuse to recognise the effect of vaccination upon the individual that they have failed to make any real progress in winning over scientific opinion

THE LATEST ARGUMENT FOR INFANT VACCINATION

Some medical officers of health are now advocating universal vaccination in infancy on the ground that there is apparently less risk of postvaccinal encephalitis if primary vaccination is done early in life As many people have to be vaccinated sooner or later—e g when going out to the East or if they join the Services—it is better (for the individual) to have this done in infancy There may be something in this argument, indeed, it is perhaps the strongest that can be used today, though if it were frankly put before parents its propaganda value would be doubtful But what a different argument from that originally used—namely, that unvaccinated persons were a danger to the community!

MAY INFANT VACCINATION INCREASE THE VIRULENCE OF THE "STRAIN" OF SMALLPOX ?

Antivaccinists have frequently pointed out that in the official statistics of a smallpox epidemic the case mortality in the unvaccinated group—which is nearly always much higher than in the vaccinated group—is greater (say, 15–30%) than was the estimated case mortality in prevaccination times (say, 5–15%) when all were unvaccinated I am inclined to agree with them in this, though I do not agree when they go on to contend that this is evidence that the official statistics of smallpox epidemics are not to be trusted I think that there is a possible alternative explanation—namely, that infant vaccination may tend to increase the severity of the "strain" of the disease

What has been said above indicates how this might come about We have seen that smallpox is chiefly spread by clinically trivial ambulant cases rather than by severe bedridden cases, also that mild cases in unvaccinated subjects tend to transmit their mildness (to "breed true") and therefore spread a mild strain of the disease whereas mild cases in vaccinated subjects —where the mildness is merely due to the fact that they have been previously vaccinated—often transmit a highly virulent strain Assuming that this tendency is always at work, it is easy to understand how the "strain" of the disease might in the course of time become permanently more virulent than would have been the case in an unvaccinated population Persons protected by vaccination would still get the disease in a much milder and less fatal form, but those who were unvaccinated, and also those whose vaccination had lapsed, would get it in a more severe form, so the net result might well be that the total mortality was just as great as, or even greater than, if there had been no vaccination It would all depend upon the relative proportion of the two classes in the population how it would work out If there were a large proportion of unvaccinated, or of those vaccinated who were no longer protected the mortality might actually be higher This may possibly explain why it is very uncertain just what effect vaccination has had in reducing the mortality from smallpox—i.e, its effect upon the community

The belief, so long and so firmly held, that the great reduction in smallpox mortality which followed the discovery of vaccination was due to vaccination is no longer tenable, seeing that the fall began before the introduction of vaccination and has continued steadily in spite of vaccination having largely fallen into disuse Moreover it is paralleled by a similar fall in the mortality from several other zymotics

THE CASE OF INDIA

One hesitates to refer to India, without having personal experience of that country and its problems But it is common knowledge that the toll of human life taken by smallpox in India (tens of thousands of deaths annually) continues to be appalling in spite of all efforts to combat it by vaccination, a vast amount of which is carried out The immediate cause of this great mortality is the intense virulence of the disease, which is such that only very recent vaccination will stand up against it (British troops in India had to be revaccinated every two years, which of course would be quite impracticable for the general population) One may try to explain this exceptional virulence as due to climatic conditions, the habits of the population, or neglect of hygiene but it is hard to believe that the virulence could have been as intense in prevaccination times, or the people would have been wiped out The suspicion therefore rises, and should be faced that in India, as in this country, though vaccination saves many individual lives, it may have actually made things worse for the community by intensifying the severity of the disease

I am not suggesting that India should now abandon the use of vaccination But I do think that it might be worth trying the experiment of introducing, on a sufficiently large scale, a very mild form of smallpox such as variola minor (alastrim) from the Western Hemisphere This could do no harm, and if it could be persuaded to "catch on" it might transform the entire situation More wonderful things have been successfully accomplished in the field of botany and agriculture The difficulty would be getting it to "catch on," but this might be done if inoculation with variola minor took the place of inoculation with vaccinia (vaccination) The experiment might be made in the first place in one town or district The present position is so serious that much more heroic measures than this would be justified

SUMMARY

The effect of vaccination upon the community must be distinguished from its effect upon the individual By masking the disease and making it more difficult to recognise, it may actually promote the spread of smallpox

Infant vaccination may conceivably have intensified the virulence of the "strain" of smallpox, both in this country and in India The mortality from smallpox in India might possibly be reduced by deliberately introducing a milder strain of the disease

---

Influenza

The statistics for England and Wales and the Great Towns do not indicate any serious epidemic of influenza up to the end of last year Any increases in pneumonia cases and deaths and in influenza deaths are not much more than normal for the time of year

A mild form of influenza, but of a very infectious type, has been epidemic in the North-east of the country including Newcastle upon Tyne, in parts of Lancashire including Liverpool, and in Birkenhead (Cheshire) The evidence is, however, that in these districts the epidemic has passed its peak and is on the downgrade. Serological investigations have now shown that the epidemic in Tyneside is due to virus A, and it may well be that it is identical with that which has been the cause of the Scandinavian outbreaks—virus A prime The results of further laboratory investigations are awaited

There is at present no evidence of spread of the epidemic to the Midlands and South There are, however, in many areas localised outbreaks of a mild disease with symptoms not unlike those of influenza, which has not so far been shown to be due to an influenza virus There is similarly no evidence of spread of the epidemic from the North to London

In the absence of notification of influenza the incidence of pneumonia cases and of deaths from pneumonia and influenza is used as a guide to the prevalence of the disease The following figures relate to the great towns of England and Wales

Week ended Dec.	*Pneumonia (including primary and influenzal)* Cases	*Pneumonia (including primary and influenzal)* Deaths	*Influenza deaths*
16	374	289	33
23	364	351	54
30	502	383	102

In England and Wales notifications of pneumonia numbered 688 in the week ended Dec 16, 648 in the week ended Dec 23, and 962 in the week ended Dec. 30

Smallpox at Brighton

Up to noon on Jan 9 there have been 17 patients believed to be suffering from smallpox in Brighton county borough, or in the immediate vicinity Of these, 2 have died and the diagnosis is still in question in 3 During the past week, the infection has been confined to the two original foci—the laundry to which the clothing of the initial case, an R A F officer, was sent, and the hospital in which the second case was missed for ten days

Among the laundry employees there have been 6 cases 2 worked at a receiving branch and the remainder in the main establishment The laundry is now out of production The hospital is in quarantine, and of its personnel 5 nurses and 1 domestic have been admitted to the smallpox hospital All these were employed on the ward to which the second case was admitted and nursed in a cubicle

The vaccinal state of the nursing and domestic staff at the infectious disease hospital was unsatisfactory, 27 out of 113 had never been vaccinated Among the nurses and domestics attached to the ward concerned 7 were unvaccinated Of these 3 had little contact with the patient, and did not get the disease, of the other 4, who had intimate contact, 1 died and 3 are in a serious condition The remaining 2 nurses now in the smallpox hospital have a good vaccinal history and there is still some doubt as to the diagnosis

Poliomyelitis

Poliomyelitis notifications in the last week of the year were paralytic 36 (38), non-paralytic 17 (15), total 53 (53) The figures for the previous week are in parentheses and the total number of notifications was the same in each week Total uncorrected notifications for 1950 are 8698 compared with 9195 in 1947, 2379 in 1948, and 6857 in 1949 The incidence of poliomyelitis in 1950 after correction of notifications is hardly likely to be much less than that in 1947, when it was $4^1/_2$ times greater than in any previous year since compulsory notifications began in 1912

The Third Quarter in Scotland

In Scotland[1] during the third quarter of 1950 the death-rate from all forms of tuberculosis was 43 per 100,000, and the death-rate from respiratory tuberculosis 37 per 100,000 These rates are 16 and 14 below those for the corresponding quarter of 1949, and they are 22 and 17 below the five years' average

In the third quarter the infant mortality rate—33 per 1000 registered live births—was the lowest recorded in Scotland for any quarter

---

[1] Quarterly Return of the Registrar General Scotland births, deaths and marriages registered in the quarter ended Sept 30, 1950 H M Stationery Office Pp 36 1s

Infectious Diseases in England and Wales

Disease	Week ended Dec				
	2	9	16	23	30*
Diphtheria	45	49	60	46	41
Dysentery	856	934	1242	1024	691
Encephalitis					
Infective	—	2	3	4	4
Postinfective	—	—	3	2	3
Food poisoning	203	108	98	169	147
Measles excluding rubella	12 323	14 076	14 290	14 392	17 408
Meningococcal infection	32	33	29	31	34
Ophthalmia neonatorum	33	34	23	37	21
Paratyphoid fever	8	2	5	3	6
Pneumonia primary or influenzal	497	574	686	648	962
Poliomyelitis					
Paralytic	90	73	82	38	36
Non paralytic	38	31	26	15	17
Puerperal pyrexia and fever	94	89	66	74	38
Scarlet fever	1435	1266	1356	1111	1026
Smallpox	—	—	—	—	4
Typhoid fever	1	6	2	5	—
Whooping-cough	4458	4444	4523	3735	3690

* Not including late returns

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN my friend Tom was in the Army they discovered he had a chronic illness that would make it difficult for him to practise medicine He could not contemplate the strains and irregular hours of a G.P 's work, so he joined the staff of an L C C mental hospital He is a competent doctor and a very kindly man, and he soon settled down to the undramatic and rather thankless task of making life a little less unpleasant for chronic psychotics. He took the D P M, bought a house near the hospital, and moved in with his several young children In 1948 they told him that he was to become a trainee specialist instead of an assistant medical officer "Don't want to be any more of a specialist than I am now," grumbled Tom When he was metamorphosed into a registrar he merely shrugged his shoulders Now they tell him that he must leave in the summer "Why?" asks Tom, truculently "Because you can't become a consultant," says the R H B "Don't want to be a consultant," growls Tom, "never did" "Good!" says the R H.B., "you are one of the lucky ones You can go to the Colonies with a good grace"

Tom is a bit of a Tory and I had had a hard job persuading him that the N H S was a good idea Now I can't look him in the eye at all

* * *

It is a dangerous habit, this skimming through the Tables of Contents of the journals or glancing at the titles of the articles, and then laying them aside as read. The other week, for instance, I was idly turning the pages of THE LANCET when the words "Milkman's Syndrome" caught my eye Underneath the title was this quotation "At times the bowel complaint is overlooked the wasting, weakness, paleness are what is noticed, and are thought to be due to another than the true cause" Hmm, I thought, curiously enough our milkman is wasted, weak, and pale For all I know he may well have "the bowel complaint," but as long as it's not typhoid My thoughts rambled on No wonder the poor fellows get wasted, weak, and pale, having to be out and about at some ghastly hour on these cold mornings I wondered whether the syndrome had a psychiatric component Our milkman certainly seems manic depressive—manic when asking for his money and depressed when he doesn't get it But what's this? Ye gods! Further down milkman has a capital M And his syndrome turns out to be "Multiple Spontaneous Idiopathic Symmetrical Pseudofractures" Curse these eponymous titles! But I suppose the author couldn't very well call his paper "Multiple Spontaneous Idiopathic Symmetrical Pseudofractures in Idiopathic Steatorrhœa Complicated by Refractory Macrocytic Anæmia"—he might have brought the compositors out on strike again

* * *

Even a smallpox scare—or should I say a vaccination epidemic?—has its lighter side Vaccinating contacts on New Year's Eve we found their main fear, apart from anxiety lest they spread the disease, was centred round the cocktail cabinet "This doesn't stop us drinking does it, Doc?" Small boys thrilled at the prospect of no baths, and some mothers, very much under their influence, began to think the whole thing a plot to save fuel

How different were these jolly folk from the panicky public who, for four days, rang our telephone bell on an average every seven minutes with urgent messages for the doctor to "Come and vaccinate me at once My cousin shook hands with the uncle of an ambulance man" or "I've not been out of the house for the past three months so must be specially liable to infection" Many patients refused to attend clinic or surgery on the grounds that they might catch the disease while awaiting vaccination It is difficult to keep one's temper from 8 A M until 10 P M, particularly with such patients as the woman who looked round our spotless waiting room and said "When I come to have my ears syringed I don't expect to be exposed to contacts" To the best of my knowledge there was no contact in the place My halo slipped half-circle and I told her there was nothing between her and the front door She did not take the hint, but, sunk in sables, brooded in a corner while the other patients did their best to give her the creeps

On reflection, I suppose we should be grateful to the cringing souls who preferred a guinea's worth of lymph in their own homes to State benefit in clinic and surgery, but what a pest they are in emergency

Our hopes that people would stop calling the doctor to their homes for colds because we might infect them with smallpox were short-lived The telephone engineers scored instead One who gave new life to our jaded phone told us that he had been refused entry because it was known that postal authorities had had some contact One facetious patient, looking round our five-bob a nob clinic remarked "You'll be able to retire after this" Somewhat bitterly we replied "No doubt—to the nearest asylum"

As wife and general factotum, my saddest moment came when my husband returned from vaccinating the Golden Goose in the local pantomime He was empty-handed Even an ordinary egg would have been welcomed

I must leave you now and take our temperatures My husband is looking for a rose petal under the mattress I've a nasty feeling that the M O H will have to be informed

* * *

It was my first morning as a teacher of practical anæsthetics at this Scandinavian hospital, so my ignorance of the operating theatre lay out was excusable I arrived at 7 A.M and I had been told that operating usually went on until 2 in the afternoon I undressed in a bare room resembling the steam room of a turkish bath on closing day, and put on the usual shapeless trousers, topped by a rather bedraggled collarless limp coat—gowns, it seemed, were not worn by porters, visitors, or anæsthetists Clogs were provided as footwear and I soon discovered why The theatre floors were kept continually covered with a half inch layer of acrid ammoniacal disinfectant solution in which everybody sloshed about As the morning wore on, the three or four cups of coffee I had drunk before dressing at the unholy hour of 6 A M began to take effect, and the time came when, with an intravesical pressure well-nigh unbearable, I had to teeter out of the theatre on my clogs to seek relief By now my feet felt like a Chinese maiden's, and the clogs seemed to have increased enormously in weight I stumbled along the corridor trying various doors, but none was the one I wanted Oddly enough, though everybody in the town seemed to speak and understand English well when one asked the way or wanted a tram ticket, here I found it was impossible to make myself understood I tried every variety of accent on the words that I felt sure must be of international significance, but "toilette" and "lavatoire" produced no signs of comprehension in the nurses I accosted At last my efforts were rewarded—by a cleaner who it later appeared had scrubbed for a time in Britain. Arriving with my last gasp at the door she had indicated I was about to enter when a grim secretarial lady came across the corridor and told me in clear and authoritative English "You cannot go in there, *that* is the Professor's lavatory!" Needless to say I committed the unforgivable and entered the unenterable I do not know whether the Professor heard about this lapse or my subsequent ones, but it may be significant that throughout the week I stayed at his hospital he never once said "Good morning"

* * *

Despite the ice-bound roads our bank manager rode the six miles to and fro between his home and the bank every day on his autocycle He is a large man who spends a goodly part of each day in the local One afternoon he set off home clutching a bottle of brandy, skidded, and fell, damaging the bike and dislocating his shoulder, but caring for none of it because he had saved the brandy He was not seriously perturbed by an uncomfortable night, the 15 mile journey to hospital for X ray, or having his shoulder reduced But he returned home ready for the solace of his hard-earned bottle Alas, his wife had knocked it off the kitchen table

Letters to the Editor

TREATMENT OF PERFORATED PEPTIC ULCER

SIR,—I should like to reply to some of the points raised in your leading article of Jan 6 As you say, when assessing the results of a non operative régime it must be remembered that in a proportion of the cases proof of perforation is lacking In the series reported from King George Hospital, Ilford, however, there is some circumstantial evidence that the figures have not been significantly "padded" by the inadvertent inclusion of cases other than perforations Of the 73 cases that Mr Hermon Taylor reports, 68 were examined radiographically and 65 4% showed subphrenic gas This corresponds with the experience of McElhinney and Zinniger,[1] who found subphrenic gas radiographically in 65% of 122 patients in whom the diagnosis of perforation was proved at operation Of the remaining 5 patients in the King George Hospital series, 4 had the diagnosis established at operation

No strict controls are available for the King George Hospital cases, but they may be compared with records on the same basis from Guy's Hospital and the London Hospital The results are remarkably similar

	Guy's 1946–49	*London 1946–49*	*King George 1946–50*
No of patients	75	75	73
Perforations sutured	69	65	6
Treated by aspiration only	4	7	65
Total deaths	7	10	7

Surely neither Mr Hermon Taylor nor Mr Stead suggests that gastric aspiration should be considered a rival treatment to operation Rather does their work help towards a better understanding of the therapeutic value and dangers associated with these two measures The conception of "the single final stopping of the leak which only operation can secure," and reliance on operative "closure" alone without efficient gastric decompression, still lead to tragedies from persistent leakage As Roscoe Graham[2] pointed out in his classic paper fibrin and fibrosis produce the real closure, operation can only provide the scaffolding Baritell,[3] reporting a series of 88 operations with 1 death, stressed the importance of gastric suction and stated that "water-tight closure is entirely unnecessary" McElhinney and Zinniger[1] report 128 cases with 8 deaths and they also emphasise the importance of combining gastric suction with operation

Reports of this type, taken together with the results obtained when operation is omitted, may incline opinion to the view that operation is an important accessory in treatment, to be used for increasing the safety factor after this has been balanced against the added risks

Wallington Surrey JOHN F R BENTLEY

CORONARY DISEASE AND MODERN STRESS

SIR,—As Professor Platt points out, the evidence for an especially high incidence of coronary thrombosis among the medical profession is rather shaky, but even if such a preponderance were conceded, the jump from this fact to the conclusion that special psychological stresses play an ætiological rôle is so far as to make it of interest to examine the reasons for this prevalent notion

The play of human emotions is often associated with certain precordial sensations which, for the sake of brevity, we might refer to as pangs Pangs have been a powerful influence in shaping the lay concepts of psychology throughout the ages, concepts which have become enshrined in all languages in expressions such as heartless, disheartened, and heartbreaking Pangs have also had their influence upon medicine Thought processes being rarely devoid of emotional content, the heart was at one time thought to be the main sensorium, and the brain was relegated to the rôle of a cooling sponge Again, in more recent times, we have learned to recognise a neurotic condition based on the misinterpretation of these thoracic sensations—the effort syndrome The "modern stress" theory of coronary disease seems to be founded on the same naïve conjectures, having not a shred of factual evidence to support it We seem to be dealing here with a sublimated form of Da Costa's syndrome medical theorists, too well informed to be able to convert the pangs into a private heart disease for themselves, are driven to make them into an ætiological hypothesis

---

[1] McElhinney W T Zinniger M M *Arch Surg* 1950 61 758
[2] Graham R R *Surg Gynec Obstet* 1937 64, 235
[3] Baritell A La M. *Surgery* 1947 21 25

Dr Macdonald Stewart's article bears signs suggestive of this Having ably shown the fallacies of the "modern stress" theory in the first part of his essay, he yet cannot avoid plumping into the pitfall he himself has so well demarcated The way in which he outlines the superior moral attitude proper to the prospective victim of coronary thrombosis and contrasts it with the low mentality of the "resentful and idle" majority suggests a hidden personal concern

In the time of our forefathers, gout was reputed to be the doctors' disease but being less hypocritical than our age they frankly attributed it to excessive tippling and not to superior mentality, although Sydenham could not forbear consoling himself with the observation that more wise men died of it than fools

Admittedly the question of coronary reactions to emotional stress and their possible chronic effects is both a legitimate and important one, but the only hopeful approach to it is by the methods of the physiological laboratory and not by pseudo psychological speculation

Gerontological Research Unit
University of Edinburgh

ERICH GEIRINGER

SOURCE OF DEOXYRIBONUCLEOPROTEIN FIBRILS IN PURULENT EXUDATES

SIR,—I was interested in the article of Dec 9 by Dr Armstrong and Dr White, and in your leading article of Dec 16 The liquefaction of viscous purulent exudates by deoxyribonuclease, streptokinase, and other enzymes looks as if it may become a valuable therapeutic procedure It may prove important to understand clearly the cytological changes which lead to the production of fibres of nucleic acid in such material

The tough viscous web in sputum and other purulent material usually follows a complex series of changes in the eosinophil or neutrophil leucocytes Responding to certain stimuli these cells eject long processes—filopodia—which may travel for as much as 200 µ in a single direction or in several different directions simultaneously They are tipped by one or more of the refractile cytoplasmic granules and are at first extremely slender and difficult to find in the unstained specimen In the earlier stages they may be withdrawn into the cell, but more often they reach their objective and the contents of the leucocyte are, as it were, poured down them, the nucleus participating in the activity and becoming filiform The cell becomes converted into a simple or branched thread

By this means neutrophils and eosinophils traverse considerable distances and, becoming attached to their objective, often draw themselves up to it so that they adhere closely to or surround the object Epithelial cells and dead or moribund leucocytes seem to stimulate this activity very strongly, whereas red cells appear to exert no positive tropism When the filopodium abuts upon any object it tends to run round it, probably led to do so by the surface pressures, for leucocytes can be seen in this way to embrace with equal facility an epithelial cell or an air bubble, and in preparations stained with Romanowsky stains epithelial cells may often be seen with blue cytoplasm and purple nucleus, and round them, like a tyre round a wheel, is applied the filiform nucleus of a leucocyte stained deeply purple

In some types of purulent material this filopodial activity of the leucocytes is responsible for arranging the familiar spherical leucocytes into long ranks lying between the filiform extensions of the more active cells If the material is not too thickly filled with cells, these ranks will ultimately be rolled up into a clump by the filopodia and undergo fairly rapid cytolysis

This is a brief and incomplete account of a few only of the activities of pus cells, but it will be realised that in such exudates the cells conforming to the classical description of leucocytes are often dead or moribund, whereas the living cells in a state of high activity are rendered unlike the classical description because of their filopodial changes In the article by Armstrong and White, for example, the figure "*b*" in each of the three series of photographs probably shows a preponderance of dead cells

The ejection of filopodia and some other activities of leucocytes have escaped the attention which they merit, and one hopes that this new therapeutic procedure will stimulate more interest in them In unstained material the activities are seen more readily in the eosinophil because of the higher refringence of its cytoplasm than in the neutrophil

The accompanying photographs show examples of the filopodial activity described above

Cirencester

R E HOPE SIMPSON

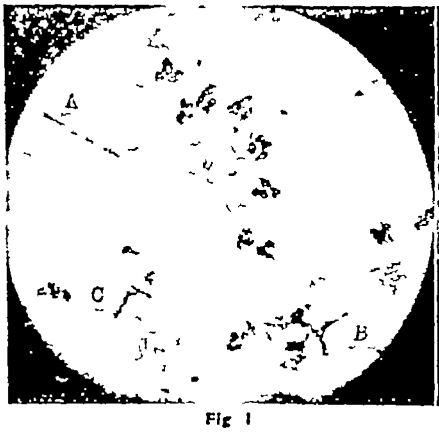


Fig 1

Fig 1—Film from purulent urine stained with Leishman stain Poly nuclear neutrophils are mostly dead or moribund A, point of departure of neutrophil by filopodial change to reach epithelial cell B Nucleus of another neutrophil can be seen re-forming round B and another round epithelial cell C.

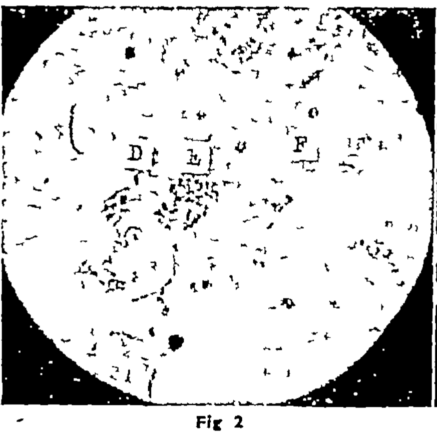


Fig 2

Fig 2—Unstained sputum : eosinophil E has reached shed epithelial cell D down filopodial pathway F

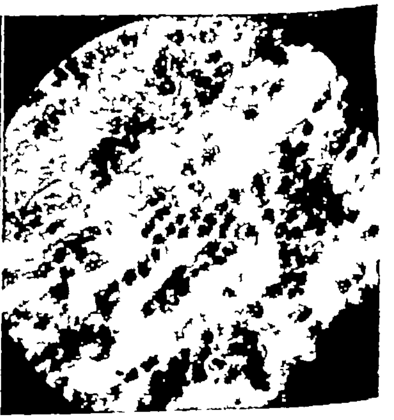


Fig 3

Fig 3—Sputum stained with Leishman stain showing dead and moribund neutrophils gathered into long ranks

WELFARE OF THE BLIND

SIR,—May we draw attention to the course that newly blinded people should follow if they wish to take full advantage of the blind welfare services ?

If a person's loss of sight has been caused or aggravated by war service (including civil defence), he or she should get in touch with St Dunstan's, 191, Marylebone Road, London, N W 1, which is responsible for such cases

Responsibility for all those whose loss of sight is not attributable to war service—that is, the civilian blind—is borne by the local authorities and the local voluntary agencies for the blind, in coöperation with the National Institute for the Blind Newly blinded civilians should therefore get in touch with the local blind welfare authority or, should there be any doubt as to the identity of that body, with the National Institute for the Blind, 224, Great Portland Street, London W 1, which gladly provides applicants with any information or advice they may require

W ASKEW
Secretary St Dunstan s

J C COLLIGAN
Secretary General
National Institute for the Blind

STUDY OF DELINQUENCY

SIR,—There are few greater attractions to the spectator than a good quarrel , and if Dr Bodman, Dr Edelston, and myself have only succeeded in bruising each other, we must at least have endeared ourselves, for the entertainment we have afforded, to your readers For when specialists in emotional health come to blows, who can help shouting " A ring, a ring ! "

After honourable war, honourable peace ! Peace treaties are I know not much in fashion nowadays , but who should be better able to resolve conflicts than the present protagonists ? And so it occurred to me to draft a treaty, by clauses, to place on record the highest common factor of agreement

This pacific overture is made, however, in the hope that Dr Edelston will not misconstrue it as battle weariness , it was really very ungenerous of him to take advantage of my chivalrous admission of the leading part that psychiatrists had played in the development of the new personality psychology (A bad beginning that, to peace negotiations I must make some other overture)

Dr Edelston bids me direct my guns upon my fellow psychologists Yes, there is much I could criticise in our own academic training, but actually there is no need More eminent psychologists than I are doing this already " Too many professional psychologists," writes Professor Vernon,[1] " in this country as well as in America, become *too* exclusively rat experts, or statisticians, or gadgeteers " How's that for blowing our own brains out ?

With that preamble of recrimination and appeasement I proceed now to the clauses of our treaty, as follows

1 All those constantly in touch with children and families —teachers general practitioners school medical officers and nurses welfare and probation officers—should be encouraged to detect maladjustment or unadjustment at its earliest stage (in so far as they are not doing so already)

2 The overcoming of the present tendency among such towards extreme pro or anti psychological psychiatric bias, regarding us alternatively as witch-doctors or nitwits , and a clearer understanding of the bearing of emotional health upon physical health education, and good behaviour

3 A thoroughgoing, yet realistic, training for clinicians of all types—to embrace whatever is relevant in our present medical and psychological teaching

4 Our conception of treatment to be widened to include as much as possible of the patient s life situation , and especially to do our best to see that every young person is firmly anchored in a family " belonging group," at best with his own parents, but otherwise with permanent parent substitutes (Not always easy, I confess again)

5 That in every case of delinquent breakdown, some one or other should be continuously responsible for the process of rehabilitation using whatever treatment, clinical or otherwise, is appropriate The position of a specialist who, with inadequate time and resources, has to give an opinion on a case which forthwith passes out of his hands can be a false one (*vide* Dr Peter Scott's letter of Dec 30)

Redhill Surrey　　D H STOTT

MEDICAL SCHEME FOR BOYS' CLUBS

SIR,—May I through your columns issue an appeal ? The London Federation of Boys' Clubs is about to launch a medical scheme by which regular routine medical inspection is to be offered to club members It has been found that much good comes of these examinations For this scheme to work we need doctors who will take part voluntarily in the club life for a minimum of about two hours in an evening every three weeks There are many other ways in which such doctors can help the many clubs in London , and these, together with details of the scheme, are outlined in a booklet which will be sent to any doctor asking for one Younger doctors on the house staffs of London hospitals are just as welcome as practitioners living near a particular club

It is hoped to issue a standard card for recording the results of medical inspections and it is felt that in time these might be of great medical and statistical value The scheme is to be in no sense a " sick parade," but a series of routine medical inspections , and the boys' own doctors under the N H S are never to be " by-passed " or made redundant No-one expects these busy practitioners to carry out routine inspections on apparently healthy adolescents and when any lesion is detected they will always be approached

FRANK FALKNER
Hon medical adviser
London Federation of Boys' Clubs

222 Blackfriars Road
London S E 1

MASS RADIOGRAPHY

SIR,—Your leading article of Dec 9 and the divers views expressed in the ensuing correspondence show that this is not the time for regional boards, or anyone else, to make a final decision about either the scope of mass radiography or the medical direction of this new diagnostic weapon

When mass radiography was first made available for civilians, it was said that eventually every man, woman, and child in Britain could be X rayed Dr James Brailsford was the first to show that this was impracticable Since the whole population cannot be X rayed, it is obvious that mass radiography should be reserved for those groups whose survey is most likely to benefit the community Therefore, the primary aim of mass radiography should be the detection of unsuspected cases of pulmonary tuberculosis not only in the most vulnerable age and occupational groups of the population, but also among those who, by reason of their calling, are most likely to disseminate widespread infection Mass radiography is thus related both to clinical and to preventive medicine For example, to discover one case of open pulmonary tuberculosis in a school teacher it would be worth while to survey many thousands, because the removal of that source of infection would eventually save the State many thousands of pounds There would also be a saving in suffering and sorrow which cannot be assessed in terms of ducats

From the groups enumerated in your leading article I would exclude " prospective employees whose employers wish them to be examined " Mass radiography is part of the National Health Service, and the Terms and Conditions of Service of Hospital Medical and Dental Staff (England and Wales), issued by the Ministry of Health on June 7, 1949, excludes from work within the scope of the National Health Service "examinations and reports required by employers (including Government Departments and local authorities) on employees or prospective employees"

---

[1] *Brit J educat Psychol* November 1950

The average cost of finding a new case of pulmonary tuberculosis is greatly reduced when "doctors' cases," where the incidence of tuberculosis is highest, are included in the routine work of a mass radiography unit By including these cases, the unit is not competing with the tuberculosis dispensaries Every doctor is advised that all suspected cases of pulmonary tuberculosis should be referred direct to the tuberculosis officer, but he is also told that mass radiography is available for those cases in which he wishes to exclude the possibility of tuberculosis before making a diagnosis Thus a diagnosis of gastric ulcer may be right nine times out of ten, but the tenth case may be acid dyspepsia associated with pulmonary tuberculosis Those of us who have established a mass radiography service for general practitioners have been amazed by the response General practitioners say that it is easier to induce their patients to attend a mass radiography unit than a tuberculosis dispensary or chest clinic with the stigma of tuberculosis Nevertheless, when a firm diagnosis of tuberculosis has been made by a mass radiography unit, there is little difficulty in inducing these patients to attend the tuberculosis dispensary in order that they may receive appropriate treatment This assumes that the mass radiography unit is fully diagnostic to the limits of its capacity Within the scope of mass radiography are all serious chest diseases, and in "doctors' cases" a relatively large number of neoplasms will be discovered in the operable stage

The value of surveying school leavers is now generally recognised, but our target should be an annual survey of all males and females between the age of 15 and 25 On the other hand, it is most difficult to induce adolescents, other than those in factories, to be surveyed after they have left school In Birmingham we attempted to arrange an annual survey through youth organisations, but the results were not impressive

Dr Hoffstaedt, in his article of Dec 9, has shown that mass radiography may be a most expensive diagnostic weapon Before it is abandoned or curtailed on that account, the cost of equipment and of film might be referred to the commission now concerned with monopolies and restrictive practices in industry It is certainly the duty of medical directors to scrutinise all accounts and to eliminate all unnecessary expenses Dr Evans and Dr Posner (Dec 23) say

> 'If it were wished to really cheapen this service, the following action would be necessary
>
> The service would have to be regarded purely as a sieve for pulmonary tuberculosis taking miniature films and repeat films of 4 × 5 in size The staff could then be reduced to radiographer assistant radiographer, dark room technician, and two clerks, clerical work would be cut down to an irreducible minimum and all cases immediately referred to a chest clinic The post of medical director would be abandoned, and a consultant chest physician would attend for two or three half sessions per week to read the miniature and large films All surveys would be arranged by a secretary under the direction of the consultant chest physician '

In reply to this suggestion, I submit that there would be no real saving but possibly an increase in expenditure If the number of clerks in a mass radiography unit was reduced from 6 to 2, the redundant 4 clerks would be required to do precisely the same work at a chest clinic If the post of medical director were abolished, his work would have to be done by an equally well qualified and well-paid chest physician, the only difference being that films would be read at the mass radiography unit and clinical work would be done at the chest clinic If all surveys were arranged by a secretary under the direction of the chest physician, this secretary would require special qualifications to enable him (*a*) to address meetings of up to 2000 employees at a factory, (*b*) to confer with joint production committees, (*c*) to meet industrialists, and (*d*) to compose the printed propaganda for his unit In most units all these duties have hitherto been performed by the medical director An adequate substitute would require an adequate salary Moreover, it is very doubtful if any layman could supervise and control the work of professional radiographers, or whether the latter would willingly agree to this

There are two claimants for the medical direction of mass radiography The majority of tuberculosis officers would like mass radiography units, as an integral part of the *tuberculosis* service, to be attached to tuberculosis dispensaries or to chest clinics The majority of medical directors would like these units to be an interdependent integral part of the *chest* service, and as such to work in close cooperation with tuberculosis dispensaries, chest clinics, thoracic units, general hospitals, school medical officers, M O H s, and, above all, general practitioners. Some inexperienced persons have suggested that the work of a mass radiography unit is so uninteresting that no one would want to be its medical director for more than a year Having had experience of all kinds of tuberculosis institutions from an open air school to a home for advanced cases, I can testify that in none of these is the work more interesting or more varied than that of a mass radiography unit, provided the latter is diagnostic to the limits of its capacity

HALLIDAY SUTHERLAND

Medical director, Birmingham Mass Radiography Unit and chairman of the Standing Committee of Medical Directors of Mass Radiography Units in England and Wales

TYPHOID FEVER IN A GENERAL HOSPITAL

SIR,—Dr Dewar (Dec 30) will doubtless be completely satisfied with my explanation that the case of subacute bacterial endocarditis, reported by Dr Curtin in your issue of Dec 16, was admitted to Sheriff Hill Infectious Diseases Hospital for investigation of suspected acute tuberculosis of the lungs in late pregnancy

It is necessary, however, to stress the vast difference between the treatment of a typhoid case in a general hospital, with the attendant risk of infection of the nursing staff and the other patients, and the care of a non infectious condition in an isolation hospital, where the patient can be segregated in a side ward or cubicle and efficiently safeguarded from the other infectious patients

A subordinate motive for my original letter of criticism was concerned with the long waiting lists for admission to the general medical wards This factor makes it still less desirable that a patient with a notifiable infectious disease should occupy a bed in a general hospital for a long time, when he could quite well have been treated in a fever hospital In my submission, it is a very regrettable tendency to admit notifiable infectious diseases to general hospitals, where the clinical approach is mainly curative, in contrast to the combined preventive and therapeutic outlook expressed in the fever hospital

I have long held the view that the modern infectious diseases hospital should not restrict its scope to the notifiable diseases, but, subject to the limits of the available accommodation and the facilities for treatment, should also accept for investigation and treatment any condition in which microbic infection is suspected or proven This would cover the throat infections, the pneumonias, the infections of the nervous system, all forms of gastro enteritis and food poisoning, obscure pyrexia, and tuberculosis At Sheriff Hill, nearly half of the bed accommodation is reserved for tuberculous of two special categories—bone and joint disease, and miliary lesions of the meninges and lungs Indeed, it was in a side ward of the pavilion devoted to the latter conditions that the patient with subacute bacterial endocarditis was treated Cases of pulmonary tuberculosis also have frequently been received in the cubicles of the hospital, and have been treated there until more appropriate accommodation was found This hospital is therefore already making a reasonable contribution to the solution of a national problem

The policy of using former isolation hospitals to provide accommodation for the tuberculous is being fully worked out in the Newcastle region In the Gateshead group, one of the two fever hospitals has been entirely given over to the treatment of pulmonary tuberculosis, leaving Sheriff Hill Hospital as the only fever hospital for an area with a population of nearly 200,000

Gateshead

JAMES GRANT
Medical Officer of Health

PUBLIC-HEALTH SALARIES

SIR,—In your article of Dec 30, you say of the new salary scales for doctors in the public health service "Unfortunately they do nothing to attract able men into the junior ranks, and little to give the service the prestige it needs" All doctors engaged in this service must surely endorse this statement If this scale is accepted, I hope that it will be with the appropriate degree of protest, and that steps will at once be taken to remedy this situation

Liverpool.

G STUART ROBERTSON

TROPIC OR TROPHIC ?

SIR,—May I call attention to my letter in your issue of Sept 30, 1944 ? In spite of Dr Burn's postulate, the logic is all in favour of tropic Atrophy does not necessarily mean degeneration by lack of nutrition , severance of a nerve causes atrophy of the corresponding muscle by inactivity while the nourishing blood supply remains intact Perhaps, in view of the derivation of the word, atrophy should not be used in this case, but it does not seem that a substitute word exists The fact that some words are in use which according to our present knowledge are misnomers but which have acquired general acceptance by tradition (e g , hysteria as derived from uterus) does not justify the creation of new misnomers with full consciousness of that fact It is to be deplored that many scientists do not attach more importance to the correct use of scientific language than the common man who, following the manner of the majority, uses I and me interchangeably, ignores the accusative of who, and does not even "feel badly" about it

Flushing N Y

ARTHUR E MEYER

THE LIQUORICE STORY

SIR,—In your annotation of Sept 23 on the interesting observations by Professor Borst and his colleagues, published in the same issue, you remarked "This fascinating investigation in Holland provides an interesting point of contact between those who work on plant hormones and the researchers in animal endocrinology" I would, therefore, like to draw your attention to the results obtained by Costello and Lynn[1] They noted that fluid extracts of glycyrrhiza contain œstrogenic principles (probably œstriol), an antihormone, benzoic acid, and two other non œstrogenic substances The deoxycortone type of reaction noted by the Dutch workers may presumably be due to œstriol, and may therefore explain the failure of the succus preparations used by them in Addison's disease and in rheumatoid arthritis

Haffkine Institute
Bombay India

ASHOK I MEHTA

---

[1] Costello C H Lynn E V *J Amer pharm Ass* 1950 39 177

THE FALSE "ACUTE ABDOMEN"

SIR,—During twenty three years at sea I have operated on four cases of perforated peptic ulcer In the same period I have seen three cases in which the symptoms resembled those of an acute abdominal disorder but recovery took place without operation In cases of board like abdominal rigidity I follow an unorthodox routine The patient is given either morphine or 'Omnopon' in fairly large doses while the operating theatre is being prepared , on board ship this takes about three hours Though frowned on by surgeons, this is, I suggest, good practice in the conditions prevailing at sea The patient is going to remain under the care of the same doctor, so there is no question of masking symptoms for another surgeon , and I believe that injection of an analgesic clarifies the diagnosis, as it did in the three cases described below In fact, it saved these three patients from operation It seems probable that had they been seen in hospital ashore, they would have been taken straight to the operating theatre for laparotomy

CASE 1 —Many years ago, at about 8 30 one morning, I saw a carpenter s mate who had woken up with acute abdominal pain He had no previous history of abdominal symptoms On examination his abdomen was board like Being in those days single handed with no nursing staff, I took a rather gloomy view of the case , but, while the operating theatre was being prepared, he was given gr $^{1}/_{3}$ morphine He gradually recovered in about four hours, and completed the three months' voyage without recurrence

Subsequent inquiry elicited the fact that the fan in his cabin had been playing on his abdomen all night , and the final diagnosis was abdominal cramp due to this cause

CASE 2 —A male passenger had had abdominal pain nine months before , no radiological evidence of gastric ulcer had been found Earlier his appendix had been removed At 8 30 A M he began to have acute abdominal pain. He ate no breakfast and treated himself with one dose of tinct chloroformi et morphinæ and later two brandies I was called to see him at 3 P M There was board like rigidity of the abdomen, more pronounced on the right side but extending into the left iliac fossa Temperature 98 2°F Pulse rate 60 per min Heart and chest normal Urine no abnormality found Perforated peptic ulcer, probably duodenal was diagnosed The patient was given gr $^{2}/_{3}$ omnopon, and the operating theatre was prepared

From then on, his condition gradually improved At 5 45 P M he was comfortable, but no intestinal sounds could be heard and there was still guarding over the gallbladder area By 8 P M he had fully recovered A diagnosis of acute cholecystitis was considered, but was discarded because the rigidity extended into the left iliac fossa and intestinal sounds were absent

CASE 3 —Four days after operating on a case of perforated duodenal ulcer, I saw a male member of the crew who reported sudden abdominal pain no diarrhœa at that time no previous attack Temperature 97 6°F Pulse rate 96 per min Vomited twice Abdomen rigid all over but not quite board like Chest and heart normal Urine trace of albumin and sugar Pupils ankle jerks, and optic discs normal

Recently perforated peptic ulcer was diagnosed and the operating theatre prepared Omnopon gr $^{1}/_{3}$ given Rigidity gradually decreased and diarrhœa ensued Final diagnosis —gastro enteritis

The possibility of tabetic gastric crisis was not investigated in the first of these cases but was excluded in the last two I have observed board like abdomens in both diabetic coma and uræmia, but these were excluded in these three cases Salt deficiency was not a causal factor in either of the last two cases, which occurred in comparatively cool weather

Goldstone and Le Marquand[1] reported cases of "acute abdomen" due to acute myositis (Bornholm disease) in which the patients were saved from operation only by the recognition of an epidemic In the cases described here, however, there was no question of an epidemic , and the onset, unlike that in all but one of the cases recorded by Goldstone and Le Marquand, was sudden

---

[1] Goldstone B W Le Marquand H S *Lancet* 1946 ii 267

Spontaneous healing of a peptic ulcer is possible, but it is difficult to believe that it occurred in each of these three cases Sometimes surgeons operate on what seem to be typical cases of perforated peptic ulcer and find no perforation , and in this connection Avid[2] mentions "formes frustes" These difficult cases usually seem to be in young patients My three cases were in young men, aged 25–35 years

On board ship cases are usually seen very early, which gives the ship's surgeon an advantage over his colleagues ashore With acute abdominal disorders the prognosis is probably very little affected by a delay in operating of up to twelve hours from the onset , and during this period, with the help of a powerful analgesic, the false "acute abdomen" will have declared itself, so that some delay in operation is justifiable

Orient Steam Navigation Company
Ltd London

H M ROYDS JONES

PURIFICATION OF VACCINE LYMPH WITH PHENOL

SIR,—Gordon[3] in 1925 found that vaccinia virus is strongly resistant to phenol, since even a 1 in 20 solution does not completely destroy it , and Stevenson and Butler[4] used 0 5% phenol to prevent accidental contamination of vaccinia in the embryonated egg Gins[5] and Lehmann[6] advocated the purification of vaccine lymph with phenol, but it was not generally used in the routine preparation of lymph Last year McClean[7] reported that phenol in a final concentration of 0 4% has no adverse effect on the potency of vaccine lymph, and will so reduce the number of contaminating bacteria that the lymph can be issued for vaccination a fortnight from the date of trituration of the crude pulp , moreover, phenolised vaccine lymph kept at a temperature below 0°C maintains its potency with a good reserve margin even after a year from the time of its preparation

TABLE I —COMPARATIVE VIABLE COUNTS

Batch no	Colony count (thousands per ml)											
	Glycerinated lymph						Phenolised lymph					
	A	B	C	D	F	F	A	B	C	D	E	F
1	∞	∞	100	60	40	20	∞	12	11	10	8	4
2	∞	∞	80	60	30	20	∞	14	14	12	6	3
3	∞	∞	60	60	30	16	∞	14	12	10	8	4
4	∞	∞	80	50	30	14	∞	10	10	9	6	3
5	∞	∞	70	60	20	14	∞	8	8	6	5	4

∞ = too many to be counted accurately
A = immediately after preparation
B = a fortnight ,,
C = 2 months ,,
D = 6 ,, ,,
E = 9 ,, ,,
F = 12 ,, ,,

These findings of McClean have been confirmed in an investigation at the Stack Medical Research Laboratories at Khartoum Five batches of vaccine lymph were prepared The bellies of five sheep, the vaccinifers, were shaved and lightly scarified with a fine wire gauze, and seed lymph of high potency was rubbed in with the gloved left hand No dressing was applied to the vaccinifers, and no antiseptic was used for the crude pulp, which was scraped four days later The takes were good and the yields soft and adequate in quantity The pulp from each sheep was divided into two equal parts one part was glycerinated in the usual routine way —i e , 4 parts by weight of 50% glycerin solution containing 0 05% clove oil were added to it, triturated, and kept at temperature below 0°C—and the second half was treated with phenol according to McClean's method[7] Thus five batches of glycerinated vaccine lymph and five phenolised batches were available for comparative bacteriological tests and potency titrations

TABLE II —COMPARATIVE POTENCY TITRATIONS

Batch no	Dilution	Glycerinated lymph					Phenolised lymph				
		A	B	C	D	E	A	B	C	D	E
1	10^{4}–10^{6}	++	++	++	++	++	++	++	++	++	++
	10^{7}	++	++	+	+	+	++	+	+	+	+
	10^{8}	+	+	+	+	+	+	+	+	+	+
2	10^{4}–10^{6}	++	++	++	++	++	++	++	++	++	++
	10^{7}	++	++	+	+	+	++	+	+	+	+
	10^{8}	+	+	+	10	10	+	+	+	+	8
3	10^{4}–10^{5}	++	++	++	++	++	++	++	++	++	++
	10^{6}	++	++	++	++	+	++	++	++	++	++
	10^{7}	+	+	+	10	8	+	+	+	+	10
	10^{8}	+	+	10	6	4	+	+	4	6	4
4	10^{4}–10^{6}	++	++	++	++	++	++	++	++	++	++
	10^{7}	+	+	+	+	+	+	+	+	+	+
	10^{8}	+	+	10	6	6	+	10	6	8	8
5	10^{4}–10^{6}	++	++	++	++	++	++	++	++	++	++
	10^{7}	+	10	4	6	3	+	+	10	4	3
	10^{8}	10	4	2	4	4	8	6	3	4	2

A = immediately after preparation
B = 2 months ,,
C = 6 ,, ,,
D = 9 ,, ,,
E = 12 ,, ,,

++ = confluent take
+ = semiconfluent take.
Numerals indicate number of discrete vesicles.

Viable counts and potency tests were carried out simultaneously immediately after preparation, after a fortnight, after 2 months, after 6 months, after 9 months, and after 12 months from the time of preparation Viable counts were done by the usual pour plate method The vaccine lymph was diluted 1 in 1000 parts in distilled water and 1 ml was added to 15 ml of melted nutrient agar, shaken thoroughly, and poured in petri dishes incubated at 37°C for 24 hours, and the colonies were counted Three plates were used for each batch, and the mean of the colony counts was taken All precautions are taken to reduce the error inherent in the plate count method Tests for the presence of hæmolytic streptococci and gas producing anaerobes were made on blood agar plates, gentian violet blood agar plates, and Robertson's cooked meat media[8] The colony counts are shown in table I

For titrating potency, albino rabbits were used The hair from both flanks was removed with a depilatory powder[9] Then each flank was divided into areas of 14 sq cm each, which were lightly scarified with a needle and had 0 1 ml of the appropriate dilution rubbed in with a glass rod The rabbits were lightly anæsthetised with ether[10] To eliminate factors due to variations in sensitivity to vaccine lymph the same rabbit was used for both the glycerinated and the phenolised vaccines, one flank for each, and each batch was tested in two rabbits The results of vaccination were read on the 4th day and again on the 6th day of vaccination The results of takes are shown in table II

It will be seen that the contaminating organisms in the phenolised batches were reduced in a fortnight to within the limits allowed by the Therapeutic Substances Regulations, 1944 , and that the phenolised lymph kept at a temperature below 0°C for a year showed no deterioration in potency and compared favourably with the glycerinated controls

Stack Medical Research Laboratories,
Khartoum

M A. HASEEB

---

[2] Avid I Companion to Surgical Studies Edinburgh 1949
[3] Gordon M H *Spec Rep Ser med Res Coun Lond* no 98, 1925
[4] Stevenson W D H Butler G G *Rep publ Hlth med Subj , Lond* no 87 1939
[5] Gins H A *Klin Wschr* 1924 3 634
[6] Lehmann W *Z Hyg InfektKr* 1937 119, 21, 513
[7] McClean D *Lancet* 1949 ii 476
[8] Ministry of Health Report of the Committee on Vaccination London 1928
[9] Mackie T J McCartney J E Handbook of Practical Bacteriology Edinburgh 1948
[10] Horgan, E S Haseeb M A *J Hyg , Camb* 1939 39, 615

Obituary

GEORGE LENTHAL CHEATLE

K C B, C V O, F R C S, Hon F A C S

George Lenthal Cheatle was born in 1865 He was educated at Merchant Taylors' School and King's College, London Hard work as a student brought him rapid qualification, and in 1887, while awaiting his house-appointments in King's College Hospital, he acted as assistant demonstrator of anatomy In 1889 he was appointed Sambrooke surgical registrar, in 1892 demonstrator of surgical pathology, and in 1893, on Lord Lister's retirement, assistant surgeon In 1900 he became full surgeon, teacher of surgical pathology, and honorary director of the pathological museum but shortly afterwards his work at King's was interrupted by his appointment as consulting surgeon to H M Forces in the South African War His service was recognised by mentions in despatches and appointment as C B

[illegible]

On his return to civilian life he carried out his routine work at King's and some smaller hospitals with vigour The accumulation of a large consulting practice was inevitable to a man of such distinction, but he remained a keen and conscientious teacher and a rabid research worker Apart from these, a growing interest in the Naval medical services was apparent when the German menace loomed on the horizon, a few years before the 1914–18 war, and he became a member of the Naval Advisory and Examining Board, and of the Admiralty Departmental Committee, Royal Naval Medical Service When war was declared he was given the rank of surgeon rear-admiral and made consulting surgeon to the Navy, serving as such throughout the war, mainly at Haslar but also at sea He was promoted K.C B in 1918

In both wars he declined the shelter of the base, deliberately accepting any risks wherever his ability could best serve the wounded In South Africa, on one occasion, he organised under fire a temporary operating-carriage in a train of wounded soldiers At Gallipoli he was in a hospital ship in waters where hospital ships could claim little immunity from enemy action

After the first world war he gave much time and thought to the reconstruction of the new King's College Hospital and its medical school General surgery, he considered, had reached such magnitude that some elements should be divorced, particularly urology and orthopædics, and the creation of these departments under distinguished specialists was largely due to his influence

In 1919 he was elected to the fellowship of King's College, and in 1923 he became senior surgeon of the hospital He also served on the committee of management and was chairman of the medical board In 1930 he retired from the active staff and was made consulting surgeon and emeritus lecturer in clinical surgery His activities, however, by no means ceased, his zeal for research was given greater scope and he at last found more time to contribute the results to the medical journals He was awarded in 1931 the Walker prize of the Royal College of Surgeons for his work on cancer, and in 1932 the honorary fellowship of the American College of Surgeons *Tumours of the Breast*, written in collaboration with Max Cutler, embodies the substance of his research into breast cancer

The year 1936 was the last landmark in this active life, when he undertook an extended lecture tour in the United States So that he might be eligible to lecture at Hines Hospital, Chicago, a privilege accorded to none but American nationals, he was granted American citizenship for one week, an almost unprecedented concession which he greatly appreciated

To this outline of his life we add the following tributes from his friends

J E writes ' As a teacher Cheatle was unorthodox for him the platform had little appeal, his intrinsic originality rebelled against the set lecture, the recital of the textbook, and he welcomed the distribution of systematic lectures to his colleagues His method of teaching was insidious and penetrating insidious since his listeners would leave with the impression that he asked their opinions because he valued them, and such corrections as he made were merely expressions of his view, penetrating, as I can affirm, for I remember to this day the lessons learnt at his tutorials more vividly than those from any other teacher He was at his best with a small class, either holding a clinical demonstration in outpatients or in his private laboratory filled to overflowing with his personal histological sections Some six of us closeted in his sanctum forgot the outside world, time meant nothing, carried away as we were by his enthusiasm in the demonstration of those beautiful sections and their significance Not only was morbid histology learnt, we were infected by his tireless energy to unravel pathological problems in those undergraduate days, the better to be equipped for their solution he inspired confidence and courage to succeed, and the urge that hard work alone could achieve success His chosen subjects were bacterial infections and the genesis of tumours, notably the latter, using as his material giant sections, cut with the giant microtome of his own design These sections had first to be studied with the naked eye, then with a low power magnifying glass, ultimately working up to the highest magnification The object of giant sections was to show the normal, the transitional, and the established growth tissue in one piece His methods demonstrated the relation of Paget's disease of the nipple to underlying carcinoma, indicating the need for radical surgery Later researches showed that areas of leucodermia, sclerodermia, and Head's points of maximum intensity were likely infecting agents of superficial malignant disease

" Lenthal Cheatle not only taught us the way to work, he was a patron of the various activities so important in the life of a medical student He took a lively interest in the medical society renamed in his time the Listerian Society, of which he was president He encouraged outdoor games, particularly lawn-tennis, and presented a challenge cup for the annual singles championship, for many years he was president of the lawn tennis club As a student he was himself a keen cricketer and a prominent member of the inter hospital cup team, in later life fishing and golf were among his interests

" As a surgeon care, patience, and precision were his outstanding qualities, but he did not lack surgical boldness and brilliance in emergency His technique followed the orthodoxy of his time, but he readily accepted and explored any novelty Although an ardent disciple of Lister and Watson Cheyne, he was among the first at King's to become wedded to aseptic surgery, though not forsaking entirely the antiseptic, especially in skin preparation. No surgical innovations are associated with his name but he was responsible for valuable modifications of the set operations which his co workers were pleased to adopt No instrument, excluding the Spencer Wells hæmostat, is more widely used than Cheatle's forceps, it will be found in every hospital, nursing home and maternity institute throughout the civilised world The grace of its shape, the poise of its neck, its utility, in many respects portrays its inventor For he like his brother Arthur H. Cheatle, was richly endowed by Nature

' Tall, slender and upright, with a winning smile, and a keen eye that missed nothing Cheatle was welcomed by every society and social scale in any country he was the perfect ambassador, as his titles cavaliere uffiziale of the Grand Cross of Italy, associate of the Order of St John of Jerusalem, and chevalier of the Legion of Honour bear testimony Yet he was simple in his tastes, very human, and imbued with an overwhelming care for the welfare of his fellow creatures Kind and generous to his patients, he also offered material aid and encouragement to students and young graduates striving to climb the slippery ladder to their ambitions, and he was energetic in his efforts to help or defend the underling

His passing marks the end of an era He assisted Lister at his last operation. Watson Cheyne, Cheatle, and Arthur Edmunds were the connecting links between the old and the new, and the great advocates of the principles and practice of Listerism Each, through life, was impelled by the magnetic influence and the noble example of the great master to research for the benefit of mankind No greater tribute could be paid to Lenthal Cheatle than that he maintained the high tradition, he did his best "

C P G W, who served with Cheatle in the South African War and the first world war, recalls how back at King's after the war as his registrar

"I became interested in his thorough investigations of carcinoma of the breast with large sections Cheatle was an enthusiast and a surgical microscopist of the first order, and there can be few surgeons who during their lifetime have had such clinical experience of cancer of the breast, for he often performed ten or more radicals per week as a routine He had a charming personality, everyone who came in contact with him was 'my dear boy,' and he was beloved by his house surgeons and registrars, and his patients worshipped him Handsome, tall, and suave, with a delightful manner, he will long be remembered at King's "

J C B recalls that early in his surgical life Cheatle's mind "was turned to, and indeed we might say swamped by, pathology", for he gave the impression of caring for little else

"He used to run into the laboratory nearly every afternoon, perhaps with another specimen which he would orientate, give an instruction as to cutting more sections from a certain specimen, pick up such sections as were ready, and hurry off home to study the same, a proceeding which often lasted till the early morning With such preoccupation he had few interests outside, and indeed was to some extent casual in practice Scientific meetings did not interest him, but anyone mentioning a problem was promptly invited to come to the laboratory and work it out, this without it entering his mind that there might be no room or conveniences He was generous almost irresponsible, in money matters it was practically impossible to get him to attend to the annual statement of accounts of the laboratory, and there was competition among cabmen to pick him up in Harley Street, about 1 45 P M Particular, almost debonair, in his dress, he retained the top hat and tail coat long after they had been discarded by others He had a mannerism of sighing deeply before answering a question, a subconscious imitation of Lord Lister as I have been told People meeting him were made to feel at home at once by his friendliness, yet he was reserved about his private life, and it is comforting to know that he passed away peacefully at the home of his daughter "

A concluding tribute comes from H O E

"Cheatle had an arresting personality He loved the unorthodox, and practised it in all he did One might have regarded him merely as a poseur if it were not for the solid merit of his clinical and pathological work He did not use a private car, and it was always a matter for astonishment when a London taxi cab of the early '20s pattern disgorged on to the steps leading to the main hall of King's College Hospital the model of late Victorian sartorial perfection which Cheatle invariably was He used to call it 'maintaining the dignity of Harley Street' He carried this elegance even into designing the white coats he wore at outpatients and during his ward visits He smoked cigarettes continually, using a long holder with a mechanical device for ridding itself of the unexpended portion of the cigarette

"A precise operator, he was always anxious to make the operation appear, as he used to say, 'like a picture in a book' To be his house surgeon was an experience, for one never knew into what unusual action Cheatle's original mind would lead him He was capable of making a withering remark to a junior who was guilty of slipshod work or lazy thinking, but one never resented it, for it was always well meant Despite all these eccentricities, his zeal was unquestioned He had a real passion for research

"He was always happy when his ward round was over, so that he could rush away to the little room in the hospital where was housed the giant microtome of his invention There his technician would be cutting and staining sections of the whole breast removed at operation Those sections that were ready for examination would be wrapped up in a brown paper parcel for Cheatle to take home to Harley Street, where, in a little room on the first floor overlooking Devonshire Street, he used to keep them in a state of apparent disarray There seemed to be thousands of them littering this room, huge plates of glass, 10 inches square It was fascinating to spend an hour or two with him there, and none would enjoy it more than Cheatle himself He was not perhaps gifted with powers of lucid explanation, and was a little impatient if one was slow to see his point, but his opinions were based on the sure ground of morbid histology, and students and junior colleagues fortunate enough to be taught by him something of the pathology of the breast as he conceived it will not readily accept any alternative views His uncompromising attitude towards his critics may, perhaps, be the reason why his work does not seem to have received quite the recognition in this country which its worth undoubtedly deserved "

Sir Lenthal Cheatle died on Jan 2 His wife, formerly Miss Clara Jopp died in 1942, and there were three sons and a daughter of the marriage

ARTHUR JOHN HALL

Kt, M A, M.D Camb, Hon D Sc Sheff, F R C P

IN 1889 Arthur Hall returned to Sheffield from Rugby, Cambridge, and Barts to join his father in general practice He soon realised that another task lay ready to his hand, and with his appointment as assistant demonstrator in physiology at the Sheffield medical school he embarked on a life of unusually strenuous endeavour

At the turn of the century provincial medical schools were mostly very poor relations of the metropolitan centres of medical education, and it was of the utmost importance to grasp the opportunities offered by the establishment of new provincial universities When its new school was opened in 1888, Sheffield had a long leeway to make up buildings, equipment, and staff were all far behind the requirements of a self-contained medical school The prospect was enough to daunt the courage of the stoutest But Arthur Hall was peculiarly suited to bring about the radical changes required A clear insight into the difficulties of the situation, combined with steady optimism, a power of clear dramatic expression on platform and in committee, single-mindedness of purpose and subordination of private interest in the main object—these and other special qualities quickly collected round him a band of devoted workers Continuously but unobtrusively he guided the development of the school, and after establishing a department of physiology he turned his attention to organising a department of pathology

A colleague relates "He was always known as 'Lord Arthur,' but 'King Arthur' might have been more appropriate since the round table technique was a familiar device with him to promote professional harmony This promotion of harmony had for him a high priority With two large general hospitals, a municipal hospital, a separate maternity hospital of international repute, and a children's hospital, the chances of professional exclusiveness, jealousy, and friction were at a premium It is not too much to claim that everyone who was a member of those medical staffs during the first thirty years of this century would acknowledge that Hall's had been the major influence in building up the present background of good will He founded a Combined Staffs Club bearing the motto *Floreat Amicitia*, which now flourishes under the name of its founder Very early in the century he also founded an abstracts club which met at his own house and pooled the results of medical reading While surrounding himself with an aura of elaborate courtesy which rendered him rather unapproachable to many, his more genuine innate qualities were candour, openness to reason, and a personal kindness for which no trouble was too great No single person will ever know the extent of his kindnesses for they were all bestowed in secrecy "

Hall's devices to attract a first-rate staff to a school growing rapidly from small beginnings were ingenious:

Not seldom he would get himself elected to a newly formed chair and hold the post for a year or two till he could find a suitable occupant. This method, known to the profession outside Sheffield as musical chairs, was successful in obviating the appointment of an unsuitable candidate merely because he happened to be the only one available at the moment of first foundation. The negotiations through which Sir Edward Mellanby was appointed to a Sheffield chair were largely instigated by Hall. He also played a major part in the events which led to the granting of a charter to the University of Sheffield in 1905.

Clinical and administrative ability are not often closely associated, but Hall was a man who, if not of the very quickest intuition, yet by the solidity of his judgment and by his powers of minute observation, was able to advance medical knowledge. And he won his reputation as an administrator against a background of clinical achievement. His handling in 1918 of the new appearance of epidemic encephalitis was a masterpiece of accuracy and soberly progressive outlook and he chose this disease as the subject of his Lumleian lectures to the Royal College of Physicians in 1923.

After he retired from the chair of medicine in 1931 he continued for many years to serve as a member of the university council and of the board of the faculty of medicine. Progressive deafness, however, led to his retirement from active participation in university affairs. Nevertheless he continued to interest himself in the progress of events in the medical school and in medicine generally.

“There was always a warm welcome for friends who visited him,’ writes G. A. C. “and his never failing sense of humour was evident in the joking references he frequently made to his deafness. Yet this deafness must have been a sad blow to one who so thoroughly enjoyed participating as a ’cellist in quartets. The only complaint he expressed about his deafness was that it prevented him hearing the voices of his grandchildren. Naturally a man of retiring disposition who disliked publicity, he was happiest in the company of one or two intimate friends. Those who were admitted to this intimacy will always remember with affection the personality in which courtesy, wisdom, generosity of nature, humour, and high principles were all blended. He was indeed the green fingered gardener of the Sheffield school of medicine full of sympathy and understanding for the plants he cared for. His energy and enthusiasm were not guided by personal ambition but by a fine sense of loyalty to local institutions and to the profession of medicine.’

His natural scientific bent had freer scope in the leisure his retirement brought, and his lively curiosity and keen observation were seen in his papers in our columns and elsewhere on such subjects as blinking, the parkinsonian smile, and cramp and salt balance. Though he gave unstintingly of his time and energy to Sheffield he had many outside interests. He had been elected F.R.C.P. in 1904 and he served the college as councillor, examiner, and censor. He examined for at least nine universities, and the quality of critical kindliness which led to this choice is made clear by A. I. G. McL.'s recollection of the membership examination.

“Hall pointed to a specimen jar containing a liver but at first I was at a loss to tell him what was wrong with it. He gently said ‘Look at the bottom of the jar,’ and there amongst the debris were things like grape skins. After that we had an animated discussion about the behaviour of hydatid cysts. When I went to Sheffield in 1934 he was already a legendary figure. He had retired from the chair of medicine in 1931, but he still retained his interest in clinical medicine, and his trim, dapper figure looking years younger than his actual age could often be seen at the Royal Hospital, where one of the wards was named after him. A man of great culture and urbanity, he was always approachable and ready to advise his younger colleagues. Of his kindness I can speak with feeling.”

As was perhaps inevitable for one who had been associated all his life with Sheffield, he was an authority on pulmonary industrial diseases and he was for some years chairman of the Medical Research Council's committee on pulmonary dust diseases and a member of the Industrial Health Research Board. In 1930 he attended the international conference on silicosis in Johannesburg. He was also a member of the Radium Commission.

In 1928 Sheffield had conferred on him an honorary D.SC. In 1936 he was knighted and the same year his friends at Sheffield presented him with his portrait by Mr. Ernest Moore (which we reproduce in part).

A. E. N. writes: “However powerful he was in dominating any situation for which he had direct responsibility, Hall never interfered with the freedom and responsibility of his colleagues or assistants. The one thing which thoroughly aroused his disapproval was lack of energy or interest in working for the good of the medical school. When the time came for his retirement he retired completely, and rigorously abstained from all interference. Thus his opinion was often spontaneously asked for. His medical teaching was sound and he conscientiously concentrated on bringing out the less gifted student. At special demonstrations he was clear and stimulating. Memory was rendered easy by punctuation with scraps of sardonic humour.

“His married life was remarkably happy, and the loss of his wife quite suddenly a few years before his own death made visible inroads into his reserve of health and enjoyment, but he endured all without complaint.”

He died on Jan. 3, at the age of 84.

GATHORNE ROBERT GIRDLESTONE

M.A., D.M. Oxfd, F.R.C.S.

As we announced last week, Mr. Girdlestone, of the Wingfield-Morris Orthopædic Hospital at Oxford, died on Dec. 30. Son of the Rev. R. B. Girdlestone, honorary canon of Christ Church, Oxford, he was born in 1881 and educated at Charterhouse, at New College, and at St. Thomas's Hospital which he entered as a university scholar in 1908. His first surgical post outside St. Thomas's was at the hospital near Oswestry now called the Robert Jones & Agnes Hunt Orthopædic Hospital, where for five years he worked both under the guidance of Sir Robert Jones and under the inspiring influence of Dame Agnes Hunt. At this time he had the misfortune to have a serious motor-cycle accident, which left him with a lung lesion. It was after this injury that he decided to dedicate his life to the care of crippled children. He had inherited his father's deeply religious nature and he entered orthopædic surgery with a sense of mission.

[Lafayette

At the beginning of the first world war Girdlestone served in the Royal Army Medical Corps, but his lung lesion prevented general service. In 1916 he was attached to the 3rd Southern General Hospital, Oxford, in charge of the orthopædic centre, an organisation which he had formed and which developed rapidly from the initial 56 beds to 400. With the help of Robert Jones, he took over some huts from the War Office which were re-erected in the grounds of what was then the Wingfield Convalescent Home, Headington, a small institution which had been founded in 1870. These huts were used by the hospital for seventeen years. In 1919 the Ministry of Pensions acquired the Wingfield Hospital as an orthopædic hospital for pensioners, though a 22-bed ward was reserved for the treatment of crippled children; but in 1922 the whole hospital was transferred from the Ministry of Pensions to the Wingfield Committee, and Girdlestone was made honorary surgeon and director. In 1930 he enlisted the sympathy of Lord Nuffield, with whose help the hospital was rebuilt and opened in 1933. His friendship with Lord Nuffield was also instrumental in gaining the latter's interest in the future of the Oxford medical school, which led to the Nuffield endowment of £2 million. In May, 1937, he was made Nuffield professor of orthopædic surgery, the first to hold a chair in orthopædic surgery in this country, but he resigned this post at the beginning of the late war He was then appointed regional orthopædic consultant to the E M S and honorary regional consultant to the Army and to the Ministry of Pensions In 1942 he was elected president of the British Orthopædic Association Outside his professional work he was a first-class golfer In his student days he represented Oxford, and only three months before his death he reached the semifinals in a competition at St Andrews

Girdlestone's entire medical life was given to building an organisation which would realise the ideal trilogy of Hugh Owen Thomas and Robert Jones for the treatment of crippling conditions "rest—surgical treatment—fresh air" To that end he launched a propaganda campaign with Robert Jones, initiated in 1919 by the publication of a plan for the organisation of orthopædics on a regional basis They referred to the pioneer work of Miss Hunt in Baschurch, the place where they had first met In 1920 both Robert Jones and Girdlestone organised the Central Council for the Care of Cripples of which for some time the latter was joint honorary secretary In 1925 he published in monograph form a scheme for the care of crippled children, basing his ideas on his experience at Headington, where the Oxford Orthopædic Region was given as an example for others to follow Already the orthopædic organisation at Oxford served, apart from the central hospital (the Wingfield-Morris), eleven outside clinics and four general hospitals In 1937, at Lord Nuffield's request, he visited South Africa to prepare a plan for the development of orthopædic surgery there This plan was subsequently fulfilled, and the National Council for the Care of Cripples in South Africa was another outcome of his visit He attracted to himself men from all countries who spent valued months and years working with and learning from him at Oxford He had a breadth of outlook that knew no geographical or national barriers

Conscious that functional recovery is the ultimate aim in traumatic surgery, he was a firm advocate of the segregation of accident cases from the care of the general surgeon to that of the orthopædic surgeon, and he was behind those who organised the accident service at the Radcliffe Infirmary, Oxford, in 1939, which, since its beginning, has been attended by the staff of the Wingfield In 1948 he suggested a plan to integrate the regional orthopædic and accident service within the frame of the new National Health Service When in that year he retired from his active duties, the posts he had created and held were occupied by younger men who had worked with him Finally, in 1949, he was one of those who asked the help of Lord Nuffield to integrate the whole of the orthopædic, traumatic, research, and teaching activities of the Oxford orthopædic region into a single structure, and Lord Nuffield offered £50,000 for the purpose When he died he was contributing to this organisation—the Nuffield Orthopædic Centre—as the culmination of his life-work

A Q W writes "Girdlestone could justifiably have said of the Wingfield what Louis XIV said of the State, but he would have been the last person in England to have done so His genuine humility would never allow him to claim more than a share in the evolution of all that the Wingfield is today Yet those who knew him and followed the growth of his cherished institution realise that in truth the Wingfield was G R G His vision and pertinacity created the physical Wingfield and overcame the difficulties which lie in the path of all pioneers That in itself was great work and called for a personality which is given to few men, but can never theless be paralleled in other branches of medicine But G R G created far more than the buildings and organisation of the hospital He inspired and maintained the spirit of the Wingfield, a spirit of clinical humility, of scientific honesty, of service, friendship, and happiness The most casual visitor must be struck by the happiness that extends all through the Wingfield medical, nursing, and lay staff, and patients

'G R G's Wingfield was no moated castle whose inmates worked in self satisfied isolation Early in the history of its evolution, G R G realised the importance of going out into the surrounding neighbourhood to help with advice on orthopædic conditions A network of clinics in hospitals and elsewhere was set up where expert diagnosis and after care by the Wingfield staff was available for a large area round Oxford In effect this meant that a regional service in orthopædics centred on Oxford was in operation for much of the counties of Oxfordshire, Buckinghamshire, and Berkshire long in advance of the National Health Service Act When the appointed day came the Oxford Regional Hospital Board, therefore, was relieved of the detailed planning of a regional orthopædic service for this had already been in existence for some years The National Health Service Act might well have kindled a feeling of jealous resentment at so personal a structure as the Wingfield had become being handed over to an unknown and untried board, but G R G showed none of this and was from the very start anxious only to help in any way he was able He did not hesitate to accept the chairmanship of the board's orthopædic surgery advisory committee, where his services were of great value in extending the orthopædic service to cover the whole region."

Such ability as a planner and organiser was but the complement of Girdlestone's outstanding merits as a surgeon Both as a clinician and as an operator he was in the first rank His original technical contributions are many, among others his method of pseudarthrosis for advanced osteoarthritis of the hip, his tendon transplant for claw toes, his procedure of cap phalangectomy for hallux valgus, and his excision of the hip-joint in severe septic arthritis of the hip Among his many written works on clinical subjects his book on *Tuberculosis of Bone and Joint* is the most widely known, and he was engaged in finishing a new edition just before he died An article by him which we shall shortly be publishing reviews infection in the operating-theatre, in which he was profoundly interested His attitude towards post operative sepsis illustrated his honesty of mind A readiness to suspect his own technique first, and that of the theatre staff only secondly, gave him an approach worthy of the best scientific tradition Undeterred by difficulties caused by the rarity of cases of appreciable sepsis, he continued steadily to aim at the ideal of complete freedom from infections

Few people are privileged to see the dreams of their youth realised, but Girdlestone was one of them. He was convinced that one day the "homes for incurables" would be replaced by institutions created to prevent the crippling consequences of many diseases, and he made the dictum of Robert Jones, "spirit of happiness and orthopædic treatment" the maxim of his life A man of great affections, tender with sufferers, a sincere friend of his friends and all who surrounded him, he will live in the hearts of those who knew him and in the Wingfield which he brought to world repute from the first wooden hut he bought to be erected in 1919 He started where his teacher had left off, and he proceeded with untiring energy along the path clearly indicated by Robert Jones and Agnes Hunt From them he took the flaring torch, and it was still in his hands when he fell

J T writes "I have never known a man who had such capacity for love and being loved He has created in the Wingfield a sanctuary where he, the most modest of souls, was venerated like a new St Francis In his simplicity, directness, and affection for the poor and the crippled he had some features in common with the *poverello* of Assisi His profound Christian beliefs, his inexhaustible energy to carry his work to a fulfilment, and his purity of appearance and bearing at all times and in all places made this parallel even closer But G R G was also a great planner and a good organiser

"As a true man of genius he never knew, or even suspected his worth He disliked public recognition and was happy sitting in the back row His modesty was apparent to the end by his refusing to have a memorial service dedicated to him It has been said of Hugh Owen Thomas that the myth woven about him during his life scarcely allows one to see the man himself I hope that the memory of G R G grows into a myth which becomes part of general medical teaching, that of a man who healed even more by the power of his love than by that of his supreme surgical skill Above all I am grateful to him for reaffirming my belief in the goodness of human nature"

In his early days at the Shropshire orthopædic hospital, Mr Girdlestone married Ina Chatterton, and she remained his companion and firm supporter till his death

CHARLES ERNEST WEST

B A, B M Oxfd, F R C S

Mr West, consulting aural surgeon to St Bartholomew's Hospital, died on New Year's Day at his home in South Devon, at the age of 77 Second son of the late C P West, of Ambleside, he received his earlier education at the Merchant Taylors' School, Crosby, where he obtained a classical scholarship admitting him to Balliol College, Oxford, in 1891 At Balliol he had a distinguished career and was in residence the unusual period of six years He was fortunate in his tutors, first Evelyn Abbott and then Sir John Conroy In his first three years he read classics, but after gaining a first in classics (mods) in 1893, he turned to chemistry and gained a first in natural science in 1895 He then joined the Oxford medical school and in 1897 won an open scholarship to St Bartholomew's Hospital In 1900 he was awarded the Brackenbury surgical scholarship and the Sir George Burrows prize, and took the B M degree Having served as house-surgeon to Mr Alfred Willett, he passed the final F R C S and was appointed a junior demonstrator of anatomy under Sir Holburt Waring At this time the hospital was improving and reorganising its special departments, and in 1902 West became first assistant to Mr A E Cumberbatch in the aural department When he succeeded Cumberbatch five years later he was an experienced and skilful operator and had already contributed a number of papers to the medical journals, besides undertaking bacteriological research with the guidance of Sir Frederick Andrewes and Lord Horder Between 1910 and 1920 he played an active part as a member of the otological section of the Royal Society of Medicine He was the new author of Diseases of the Ear in Walsham's *Surgery*, and joint author of *Operations of Aural Surgery* written principally for the aid of house-surgeons A joint paper on experience and results in operations on the labyrinth, which he read at the Royal Society of Medicine was the first important British report on this subject written from personal experience

After more than a decade in which he continued to carry on a large and increasing hospital and private practice, West startled his friends by deciding to retire, and he left London in 1921 He was elected consultant aural surgeon and a governor of St Bartholomew's Hospital, but went to live at Flushing, near Falmouth, where, after a strenuous life, he was able to enjoy one of his favourite hobbies, sailing and motor-boating Some years later he left Cornwall and moved to Sturminster in Dorset, where during the late war he joined the Home Guard, serving as major and medical officer of the 4th Dorset battalion In the first world war he had held a Territorial commission in the R A M C, and had been attached to the (Military) Hospital at Camberwell with other members of the St Bartholomew's staff, under Sir D'Arcy Power as commandant After the second war he left Dorset and took up residence at Budleigh Salterton in Devon.

With those who knew him well, West was a brilliant conversationalist but he was reserved and modest about his accomplishments and never sought society He was a keen critic of men and affairs and a connoisseur of good things, from wines to Persian carpets He was fond of writing and wrote well, at one time often contributing to the public press articles (usually anonymous) on non-professional subjects Though hardly a wit, he had a keen sense of humour—sometimes rather pungent He was a fearless speaker and a man of strong convictions, capable of rapid decisions With his gift of repartee he might have made a name for himself at the Bar, or with his talent for administration he might have become a captain of industry In the early days of motoring it was always a delight to accompany him to Olympia, for he was a man of many interests, and at the annual motor show he never failed quickly to recognise developments of practical importance His appreciation of music induced him to possess himself of a harp, on which he was no mean performer

West first married in 1908 After the death of his wife some years later, he married Miss Kathleen McCrossan, who was his devoted companion to the end He had no children

S S

THOMAS FRASER

C B E, D S O, M A, M.B, LL D Aberd, D L

By the death of Dr Thomas Fraser on Jan 2, Aberdeen has lost one of its most distinguished medical men and a well-beloved physician

He was born in 1872, the son of Provost Thomas Fraser of Kintore, Aberdeenshire From Robert Gordon's College he proceeded to Aberdeen University, graduating M A in 1894 and M B four years later While in general practice in the northern district of Aberdeen he was appointed assistant in the university department of materia medica and he was also clinical tutor at the Aberdeen Royal Infirmary

[MacMahon

Early in his medical career Fraser took a keen interest in diabetes and he did research of distinction in this field Along with John Rennie, D SC, he made extracts of the islet tissue of the pancreas in *Lophius piscatorius*, the angler fish, of which, as Rennie and he remarked in their paper in the *Biochemical Journal* (1907), there was an ample supply at the Aberdeen fish market Fraser treated a series of diabetic patients with this extract, and in one patient he gave the extract by subcutaneous injection for four days, but he abandoned the method on account of the amount of the reaction caused by the hypodermic injection Accurate and easy methods were not yet available for estimation of the blood-sugar, though a tentative method, curiously enough, was published in the same volume of the *Biochemical Journal* by Edie and Spence It is probably true to assume that this attempt to use an insulin extract was the first on record, anticipating the work of Banting, Best, and Macleod in 1921

The outbreak of war in 1914 found Fraser mobilised with the 1st Highland field ambulance, and he was in command of the 89th field ambulance at the landing at Helles in 1915 Later he saw action in Gallipoli, Egypt, and France, where he commanded the 51st Highland casualty-clearing station and later was A.D.M.S to the 47th London division For his services he was awarded the D S O, was five times mentioned in despatches, and was appointed C B E in 1920

At the end of the war he returned to his practice in Aberdeen, where his skill, wisdom, and unremitting effort earned the respect and affection of many patients, both in town and county, for as A. L writes "Fraser's dignified manner, his sound knowledge, and his wisdom were qualities which gave to his visits a peculiar charm and value, and although always busy he always had time to talk with either a patient or a colleague" He was appointed physician to the wards of the Aberdeen Royal Infirmary and lecturer in clinical medicine at Aberdeen University In his ward rounds he met the large number of post-war students, many of whom had themselves seen service, and to these he imparted both sound clinical teaching and the wisdom acquired in medical practice He had taken a full share in the discussion and negotiations before the introduction of National Health Insurance in 1911, and time had shown the wisdom of his advice Now in the '20s he again took a prominent part in the medical welfare of the north-east of Scotland

The joint hospital medical scheme had been a creation in the minds of the late Prof Matthew Hay and Sir Ashley Mackintosh, and Dr Fraser presided over the meetings of the Aberdeen Medico Chirurgical Society where the details of this important scheme were promulgated in 1927 His personal influence was of value in raising the large sum of £600,000 required to complete this great concept in 1936

Many honours came to him in the course of these years He was elected president of the Aberdeen Medico Chirurgical Society in 1927 He served on the council of the British Medical Association and he held the presidency from 1939 to 1942 He was a member of the General Medical Council from 1941 to 1946 His own university conferred on him the degree of LL D in 1939 and his city made him deputy lieutenant He is survived by his wife and two sons

HERBERT FRENCH

C V O, C B E, D M Oxfd, F R C P

Dr Herbert French, consulting physician to Guy's Hospital and formerly physician to H M Household, died in London on Jan 1, at the age of 75

He entered Guy's as a student in 1898, after taking a first-class in the final honours school of physiology at Oxford, where he had been a scholar of Christ Church As a student he won many prizes, and two years after qualifying in 1900 he was awarded the Radcliffe travelling fellowship In the same year he took the M R C P and was appointed medical registrar at Guy's His success in this post led to his election as assistant physician in 1906

[Weston s Studios

Up to the time of French's appointment Guy's had had few Oxford graduates on its staff, but in the next few years Hurst, Hunt, and Poulton were appointed, so that in 1914 all the four assistant physicians were Oxford men In 1907 French was elected F R C P and the following year he delivered the Goulstonian lectures on Medical Diseases of Pregnant Women On the retirement of Sir William Hale-White in 1917 French became physician to the hospital

In the first world war the foresight of Lord Haldane, at the War Office, had ensured that the services of many London physicians and surgeons should be available to the Army by giving them commissions in the Territorial Army on a part time basis, so that while continuing their civilian hospital work they could attend military hospitals in the London area. Soon after the outbreak of hostilities French was in khaki and he performed military duties throughout the war His programme was already full, for he had quickly built up a large consulting practice and his services were sought by general practitioners all over the country Nor did he neglect his duties at Guy's, where he was a popular and effective teacher

Up till about 1920 it was the custom for the assistant physicians at Guy's—and, indeed, at most other teaching hospitals—to do all the routine necropsies, and the experience gained by performing three or four post-mortems every week for many years laid the foundation of the remarkable clinical sense of the physicians of that epoch French, like his seniors and contemporaries, was not a specialist Nor would he have claimed to be a research-worker His interests embraced the whole field of medicine and by training and experience he was a sound all-round physician This outlook was appropriately reflected in his contributions to medical literature, which consisted mainly of articles in works of reference, such as Allbutt's *System of Medicine* and English's *System of Treatment*, in which his gift for lucid exposition found a worthy outlet His magnum opus, the still widely read *Index of Differential Diagnosis*, was a not unsuccessful attempt to approach clinical medicine through symptoms rather than by formal descriptions of diseases His small book, with Dr E E T Nuthall, on *Medical Laboratory Methods* was one of the earliest books for students on this subject

When he resigned from his hospital appointments in 1929 he was at the height of his fame But he was perhaps wise to retire at an age when he could still enjoy his leisure after so busy and exacting a professional career At his country home, Cudworth Manor, Newdigate, he indulged his taste for agriculture and he became a fruit-farmer, jam-maker, and cider-maker

One of his students recalls waiting on the steps of the colonnade at Guy's for French's handsome well-dressed figure, "for he was one of the few London consultants who did not change his sartorial habits in the 1914–18 war Up to his last round he always arrived in tail coat, top hat, white spats, and carrying a gold headed cane His teaching was always popular both for its intrinsic worth and also perhaps, for his habit of retiring in the middle of the round to the ward theatre so that teaching could continue while he and we indulged in a cigarette His hospitality will also be gratefully remembered In those days it was the practice of all members of the staff to give dinner parties for their firms every three months, and those at French's house were on a lavish scale, often ending with a flutter at roulette. He gave hilarious dances at Cudworth, where a guest might don wellingtons and help feed the pigs

P T *writes* "*French took great trouble with his students* and was especially keen on teaching them diagnosis—the methods of diagnosis and complications of disease One striking instance of his method was that he trained himself to imitate various convulsions, fits, and characteristic gaits *and to repeat these before his class of students* There must still be some of his former pupils who have seen Dr French having a realistic epileptic fit on the floor of the ward or demonstration room He was also equally keen on the routine work of having the clinical reports bound and indexed at the end of the year French commenced this work early in January many registrars were a year or more behindhand with this part of their work "

Dr French leaves a son and a daughter by his first marriage to Amy, daughter of Sir James Sawyer She died in 1946, and in 1948 he married Mrs Nora McDonald, who survives him

SIR PHILIP PANTON

W H McM writes "*Meeting Panton for discussion* was always a pleasure Seated beside him at his desk in the ministerial office which he shared with three others, one listened to a quiet persuasive voice advocating a change in the work or personnel of the laboratory A dissenting reply would cause his spectacles to slip down his *nose* and the corners of his mouth to fall in mild astonishment, a trace of firmness would then be discernible through the soft blueness of his eyes as they turned towards you When you eventually agreed and saw the wisdom of his argument—and you could be sure that any move he proposed would be to the advantage of all concerned—he would smile generously, opening his mouth in almost a gasp in a way which was highly characteristic At lunch at St Stephen s Restaurant after the interview he would inquire after many acquaintances, including the technicians and their families And then, pipe in hand, he returned across Parliament Square, waving farewell as he disappeared behind the sandbagged approach to Caxton House West His letters, often written hurriedly in an untidy hand, were notable for their conciseness and clarity, few of them ending without a sly touch of humour In committee he was sympathetic, unhurried, and watchful, having the knack of leading the meeting back to the point But he could be firm if opposed and the person who was not impressed with the advantages to the community of a service in clinical pathology might meet with a most withering and quite unexpected retort On the occasion of his pastoral visits red letter days in the laboratories, he found time to visit the pathologists in their homes, and he accepted invitations to speak in American hospitals

'At Otter's Pool he lived surrounded by the treasures he prized—books, portraits, and seascapes His bedroom opened on to a veranda which overlooked the lawn and his beloved watergarden, designed by him and largely fashioned with his own hands, for he was adept at building a wall, improvising a rustic bridge, or constructing a pool It was a garden such as would have delighted William Shenstone, while the waters were a paradise of ripples and shade for the fish he befriended But the regular visitor might notice changes in the landscape and colourful islands would appear in the waterways Beneath the veranda was the loggia adorned with stuffed birds, relics of his boyhood here on summer evenings he would reminisce on his early trips to New Zealand and the Faroes He was for his age unusually tolerant of cold and his habit of insisting on half open doors was sometimes hard to endure The grey flannel trousers, the shaggy Harris jacket and the pipe were old and trusted friends, as was his faithful Wu His illness showed itself not long after retirement and regretfully he laid his spade and wheelbarrow aside , but he continued to plan fresh improvements and enjoyed much of his time in the garden. For the rest he sat in his wicker armchair watching for the squirrel in the blue spruce tree and writing short stories which were fun to read At first he continued to attend meetings because of the opportunity they provided of seeing friends, but the journeys overtired him and he accepted defeat philosophically and with his usual good humour The mists of late autumn then settled on the pools and he saw the leaves of his favourite yellow catalpa fall for the last time on to the dewy grass "

SIR LEONARD PARSONS

R E S writes "The obituaries in the medical journals, and the moving address by Prof T L Hardy at the memorial service in Birmingham Cathedral, emphasised that Sir Leonard Parsons used his great gifts to great purpose As one living on the periphery of the Birmingham region, I would like to pay credit to another of his varied activities—his desire to make the National Health Service work for the good of all Perhaps this is typified by the entry opposite his name in the consultants' directory, that he was a specialist in general medicine and pædiatrics and that he was available anywhere in the region He willingly travelled any distance without thought of reward and often at great personal inconvenience If possible he preferred a consultation not to interfere with his going to church or the family lunch, especially when the grandchildren were present, but otherwise nothing stood in his way As he grew older so he seemed ever more willing to help others, especially mothers in distress If his example of coming to the periphery is followed by the younger generation and if credit for good work done there is appreciated centrally as it was by Sir Leonard Parsons, we can look forward to a fraternity living and striving together for a happier country "

Appointments

ALEXANDER, J G U O M.B Lond consultant in bacteriology Hull Royal Infirmary

DROLLER HUGO M.D Munich, M R C P M R C.P.E consultant geriatric physician hospitals in No 21 (Leeds A) and No 22 (Leeds B) hospital management committee groups

FARR F J M B Brist D M R.E consultant in radiology, hospitals in No 11 (Dewsbury Batley and Mirfield) hospital management committee group

FORSTER, WILLIAM M.B Durb D P M psychiatrist Storthes Hall Hospital Kirkburton Yorks

HARRISON E J M.B.E M.A M.B Camb D P M psychiatrist, Bootham Park Hospital York.

JARMAN, D E M R.C S psychiatrist Storthes Hall Hospital, Kirkburton Yorks

KENNEDY, A F O B.E M.D Dubl M R C P I asst senior M O South East Metropolitan Regional Hospital Board

O BRIEN NORAH L.R C P I M.O Tanganyika

PICKUP J D M D Leeds D C H consultant in pædiatrics hospitals in No 8 (Pontefract and Castleford) No 9 (Wakefield A) and No 11 (Dewsbury Batley and Mirfield) hospital management committee groups

REID FRANK M B Leeds D M R D consultant radiologist, hospitals in Harrogate and Ripon hospital management committee group

ROGERS A C M.R C.S D.M R D consultant radiologist hospitals in Hull A and B and East Riding hospital management committee groups

SHILLITOE, A J M B Lond M.R C.P consultant in pathology Hull Royal Infirmary

SIMONS E. L M.B Camb consultant in pathology hospitals in Goole Howden and Selby, and Pontefract and Castleford hospital management committee groups

SIMPSON R A H M R C.S appointed factory doctor Lydd district Kent

SWEETNAM W P M.D Manc M R C.P D.P.H D C H consultant pædiatrician hospitals in Huddersfield and Halifax hospital management committee groups

---

News

University of Oxford

On Jan 16, convocation will be asked to approve a proposal to confer the honorary degree of D C L on Sir Godfrey Huggins, F R C S , prime minister of Southern Rhodesia

Queen's University, Belfast

On Dec 20, the following degrees and diplomas were conferred

M.D—R. D N Blair Basil Blowett, Brian Mullally

M.B , B Ch , B A O—C G Alexander S A Agnew Elizabeth F Bennett J B Bowden W A Boyd C F Brennan T D Brown J M R Campbell Janet C Davidson P J Devlin D A Elliott N P Ellison Patricia E Ferguson A G Fullerton W J Glover Ferdinand Hillman S R A Hogg Thomas Horner D W Ingram D H Johnston Arthur Jones Dorothea Kelso, Mca W Kelso W J Kernohan Frances E W Kinnaird A L Kirkland Harold Korentager R S Lindsay Doreen E Linton C R Locker J C H Loughridge, M J Lyons W T E McCaughey Ephraim McFall M J McKenna Edith M McKinney A G McKnight Frances M McQuitty W N McWilliam, R. G S Malone V J Marmion J E H Mercer N G Metrustry H A Millar George Moles M. H Moles Sean Moore J F O Sullivan G C Patterson J N Patterson A C C Pinion Norah I Rottger J L Russell, I McC Todd, Mary Uprichard W G Wade J A Weaver, C R Whitfield J S Willman Sheila M Wilson, H G Wright Sandra Wylie

C P H—A C Darrah R Logan F V Maclaine, S H Moore P N Newsam W T Orton, W J Patterson J Simpson E M Wells

Order of St John of Jerusalem

The King has sanctioned the following promotions in, and appointments to, this order

As Knight—C Gardiner Hill M B

As Commanders—E P Scott M B R V S Cooper M B W B Fox M B J R Hanna M B , C S C Prance, M B N S B Vinter M B E M Humphery, M B Colonel K B Fraser M B

As Associate Commanders—Major S K Engineer F R.C.P.F

As Officers—S I A Laidlaw M D B LaHaye M D C H Vernon F R C.S B L Steele M R C.S C E H Gater L.R.C.P E , H E Thomas M B L G Norman, M D

As Associate Officers—B B Rai M B K B M. S Mahmood M B Lieut -Colonel P M Petigara M B Miss B Rose M B

Royal College of Surgeons in Ireland

The president and council of the college invite the submission of essays before Feb 1, 1952, for the Carmichael prizes (£150 and £100)

According to Mr Carmichael s will the essays should deal with the improvement of the medical profession with the view of rendering it more useful to the public and a more respectable body than it is at present The authors are also asked to consider the preliminary and moral education of medical and surgical students as well as the mode of conducting their professional studies Mr Carmichael also wished the authors to consider the most practical mode of rendering the qualifying examination as demonstrative as possible

Further particulars may be had from the registrar of the college, Dublin

Faculty of Radiologists

The faculty is holding a weekend postgraduate course at the Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2 on Feb 17 and 18 Applications for enrolment should be sent to the secretary of the faculty, 45 Lincoln s Inn Fields, W C 2

Harveian Society of London

The Buckston Browne prize for 1950 has been awarded to Dr C J Gavey, F.R C.P , for his essay on the Management of the Hopeless Case

King Edward's Hospital Fund for London

The Fund has received a further instalment of £100 000 from the Nuffield Trust for the Special Areas Lord Nuffield provided that loans repaid to this trust should pass to King Edward s Hospital Fund In all £1,350,000 has now been received

The King has sent his annual subscription of £1000 for 1951 to the Fund

Prison Medical Services

Dr H K Snell, principal medical officer of Wormwood Scrubs Prison, has been appointed to be director of Prison Medical Services in succession to Dr H T P Young, who retired on Dec 31

Dr Snell qualified from King's College Hospital in 1921 and after holding house appointments there took his M B Lond in 1924 and his M D three years later He has served as medical officer at Wandsworth and Parkhurst prisons and at Broadmoor asylum His published work includes papers on the influence of war on drunkenness and attempted suicide

Society of Chemical Industry

The 70th annual general meeting of this society will be held in London from July 9 to 13, at the *Imperial College of Science and Technology, South Kensington*

Empire Rheumatism Council

Lord Horder, will take the chair at the annual general meeting of the council to be held at 41, Portland Place, London, W 1, on Wednesday, Jan 24, at 6 p m

St John Ambulance Brigade

Mr Frank Edwards, F R C S E, of Shrewsbury, has been appointed surgeon in chief of the brigade in succession to Dr Corbet Fletcher, of Hampstead, who has resigned Dr Marcus Scott, of Newington Causeway, London, succeeds Mr Edwards as deputy surgeon in chief

Institute of Hospital Administrators

The address of this institute and of its journal the *Hospital* is *75, Portland Place* London, W 1

Irish Gerontological Society

This society was founded on Dec 6 The following officers were elected president, Prof W J E Jessop, secretary, Dr John Fleetwood, treasurer, Dr Paul Holland The secretary may be addressed at the department of physiology, Royal College of Surgeons, Dublin

Community Mental Health

Dr Russell Brain, P R C P, will open the conference on Community Mental Health in Practice which the National Association for Mental Health is holding at St Pancras Town Hall, London, W C 1, from March 12 to 13 Other speakers will include Dr T A. Ratcliffe, Dr Fanny Wride, Dr Mary Capes, Dr T M Ling, Dr Roger Tredgold, Dr Felix Post, and Dr J W Affleck Further information may be had from the *conference secretary*, 39, Queen Anne Street, W 1

Volunteers for a Cold

The Common Cold Research Unit at Harvard Hospital, Salisbury, needs more volunteers urgently because the island experiment, described in our columns last week, has given new ideas for studying the transfer of natural colds The unit is also trying to find out why school-children play such an important rôle in the spread of the common cold

Since the experiments at Salisbury started in 1946 over 2000 volunteers have visited the unit, some of them have paid as many as four visits But more volunteers, aged 18–40, are still needed They are offered 10 days' holiday with free travel warrant and pocket-money Applications should be sent *to the medical officer*, Harvard Hospital, Salisbury

Births, Marriages, and Deaths

BIRTHS

Browne —On Dec 25 at Newcastle upon Tyne, the wife of Prof R C Browne—a daughter

French —On Dec 31 in Oxford the wife of Dr John French —a son

Habibis —On Dec 23, in London, to Dr Stella Murray wife of Dr H S Habibis—a son

Sears —On Dec 31 in London to Dr Janet Sears (née Conn), wife of Dr H T N Sears—a daughter

Stones —On Jan 6 in Liverpool the wife of Dr P B Stones —a son

MARRIAGES

Hewitt—Jago —On Jan 9 in London Douglas Hewitt M A to Margaret Jago M B

DEATHS

Campbell.—On Jan 3 at Dundee Peter Campbell M B Edin aged 94

Cathcart —On Jan 4 at Broadstairs George Clark Cathcart M A M D Edin aged 90

Clark —On Jan 1 Agnes Catherine Clark M B Camb D A

Greenwood —On Jan 3 at Darlington Alan Young Greenwood M D Edin

Hardy —On Jan 4 at Weybridge Surrey Francis Alexander Hardy M D Edin aged 78

Lloyd —On Jan 4 at Milford-on Sea Hants Robert Archer Lloyd D.S O M D Lond lieut -colonel I M.S retd aged 72

Maynard —On Jan 6 in London Edwin Maynard M D Durh, F R C S D P H

Pitt —On Jan 3 in London Clive Nelson Pitt M B Sydney

Sansom —On Jan 6 at St Leonards Sussex Charles Lane Sansom C.M G F R C.S E D P H Kt of Order of Isabella Catolica of Spain aged 88

Sansom —On Jan 2 John Raymond Eden Sansom, M B Brist aged 54

West —On Jan 1 at Budleigh Salterton Charles Ernest West B.A Oxfd F R C.S aged 77

Society for the Study of Fertility

The second annual conference of this society will be held at *Girton College, Cambridge, on June 20 and 21* Further particulars may be had from the secretary, Dr G I M Swyer, University College Hospital Medical School, London W C 1

Films on Child Health

Prof A V Neale will take the chair at a meeting of the medical committee of the Scientific Film Association on Jan 15 at 5 P M, at 1, Wimpole Street, London, W 1, when some films on child health will be shown and discussed.

In our advertisement columns application is invited for the post of junior assistant editor of The Lancet

At the invitation of the Postgraduate Federations of Australia and New Zealand Dr William Pickles, of Aysgarth, is to give a series of lectures in these countries He is leaving on Jan 19 and will be away until late June

Diary of the Week

JAN 14 TO 20

Monday, 15th

Hunterian Society
8 30 P M (Mansion House E C 4) Prof F Orban (Liège) Arteriographic Approach to the Study of Arteritis

University of Durham
5 15 P M (Royal Victoria Infirmary Newcastle upon Tyne) Prof J Z Young, F R.S Experiments in Learning (Rutherford Morison lecture)

Tuesday, 16th

British Postgraduate Medical Federation
5 30 P M (London School of Hygiene Keppel Street W.C 1) Prof Henry Barcroft Circulation in the Human Limb.

Institute of Dermatology, St John s Hospital Lisle Street, W C 2
5 P M Dr M S Thomson Zoonoses (Parasitic Infections).

Eugenics Society
5 30 P M (Burlington House Piccadilly, W 1) Dr C O Carter Congenital Malformations

Society for the Study of Addiction
4 P M (11 Chandos Street W 1) Dr J A Hobson Clinical Experiences in the Treatment of Alcoholism

Wednesday, 17th

Institute of Dermatology
5 P M Dr R W Riddell Medical Mycology

Royal Microscopical Society, Tavistock House South, Tavistock Square W C 1
6 P M Dr G M Findlay The Virus and the Cell

Harveian Society of London 11, Chandos Street W 1
8 45 P.M Dr R R Trail Continuing Problem of Phthisis.

Medico Chirurgical Society of Edinburgh
8 30 P M (Royal College of Surgeons, 18 Nicolson Street Edinburgh) Prof E F Finch Approach to Specialism.

Thursday, 18th

University College Gower Street W C 1
5 15 P M Mr F Bergel D SC Physico chemical Properties and Pharmacological Activity of Drugs (First of two lectures)

British Postgraduate Medical Federation
5 30 P M Dr G D Dawson Cerebral Responses to Peripheral Stimuli in Man

St George s Hospital Medical School, Hyde Park Corner S W 1
4 30 P M Dr Denis Williams Neurology lecture-demonstration

Faculty of Radiologists
8 15 P M (32, Welbeck Street W 1) Dr W St. C Symmers, Dr R Bodley Scott Dr F Campbell Golding The Reticuloses

Royal Society of Tropical Medicine and Hygiene 26 Portland Place W 1
7 30 P M Prof René Mouchet The Work of the Foreami (Fonds Reine Elisabeth pour l Assistance Médicale aux Indigènes) in the Belgian Congo

Liverpool Medical Institution, 114, Mount Pleasant Liverpool, 3
8 P M Mr J A Shepherd Inguinal Hernia

Friday, 19th

Faculty of Radiologists
10 30 A M (1 Wimpole Street, W 1) Dr Brian Russell, Prof R McWhirter Dr D G Galton Dr J D N Nabarro Dr John Boland The Reticuloses.
2 15 P M (Royal College of Surgeons Lincoln s Inn Fields W C 2) Dr W M Levitt Dr Gwen Hilton Dr Geoffrey Boden The Reticuloses

Medical Women s Federation
8 30 P M (Royal Free Hospital School of Medicine, W C 1) Mr L L Whytehead Recent Developments in Cardiac Surgery at Guy s Hospital

Saturday, 20th

South East Metropolitan Regional Tuberculosis Society
10 30 A M (Chest Clinic Town Hall Walworth Road S E 1) Dr W G Tillman Tuberculous Conditions of the Skin Dr King Turner Oral Conditions in Pulmonary Tuberculosis Dr E K Pritchard Domiciliary Treatment of Pulmonary Tuberculosis

PROPER USE OF THE HOSPITAL IN TREATMENT OF THE AGED SICK

LORD AMULREE
M A , M.D Camb , F R C P
ASSISTANT PHYSICIAN

A N EXTON SMITH
M.A , M B Camb , M.R C P

G S CROCKETT
M.A , M B Camb M R C P
MEDICAL REGISTRARS

UNIVERSITY COLLEGE HOSPITAL

SINCE the introduction of the National Health Service, wo years ago, one of the more formidable problems has een the care of the aged sick General practitioners hroughout the country know well the difficulties of etting their aged patients into hospital Harold tassen, in an article called "Granny is Gone," has ingled out for criticism this aspect of the health service n Britain, and tells the story of one old lady who died f pneumonia, because she could not be found a bed in ospital (see Ogilvie 1950) We hope to show in this rticle how a service, based on a hospital, can be evolved o provide better facilities for the care of the aged sick

Short Stay In Hospital

We have already described the state of affairs in St Pancras Hospital when this work was begun (Exton-Smith and Crockett 1949) It is now possible to give figures of the results of a year's treatment, and in so doing the patients have been divided into two categories In the first category are the "inherited" patients (those present at the time of the take over) , in the second category the "new" patients (those admitted during the year June 1, 1949, to May 31, 1950)

The disposal, over a year, of 155 inherited patients is shown in table I These bare figures give rather a gloomy view of the chances of rehabilitation and ultimate discharge of patients who have been in hospital for more than two years We can say, however, that though 95% of these patients were at one time bedridden, by the end of the year their physical state and mental outlook had improved so much that the bedridden cases had been reduced to 10% The patients composing this 10% have gross physical deformities which make it impossible for them to sit in chairs Many of these deformities we believe were preventable

Table II shows the disposal, over a year, of 89 new patients Of the 29 remaining in the hospital, we consider that 18 (20% of the 89) are suitable for hostel accommodation , and in fact some of these patients are now awaiting the opening of a hostel which is to be attached to the hospital Only 11 of the 29 (about 13% of the 89) are regarded as irremediable Only a small number of new patients were admitted during the year, because the total number of beds allocated to aged patients is being reduced from 155 to 120

The considerable difference in the average length of stay of the two groups of patients has led us to consider whether these groups were comparable In one way they were not, for none of the inherited patients had been admitted direct from home they had come from other hospitals where they had usually already spent several months, and they were transferred to St Pancras Hospital because at that time there was no solution to their problem other than continued hospital care

We contend that in many of these cases this solution was not the only one and that if this type of patient be dealt with in the manner we outline below many needless hospital admissions will be avoided If so, a great saving will be made in hospital beds, the maintenance of which costs the community so much money and staff Indeed, if the existing beds were kept free of those who do not require hospital care, the 6000 hospital beds for the chronic sick* now unused through lack of nursing staff might turn out to be redundant We believe that the demand for still more nursing recruits, at a time when there are more nurses in the country than there ever has been in the past, is unjustified

Table I shows that 155 patients have been in hospital for an average of thirty-two months (at a cost of about £220,000) We believe that only in very exceptional cases need a patient remain in hospital for as long as thirty two months Table II shows that the average length of stay of the "new" patients is about ten weeks This suggests that if, in a period of 32 months, these 155 hospital beds had been employed for their proper purpose—the active treatment of the sick—they could have accommodated 1200 "new" patients at the same cost to the hospital This turnover in itself would have eliminated a long waiting list The longer the aged patient must wait before gaining admission to hospital the more difficult and longer his treatment becomes Waiting lists are thus conducive to long stay in hospital, the two tending to produce a vicious circle as the turnover diminishes

---

* Answer to Parliamentary Questions *Hansard* March 16, 1950

TABLE I—DISPOSAL OF "INHERITED" PATIENTS DURING A YEAR

—	No in hospital Jan 1, 1949	Disposal between Jan 1 1949 and Dec. 31 1949				Average length of stay		Average age (years)
		(*a*) Died	(*b*) Discharged	(*c*) Transferred	(*d*) Remain	Groups (*a*) (*b*) and (*c*)	Group (*d*)	
Males	74	12	6	2	54	28 months	33 months	71
Females	81	13	2	4	62	30 months	34 months	75
Total	155	25 (*16*%)	8 (*5*%)	6 (*4*%)	116 (*75*%)	—	—	—

TABLE II—DISPOSAL OF NEW PATIENTS ADMITTED BETWEEN JUNE 1, 1949, AND MAY 31, 1950

—	No admitted	Disposal between June 1, 1949 and May 31 1950				Average length of stay		Average age (years)
		(*a*) Died	(*b*) Discharged	(*c*) Transferred	(*d*) Remain	Groups (*a*) (*b*) and (*c*)	Group (*d*)	
Males	39	13	10	3	13	8 weeks	9 weeks	70
Females	50	13	13	8	16	11 weeks	14 weeks	77
Total	89	26 (*29*%)	23 (*26*%)	11 (*12*%)	29 (*33*%)	—	—	—

Society of Chemical Industry

The 70th annual general meeting of this society will be held in London from July 9 to 13, at the Imperial College of Science and Technology, South Kensington

Empire Rheumatism Council

Lord Horder, will take the chair at the annual general meeting of the council to be held at 41, Portland Place, London, W 1, on Wednesday, Jan 24, at 6 p m

St John Ambulance Brigade

Mr Frank Edwards, F.R C S E , of Shrewsbury, has been appointed surgeon in chief of the brigade in succession to Dr Corbet Fletcher, of Hampstead, who has resigned Dr Marcus Scott, of Newington Causeway, London, succeeds Mr Edwards as deputy surgeon in chief

Institute of Hospital Administrators

The address of this institute and of its journal the *Hospital* is 75, Portland Place, London, W 1

Irish Gerontological Society

This society was founded on Dec 6 The following officers were elected president, Prof W J E Jessop , secretary, Dr John Fleetwood , treasurer, Dr Paul Holland The secretary may be addressed at the department of physiology, Royal College of Surgeons, Dublin

Community Mental Health

Dr Russell Brain, P R C.P , will open the conference on Community Mental Health in Practice which the National Association for Mental Health is holding at St Pancras Town Hall, London, W C 1, from March 12 to 13 Other speakers will include Dr T A Ratcliffe, Dr Fanny Wride, Dr Mary Capes, Dr T M Ling, Dr Roger Tredgold, Dr Felix Post, and Dr J W Affleck Further information may be had from the conference secretary, 39, Queen Anne Street, W 1

Volunteers for a Cold

The Common Cold Research Unit at Harvard Hospital, Salisbury, needs more volunteers urgently because the island experiment, described in our columns last week, has given new ideas for studying the transfer of natural colds The unit is also trying to find out why school children play such an important rôle in the spread of the common cold

Since the experiments at Salisbury started in 1946 over 2000 volunteers have visited the unit, some of them have paid as many as four visits But more volunteers, aged 18–40, are still needed They are offered 10 days' holiday with free travel warrant and pocket-money Applications should be sent to the medical officer, Harvard Hospital, Salisbury

---

Births, Marriages, and Deaths

BIRTHS

BROWNE —On Dec. 25, at Newcastle upon Tyne, the wife of Prof. R. C Browne—a daughter

FRENCH —On Dec 31 in Oxford, the wife of Dr John French—a son

HABIBIS —On Dec 23 in London to Dr Stella Murray wife of Dr H S Habibis—a son

SEARS —On Dec 31 in London, to Dr Janet Sears (née Conn) wife of Dr H T N Sears—a daughter

STONES —On Jan 6 in Liverpool, the wife of Dr P B Stones—a son

MARRIAGES

HEWITT—JAGO —On Jan 9 in London, Douglas Hewitt M A , to Margaret Jago M B

DEATHS

CAMPBELL.—On Jan 3 at Dundee Peter Campbell M B Edin aged 94

CATHCART —On Jan 4 at Broadstairs George Clark Cathcart M A M D Edin aged 90

CLARK —On Jan 1 Agnes Catherine Clark M B Camb D A

GREENWOOD —On Jan 3 at Darlington Alan Young Greenwood M D Edin

HARDY —On Jan 4 at Weybridge Surrey Francis Alexander Hardy M D Edin aged 78

LLOYD —On Jan 4 at Milford-on Sea Hants Robert Archer Lloyd D.S O M D Lond lieut colonel I M S retd aged 72

MAYNARD —On Jan 6 in London, Edwin Maynard M D Durh F R C.S D P H

PITT —On Jan 3 in London Clive Nelson Pitt M B Sydney

SANSOM —On Jan 6 at St Leonards Sussex Charles Lane Sansom C M G F R C S E D P H Kt of Order of Isabella Catolica of Spain aged 88

SANSOM —On Jan 2 John Raymond Eden Sansom M B Brist aged 54

WEST —On Jan 1 at Budleigh Salterton Charles Ernest West B.A Oxfd F R C.S aged 77

Society for the Study of Fertility

The second annual conference of this society will be held at Girton College, Cambridge, on June 20 and 21 Further particulars may be had from the secretary, Dr G I M Swyer, University College Hospital Medical School, London, W C 1

Films on Child Health

Prof A V Neale will take the chair at a meeting of the medical committee of the Scientific Film Association on Jan 15 at 5 P M , at 1, Wimpole Street, London, W 1, when some films on child health will be shown and discussed.

In our advertisement columns application is invited for the post of *junior assistant editor of* THE LANCET

At the invitation of the Postgraduate Federations of Australia and New Zealand Dr William Pickles, of Aysgarth, is to give a series of lectures in these countries He is leaving on Jan 19 and will be away until late June

---

Diary of the Week

JAN 14 TO 20

Monday, 15th

HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Prof F Orban (Liège) *Arteriographic Approach to the Study of Arteritis*

UNIVERSITY OF DURHAM
5 15 P M (Royal Victoria Infirmary Newcastle upon Tyne) Prof J Z Young, F R.S Experiments in Learning (Rutherford Morison lecture)

Tuesday, 16th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene Keppel Street, W.C.1) Prof Henry Barcroft Circulation in the Human Limbs.

INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle Street, W C 2
5 P M Dr M S Thomson Zoonoses (Parasitic Infections).

EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly, W 1) Dr C. O Carter Congenital Malformations

SOCIETY FOR THE STUDY OF ADDICTION
4 P M (11, Chandos Street W 1) Dr J A Hobson Clinical Experiences in the Treatment of Alcoholism

Wednesday, 17th

INSTITUTE OF DERMATOLOGY
5 P M Dr R W Riddell Medical Mycology

ROYAL MICROSCOPICAL SOCIETY, Tavistock House South, Tavistock Square W C 1
6 P.M Dr G M Findlay The Virus and the Cell

HARVEIAN SOCIETY OF LONDON, 11, Chandos Street W 1
8 45 P M Dr R R Trail Continuing Problem of Phthisis

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons, 18, Nicolson Street, Edinburgh) Prof E F Finch Approach to Specialism.

Thursday, 18th

UNIVERSITY COLLEGE Gower Street W C 1
5 15 P M Mr F Bergel D.SC Physico-chemical Properties and Pharmacological Activity of Drugs (First of two lectures)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Dr G D Dawson Cerebral Responses to Peripheral Stimuli in Man

ST GEORGE S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner S W 1
4 30 P M Dr Denis Williams Neurology lecture-demonstration

FACULTY OF RADIOLOGISTS
8 15 P M (32 Welbeck Street W 1) Dr W St. C Symmers, Dr R Bodley Scott Dr F Campbell Golding The Reticuloses

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE 26 Portland Place W 1
7 30 P M Prof René Mouchet The Work of the 'Foreami (Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes) in the Belgian Congo

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P M Mr J A Shepherd Inguinal Hernia

Friday, 19th

FACULTY OF RADIOLOGISTS
10 30 A M (1 Wimpole Street, W 1) Dr Brian Russell Prof R McWhirter Dr D G Galton Dr J D N Nabarro Dr John Boland The Reticuloses.
2 15 P M (Royal College of Surgeons, Lincoln s Inn Fields W C 2) Dr W M Levitt Dr Gwen Hilton Dr Geoffrey Boden The Reticuloses

MEDICAL WOMEN S FEDERATION
8 30 P M (Royal Free Hospital School of Medicine W C 1) Mr L L Whytehead Recent Developments in Cardiac Surgery at Guy s Hospital

Saturday, 20th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
10 30 A M (Chest Clinic Town Hall Walworth Road S E.1) Dr W G Tillman Tuberculous Conditions of the Skin Dr King Turner *Oral Conditions in Pulmonary Tuberculosis* Dr E K Pritchard : Domiciliary Treatment of Pulmonary Tuberculosis

bowel action can be produced at a convenient and predictable time

Medicolegal Reasons

We have found that many patients have been kept n bed after a fall, irrespective of whether or not they have sustained any real injury Some hospitals have been prompted to withhold attempts at rehabilitation of patients who have a tendency to fall for fear of adverse criticism in the coroner's court A tendency to falling is almost universal in aged patients, but can hardly justify such a nihilistic attitude as that In our unit 102 patients who were formerly bedridden now spend the greater part of the day sitting in chairs, or take part in walking exercises in the ward and gymnasium Except one patient who slipped on the floor (which was formerly kept highly polished) none has sustained any serious injury

Reasons of Expediency

It is always easier to keep aged patients in bed than to get them up, but the enthusiasm of the ward sisters in encouraging patients to activity does much to counteract such laissez faire Some believe, mostly out of sentiment, that people should be put to bed merely because they are old and "deserve a rest"

We have recently seen a lady of 91 who, after bronchopneumonia three years ago, had been kept in bed by well meaning and consequently overburdened relatives After two days in hospital she was sitting in a chair, and within six days she was walking She was in hospital only twenty-nine days and was able to return home fully ambulant

On the other hand, directly they are admitted to hospital, some patients who were ambulant at home lose their ability to get about For those living alone the stimulus to remain active is that of self preservation There are many without friends and relatives, and to survive they must at least be able to get to their front door to admit food and succour Once in hospital, such patients are often waited on hand and foot, the stimulus to activity is lost, they find no familiar pieces of furniture on which to drag themselves around, and they quickly cease to be mobile Here is a true iatrogenic loss of locomotion

Blind patients need not be kept in bed If they are led round the ward each day they soon come to know it as well as the familiar surroundings of their own home

DISCHARGE FROM HOSPITAL

Though it is a relatively simple matter to aid the recovery of the aged sick admitted to hospital, their ultimate discharge often presents a formidable problem Naturally the rate of turnover directly depends on the ease with which the patients can be discharged. Those who have been treated successfully in hospital can either be returned home or be sent to hostel accommodation

Return home—The difficulty of discharging a patient to his home is due not only (as some would have it) to the unwillingness of relatives to look after their aged parents but also to less obvious causes As a person gets older he adapts his life to his failing faculties, and his daily habits in the home are modified to fit in with what he can manage without assistance The sudden onset of an incapacity, be it major or minor, will upset the delicate balance between what the person can do and what he needs to do to continue his normal existence at home This precarious balance, which has been steadily built up over the course of years, can rarely be restored once the patient has been admitted to hospital, even though the precipitating incapacity which led to admission has been removed Where the balance before admission is not so critical, it is possible to discharge the patient to his home Nevertheless, such patients will usually need a home help, meals on wheels service, and outpatient supervision to enable them to carry on their home life successfully

Hostel accommodation—Where the balance between ability and necessity has become more precarious even the provision of these services will not allow the person to return home, and some form of hostel accommodation is essential Hostels for the aged are sadly lacking in most areas At the moment some 45% of the patients in this hospital have enough functional capacity to live fuller lives in a hostel than they are enjoying at present in hospital, but they remain because we lack other accommodation

Long stay annexes—A few patients still have considerable disability even after months of intensive treatment They need continued physical assistance and some general nursing care for their well being This type of patient is best cared for in the so called long stay annexe In collaboration with the Emergency Bed Service we have been able to transfer such patients to nursing homes under the control of the regional hospital board, and at the same time patients on the Emergency Bed Service waiting list have been admitted to the vacant hospital beds

Domiciliary Visits

We have already mentioned the part played by a domiciliary visit in promoting a quick turnover of patients But there are also other aspects of these visits to be considered

PURPOSE AND VALUE OF HOME VISITS

1 It is necessary *to establish a base line*, or a common standard, by which to judge the urgency of the need for admission to hospital The necessity arises from the present shortage of beds for the aged sick for we have to ensure that the available beds are used to the best advantage If such a common standard is to be maintained a physician from the hospital must visit the patients in their own homes, otherwise the hospital has to rely on reports from general practitioners, who may have different standards and use different criteria in judging the urgency of admission

Though adverse social conditions rather than physical disabilities sometimes make admission necessary, we find this exceptional The initial visit must therefore be made by a doctor who assesses the physical need, rather than by an almoner who will assess the social need (cf Macdonald 1950)

2 *To evaluate waiting lists*—We have received from time to time a list of patients on the "chronic" waiting list of the Emergency Bed Service for the St Pancras area When we visited such patients we often found that the physical condition had changed since their names were put on the waiting list, and in many cases the E B S had not been informed of such changes Thus some patients had died, others had already been admitted to a hospital, and many had recovered The particular value of a domiciliary visit may be illustrated by the following case

We were asked to see a woman aged 90, who was said to require urgent admission because of gangrene of the leg She was living in reasonable comfort in a first-floor flat and was cared for by an elderly friend On examination she was very weak, but not in pain There was auricular fibrillation and the left leg was blue and cold up to the groin, with no femoral pulse She did not want to come into hospital and the friend, who realised that she was dying, was most anxious that she should spend her last hours at home It seemed the kindest thing for them both to leave them be, for the friend was managing adequately and the patient was receiving attention from the district nurse We consulted with the patient's doctor who agreed to this course

3 *To assess the patient in his environment*—It is becoming clearer and clearer that by observing and treating a patient in a hospital, isolated from his normal environment, we may be going only half way towards promoting recovery in its broadest sense The hospital

Economic considerations aside, it is clearly right and proper that patients should spend as short a time as possible in hospital The results to patients of long stay and neglect in Public Assistance institutions and hospitals are well known, and are responsible for the evil reputations of such institutions As this geriatric unit, like most others, has grown up in what was once a municipal infirmary, it is satisfying to find that already the quick turnover has changed the attitude of prospective patients in the district They are no longer hesitant about agreeing to admission, they no longer feel that their entry here will be the beginning of their "way to dusty death"

Attainment of a Quick Turnover

The way in which such a quick turnover can be achieved may be considered in three sections domiciliary and outpatient treatment, ward treatment, and discharge from hospital

DOMICILIARY AND OUTPATIENT TREATMENT

Every patient who requires early treatment to ensure his quick recovery must be admitted without delay In order to select these cases, whenever a practitioner requests admission for a patient we see that patient in his own home or in the outpatient department Most of them do not attend outpatients in the first instance as a rule they have already taken to their beds, and so are seen in their homes For every new patient attending the outpatient department, 4 are seen for the first time at home

Great psychological benefit results to the patient from a visit by hospital doctors he becomes at once an individual (rather than a mere name on a waiting list), known personally to the doctors who will be looking after him in hospital Many patients receive outpatient treatment in the physiotherapy and occupational therapy departments, and these are brought to hospital by car or ambulance

Large scale domiciliary treatment, as practised by Dr Bluestone (1949) at the Montefiore Hospital, New York, would reduce still further the numbers requiring hospital admission, and lessen the period of stay for those already in hospital

WARD TREATMENT

Various detailed articles on the adaptation of modern therapeutic measures to the care of the elderly sick have appeared (Howell 1950, Cosin 1949, Warren 1948a, Crockett and Exton Smith 1950) The geriatric ward differs from the acute general ward in one important way In the general ward, it is traditional for a patient to be in bed Whatever the reason for his entry to hospital—be it merely the balancing of his diabetes, or the investigation of renal function—he is put to bed and kept there, for the convenience of doctors and to maintain, for the sake of the nursing staff, the orderly appearance of the ward The diabetic accurately balanced for his immobile hospital existence will require, on returning to an active life, a radical change in his insulin dosage, but he will suffer no permanent harm For the aged patient, on the other hand, such immobilisation is often disastrous, ending in permanent bedfastness

Many of the reasons given for keeping patients in bed are not valid for the elderly These reasons can be conveniently classified as medical, hygienic, and medico legal, and reasons to do with expediency

Medical Reasons for Rest in Bed

Heart disease—Rest in bed in a young patient considerably reduces the amount of work the heart has to do On the other hand, in the aged patient, whose normal activity is already considerably reduced by other than cardiac factors, long continued bed rest produces little further reduction in the work of th heart Bain (1950) states that three weeks in bed afte coronary thrombosis is quite long enough for an aged patient Gavey (1949) agrees that three weeks is th optimum period of rest after coronary thrombosis, and in some cases a commode may be used after one week

Patients with congestive cardiac failure or angi need not necessarily be kept in bed, but should allowed as much activity as their dyspnœa or pa permits

Hypertension—Some degree of hypertension, especial systolic, is a usual concomitant of old age, and no patie need be restricted in his activity or confined to b because of high sphygmomanometric readings alone

Hemiplegia—As soon as the period of shock followi a cerebrovascular accident is over, the patient mu become as active as possible Generally a week aft the onset of a hemiplegia, he may sit in a chair an start his exercises (Warren 1948b) Patients wi hemiplegia are often left in bed for many months befo their treatment is considered, by this time the lim are contracted, stiff, and painful to a degree for whi the paralysis alone cannot be blamed Even wh walking is never achieved the patient should re educated sufficiently to lead a "chair borne" existen and not put back to bed as "hopeless"

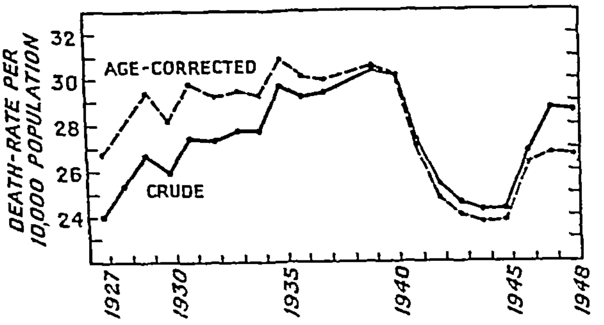
Arthritis—Even as little as 15° of limitation of exte sion of the knees, in the presence of restricted ank movement, will prevent a patient walking, and su minor degrees of deformity easily develop insidious beneath the bedclothes A long period in bed or encourages stiff painful joint deformities The resti of a joint with chronic arthritis may temporarily relie pain, but any later attempt to recover function w bring with it more pain than ever before, so rest or alleviates pain at the expense of function

Varicose ulcers—Although varicose ulcers may treated effectively by measures involving rest in b this is by no means essential In fact, most patien with varicose ulcers need not be admitted to hospi at all Treated at home by the Dickson Wright 'Elast plast' method, they should remain ambulant (Riv 1951), and this is very desirable, for they are a to retain their independence, and do not become a burd to their relatives

Neurological and orthopædic conditions—Many su conditions may ultimately prevent patients walking e g, late motor neurone disease, disseminated scleros tabes dorsalis, and ununited fractures of the lower lim For patients with such disorders rehabilitation will n be complete, but they should be encouraged to achie as much functional activity as possible They c usually be taught to get about in wheel chairs, and th live as full a life as possible within the limits of t disability Moreover, deterioration may be slow down, particularly in tabes

Hygienic Reasons

It is an almost universal custom to keep an incontine patient in bed Conversely, one often finds that elde patients confined to bed for long periods beco incontinent Very often the simple measure of gett such patients up suffices to remedy their incontinen For those who remain incontinent when sitting out bed there are two devices which prevent continu soaking of their clothes For men, the use of cond drainage is invaluable A condom, from which rubb tubing leads to a bottle, is fitted over the penis, and this way an intra urethral catheter, and hence t danger of a urinary infection, are avoided Wom incontinent of urine (and of fæces) can be sat on a commo chair throughout the day, an inflated rubber ring bei interposed to prevent pressure sores Fæcal incontinen often responds to regular enemata, by means of whi



g 1—Mortality from circulatory diseases in Norway in 1927-48 Standard population = population of Norway in 1940

om these diseases in Norway in the period 1927–48 927 was chosen as the first year to be studied because was then that Norway adopted the inter Scandinavian omenclature of causes of death However, in 1941 he Statistical Central Bureau, which handles the gures for causes of death, adopted the international omenclature It has therefore been necessary to egroup the diagnoses of causes of death for the years 941–48 so that they tally as closely as possible with he diagnoses according to the inter Scandinavian omenclature, this regrouping was made in accordance vith directions given by the Statistical Central Bureau Table I shows the synonymous diagnoses of the two omenclatures

MORTALITY FIGURES

Fig 1 shows that until 1940 there was a steady rise n mortality from circulatory diseases This rise was smaller with correction for age than without such correction—a feature which reflects the influence of the changing age distribution of the community From 1941 onwards there was a sharp fall in mortality, which was lowest in 1943–45 When the war ended mortality rose sharply The rise before the war, the decline during the war, and the subsequent rise are equally pronounced for each sex Expressing the mortality in 1938–40 as 100 (with correction for age), the comparable figure for 1943–45 was 78 7 for men and 78 6 for women, and for 1946–48 it was 87 3 for men and 88 1 for women

This decline began in the year that the inter-Scandinavian nomenclature was replaced by the international nomenclature We have concluded, however, that the change over can account for no more than a small part of the war time decline, and the subsequent rapid rise to the pre war level strongly suggests that the decline was real

TABLE I—CAUSES OF DEATH ACCORDING TO THE INTERNATIONAL AND THE INTER SCANDINAVIAN NOMENCLATURES

International	Inter Scandinavian
Pericarditis Endocarditis acuta et subacuta Endocarditis chronica (vitium organ icum cordis) Alii morbi cordis	Pericarditis Endocarditis acuta Endocarditis chronica (vitium cordis)
Myocarditis acuta et chronica degen eratio myocardii infarctum cordis	Myocarditis chronica
Arteriosclerosis universalis Arterio sclerosis cordis embolia thrombosis aneurysma arteriæ coronariæ angina pectoris	Arteriosclerosis
Embolia et thrombosis cerebri Con gestio pulmonum œdema embolia infarctum thrombosis pulmonum	Embolia
Aneurysma (sine aorta)	Aneurysma (sine aorta)
Gangræna	Gangræna senilis
Morbi venarum	Morbi venarum
Alii morbi organ circulat	Alii morbi organ circulat
Hæmorrhagia cerebri apoplexia	Apoplexia
Nephritis chronica	Nephritis chronica

Throughout the period from 1927 to 1948 the mortality from these diseases was highest in the oldest age groups Before the war the increase in mortality was confined to those over 60 years of age, and was greatest among those aged 80 years or more The decline during the war affected all age groups, but was greatest in the youngest groups Expressing mortality in 1938–40 as 100, then in 1943–45 it was 69 among those aged 20–39 years, 71 in those aged 40–59 years, 75 in those aged 60–79 years, and 89 in those aged 80 years or more (table II) The post war rise involved all ages over 40

In estimating the number of deaths from each separate cause between 1927 and 1948, we are hampered by the big changes during this time both in diagnostic criteria and in the system of statistical registration, and thus we must be most cautious in drawing conclusions Throughout the period, however, there were four main causes of death according to the inter Scandinavian nomenclature apoplexy, arteriosclerosis, chronic myo carditis, and chronic endocarditis (valvular disease of the heart) Chronic nephritis was a rather less important cause, and the other causes, both individually and collectively, played a minor part

TABLE II—MORTALITY IN 1943–45(a) AND 1946–48(b) RELATED TO MORTALITY IN 1938–40 WHICH IS EXPRESSED AS 100

Causes of death	Age-groups (years)									
	20–39		40–59		60–79		80 and over		All ages	
	a	b	a	b	a	b	a	b	a	b
Apoplexy			67	73	80	89	96	102	85	95
Arteriosclerosis			57	71	52	57	61	65	60	65
Chronic myocarditis			86	100	83	104	104	112	92	112
Chronic endocarditis	75	75	92	105	98	126	151	191	112	143
Chronic nephritis	50	50	47	43	51	46	50	41	50	46
All causes	69	58	71	77	75	88	89	97	81	93

During the whole period, apoplexy was the most important cause The mortality from this cause rose somewhat before the war, but only among those aged 80 years or more During the war there was a distinct, but not very well marked, decline for all age groups, and this was most evident in the youngest groups (see table II) Since the war there has been a definite rise in all age groups

Arteriosclerosis was for a long time the next most common cause, but from the middle 30s deaths from this cause declined considerably (fig 2) The decline was certainly not due to this disease having become more rare, it is attributable rather to the change in nomenclature, the main effect of which was an increase in notifications of death from chronic myocarditis, under which heading cardiac infarction is now registered (see table I) The decline in mortality from arterio sclerosis was accentuated during the war, but since then deaths from this cause have definitely increased

The greatest rise was in deaths from chronic myo carditis, the rise being most prominent in the oldest age group (fig 3) However, deaths from this cause also declined during the war, and after the war again rose

It is more difficult to judge mortality from chronic endocarditis because since 1941 this cause has been included with "other diseases of the heart" The figures from 1941 onwards are therefore misleadingly high (table II)

The most striking features of the chronic-nephritis figures (table II) are the conspicuous decline during the war and the comparatively moderate rise after the war doctor visiting the patient's home before admitting him to hospital will at once gain valuable information on which the whole treatment, course, and prognosis may be planned It is possible to see how the patient was managing to cope with his everyday life before his illness, or, in some cases, despite his illness Further, the relatives and others helping the patient will nearly always be at hand, and all the circumstances of the case can be discussed with them The relatives must never be given the impression that "granny is going away for good", the idea should be inculcated that the stay in hospital is only likely to be temporary, so that granny's room is not given up the moment she goes out of it Also the strain the illness is throwing on those helping can be judged This is an important point in assessing the necessity for admission Incontinence, bed sores, and restless confusion at night are all conditions imposing on the relatives a nursing burden that very few can support

Finally, it is useful from the standpoint of prognosis to know the details of the patient's home—the number of stairs, the situation of water and lavatory, the proximity of shops, and the willingness of relatives to help On these facts one may often predict whether the patient will be able to return home once hospital treatment is finished

4 *To make contact with general practitioners*—Whereas formerly the plight of many old people was brought to our notice by such bodies as the Family Welfare Association, we now find that general practitioners seek our help in the first instance The general practitioner is, we hope, reassured to feel that he is not having to deal unaided with his aged sick, who are often among his most exacting patients By discussion with him the patient's management can be unified, and the usual dichotomy between home care and hospital care avoided Moreover, the bond between the general practitioner and his local hospital, which is rapidly weakening elsewhere, is in this particular service strengthened

RESULTS OF HOME VISITS

The following figures show the care arranged as a result of 127 domiciliary visits between June 1, 1949, and May 31, 1950

The condition of some of these patients was investigated because they had been on the E B S "chronic" waiting list for some time When the visits were made a few were found to have been admitted elsewhere or to have died

Disposal		*No of patients*
Admitted immediately	to St Pancras Hospital	35
Admitted subsequently		20
Awaiting admission		4
Admitted elsewhere		18
Admitted elsewhere by our arrangement		5
Outpatient and domiciliary treatment		21
Nothing needed		11
Died		10
Refused treatment		3
Total		127

We do not intend, in this paper, to analyse these results at any length Two interesting points, however, may be mentioned Of the 55 patients admitted after being seen in their homes, 7 had conditions which we think might have been prevented by earlier medical treatment at home If these 7 patients had seen a doctor earlier they would not have reached the state of neglect which finally necessitated their admission to hospital Moreover, a further 9 patients need not have come into hospital if better social services—such as the provision of night sitters in, more domestic help, and a laundry service—had been available Another 4 patients were admitted while aged relatives on whom they were dependent were themselves undergoing hospital tre ment We should also like to emphasise that in no c was a patient's admission to hospital refused when medical condition was so serious as to demand it

Further Development of the Service

In order to prevent such states of affairs, and improve the geriatric service, Dr D H Geffen, medi officer of health of the borough, has started a St Panc Association for the Care of the Aged A club for people has also been formed, which a doctor from hospital is to attend, so that those who seek medi advice can readily obtain it Welfare workers visit old people who are incapacitated in their hom especially those living alone At the same time th will be a close link with the geriatric outpatient depa ment and the outpatient services of the hospital. Th measures, it is hoped, will ensure that the plight many old people will become known to the medi authorities earlier, and granny will not be found to ha "gone" while waiting for a hospital bed to be fou for her

We wish to acknowledge with gratitude the coöperation have received in our work from Dr D H Geffen, and fr Major F Hannan of the Emergency Bed Service

REFERENCES

Bain, C (1950) *Lancet*, i, 861
Bluestone E M (1949) Home Care New York
Cosin L Z (1949) *Brit J phys Med* 11, 162
Crockett, G S, Exton-Smith, A N (1950) *Ibid*, 13, 73
Exton-Smith A N Crockett G S (1949) *Lancet*, i 1016
Gavey, C J (1949) *Ibid*, ii 725
Howell T H (1950) Old Age London
Macdonald D M (1950) *Almoner*, 2, 227
Ogilvie W H (1950) *Brit med J* i, 683
Rivlin, S M (1951) Treatment of Varicose Veins, and th
Complications London.
Warren M. (1948a) *Brit J phys Med* 11 167
— (1948b) *Med Pr* 219, 396

MORTALITY FROM CIRCULATORY DISEASES IN NORWAY 1940-1945

Axel Strøm
M D Oslo
PROFESSOR
OF HYGIENE

R Adelsten Jensen
M D Oslo
ASSISTANT PHYSICIAN,
INSTITUTE OF HYGIENE

UNIVERSITY OF OSLO

In recent decades the proportion of deaths attribut to diseases of the circulatory system has increa greatly, and in civilised communities this group diseases is now the most important cause of dea Some of this increase is certainly more apparent th real, owing to the greater average length of life, mo attendance on doctors, and more accurate diagnos and there may have been some shift in diagnoses fro other groups to the circulatory group (Moriyam 1948, Woolsey and Moriyama 1948) But the possibil that there may also be a true rise in the mortality fr this group of diseases, and notably from diseases of t coronary arteries, cannot be dismissed

One explanation of the supposed increase in prevalen of these diseases is that this is connected with an increa consumption of foods containing fats and cholester If this is proved correct, ideas both on treatment a on the composition of an optimal dietary will profoundly affected

SCOPE OF INVESTIGATION

During the late war national dietaries were great changed in most European countries occupied by t enemy Food became scarce, and the shortage w primarily of foods containing fat and cholesterol the same time there was increased nervous stra which has also been held to provoke circulatory diseas In view of these facts we have investigated the mortali

TABLE III—MORTALITY FROM APOPLEXY, CHRONIC NEPHRITIS, AND ARTERIOSCLEROSIS PLUS CHRONIC MYOCARDITIS, IN URBAN AND RURAL AREAS IN 1938–40 AND 1943–45

Areas	Apoplexy		Chronic nephritis		Arterio sclerosis plus chronic myocarditis	
	1938–40	1943–45	1938–40	1943–45	1938–40	1943–45
rban						
No of deaths	2771	2467	693	351	2870	2042
Deaths per 10 000 pop per year	11 1	9 6	2 8	1 4	11 5	7 8
Relative mortality	100 0	87 1	100 0	50 0	100 0	69 4
ural						
No of deaths	6171	5437	1402	768	6225	5039
Deaths per 10 000 pop per year	9 8	8 3	2 2	1 2	9 9	7 7
Relative mortality	100 0	84 6	100 0	52 5	100 0	77 7

Lacking data on the sex and age distribution of the population in urban and rural areas, we have been obliged to limit our further comparisons to Oslo on the one hand and the whole of Norway on the other In Oslo before the war, the adjustment of the dietary to modern standards, with a plentiful supply of "protective" foods, was fairly far advanced, and the war time food restrictions were more severe in this city than in the country as a whole Table IV shows that, for both sexes and for all ages combined, the decline was somewhat *smaller* in Oslo than in the whole country This is not in keeping with the hypothesis that food restrictions lessened mortality, but close study of the table shows that the comparatively small decline in Oslo was chiefly among women aged 80 and over Among younger women and among men in all age groups, the decline was greater in Oslo than in the whole country, and we are tempted to ask Was not the factor responsible for the decline in mortality really more effective in Oslo than in the country as a whole, this feature being obscured by more accurate diagnoses in Oslo during the later years in the case of the oldest women ?

Comparing the causes of death, one by one, we find that the mortality from apoplexy and chronic nephritis declined somewhat less in Oslo than in the whole country, whereas mortality from arteriosclerosis plus chronic myocarditis declined almost equally in the two areas However, under the age of 80 the decline in mortality from arteriosclerosis and myocarditis was greater in Oslo than in all Norway Here again, the over-80 age group forces up the total figure for Oslo, and we must again ask whether more accurate diagnosis in this age group during the later years did not play a part, camouflaging a decline

TABLE IV—MORTALITY FROM CIRCULATORY DISEASES IN ALL NORWAY AND IN OSLO IN 1943–45 RELATED TO MORTALITY IN 1938–40 WHICH IS EXPRESSED AS 100

Age (yr)	Men		Women		Both sexes	
	All Norway	Oslo	All Norway	Oslo	All Norway	Oslo
40–59	80 9	68 1	73 0	54 7	76 2	63 1
60–79	77 6	66 8	75 7	76 5	76 9	72 1
80 +	87 8	85 0	91 3	107 3	88 9	99 5
All ages						
Direct calculation	83 3	81 1	83 8	90 4	83 4	86 5
Standardised calculation	78 7	75 4	78 6	84 5	78 6	81 1

The standard population is that of Norway in 1940 The direct calculation is computed from crude death rates and the standardised calculation from the standardised death rates

CONCLUSION

More definite conclusions are impossible Our investigations have yielded, not certain proof, but several pieces of evidence for the dietary hypothesis We have, moreover, been unable to find an alternative explanation of this remarkable decline

SUMMARY

Before the late war mortality from diseases of the circulatory system was rising each year in Norway This rise ceased during the war, and from 1941 to 1943–45 there was a well marked fall in mortality from these diseases Since the war there has been a rapid rise in mortality towards the pre war level

The war time decline in mortality was equally evident for both sexes and all ages, and it involved all the most important causes of death from circulatory diseases This also applies to the post war rise

The war time decline coincided with severe dietary restrictions The supply of calories was reduced, and this reduction was principally of foods containing fat, including those rich in cholesterol

REFERENCES

Moriyama I M. (1948) *Publ Hlth Rep, Wash* 63, 537
Strom, A (1948) *Acta med scand* suppl 214
Woolsey Th D, Moriyama I M. (1948) *Publ Hlth Rep, Wash* 63, 1247

LATERALLY PLACED CERVICAL DISCS

REVIEW OF TWELVE CASES

MICHAEL JEFFERSON
M A, B Sc, B M Oxfd, M R C P
LECTURER IN NEUROLOGY IN THE UNIVERSITY OF BIRMINGHAM

Stookey (1928) drew attention to certain syndromes resulting from pressure on the spinal cord or its attached roots by nodular tumours taking origin from the intervertebral discs in the cervical region These tumours, which he believed were neoplastic, he designated ventral extradural chondromas Arising usually in or near the midline they impinged on the cord from its anterior surface, thereby dislocating it backwards The clinical picture was commonly one of total cord compression, though at times it resembled that of the Brown Séquard syndrome Very rarely the tumour might be placed so far laterally as to damage nerve roots while leaving the cord unharmed

Earlier workers had described such tumours under different titles, such as chondromata, fibrochondromata, osteochondromata, enchondromata, chondrochordomata, and so on For example, Gowers (1886), discussing compression of the spinal cord, refers to enchondroma "springing from the bones or intervertebral tissues" as a possible cause, and Oppenheim (1911) mentions just such a case, in which a spinal chondroma had been removed during life More recently Elsberg (1916, 1925) and Adson (1925) reported finding a chondroma at exploratory operation in cases believed to be due to intrinsic spinal neoplasms

Following Stookey's (1928) paper, other reports soon began to appear Elsberg (1931) stated that he had found ventral extradural chondromata in 15 cases out of 200 explored for spinal tumour He drew attention to the important work of Schmorl (1929) and Andrae (1929) on the pathological anatomy of the intervertebral discs, and commented on the close histological resemblance between the ventral chondromata and intervertebral discs He felt nevertheless that there was not a complete identity, for the former showed unmistakable hyperplasia and in that sense were to be regarded as neoplasms, though of admittedly limited activity Bucy (1930) and Alpers et al (1933) had also taken them to be true neoplasms, but it shortly came to be widely accepted

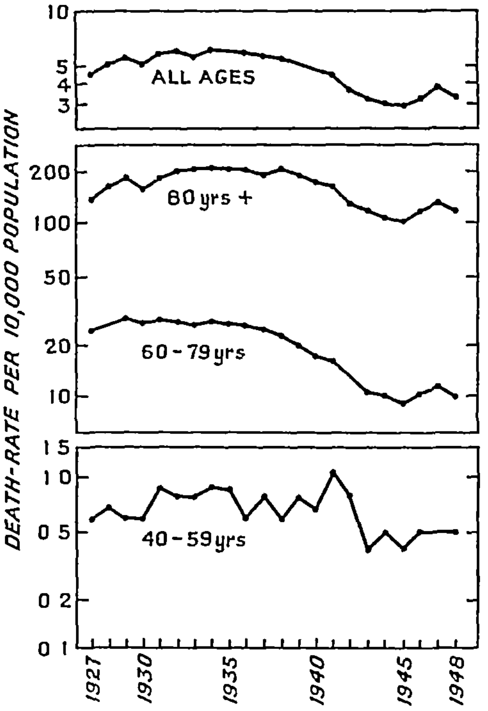


Fig 2—Mortality from arteriosclerosis in Norway in 1927-48, by age-groups

The following conclusions can be drawn

1 During the war one or more factors brought about a definite decline in mortality from diseases of the circulatory system in Norway These factors have in the main not operated since the war, and mortality has again risen
2 These factors affected all the most important causes of death from circulatory diseases, for both sexes and every age group

CHANGES IN DIET

It is natural to seek a solution in the dietary changes, which began before mortality from circulatory diseases started to decline Comparison of the dietaries of working class families in Oslo before and during the war (Strøm 1948) shows that during the war there was a considerable decline in the consumption of meat and meat products, whole milk, cream, margarine and other fats (but not butter), cheese, eggs, fruit and berries, sugar, and coffee On the other hand, there was a rise in the consumption of fish, skimmed milk, cereals, potatoes and vegetables The average calorie content of the food eaten fell from 3470 per man value per day in 1936-37 to 2850 in 1942-45 This led to widespread loss of weight The calorie reduction was chiefly in the fat component, which fell from 159 to 71 g per day, and the cholesterol content was reduced accordingly The average protein content of the diet fell from 115 to 93 g per day, while the consumption of carbohydrates rose from 395 to 429 g

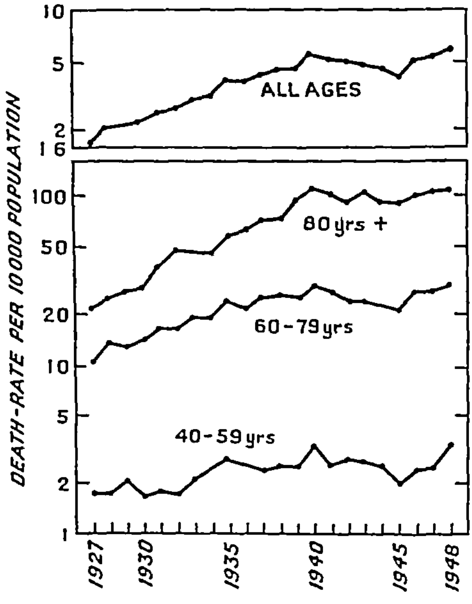


Fig 3—Mortality from chronic myocarditis in Norway in 1927 48 by age-groups.

We have obtained from the ministry of supplies data on the estimated annual consumption between 1938 and 1948 of the main sources of cholesterol—milk, cream, butter, cheese, and eggs These figures are approximate, but, as fig 4 shows, there is close correlation between the curve for consumption of fat contained in these foods and the curve for mortality from circulatory diseases, with correction for age We must, however, beware of regarding this evidence as decisive Similar correlation could undoubtedly be demonstrated between mortality and trends in other commodities, such as sugar, coffee, tobacco, textiles, and footwear, yet the last two of these can hardly have exerted any influence on mortality

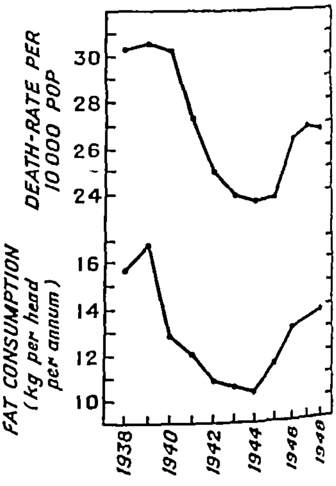


Fig 4—Mortality from circulatory disease, corrected for age, consumption of fat in form of butter, milk cheese and eggs

TOWN AND COUNTRY

If the changes in the dietary account for the lessened mortality, the decline should be greater in urban than in rural areas The food restrictions, though applying throughout the country, made themselves felt most in the towns Indeed, in some rural areas the diet of the population improved during the war, because the farmers consumed more of their own produce

To our surprise we found that the mortality declined just as much in the rural as in the urban areas In the period 1938-40 the mortality in the urban areas was 33 5 per 10,000 population, while in the rural areas 28 6 The corresponding figures for 1943-45 were 26 9 and 23 3 Expressing mortality in 1938-40 as 100, in 1943-45 it was 80 3 in the urban areas and 81 5 in the rural areas—an insignificant difference between the two areas

However, comparison of the behaviour of each cause of death in town and in country gives a different result. Table III shows that mortality from apoplexy declined somewhat less in the urban than in the rural areas, while mortality from chronic nephritis declined about equally in the two areas, but mortality from arteriosclerosis and chronic myocarditis (combined because of the change in nomenclature) fell much more in town than in country Expressing the mortality from these two diseases in 1938-40 as 100, in 1943-45 it was 69 4 in the urban areas and 77 7 in the rural areas It is precisely these diseases that might decrease most with reduction in the supply of fats and cholesterol

FUNCTION OF ERECTORES SPINÆ IN FLEXION OF THE TRUNK

W F Floyd
B Sc Lond, F.Inst.P, A.M I E.E
SENIOR LECTURER IN PHYSIOLOGY

P H S Silver
M.B Lond
SENIOR DEMONSTRATOR OF ANATOMY

MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON

Fick (1911) believed that the erectores spinæ relax when the vertebral column is fully flexed This means that when a man is bending down to the ground or sitting with a "round back"—both positions in which the vertebral column is in full flexion—the attitude of his spine is maintained by the ligaments and not by activity in his erectores spinæ At that time Fick's hypothesis was not supported by any experimental evidence, but the technique of electromyography has made it possible to study the action of the spinal muscles in a normal man, and we are now reporting some relevant electromyographic findings

METHOD

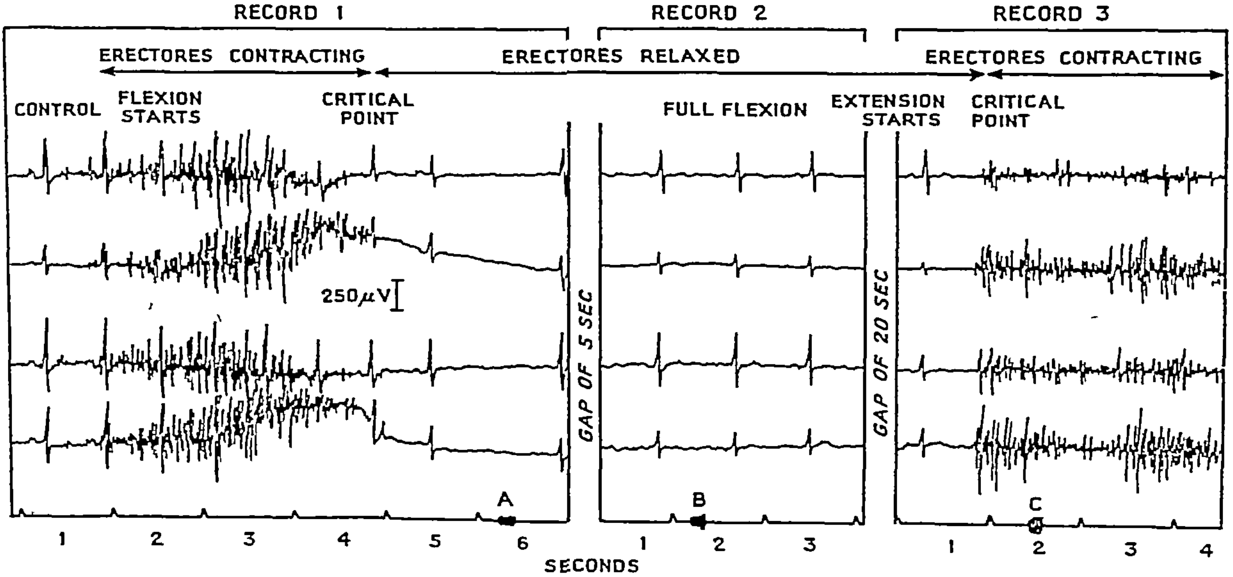
A six channel amplifier with ink-writing oscillographs was used (standard Ediswan electro encephalograph) and surface electrodes The method is painless and does not disturb the muscle in any way With this apparatus the action of three parts of the two erectores could be recorded simultaneously

When the upper parts of the erectores are studied the trapezius, rhomboids, &c, interfere with the record, unless special precautions are taken Nevertheless we have some evidence to show that the upper part of the muscle in the thoracic region behaves in the same manner as the lumbar part The lower thoracic and lumbar parts of the muscle are simpler to study experimentally, and the *thoracolumbar region, being the most mobile* part of the trunk, is the part most commonly injured and of special clinical interest

The electrodes were concave silver plates 1 cm in diameter, and were held in position with adhesive plaster on the skin over the erectores at the levels of the spines T10, T12, L2, and L4 When the muscle is in action, the sum of the motor unit action potentials in the vicinity is picked up by the electrodes and appears as a complex deflection on the recording pens This is a modification of the method of Floyd and Silver (1950) Deeper parts of the muscles were investigated with needle electrodes and cathode ray tube recording, but the findings were similar to those demonstrated with surface electrodes We have failed to demonstrate activity in the deep parts of the erectores—e g, in the multifidi—when the surface electrodes fail to show activity

RESULTS

The results of this study are summarised in the accompanying figure, which shows a simultaneous recording on four channels, the upper two from the left, and the lower two from the right erector spinæ All records are interrupted by the electrocardiographic complex, which is always present in electromyographic records of the trunk



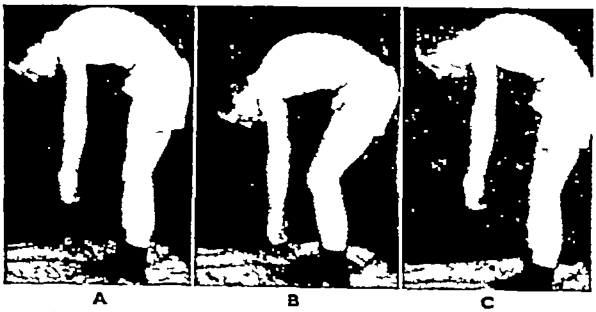
Electromyographic pattern of activity for thoracolumbar parts of erectores spinæ muscles. I from the left thoracolumbar region with the electrodes over the most prominent part of the erector spinæ opposite the spines of vertebræ T10 and T12. II from the left lower lumbar region with the electrodes similarly placed opposite the spines of vertebræ L2 and L4 III and IV, from corresponding areas of the right erector spinæ

Records 1 2 and 3 are three excerpts from a single tracing obtained while the man bent down to the ground and up again In the intervals between records 1 and 2 and between records 2 and 3 the tracing was identical with record 2. The photographs were taken at the times marked A B and C on the chart.

During the *control period the trunk was upright*, and the erectores show minimal activity for about 1 sec. The activity increases at the beginning of sec. 2 as the man bends forwards and it continues to increase for 2 sec. By the beginning of sec. 5 the erectores are relaxed again and photograph A shows the man's position immediately after relaxation

When the man remains bent down to the ground (photograph B) relaxation continues as shown in record 2. The contour of the back in photographs A and B is the same only the position of hips and knees is altered

The electrocardiographic complex occurs in all three records and is especially obvious in record 2 where there is no muscular activity



Record 3 shows that the erectores suddenly become active again when the trunk is raised Note that the erectores are not activated at the initiation of this movement only the hips extend Photograph C shows the man's position immediately after the erectores were reactivated; note the general similarity with photograph A.

defects that seem only the more genuine by conforming to the expected boundaries In my opinion sensory changes are almost always restricted to a slight diminution of acuity of pinprick and two point discrimination on the palmar surface only of the digital phalanges, which are the seat of subjective dysæsthesia, the rest of the dermatome area appears normal with ordinary clinical tests As regards the arm reflexes there is so much personal variety in their major segmental innervation that again no absolute constancy is found It is undoubtedly true that depression or abolition of the triceps jerk most often indicates a lesion of C7 root, and that the supinator and biceps jerks are impaired with lesions of C6 root However, the triceps reflex can be implicated at times with affections of either C6 or D1 rootlets, conversely, the supinator and the biceps reflexes may be altered by lesions of the C7 root

Straight radiography of the cervical spine in patients with radicular neuralgic complaints is not always helpful or reliable. Many apparently normal people over the age of 40 show radiological proof of degenerative arthritis in the neck (Davies 1945) These changes are usually most evident in the lower cervical spine, commonly from the level of C5 vertebral body downwards There is narrowing, often considerable, of the intervertebral disc (as seen in the lateral projection) at one or more of the interspaces C5–6, C6–7, and C7–D1, and the margins of the vertebral bodies adjacent to the affected space show sclerosis, with or without osteophytes Alternatively, in some cases the proliferative marginal changes are very pronounced, while loss of disc space is minimal or even absent In either group, however, the radiological appearances strongly suggest a pathological state of the relevant intervertebral discs The fact that the patients are symptom free is simply confirmation in the living of Schmorl's necropsy demonstration of the frequency of symptomless rupture of an intervertebral disc Conversely it is well known that the absence of radiological signs in the neck cannot be taken to mean that the intervertebral discs are healthy (Hanflig 1936, Spurling and Scoville 1944, Davies 1945) It follows that hypertrophic changes, even when associated with the grossest reduction of an interspace, in a patient with symptoms of segmental brachial neuralgia may be merely coincidental and do not necessarily define the level of the protrusion In the present cases 2 patients gave normal cervical radiograms, yet 1 of these was proved at operation to have a large disc protrusion at C5–6, and the other had clinical signs of prolapse at C6–7 Of the 10 remaining patients 7 had abnormalities at a single interspace, and 3 at two interspaces, in only 6 did the radiological signs coincide exactly with the level of root compression as determined clinically, myelographically, or operatively

Treatment

That effective treatment of segmental arm pain due to prolapsed disc is possible by simple measures is widely recognised but has recently been a little obscured by the flood of papers on its surgical cure The most generally useful method of treatment is plaster immobilisation of the neck, the cast being designed to include the head and upper chest to ensure really strict immobilisation Symptoms are almost invariably relieved by this procedure, sometimes with the most gratifying speed In the present series of cases only 1 patient had a partial relapse after removal of the collar Although he then did well with physiotherapy, such cases are often best treated by the provision of a leather collar which can be worn indefinitely Sling traction of the neck by Sayre's method has its advocates (Turner and Oppenheimer 1936, Hanflig 1943), but it means that the patient must be kept in bed lying on his back, whereas the patient in plaster can be fully ambulant and need not even remain in hospital Physiotherapy, in the form of massage, radiant heat, or diathermy with active graduated physical exercises, has a definite place in treatment where symptoms are not severe

Operation should properly be reserved for those whose symptoms are of long duration and are known to resist more modest courses of action In this context, however, it may be recalled that the morbid anatomy of protruded cervical disc often differs in some respects from that of protruded lumbar disc The lumbar nerve roots are usually injured by herniations of more or less discrete disc substance, whereas in the neck this is seldom so More often, as Elsberg emphasised long ago, there is an accompanying bony and fibrocartilaginous proliferation, arising from the margins of the vertebral bodies and from the annulus fibrosus, which may be the major element in causing stretching or compression of the nerve root From the surgical point of view it can be far more difficult, technically, to remove such a secondary tumefaction adequately, than to ablate the extruded disc matter itself Thus decompression of the root may perforce be incomplete, or transient, for there is no guarantee that further proliferation will not take place postoperatively Unfortunately it is impossible to gauge, before exploration, how far root damage is due to one factor rather than to the other These facts in themselves may be taken as an argument against too hasty recourse to surgery

Finally it has to be admitted that, although surgical treatment carries no more than the usual anæsthetic risk to life, operation does bring with it a small but definite hazard to the spinal cord, as Michelsen has pointed out, and as 1 of the 4 cases submitted to surgery in this series bears witness

SUMMARY

A brief historical introduction to the subject of cervical disc prolapse is given

The main features of 12 cases with radicular brachial neuralgia from lateral disc prolapse are summarised, their treatment indicated, and illustrative examples given

The levels of disc protrusion are discussed, the symptoms and signs of involvement of various radicles are considered, and the usefulness of radiological findings assessed

A plea for conservative treatment is entered

My thanks are due to Professor Cloake for allowing me to re-examine and make observations on his patients

REFERENCES

Adson A W (1925) *Northn Med* 24 309
Andrae, R (1929) *Beitr path Anat* 82 464
Alpers B J, Grant F C Yaskin J C (1933) *Ann Surg* 97, 10
Bradford F K Spurling R G (1941) The Intervertebral Dis
London
Browder, J Watson R (1945) *N Y St J Med* 45, 730
Bucy, P C (1930) *J Amer med Ass* 94, 1552
— Chenault, H (1944) *Ibid* 126 26
Davies H (1945) *Brit J Radiol* 18 1
Elliott F A, Kremer M (1945) *Lancet* I, 4
Elsberg C A (1916) Diseases of the Spinal Cord and its Membrane
Philadelphia
— (1925) Tumors of the Spinal Cord New York
— (1931) *Bull neurol Inst N Y* 1, 350
Foerster O (1933) *Brain* 56 1
Gowers W R (1886) Diseases of the Nervous System London
Hanflig S S (1936) *J Amer med Ass* 106 523
— (1943) *Arch Surg* 46, 652
Hawk W A (1936) *Brain* 59 204
Keegan J J (1947) *Arch Surg* 55 246
Kristoff F V Odom, G L (1947) *Ibid* 54, 287
Love, J G Walsh M N (1938) *J Amer med Ass* 111 396
— — (1940) *Arch Surg* 40 454
Michelsen J J (1947) *Surg Clin N Amer* 27, 1240
— Mixter W J (1944) *New Engl J Med* 231 279
Mixter W J Ayer J B (1935) *Ibid* 213 385
— Barr J S (1934) *Ibid* 211, 210
Oppenheim H (1911) Textbook of Nervous Diseases Edinburgh
Peet M M Echols D H (1934) *Arch Neurol Psychiat* 32 9
Schmorl G C (1929) *Fortschr Roentgenstr* 40 629
Semmes R E (1948) *Amer J Surg* 75 137
— Murphey F (1943) *J Amer med Ass* 121 1209
Spurling, R G Scoville W B (1944) *Surg Gynec Obstet* 78 350
Stookey B (1928) *Arch Neurol Psychiat* 20 275
— (1940) *Arch Surg* 40 417
Turner E L Oppenheimer A (1936) *Ann intern Med* 10, 427

FUNCTION OF ERECTORES SPINÆ IN FLEXION OF THE TRUNK

W F Floyd
B Sc Lond, F Inst.P, A.M I.E.E
SENIOR LECTURER IN PHYSIOLOGY

P H S Silver
M.B Lond
SENIOR DEMONSTRATOR OF ANATOMY

MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON

Fick (1911) believed that the erectores spinæ relax when the vertebral column is fully flexed This means that when a man is bending down to the ground or sitting with a "round back"—both positions in which the vertebral column is in full flexion—the attitude of his spine is maintained by the ligaments and not by activity in his erectores spinæ At that time Fick's hypothesis was not supported by any experimental evidence, but the technique of electromyography has made it possible to study the action of the spinal muscles in a normal man, and we are now reporting some relevant electromyographic findings

METHOD

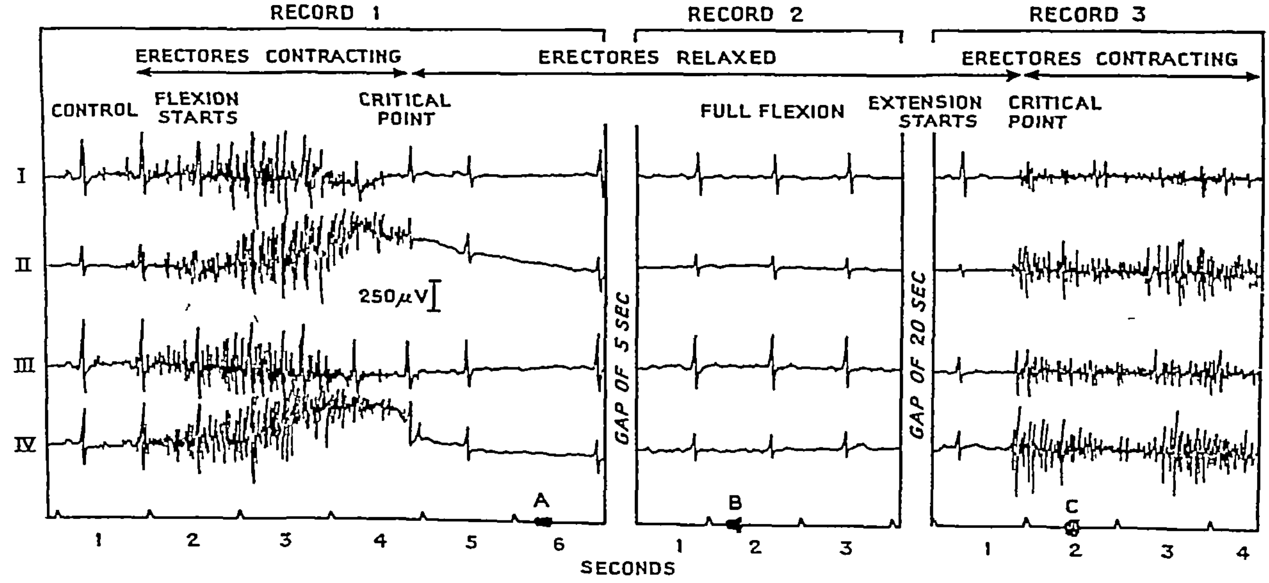
A six channel amplifier with ink-writing oscillographs was used (standard Ediswan electro encephalograph) and urface electrodes The method is painless and does not isturb the muscle in any way With this apparatus he action of three parts of the two erectores could be ecorded simultaneously

When the upper parts of the erectores are studied the trapezius, rhomboids, &c, interfere with the record, unless special precautions are taken Nevertheless we have some evidence to show that the upper part of the muscle in the thoracic region behaves in the same manner as the lumbar part The lower thoracic and lumbar parts of the muscle are simpler to study experimentally, and the thoracolumbar region, being the most mobile part of the trunk, is the part most commonly injured and of special clinical interest

The electrodes were concave silver plates 1 cm in diameter, and were held in position with adhesive plaster on the skin over the erectores at the levels of the spines T10, T12, L2, and L4 When the muscle is in action, the sum of the motor unit action potentials in the vicinity is picked up by the electrodes and appears as a complex deflection on the recording pens This is a modification of the method of Floyd and Silver (1950) Deeper parts of the muscles were investigated with needle electrodes and cathode ray tube recording, but the findings were similar to those demonstrated with surface electrodes We have failed to demonstrate activity in the deep parts of the erectores—e g, in the multifidi—when the surface electrodes fail to show activity

RESULTS

The results of this study are summarised in the accompanying figure, which shows a simultaneous recording on four channels, the upper two from the left, and the lower two from the right erector spinæ All records are interrupted by the electrocardiographic complex, which is always present in electromyographic records of the trunk



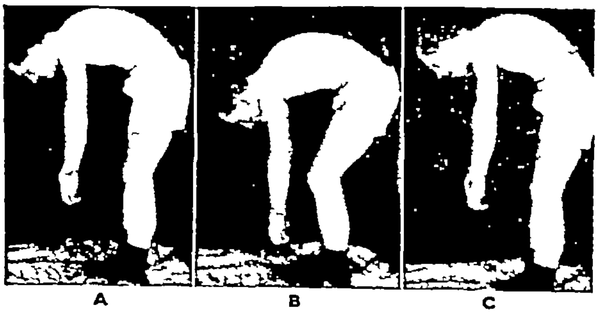
Electromyographic pattern of activity for thoracolumbar parts of erectores spinæ muscles I from the left thoracolumbar region with the electrodes over the most prominent part of the erector spinæ opposite the spines of vertebræ T10 and T12. II from the left lower lumbar region with the electrodes similarly placed opposite the spines of vertebræ L2 and L4 III and IV, from corresponding areas of the right erector spinæ

Records 1 2 and 3 are three excerpts from a single tracing obtained while the man bent down to the ground and up again In the intervals between records 1 and 2 and between records 2 and 3 the tracing was identical with record 2. The photographs were taken at the times marked A B and C on the chart.

During the control period the trunk was upright, and the erectores show minimal activity for about 1 sec. The activity increases at the beginning of sec. 2 as the man bends forwards and it continues to increase for 2 sec. By the beginning of sec. 5 the erectores are relaxed again and photograph A shows the man's position immediately after relaxation

When the man remains bent down to the ground (photograph B) relaxation continues as shown in record 2. The contour of the back in photographs A and B is the same; only the position of hips and knees is altered

The electrocardiographic complex occurs in all three records and is especially obvious in record 2 where there is no muscular activity



Record 3 shows that the erectores suddenly become active again when the trunk is raised Note that the erectores are not activated at the initiation of this movement only the hips extend Photograph C shows the man's position immediately after the erectores were reactivated; note the general similarity with photograph A.

During the 1st sec of record 1 the man was standing upright, and the trace shows minimal activity in the erectores About 1 sec from the beginning of the record the man began to bend forwards, and the vertebral column and hip joints began to flex The activity in the erectores increased considerably for about 2 sec as the man leaned further and further forwards, and the muscles acted as anti gravity muscles to prevent the trunk from falling forwards By the beginning of the 5th sec of record 1 the erectores relaxed once more, in spite of the fact that the man was leaning forwards The photograph A, to show the position of the trunk when the erectores were relaxed, was taken at the moment shown by the signal mark A in record 1, and this photograph shows approximately the critical position for relaxation of the erectores spinæ in this man when leaning forward The spine was now fully flexed, and the erectores were relaxed and no longer acted as antigravity muscles Their function, that of maintaining the position of the flexed spine, must therefore have been taken over by non contractile tissue Bending further downwards was achieved only by flexing the hip joints photograph B, taken at signal mark B in record 2 shows that the attitude of the back was unchanged, but the hips were more flexed than in photograph A, and the erectores were still inactive

When the man began to raise himself again to the upright position, the movement began by an extension of the hip joints During this phase of the movement, the last part of which is shown in the 1st sec of record 3, there was no activity in the erectores At the beginning of the 2nd sec, however, the erectores became active again Photograph C, taken at signal mark C in record 3, shows the man's position approximately at this moment when the erectores contracted The activity in the erectores continued until the man once more returned to the upright position Note the similarity between photographs A and C

DISCUSSION

It is known that posture is maintained by muscle action and that the function of ligaments is to limit the extremes of movement (Wiles 1935, 1937, 1949) During the initial stages of trunk flexion in standing the movement is controlled by the erectores spinæ, but, when the fully flexed position is reached, the ligaments alone are concerned with maintaining the position

In the position of full flexion in sitting—Andry's (1743) "bad posture"—the electromyographic studies show that the erectores are relaxed This position is often maintained comfortably for a relatively long time compared with the discomfort from a fully extended knee joint which becomes painful within a few minutes This difference we attribute to the presence of the elastic ligamenta flava in the spine, and we regard this phenomenon not as an exception to the generally accepted ideas about the ability of ligaments to stand strain indefinitely but as a special case in view of the presence of the specialised elastic ligaments However, we do not suggest that this position can be maintained indefinitely without discomfort, because certain people experience backache if they sit in the fully flexed position for a sufficient time—e g, patients sitting in bed with only the thoracic part of the vertebral column supported, motor car drivers, &c

Presumably stretch receptors in the ligamenta flava and other ligaments are stimulated when these ligaments are stretched, and the afferent impulses from the stretch receptors cause reflex inhibition of the erectores spinæ We do not at present possess a suitable laboratory animal for studying this reflex in detail, and have no direct experimental evidence to support this hypothesis For this reason, at present, we prefer to speak of the relaxation' rather than the reflex inhibition" of the erectores Such a reflex inhibitory mechanism, however, seems the most likely explanation

The phenomenon can be useful clinically in differentiating back pain originating in muscle and back pain originating in ligaments If a patient with pain in th back can be persuaded to bend to the fully flexed position pain from ligaments should get progressively worse whereas pain from muscle should improve (but wil not necessarily disappear altogether) This has bee demonstrated clinically in some cases

The main interest, however, lies in the insight whic we now have into the mechanism of injury to the annulu fibrosus This injury often occurs when the spine i flexed (Wiles 1949) In this position the strain of th trunk falls on the ligaments Owing to mechanical factor tensions of about 1500 lb (Bradford and Spurling 194 operate on these ligaments, plus any additional loa which is being carried The erectores spinæ do not shar in bearing the load The strain falls on the elasti ligamenta flava and the other less elastic ligament including the annulus fibrosus These relatively inelasti structures are most easily damaged Hence injury ca result in apparently trivial circumstances—e g, tying shoe lace (Jackson 1950) The patient need not hav been lifting or lowering a weight (apart from h body weight)

The relaxation of the erectores spinæ in the full flexed position is in no sense "the cause" of ruptur of the annulus fibrosus, it is only a contributory fac which can operate only in the circumstances described

SUMMARY

Observations are described which show that ful flexion of the spine is accompanied by relaxation of th erectores spinæ Consequently in this position furthe flexion is limited only by the intervertebral ligament It is thought that there are limits to the time for whic the ligaments can support this tension—e g, in sittin—just as there are limits to the tension which th ligaments can withstand in weight lifting

Some clinical implications are described in backach and the mechanism of rupture of the annulus fibrosus

REFERENCES

Andry N (1743) Orthopædia London vol I book 2 p 86
Bradford F K Spurling R G (1945) The Intervertebral Di- 2nd ed Springfield, Ill p 28
Fick R (1911) Handbuch der Anatomie und Mechanik der Gelenk Jena vol III
Floyd W F Silver P H S (1950) *J Anat Lond* 84 13
Jackson H (1950) *Proc R Soc Med* 43 638
Wiles P (1935) *Practitioner* 135 318
— (1937) *Lancet* 1, 911
— (1949) Essentials of Orthopædics 2nd ed, London

THIOURACIL COMPOUNDS IN THE PREVENTION OF PAROXYSMAL CARDIAC ARRHYTHMIA

H D RUSKIN
M B Witwatersrand, M R C P
MEDICAL REGISTRAR, JOHANNESBURG GENERAL HOSPITAL, I
CONSULTING PHYSICIAN, KRUGERSDORP HOSPITAL, TRANSVA

MANY drugs and manœuvres are advocated for termin ting a paroxysm of cardiac arrhythmia, but there a few methods of preventing such attacks Of these th best known are the administration of quinidine an digitalis (Linenthal and Freedberg 1949), dehydratio (Gold 1948), and sympathetic denervation (White a Smithwick 1941) Not uncommonly these measur fail, and, with quinidine, problems of dosage an toxicity may arise

Because thiouracil compounds are effective in th control of angina pectoris, and because the factors whic precipitate attacks of angina and the paroxysmal cardi arrhythmias are mainly identical, I thought that the drugs might prove of value in preventing the latter. Since October, 1949, thiouracil derivatives have been administered to seven patients, in all of whom previous treatment with quinidine and digitalis had been unsatisfactory, because it failed or caused untoward reactions. Four of these patients were women and three were men, their ages varying from 22 to 67 years. The frequency of the attacks varied greatly: in four cases these were a daily occurrence, in two cases there were several bouts each week, and in one case several each month. One patient was admitted to hospital because of the severity of the attacks, whereas the remainder were treated as outpatients.

Of the seven patients, two had apparently normal hearts, three had hypertensive heart disease, and two had rheumatic valvular disease. None showed evidence of thyrotoxicosis. Electrocardiographic proof of the arrhythmia was obtained in six cases, three had supraventricular tachycardia, two auricular flutter with auriculo-ventricular block, and two auricular fibrillation.

CASE REPORTS

Case 1.—A married woman, aged 60, was admitted to the Johannesburg Hospital on July 18, 1949, complaining of attacks of palpitation and breathlessness of 8 years' duration, which had become more severe and more frequent in the past few months, when they had been lasting for hours or even days. They were usually precipitated by exertion and by emotional disturbance.

The patient was very obese and distinctly cyanosed; pulse-rate 200 per min., and blood-pressure (B.P.) 170/110 mm. Hg. The electrocardiogram showed auricular flutter with 2 : 1 auriculo-ventricular block. The attack was terminated in 6 hours by means of gr. $^1/_4$ of morphine and gr. 6 of quinidine orally every 2 hours. Despite continued administration of gr. 6 of quinidine at 8-hourly intervals 2 days later she had a further paroxysm, with a ventricular rate of 140 per min. Digitalisation (digoxin 1 mg. intravenously, followed by 0·25 mg. daily by mouth), combined with gr. 3 of quinidine 3-hourly and later 2-hourly, did not prevent the paroxysms, which recurred with a ventricular rate varying from 140 to 220 per min. During some of the attacks she became extremely dyspnœic and cyanosed, with a fall of B.P. to 80/60 mm. Hg; and on several occasions when the attack had continued for more than 6 hours, congestive cardiac failure developed, necessitating strict salt restriction and the administration of mercurial diuretics. Additional remedies, such as intravenous procaine, aminophylline, and 'Neosynephrin,' were tried at different times in an attempt to terminate the more severe attacks, but gr. 3 of quinidine intravenously proved the most effective.

Between paroxysms the pulse-rate was 80 per min. and the B.P. 180/110 mm. Hg, the electrocardiogram revealed a normal rhythm with evidence suggestive of left ventricular hypertrophy. Radiologically the heart was enlarged with a hypertensive configuration.

On Oct. 10 treatment with methyl thiouracil—0·6 g. daily in three divided doses—was begun, while the patient continued to take gr. 6 of quinidine at 4-hourly intervals. Except for one mild attack, on the second day of this treatment there followed a period of freedom from attacks which lasted almost 3 months, the patient becoming ambulatory within a fortnight after having been bedridden for 8 weeks. The dose of quinidine was decreased until it was finally discontinued at the end of one month. The basal metabolic rate shortly after the start of treatment with methyl thiouracil was + 28%.

After her discharge from hospital on Dec. 2 the patient remained free of attacks until Dec. 23, when she was frightened by a flash of lightning and immediately developed a paroxysm. Several further attacks occurred during an emotional crisis occasioned by the sudden illness of her husband.

She was readmitted to hospital on Jan. 6, 1950. While taking methyl thiouracil, she continued to have mild bouts which were terminated promptly by quinidine intravenously in gr. 3 doses. The basal metabolic rate on Jan. 16 was +25% and the blood-cholesterol 270 mg. per 100 ml. The electrocardiographic pattern recorded during paroxysms was the same as before. Propyl thiouracil—0·6 g. and later 1·2 g. daily—was substituted for the methyl preparation. The attacks became still less frequent and more readily controlled by intravenous quinidine. On March 10, the daily dose of propyl thiouracil was reduced to 0·6 g. in three divided doses, and gr. 6 of quinidine was added to each dose. Since then the attacks have become infrequent and less severe, each responding promptly to gr. 3 of quinidine intravenously.

After administration of methyl thiouracil this patient, previously completely incapacitated and at times dangerously ill, was able to lead a comparatively normal life. While she is still not entirely free of paroxysms, they are now infrequent, mild, and easily controlled.

Case 2.—A 36-year-old housewife first consulted me in November, 1948, with a 28-year history of paroxysmal tachycardia. During the past few years the attacks, which had been occurring almost daily, were usually short and were often terminated by deep breathing or drinking iced water. They were usually precipitated by physical exertion or emotional stress and were more prone to come on before and during menses. Throughout her first pregnancy in 1947 she was completely free of attacks.

The patient was a well-developed, apprehensive young woman with no demonstrable cardiovascular abnormality other than persistent tachycardia at a rate of 100 per min. There was no clinical evidence of thyrotoxicosis and repeated basal metabolic rate determinations were normal. The B.P. was 130/80 mm. Hg, and radiologically the cardiac shadow was normal. An electrocardiogram obtained during an attack in 1945 showed supraventricular tachycardia at a rate of 160 per min. Between paroxysms, at rest and after exercise, the electrocardiogram was normal.

One year later—in 1949—her condition was unchanged. Treatment with propyl thiouracil in a daily dosage of 0·6 g., given in three divided doses, was started, and within a week the bouts of palpitation had ceased. After 8 weeks, owing to the severe nausea and vomiting of pregnancy, she discontinued the drug, and she then had a further four severe attacks within 2 weeks; on recommencing the drug the attacks again ceased. Because during a previous pregnancy she had been completely free from attacks it was decided to exclude the present pregnancy as the cause of her recent improvement. The drug was therefore again discontinued; but within 10 days there was an unusually severe attack lasting twenty-four hours followed by a series of shorter bouts at brief intervals. Within 5 days of recommencing propyl thiouracil in the daily dosage of 0·3 g., the paroxysms again ceased completely and have not recurred.

The prompt and complete control of the frequent paroxysms while taking propyl thiouracil, and their early recurrence on discontinuing the drug, are noteworthy features in this case.

Case 3.—A moderately obese 50-year-old man had been experiencing occasional attacks of palpitation for 7 years until 3 years ago when he began to have three or four attacks each week. The paroxysms, each lasting 6–8 hours, occurred usually at night when he was tired or worried, and could usually be terminated within a few hours by gr. 6 of quinidine.

In 1948 no clinical evidence of cardiovascular disease was found, the resting pulse-rate being 72 per min. and the B.P. 130/90 mm. Hg. Radiologically the cardiac shadow was normal, and the basal metabolic rate was − 5%. The electrocardiogram was normal at rest and after exercise, but during a paroxysm it showed auricular fibrillation. Quinidine in doses of gr. 6 thrice daily failed to prevent the attacks, and increase in the dosage was impracticable as it caused diarrhœa. Digitalis likewise proved ineffective.

In November, 1949, the paroxysms were occurring every night. Methyl thiouracil treatment was started with 0·6 g. daily in three divided doses. No improvement was noted after one month, so gr. 6 of quinidine was given with each dose of methyl thiouracil. The attacks ceased promptly. Propyl thiouracil was substituted for methyl thiouracil in the same dosage and quinidine was omitted, but the nocturnal paroxysms returned within a few days. Next, the total daily dose of propyl thiouracil was given at bedtime but no improvement ensued, so a single combined dose of 0·3 g. of propyl thiouracil with gr. 6 of quinidine was given at night. On this régime the attacks soon became fewer and shorter; but because paroxysms began to occur also during the daytime, 0·2 g. of propyl thiouracil was given with gr. 6 of quinidine every 8 hours, and within a few days the attacks ceased except for an occasional mild paroxysm.

This case demonstrates the value of the use of thiouracil together with quinidine for the control of paroxysmal auricular fibrillation, where neither alone has proved effective.

Case 4.—A 22-year-old man, a university student, was seen in 1947 because of infrequent attacks of rapid heart action, of one year's duration, each bout lasting 6–12 hours. He had had three attacks of rheumatic fever. Clinical and radiological examination revealed gross cardiac enlargement with mitral stenosis and aortic incompetence. The resting pulse-rate was 80 per min., and the B.P. 120/70 mm. Hg. Between attacks the electrocardiogram was normal except for the presence of mitral P waves. The paroxysms were relieved by the administration of gr. 9 of quinidine daily. During the ensuing months, the attacks became more frequent and severe; and in 1948, despite gr. 18 of quinidine daily, he was experiencing weekly paroxysms with a regular rhythm and a rate varying from 130 to 180 per min. To induce dehydration supplementary therapy was instituted with ammonium chloride, mercurial diuretics, and salt restriction; but these had no effect.

During 1949, his condition deteriorated: despite digitalisation and the daily administration of gr. 30 of quinidine, two attacks of arrhythmia were occurring each week. These attacks were longer, persisting for 6–12 hours, and were terminated only after three or four doses of gr. 9 of quinidine had been taken at hourly intervals. Invariably the omission of a single routine dose of quinidine was promptly followed by a paroxysm, which was sometimes precipitated by emotional stress or undue physical exertion. Nevertheless, he had been able to lead a fairly active university life.

Re-examination in December, 1949, showed a further increase in the size of the heart although there were no signs of congestive cardiac failure. An electrocardiogram during an attack showed auricular flutter (auricular rate 240, ventricular rate 90 per min.) with a varying auriculo-ventricular block resulting in a very irregular pulse.

While treatment with digitalis and quinidine continued, methyl thiouracil in daily doses of 0·6 g. was instituted. After 2 months, there having been no diminution in the frequency or severity of the attacks, propyl thiouracil was substituted and was given at the higher dosage level of 1·0 g., and later of 1·2 g. daily; but again no preventive effect was noted.

This case demonstrates the failure of thiouracil derivatives to prevent attacks of auricular flutter in a patient suffering from valvular heart disease of rheumatic origin with gross cardiac enlargement.

Case 5.—A 67-year-old widow, first examined in July, 1946, complained of daily attacks of palpitation lasting from a few seconds up to 8 hours, which began with the menopause in 1932. She was anxious and moderately obese, with a pulse-rate of 84 per min. and a B.P. of 190/110 mm. Hg. No clinical evidence of thyrotoxicosis was apparent. Orthodiascopic examination showed unfolding of the aorta and an increase in cardiac size due to left ventricular enlargement. The electrocardiogram was normal between attacks but showed the presence of auricular fibrillation during a paroxysm.

Quinidine was prescribed in a daily dosage of gr. 9 and the attacks became less frequent; but because of nausea the patient would not continue to take this drug. Digitalis was thereupon substituted, with subsequent improvement; but she discontinued this drug of her own accord.

In 1949 chronic lymphatic leukæmia was diagnosed. The paroxysmal auricular fibrillation had persisted, but the cardiovascular state had not deteriorated. Propyl thiouracil—0·6 g. daily—was prescribed in January, 1950. The effect was immediate, there being only one subsequent attack of fibrillation. Since the leucocyte count fell rapidly from 48,000 to 24,000 per c.mm., the dose of propyl thiouracil was reduced to 0·15 g. daily; and thereafter she had two more paroxysms. Since then she has remained completely free of bouts while taking 0·3 g. of propyl thiouracil daily; and the improvement in her emotional state, in her sense of well-being, and in her loss of heart consciousness has been most striking.

This case demonstrates the immediate and complete inhibition of very frequent paroxysms of auricular fibrillation by means of propyl thiouracil without quinidine or digitalis.

Case 6.—A 47-year-old merchant presented himself in January, 1950, with the complaint that for 2 years he had suffered from attacks of racing of his heart two or three times each month, following emotional stress. He experienced a sense of constriction of his chest when emotionally upset, but not on exertion. Clinical examination revealed pulsus bisferiens at a rate of 80 per min. with occasional extrasystoles, a blood-pressure of 110/80 mm. Hg, and the auscultatory signs of aortic stenosis and incompetence with mitral stenosis. On X-ray screening the heart was found to be enlarged owing to hypertrophy of the left ventricle. The electrocardiogram with the patient at rest showed a normal rhythm and evidence of left ventricular hypertrophy. Although no changes in the S–T segment took place after exercise, the precordial constriction was regarded as anginal. A tracing during a paroxysm revealed supraventricular tachycardia. Treatment with digoxin had failed to influence the symptoms.

Propyl thiouracil—0·6 g. daily—was prescribed, and within a few days the attacks of precordial constriction after excitement ceased. The patient has remained free of paroxysmal tachycardia for three months on a maintenance dose of 0·3 g. of the drug daily.

In this case paroxysms of arrhythmia were always infrequent; but since treatment with thiouracil was started the period of freedom from attacks has exceeded the duration of the natural intervals in the past.

Case 7.—A housewife, aged 43, was seen in July, 1948, with the history that for 3 years she had suffered from bouts of palpitation lasting $^1/_2$–2 hours, each bout starting and ending suddenly. The number of these attacks varied from several in a day to one in a month. She appeared anxious and tremulous, the pulse-rate being 96 per min. and the blood-pressure 180/110 mm. Hg, but no signs of thyrotoxicosis were evident. Screening of the heart showed prominence of the left ventricle and a normal transverse diameter. An electrocardiogram obtained between attacks revealed evidence of left ventricular hypertrophy. The basal metabolic rate was +14%.

During the ensuing 6 months she remained moderately free of paroxysms while taking gr. 9 of quinidine daily together with small doses of phenobarbitone. Subsequently, after several attacks lasting 6–8 hours, the dosage of quinidine was increased to gr. 15 daily. She apparently discontinued treatment; and when she was again seen in February, 1950, the paroxysms were occurring three to four times each week and were lasting up to an hour. The B.P. was 160/100 mm. Hg and the electrocardiogram was unchanged; but the cardiac shadow had increased by 0·5 cm. in its transverse diameter. Her family doctor witnessed an attack in which the pulse-rate was 120 per min. and the rhythm regular. Methyl thiouracil was prescribed in the daily dosage of 0·6 g.; and within a week she had become free of paroxysms except for an occasional bout lasting only a few minutes. Within a few days of her discontinuing the drug, because of an intercurrent infection, the bouts recurred; but they again ceased shortly after treatment was resumed.

Electrocardiographic proof of the nature of the arrhythmia was not obtained in this case, but the attacks were probably due to supraventricular tachycardia.

DISCUSSION

The rôle of emotional stress in precipitating extrasystoles, paroxysmal auricular tachycardia, and auricular fibrillation in individuals with normal or diseased hearts has been demonstrated by Duncan et al. (1949). In each of the cases in the present study there was obvious emotional disturbance with anxiety or depression, while in several there was clear evidence of the precipitation of attacks of arrhythmia by emotional stress. Emotional stimuli are thought to produce this effect through the autonomic nervous system and the endocrine glands—particularly the thyroid and adrenal (Katz et al. 1947).

Circulating adrenaline increases under a variety of circumstances, prominent among which are emotional stress and physical effort; and adrenaline tends to accumulate in the myocardium, on which it has an anoxiating effect (Green et al. 1942). This effect is augmented and intensified by thyroxine (Raab 1945a), while thiouracil diminishes the sensitivity of the normal heart to adrenaline (Raab 1945b). On the supposition that an excess of circulating adrenaline was responsible for precipitating attacks of angina pectoris this condition was successfully treated with thiouracil (Raab 1945c)

The rapidity with which some cases of angina pectoris or paroxysmal arrhythmia respond to treatment with thiouracil compounds, and the early relapses when such treatment is discontinued, suggest a similar mode of action of the drugs in these two conditions Possibly thiouracil exerts a direct effect on the myocardium and its action apparently does not depend on reduction in the rate of metabolism Where the drug proved effective the attacks were brought under control within a week, whereas where no response was noted within this period no effect was obtained from further administration of the drug

Of the seven patients studied in the present series, six had failed to respond adequately to quinidine In those patients that do respond to quinidine, the maintenance dose of this drug may perhaps be reduced by the addition of a thiouracil compound Conversely, where the response to thiouracil is complete, the dosage can probably be reduced by the additional administration of quinidine

Although this preliminary study has not definitely established the relative therapeutic value of the thiouracil compounds compared with quinidine or digitalis, further trials of the former drugs in the preventive treatment of the paroxysmal cardiac arrhythmias would appear to be warranted.

SUMMARY

Methyl and/or propyl thiouracil was administered in seven cases of paroxysmal cardiac arrhythmia

In four the paroxysms were completely prevented , in two they became less frequent and less severe , and in one there was no response

In two patients the combination of a thiouracil compound with quinidine was more effective than either drug alone

It is a pleasure to record my gratitude to Dr M. M. Suzman, of Johannesburg, for his help in the preparation of this paper

REFERENCES

Duncan C H. Stevenson I P Ripley H S (1949) *Psychosom Med* 12 23

Gold H (1948) *Amer J Med* 5 110

Green H D Wegria R Boyer N H (1942) *J Pharmacol* 76 378

Katz L N., Winton S S Megibow R S (1947) *Ann intern Med* 27, 261

Linenthal A. J Freedberg A. S (1949) *New Engl J Med* 241 570 612

Raab W (1945a) *J Pharmacol* 82 330

— (1945b) *J Lab clin Med* 30 774

— (1945c) *J Amer med Ass* 128 249

White J C., Smithwick R H (1941) The Autonomic Nervous System. London.

TRIAL OF β-NAPHTHYL-DI-2-CHLOROETHYLAMINE IN LEUKÆMIA, HODGKIN'S DISEASE, AND ALLIED DISORDERS

C GARDIKAS

M.D Athens M.Sc Ph.D Manc

REGISTRAR

JOHN F WILKINSON

M.D M.Sc Ph.D Manc , F.R C.P , F.R.I.C

PHYSICIAN AND DIRECTOR, DEPARTMENT OF HÆMATOLOGY

MANCHESTER ROYAL INFIRMARY

SINCE the war time investigations of Wilkinson, begun in 1942, on the cytotoxic effects of β chloro alkylamines and their therapeutic value in leukæmias and reticulosis (Wilkinson and Fletcher 1947) many groups of workers have reported similar observations

Widely different degrees of benefit have been described In our series of over a hundred cases of chronic leukæmia, Hodgkin s disease and allied disorders treated usually with the nitrogen mustard tris β chloroethylamine hydrochloride (' HN3) intravenously, satisfactory remissions have been obtained in at least 80% of the cases (Gardikas and Wilkinson, to be published)

Since the therapeutic effects of this type of substance have been confirmed, intensive search has been made for similar compounds that might exert more effective and more prolonged effects without their general cytotoxic effects At the same time, the greater convenience and safety in unskilled hands of substances suitable for oral administration would circumvent some of the inherent difficulties of the present intravenous treatment Burchenal (1948) has reported his experience with two nitrogen mustard derivatives—the 1 3 propane diamine NNN N tetrakis (2 chloroethyl) dihydrochloride (' SK136 ') and the 1 3 propane diamine 2 chloro NNN'N' tetrakis (2 chloroethyl) dihydrochloride (' SK137 ') Both products were tried in leukæmia but showed no advantages over the original nitrogen mustards Craver (1948) also has reported similar negative results Haddow et al (1948) prepared a series of aromatic nitrogen mustards, and one of these products, β naphthyl di 2 chloroethylamine (' R48 '), has been subjected to clinical trials by several groups of workers under the ægis of the Medical Research Council. The present report summarises our results in this therapeutic trial. Matthews (1950) has already reported the results obtained by another group in these trials

CLINICAL MATERIAL

Twenty five patients (eleven male and fourteen female) have been treated with R48 in this series There were eight cases of chronic lymphatic leukæmia, five of chronic myeloid leukæmia, two of acute leukæmia, seven of Hodgkin's disease one of lymphosarcoma, one of giant follicular reticulosis, and one of mycosis fungoides The patients were adults aged 17–69, except for one child aged 12 years

Diagnoses of the particular diseases were made by the usual clinical and pathological observations, including marrow biopsy in all cases, gland biopsy in all cases of Hodgkin s disease lymphosarcoma and giant follicular reticulosis, and skin biopsy in the case of mycosis fungoides

DOSAGE AND METHOD OF USE

β naphthyl di 2-chloroethylamine (R48) was given by mouth in divided doses three times daily to a total of 100–400 mg daily In chronic leukæmia the treatment was usually continued until the white cell count had fallen to about 20,000 per c mm , unless toxic symptoms necessitated an earlier discontinuance of the treatment In Hodgkin s disease or other reticuloses in which there was little leucocytosis before the start of the treatment, the criteria for the continuation of treatment were less rigid in view of our experience with intravenous therapy As a rule the treatment was continued until a white cell count of about 3000–4000 per c mm was reached, or until clinical symptoms and signs—e g , lymphadenopathy—had disappeared After preliminary trials had established a safe line of procedure, the patients, while under treatment with R48, were seen regularly at weekly or fortnightly intervals for blood-counts and clinical examination When the initial course had been completed and remission obtained, the treatment was discontinued, the patient still being followed up at fortnightly or monthly visits and further courses being given when required Attempts to introduce a maintenance dose in the hope that the duration of the remission could be prolonged considerably were not satisfactory, for we noted that usually a very small maintenance dose remained ineffective, whereas a larger one might produce leucopenia

TOXIC EFFECTS

In one patient with chronic lymphatic leukæmia treatment with R48 produced gross hæmaturia necessitating a discontinuance of treatment and another patient developed a moderate dysuria with microscopical hæmaturia , but both conditions cleared completely as soon as treatment was stopped A generalised purpuric rash developed in another patient without thrombocytopenia, but cleared satisfactorily In two other cases a transient maculopapular rash was noted, but further treatment was given uneventfully In no case was there any relation between the appearance of toxic symptoms and the daily or total dose of the drug administered

RESULTS*

Acute Leukæmia

Two patients with acute leukæmia were treated with R48 One was given total doses of 6 8 g in 17 days, and the other 21 6 g in 30 days The disease followed its usual course without any symptomatic relief or objective improvement

Chronic Myeloid Leukæmia

Five cases of chronic myeloid leukæmia were treated In two cases satisfactory clinical and hæmatological remissions were obtained the white cell counts fell from 139,000 to 13,600 per c mm and from 233,000 to 16,000 per c mm , the hæmoglobin values rose moderately , the general condition improved , and the feeling of well being returned Splenomegaly regressed considerably in one patient but remained almost unaffected in the other Both patients have had repeated courses , both are alive and well with fairly good working capacity 20 and 22 months after the institution of the treatment In the third case there was no improvement, though the white cell count fell from 158,000 to 42,000 per c mm , the patient died 2 months after R48 treatment was started, but by then he had reached a very advanced stage, having received treatment previously with urethane and other agents for 30 months The fourth case was in a boy, aged 17 with 6 months' history of subjective symptoms and presenting a typical clinical and hæmatological picture of chronic myeloid leukæmia He had had no previous treatment and was given R48 300 mg daily for 30 days—a total dose of 9 g At the end of this period the lymph node and splenic enlargements remained the same and the white cell count rose from 120,000 per c mm before treatment to 290,000 per c mm Subsequent treatment with intravenous tris β chloroethylamine produced very rapidly a good remission Another patient has had treatment for only a short time but is responding satisfactorily

Chronic Lymphatic Leukæmia

Eight cases of chronic lymphatic leukæmia were treated In two the results were satisfactory , good and long remissions were obtained, and both patients are well, with full working capacity, 22 and 20 months after the start of treatment with R48 Two other patients presented only remissions in their constitutional symptoms but no reduction of lymphadenopathy They have not yet returned to work 19 and 4 months since treatment with R48 was first given In three other patients, although the white cell counts returned to normal, the lymph node and splenic enlargements showed no changes, the anæmia did not improve, and the patients died 1, 1, and 9 months after treatment with R48 had been begun, without any apparent relief of the clinical course of the disease Another patient has had treatment for only a short time

Hodgkin's Disease

Seven patients have been treated In three the results were very good and the involved tissues regressed completely or almost completely The quantities required to produce these remissions were 5 g in 50 days, 45 g in 150 days, and 24 g in 60 days The general condition was good in all three cases and has remained good until now, 7, 20, and 24 months since treatment began Another patient was a woman of 45 who had previously been treated with intravenous tris β chloroethylamine for 2 years, which had produced such remarkably good results in this time that she had continued to run a very busy company and had regained her well being , she has gained so much weight as to render it very difficult to give intravenous therapy owing to poor access to veins, and so for over 12 months now she has been maintained on R48 with good response One patient has severe Hodgkin's disease involving soft tissues and skeletal structures and has responded quite well to intravenous therapy Owing to technical difficulty with her veins also, she has been put on to R48 orally, but the response is not very good In two other cases the treatment failed and both patients died after having received 3 3 g in 24 days and 3 4 g in 17 days

Miscellaneous Diseases

One patient with lymphosarcoma showed no improvement and died after having received 8 7 g of R48 in 3 days

In a patient with giant follicular reticulosis with generalised severe lymphadenopathy, treatment with R48 for 32 days (total dose 6 4 g) did not affect the disease On the contrary, the pre existing glands increased somewhat and additional glands became enlarged during the treatment Subsequently a course of tris β chloroethylamine was given, with considerable diminution in size of the lymph nodes

Finally, a case of mycosis fungoides treated with R48 is reported

Mrs A , aged 40, had noted a red patch on the left thigh for many years Since November, 1948, new red patches had appeared on both lower extremities A further spread had occurred in August, 1949, when similar lesions appeared on the forearms At the beginning of October, 1949, a vesicle appeared in the original lesion of the left thigh, and soon an ulcer formed Skin biopsy confirmed the diagnosis of mycosis fungoides Apart from the skin lesion the general condition was very good On the internal surface of the left thigh there was a tumour 5 cm in diameter, with a deep on oozing ulcer , the base of the ulcer was covered with necrotic greyish substance In addition, there were about a dozen patches (about ³/₄ in diam) located on both legs, both forearms, and the left breast The patches were red and well defined , few of them were infiltrated, and the skin over them was scaly After X ray irradiation the ulcer healed towards the end of December, 1949, but a month later a new ulcer appeared on the same thigh with the same characteristics as the first ulceration This time the patient was given a course of R48, starting on Jan 18, 1950, with a daily dose of 100 mg Two weeks later a definite improvement was already noticeable , the base of the ulcer began to dry and in two months, after 5 5 g of R48 had been given the ulcer was completely healed The hæmatological picture remained unaffected throughout the treatment (red cells about 4 500 000 per c mm , Hb 90–100%, and white cells 9000–13,000 per c mm)

The beneficial effects of nitrogen mustard in some cases of mycosis fungoides have been described by Henstell et al (1947), Osborne et al (1947), Philpott et al (1947), and Craver (1948)

DISCUSSION

Despite the small number and diversity of cases treated with R48, certain facts seem suggestive in the comparison of R48 with nitrogen mustard by intravenous administration

(1) The effect of R48 has been inferior to that of intravenous nitrogen mustard In our experience, in over 80% of patients with chronic leukæmia or Hodgkin's disease satisfactory remission follows the first course of nitrogen mustard injections The remission includes a return of the white cell count to normal, a rise in the hæmoglobin level considerable regression or total disappearance of enlarge

---

*Further details of the cases treated are given in a table obtainable on request from THE LANCET Office 7 Adam Street Adelphi London W C 2 ment of spleen or lymph nodes, and return of feeling of well being Our experience with R48 has not been equally satisfactory Remissions, when obtained, have been, in most cases, only partial The white-cell count returned to normal, but spleen and node masses either remained completely unaffected or were only partially obliterated

Thus a discrepancy between the effect of the treatment on the white cells, on the one hand, and on enlarged spleen and lymph nodes, on the other, was observed in most cases, and we consider this discrepancy to be a serious drawback—first because the leucocytosis constitutes only one element of the disease, and secondly because a fall of the white cell count necessitates discontinuance of treatment for fear of a severe leucopenia, and one has to wait until the white cell count rises before another form of treatment, such as intravenous nitrogen mustard, is given

(2) Whereas treatment with intravenous β-chloro alkylamine induces remissions quickly (usually within 20–30 days), the time in which R48 induced remissions varied widely The lengths of time between the beginning of the course and the restoration of the white cell count to normal in cases of chronic leukæmia were

Case no	*Type of leukæmia*	*No of days*	*Total dose (g)*
1	Lymphatic	21	6 6
2	Lymphatic	60	18 0
3	Lymphatic	34	13·6
4	Lymphatic	50	9 0
5	Myeloid	100	40 0
6	Myeloid	50	12 4

In cases of Hodgkin's disease the times from the start of treatment to the optimal regression of enlarged masses were

Case no	*No of days*	*Total dose (g)*
7	150	45 0
8	60	24 0
9	50	50 0

This wide variation in the length of the courses constitutes another drawback of R48 treatment, because it necessitates a long stay in hospital or frequent visits to the outpatient clinics

In brief, therefore, our impression from the therapeutic trial of R48 has been disappointing in many respects, for it does not seem to replace satisfactorily treatment with β chloro alkylamines On the other hand, R48 is effective by mouth in some cases and may therefore be of value in cases where intravenous administration is technically difficult or impossible

SUMMARY

Twenty-five patients were treated with β naphthyl di-2 chloroethylamine (R48) by mouth

Of eight patients with chronic lymphatic leukæmia, two responded to the treatment satisfactorily, in two the results were poor, and three died soon after the first course of treatment Another patient is still in the first course

Of five patients with chronic myeloid leukæmia, two showed a satisfactory response, one did not respond at all, one died soon after the first course was completed, and one is still in the first course

Of seven patients with Hodgkin's disease four responded well to the treatment, one did not respond at all, and two died.

No response was obtained in a patient with lymphosarcoma and in a patient with giant follicular reticulosis, one patient with mycosis fungoides responded well.

The results as a whole have been inferior to those obtained with the β-chloro alkylamines intravenously

This work was done during the tenure of the Sybil Mary Pilkington Fellowship by one of us (C G) and as part of a special investigation for the Medical Research Council, from whom a research grant was received Our thanks are due to Prof A Haddow for the supply of R48

References at foot of next column

ACROSCLEROSIS

T R LITTLER
M B Lpool, M R C P
MEDICAL REGISTRAR

S CANTER
M.D Lpool, D P.H.
PHYSICIAN TO THE DEPARTMENT OF DERMATOLOGY

BIRKENHEAD GENERAL HOSPITAL

ACROSCLEROSIS is relatively rare, and there is much conflict of opinion about whether it is an independent clinical syndrome or not

Acrosclerosis, scleroderma, sclerœdema adultorum, and dermatomyositis have been grouped together as dermatoscleroses, because hardening of the skin is common to all of them at some time during their course (O'Leary 1943) They have other features, such as (1) involvement of the body musculature (this occurs in acrosclerosis, scleroderma, and dermatomyositis, but not in sclerœdema adultorum), (2) a tendency for the cutaneous involvement to be self limited, the œdema subsiding and leaving various degrees of atrophy, (3) pigmentation, which may occasionally be marked, and (4) calcinosis, or deposition of calcium in the skin and muscles (this is common to all except sclerœdema adultorum)

Difficulty arises in establishing these four conditions as separate entities Scleroderma and dermatomyositis have been regarded as one and the same disease (Dowling 1940, Freudenthal 1940), and Sellei (1934) was much criticised for suggesting that acrosclerosis should be considered quite apart from scleroderma Sellei is supported by O'Leary and Waisman (1943), who tabulate the differences—especially in sex incidence, prodromal symptoms, sites of lesions, prognosis, and pathogenesis—between the two conditions

The cardinal feature of acrosclerosis is its invariable association with the Raynaud phenomenon, this is usually well established months or years before the skin lesions appear, but occasionally the vasomotor and cutaneous signs appear almost simultaneously O'Leary and Waisman (1943) suggest that sclerodactylia must be regarded as a potential complication of Raynaud's syndrome Raynaud himself noted the association of *acral cutaneous sclerosis with the vasomotor symptoms* which now bear his name

CLINICAL PICTURE

Changes in Skin

The cutaneous changes are essentially those of typical scleroderma, but they are confined to the distal parts of the extremities, the face, and the neck Over the fingers and hands the skin is thin, smooth, shiny, and tense The colour may be altered by pigmentary changes or by vascular disturbance, appearing coppery owing to increased pigmentation, or dusky or frankly cyanotic owing to impairment of circulation The fingers are characteristically rigid and held in a position of semiflexion and the skin over the dorsum of the hands is so adherent to the underlying structures that it is impossible to pick it up between the thumb and index finger These changes of the fingers and hands persist beyond the level of the wrists and merge into normal skin on the forearms Trophic changes—e g, ulcers—are commonly found on the backs of the fingers, and

---

DR. GARDIKAS, DR WILKINSON REFERENCES

Burchenal J H (1948) *Radiology* 50, 494
Craver L F (1948) *Ibid* p 486
Haddow A Kon G A R, Ross W C J (1948) *Nature Lond* 162 824
Henstell H H, Tober J N Newman B A (1947) *Blood* 2 564
Matthews W B (1950) *Lancet* i 896
Osborne E D Jordon J W Hoak F C Pschierer F J (1947) *J Amer med Ass* 135 1123
Philpott O S Woodburne A. R Waldriff G A. (1947) *Ibid* p 631
Wilkinson J F Fletcher F (1947) *Lancet* ii 540

patient developed a moderate dysuria with microscopical hæmaturia , but both conditions cleared completely as soon as treatment was stopped A generalised purpuric rash developed in another patient without thrombocytopenia, but cleared satisfactorily In two other cases a transient maculopapular rash was noted, but further treatment was given uneventfully In no case was there any relation between the appearance of toxic symptoms and the daily or total dose of the drug administered

RESULTS*

Acute Leukæmia

Two patients with acute leukæmia were treated with R48 One was given total doses of 6 8 g in 17 days, and the other 21 6 g in 30 days The disease followed its usual course without any symptomatic relief or objective improvement

Chronic Myeloid Leukæmia

Five cases of chronic myeloid leukæmia were treated In two cases satisfactory clinical and hæmatological remissions were obtained the white cell counts fell from 139,000 to 13,000 per c mm and from 233,000 to 16,000 per c mm , the hæmoglobin values rose moderately , the general condition improved , and the feeling of well being returned Splenomegaly regressed considerably in one patient but remained almost unaffected in the other Both patients have had repeated courses , both are alive and well with fairly good working capacity 20 and 22 months after the institution of the treatment In the third case there was no improvement, though the white cell count fell from 158,000 to 42,000 per c mm , the patient died 2 months after R48 treatment was started, but by then he had reached a very advanced stage, having received treatment previously with urethane and other agents for 30 months The fourth case was in a boy, aged 17 with 6 months' history of subjective symptoms and presenting a typical clinical and hæmatological picture of chronic myeloid leukæmia He had had no previous treatment and was given R48 300 mg daily for 30 days—a total dose of 9 g At the end of this period the lymph node and splenic enlargements remained the same, and the white cell count rose from 120,000 per c mm before treatment to 290,000 per c mm Subsequent treatment with intravenous tris β chloroethylamine produced very rapidly a good remission Another patient has had treatment for only a short time but is responding satisfactorily

Chronic Lymphatic Leukæmia

Eight cases of chronic lymphatic leukæmia were treated In two the results were satisfactory , good and long remissions were obtained, and both patients are well, with full working capacity, 22 and 20 months after the start of treatment with R48 Two other patients presented only remissions in their constitutional symptoms but no reduction of lymphadenopathy They have not yet returned to work 19 and 4 months since treatment with R48 was first given In three other patients, although the white cell counts returned to normal, the lymph node and splenic enlargements showed no changes, the anæmia did not improve, and the patients died 1, 1, and 9 months after treatment with R48 had been begun, without any apparent relief of the clinical course of the disease Another patient has had treatment for only a short time

Hodgkin's Disease

Seven patients have been treated In three the results were very good and the involved tissues regressed completely or almost completely The quantities required to produce these remissions were 5 g in 50 days, 45 g in 150 days, and 24 g in 60 days The general condition was good in all three cases and has remained good until now, 7, 20, and 24 months since treatment began Another patient was a woman of 45 who had previously been treated with intravenous tris β chloroethylamine for 2 years, which had produced such remarkably good results in this time that she had continued to run a very busy company and had regained her well being, she had gained so much weight as to render it very difficult to give intravenous therapy owing to poor access to veins, and so for over 12 months now she has been maintained on R48 with good response One patient has severe Hodgkin's disease involving soft tissues and skeletal structures, and has responded quite well to intravenous therapy Owing to technical difficulty with her veins also, she has been put on to R48 orally, but the response is not very good In two other cases the treatment failed and both patients died after having received 3 3 g in 24 days and 3 4 g in 17 days

Miscellaneous Diseases

One patient with lymphosarcoma showed no improvement and died after having received 8 7 g of R48 in 30 days

In a patient with giant follicular reticulosis with generalised severe lymphadenopathy, treatment with R48 for 32 days (total dose 6 4 g) did not affect the disease On the contrary, the pre existing glands increased somewhat and additional glands became enlarged during the treatment Subsequently a course of tris β chloroethylamine was given, with considerable diminution in size of the lymph nodes

Finally, a case of mycosis fungoides treated with R48 is reported

Mrs A , aged 40, had noted a red patch on the left thigh for many years Since November, 1948, new red patches had appeared on both lower extremities A further spread had occurred in August, 1949, when similar lesions appeared on the forearms At the beginning of October, 1949, a vesicle appeared in the original lesion of the left thigh, and soon an ulcer formed Skin biopsy confirmed the diagnosis of mycosis fungoides Apart from the skin lesion the general condition was very good On the internal surface of the left thigh there was a tumour 5 cm in diameter, with a deep oval oozing ulcer the base of the ulcer was covered with necrotic greyish substance In addition, there were about a dozen patches (about $^3/_4$ in diam) located on both legs, both forearms, and the left breast The patches were red and well defined , few of them were infiltrated, and the skin over them was scaly After X ray irradiation the ulcer healed towards the end of December, 1949, but a month later a new ulcer appeared on the same thigh with the same characteristics as the first ulceration This time the patient was given a course of R48, starting on Jan 18, 1950, with a daily dose of 100 mg Two weeks later a definite improvement was already noticeable , the base of the ulcer began to dry and in two months, after 5 5 g of R48 had been given, the ulcer was completely healed The hæmatological picture remained unaffected throughout the treatment (red cells about 4,500 000 per c mm , Hb 90–100%, and white cells 9000–13,000 per c mm)

The beneficial effects of nitrogen mustard in some cases of mycosis fungoides have been described by Henstell et al (1947), Osborne et al (1947), Philpott et al (1947), and Craver (1948)

DISCUSSION

Despite the small number and diversity of cases treated with R48, certain facts seem suggestive in the comparison of R48 with nitrogen mustard by intravenous administration

(1) The effect of R48 has been inferior to that of intravenous nitrogen mustard In our experience, in over 80% of patients with chronic leukæmia or Hodgkin's disease satisfactory remission follows the first course of nitrogen mustard injections The remission includes a return of the white cell count to normal, a rise in the hæmoglobin level, considerable regression or total disappearance of enlarge-

---

*Further details of the cases treated are given in a table obtainable on request from THE LANCET Office 7 Adam Street Adelphi London W C 2 ment of spleen or lymph nodes, and return of feeling of well being Our experience with R4S has not been equally satisfactory Remissions, when obtained, have been, in most cases, only partial The white-cell count returned to normal, but spleen and node masses either remained completely unaffected or were only partially obliterated

Thus a discrepancy between the effect of the treatment on the white cells, on the one hand, and on enlarged spleen and lymph nodes, on the other, was observed in most cases, and we consider this discrepancy to be a serious drawback—first because the leucocytosis constitutes only one element of the disease, and secondly because a fall of the white cell count necessitates discontinuance of treatment for fear of a severe leucopenia, and one has to wait until the white cell count rises before another form of treatment, such as intravenous nitrogen mustard, is given

(2) Whereas treatment with intravenous β-chloro alkylamine induces remissions quickly (usually within 20–30 days) the time in which R4S induced remissions varied widely The lengths of time between the beginning of the course and the restoration of the white-cell count to normal in cases of chronic leukæmia were

Case no	*Type of leukæmia*	*No of days*	*Total dose (g)*
1	Lymphatic	21	6·6
2	Lymphatic	60	18 0
3	Lymphatic	34	13·6
4	Lymphatic	50	9 0
5	Myeloid	100	40 0
6	Myeloid	50	12 4

In cases of Hodgkin s disease the times from the start of treatment to the optimal regression of enlarged masses were

Case no.	*No of days*	*Total dose (g)*
7	150	45·0
8	60	24 0
9	50	50 0

This wide variation in the length of the courses constitutes another drawback of R4S treatment, because it necessitates a long stay in hospital or frequent visits to the outpatient clinics

In brief, therefore our impression from the therapeutic trial of R4S has been disappointing in many respects, for it does not seem to replace satisfactorily treatment with β chloro alkylamines On the other hand, R4S is effective by mouth in some cases and may therefore be of value in cases where intravenous administration is technically difficult or impossible

SUMMARY

Twenty five patients were treated with β naphthyl di-2-chloroethylamine (R4S) by mouth

Of eight patients with chronic lymphatic leukæmia, two responded to the treatment satisfactorily, in two the results were poor, and three died soon after the first course of treatment Another patient is still in the first course

Of five patients with chronic myeloid leukæmia, two showed a satisfactory response one did not respond at all, one died soon after the first course was completed, and one is still in the first course

Of seven patients with Hodgkin s disease four responded well to the treatment one did not respond at all, and two died

No response was obtained in a patient with lymphosarcoma and in a patient with giant follicular reticulosis, one patient with mycosis fungoides responded well.

The results as a whole have been inferior to those obtained with the β-chloro-alkylamines intravenously

This work was done during the tenure of the Sybil Mary Pilkington Fellowship by one of us (C G) and as part of a special investigation for the Medical Research Council, from whom a research grant was received. Our thanks are due to Prof A. Haddow for the supply of R4S

References at foot of next column

ACROSCLEROSIS

T R Littler
M B Lpool, M R C P
MEDICAL REGISTRAR

S Canter
M.D Lpool, D.P.H.
PHYSICIAN TO THE DEPARTMENT OF DERMATOLOGY

BIRKENHEAD GENERAL HOSPITAL

Acrosclerosis is relatively rare, and there is much conflict of opinion about whether it is an independent clinical syndrome or not

Acrosclerosis scleroderma, sclerœdema adultorum, and dermatomyositis have been grouped together as dermatoscleroses because hardening of the skin is common to all of them at some time during their course (O'Leary 1943) They have other features, such as (1) involvement of the body musculature (this occurs in acrosclerosis, scleroderma, and dermatomyositis, but not in sclerœdema adultorum), (2) a tendency for the cutaneous involvement to be self-limited, the œdema subsiding and leaving various degrees of atrophy, (3) pigmentation, which may occasionally be marked, and (4) calcinosis, or deposition of calcium in the skin and muscles (this is common to all except sclerœdema adultorum)

Difficulty arises in establishing these four conditions as separate entities Scleroderma and dermatomyositis have been regarded as one and the same disease (Dowling 1940, Freudenthal 1940), and Sellei (1934) was much criticised for suggesting that acrosclerosis should be considered quite apart from scleroderma Sellei is supported by O'Leary and Waisman (1943), who tabulate the differences—especially in sex incidence, prodromal symptoms sites of lesions prognosis and pathogenesis—between the two conditions

The cardinal feature of acrosclerosis is its invariable association with the Raynaud phenomenon, this is usually well established months or years before the skin lesions appear, but occasionally the vasomotor and cutaneous signs appear almost simultaneously O'Leary and Waisman (1943) suggest that sclerodactylia must be regarded as a potential complication of Raynaud's syndrome Raynaud himself noted the association of acral cutaneous sclerosis with the vasomotor symptoms which now bear his name

CLINICAL PICTURE

Changes in Skin

The cutaneous changes are essentially those of typical scleroderma, but they are confined to the distal parts of the extremities, the face, and the neck. Over the fingers and hands the skin is thin, smooth shiny, and tense The colour may be altered by pigmentary changes or by vascular disturbance, appearing coppery owing to increased pigmentation, or dusky or frankly cyanotic owing to impairment of circulation The fingers are characteristically rigid and held in a position of semiflexion and the skin over the dorsum of the hands is so adherent to the underlying structures that it is impossible to pick it up between the thumb and index finger These changes of the fingers and hands persist beyond the level of the wrists and merge into normal skin on the forearms Trophic changes—e.g, ulcers—are commonly found on the backs of the fingers, and

---

DR GARDIKAS, DR WILKINSON REFERENCES

Burchenal J H (1948) *Radiology* 50 494
Craver L F (1948) *Ibid* p 486
Haddow A Kon G A. R Ross W C J (1948) *Nature Lond* 162 824
Henstell H H Tober J N Newman B A (1947) *Blood* 2 564
Matthews W B (1950) *Lancet* i 896
Osborne E D., Jordon J W Hoak F C., Pschierer F J (1947) *J Amer med Ass* 135 1123
Philpott, O S Woodburne A. R. Waldriff G A. (1947) *Ibid* p 631
Wilkinson J F., Fletcher F (1947) *Lancet* ii 540

the hands are cold and often moist A similar condition, but usually less severe, is found on the lower extremities Here abnormal skin usually merges with normal skin below the knee, and deformity is not as apparent as it is in the hands, but clawing of the toes and complete immobility of the ankles may ensue The feet are cold, yet sweating

Calcium may be deposited in the soft tissues, when this true calcinosis coincides with sclerodermatous skin changes it constitutes the Thibierge Weissenbach syndrome (Lindsay et al 1943)

Facial sclerosis may coincide with the appearance of sclerodactylia, or its onset may be delayed for some years (Ormsby and Montgomery 1948) As the condition develops, the skin of the face becomes drawn and taut, and all its mobility is lost The lips are thinned and radially furrowed, and small furrows may appear on the chin The nose is prominent, sharp, and pinched, giving the patient a rather "peaked" expression, because the skin is stretched taut over the underlying cartilage The skin of the eyelids is involved, and the process also spreads down the neck to the clavicles, where it gradually merges with normal skin covering the thorax and shoulders In the fully established case the face may appear like that of a corpse (Ormsby and Montgomery 1948), with pigmentation of the facial skin and telangiectasis, the coppery hue suggesting Addison's disease Pruritus is uncommon, the first symptom of any skin change is stiffness In contrast to true scleroderma, acrosclerosis does not progress but remains confined to the face and extremities for many years, it may partly regress even after twenty years (O'Leary and Waisman 1943)

Histologically the skin resembles that seen in diffuse scleroderma (O'Leary 1943) The first published notes on the histology of this type of cutaneous lesion were those of Crocker (1880), who found the epidermis unaltered except for pigmentation and the occasional presence of a few wandering leucocytes, the corium with papillæ less prominent than usual and with perivascular lymphocytic infiltrations, and the ducts of the glands obliterated by fibrous tissue Modern histopathologists have elaborated further, and attention is now focused on the collagen tissues of the body (O'Leary and Waisman 1943, Ormsby and Montgomery 1948, Klemperer et al 1942, O'Leary and Nomland 1930, Lewis 1940, Freudenthal 1940) The first sign is an œdema of the collagen bundles in the cutis, which causes swelling and separation of the bundles As the process continues, its sclerosing nature is made manifest, the bundles losing their fine fibrillary structure and becoming hyalinised and matted together Changes in the elastic tissue are variable, some workers recording absence of, or diminution in the number of, elastic fibres, whereas others find these normal or possibly thickened The vessels may show "cuffing" with mononuclear cells, chiefly lymphocytes, and plasma cells, and obliterative sclerosing changes chiefly involving the intima The epidermal changes are not well marked and are only secondary to the œdema and sclerosis of the underlying tissue The epidermis is thinned, and the rete pegs are flattened and fewer than normal (Freudenthal 1940) Subcutaneous fat is absent, and there is atrophy of the dermal appendages, the sweat glands being probably least affected (Ormsby and Montgomery 1948) Increased melanin pigmentation may be seen

Arthralgia

As well as the more obvious cutaneous manifestations, arthralgia and dysphagia may accompany acrosclerosis The arthralgia may, as with the Raynaud phenomena, be a premonitory symptom, but Sellei (1934) refers to changes in the joints, in addition to the flexion of the phalanges, which he terms pseudo arthritis deformans

Dysphagia

The dysphagia is of several kinds (1) difficulty in initiating deglutition, owing to the rigidity of the face, (2) difficulty in opening the mouth and in mastication, and (3) true dysphagia, which is present in over 10% of the patients (Ormsby and Montgomery 1948) A retrosternal burning sensation may be the first symptom of œsophageal involvement Involvement of the œsophagus can be detected by radioscopy or by endoscopy, including biopsy

The œsophageal changes are apparently identical with those of scleroderma and have been well described by Olsen et al (1945) Dysphagia in scleroderma was first recorded by Ehrmann (1903), who did an œsophagoscopy and noted changes in the œsophageal mucosa Schmidt (1916) reported on the radiological appearances after a barium swallow in a patient who had scleroderma with dysphagia although no lesion was detected in the œsophagus, fifteen minutes was required to allow for passage of the barium into the stomach, and the greatest delay was noticed at the cardia, where peristalsis was less than normal In 15 of 18 cases of acrosclerosis reported by Olsen et al (1945) conclusive radiological findings were demonstrable œsophageal dilatation with atony of the œsophageal musculature was noted in 6 (*peristalsis was decreased or absent in these*), apparent spasm at the cardia, with obstruction, was noted in 4, and the passage of barium was slower than normal The radiological diagnosis in all these cases was one of cardiospasm This finding supports the clinical manifestations, the patients often localising their symptoms to the lower end of the œsophagus Olsen et al (1945) observe that œsophageal lesions tend to occur in advanced cases of acrosclerosis, and therefore the prognosis is not good, and they correlate Raynaud phenomena and cardiospasm as being due to disturbance of the autonomic nervous system They suggest that some common ætiological factor exists in the vasomotor, dermatological, and œsophageal disturbances observed in acrosclerosis. The œsophageal dysfunction can be traced from simple delay in the passage of barium to stricture formation in the lower part of the œsophagus Histologically the picture is one of sclerosis of the connective tissues The submucosa is infiltrated with round cells, and there is well marked perivascular infiltration, with fragmentation of the elastic fibres and atrophy of the muscularis Finally, Olsen et al (1945) comment that œsophageal disturbances are extremely rare in patients exhibiting the Raynaud syndrome alone Lindsay et al (1943) have described œsophageal changes in scleroderma resembling those described by Olsen et al (1945) in acrosclerosis

Changes in Muscle

These are well known in scleroderma but are regarded as inconstant in acrosclerosis (O'Leary 1943) O'Leary and Waisman (1943) described interstitial inflammation and homogenisation of muscle bundles The histological picture in cases which show muscle involvement is similar to that found in generalised scleroderma, and has been fully described by Freudenthal (1940), it includes œdema, hyalinisation of fibres, abnormal staining reactions, and loss or blurring of cross striations The nuclei are often increased in number and are characteristically arranged in longitudinal rows along the sarcolemma (Freudenthal 1940) Infiltration is variable, when it occurs the cells are mononuclears—usually lymphocytes—with occasional plasma cells Occasionally the lymphocytes aggregate together, and these little colonies are called "lymphorrhages" These lesions were first described by Weigert (1901) in myasthenia gravis. Buzzard (1905) suggested the term "lymphorrhage" because the lymphocytic aggregations resemble capillary diapedesis of red blood cells Dudgeon and Urquhart (1926) have described these lymphocytic infiltrations in scleroderma Since germ centres are present, these "lymphorrhages" are thought by some workers to represent aberrant lymphatic tissue because of their high degree of differentiation

Changes in Lungs

Very rarely there are cystic changes in the lungs in scleroderma and acrosclerosis These cysts vary in size and may be found towards the periphery of the lung, away from the hilum, they are multiple, close together, and supported by narrow septa These changes are summarised by Dostrovsky (1947) as a sclerotic change in the lungs, followed by dissolution of the alveoli, with cyst formation

CASE RECORD

A childless married woman, aged 46, was first seen in January, 1947, with about a year's history of typical Raynaud phenomena Before this she had always enjoyed good health There was nothing relevant in her family history The Raynaud attacks were aggravated by exposure to cold, but they also occurred spontaneously, and during an attack the finger tips of both hands became cyanosed and numb The cyanosis began as a light bluish tint, later became a deeper blue, and gradually spread proximally towards the base of the fingers The condition subsided after a few minutes, and the colour of the skin became normal About a year after the onset of the Raynaud attacks the patient had noticed the onset of stiffness in the fingers and hands There had been no arthralgia, but the patient had speedily become incapable of moving her fingers or wrists Within a month the skin of her face, neck, and hands had become coppery and, as this pigmentation had subsided, all these areas had become sclerotic Lastly the feet had become affected, but never to the same extent as the other parts

On admission in February, 1947, the skin over the wrists, hands, and fingers was thin smooth, shiny, and tense The fingers and wrists were rigid, the fingers being held in a position of semi flexion and there was slight ulnar deviation at the wrists It was impossible to pinch up a fold of skin between the finger and thumb, and the affected skin traced up the arm, gradually merged into normal skin in the region of the elbows Frequent Raynaud phenomena were noted The facies was typical of the condition The skin was volved to a level just covering the shoulders and beneath oth clavicles, and then it merged almost imperceptibly ith more normal skin Similar, but less severe, changes ere present in both lower extremities and limited movement as present at both ankle joints Increased pigmentation f patchy distribution on the neck and on the dorsum of rists and hands was noted The blood pressure was 108/65 m Hg but no gross abnormality was detected in the espiratory, alimentary, or central nervous systems

Investigations—A blood count and the erythrocyte edimentation rate (E.S.R.) were normal The blood uric acid evel was 2 mg per 100 ml and blood calcium level 10 5 mg er 100 ml Radiography revealed no evidence of pulmonary isease, and there were no visible cervical ribs Radiograms f the hands showed sclerosis of the tips of the terminal halanges thought to be due to impaired blood supply

Treatment—In view of the Raynaud phenomena, sympa hectomy was considered, and the patient was seen in con ultation with Mr J Bagot Oldham, who reported I am ery doubtful about the advisability of sympathectomy here, ecause sclerodactyly is well marked, and this condition is ot benefited by sympathectomy I might try the effect f a paravertebral block but, unless its result is very striking, am opposed to any operation In view of these findings, the patient was discharged from hospital the treatment advised being physiotherapy, and thyroid extract by mouth This treatment was continued for some months without any material benefit to the patient, and she subsequently discontinued her attendance at the hospital and was not seen again until November 1948

On examination in November, 1948, there was no significant change in her condition, but she had become very distressed owing to her inability to perform any useful tasks

Readmission—She was readmitted in March 1949, the physical signs being the same as on her previous examination A new feature, not noted on her previous admission was the appearance of scars due to ulceration of the skin on the fingers Apart from these trophic changes the fingers were cylindrical and tapering at their tips, and were still held rigidly in a position of semi flexion, the extremities being cold and sweating

Investigations—A Wassermann reaction was negative A blood count showed slight hypochromic anæmia but no other abnormality The blood calcium level was 8 6 mg per 100 ml serum potassium 18 5 mg per 100 ml, serum sodium 294 mg per 100 ml, and blood urea 22 mg per 100 ml The Kepler factor was 33, suggesting that the patient had not got Addison's disease Plasma protein levels, albumin globulin ratio, E S R, and urine were normal A fractional test-meal showed hypochlorhydria Electrocardiography was normal Radiography of the chest showed no evidence of pulmonary disease, no cystic changes, and a normal cardiac outline After a barium swallow there was delay in passage of the barium through the œsophagus, but contractions were visible at all levels Radiography of the soft tissues showed no evidence of calcinosis, and of the wrists showed decalcification of bones only

Biopsy—Skin showed atrophy of the epithelium, with flattening and diminution in number of the rete pegs (papillæ) Some of the small blood vessels in the corium showed scanty perivascular lymphocytic infiltration Subcutaneous fat was practically absent, and the glands were compressed by sclerosis of the fibrous connective tissue Muscle showed non specific changes only

Treatment—The patient's repeated requests for treatment presented a difficult problem On rather empirical grounds, but supported by the low serum calcium levels, she was given calciferol 100,000 units daily, together with physio therapy, including inunction with bland oils One treatment with thorium X was given to the fingers This caused slight reddening of the skin, but neither the calciferol (which subsequently raised the serum calcium level to 9 8 mg per 100 ml) nor the thorium X produced any recognisable improvement

DIFFERENTIAL DIAGNOSIS

The earliest manifestations of acrosclerosis are the Raynaud phenomena, and until the skin changes appear the diagnosis of acrosclerosis does not arise Superficial examination may lead to a momentary confusion with rheumatoid arthritis Raynaud phenomena are seen in both conditions, and the ulnar deviation and position of flexion of the fingers are common to both Closer examination confirms, however, that the changes are not primarily articular or periarticular, and any deformities that have arisen are due to the contraction of the skin over the underlying tissues. In this way an entire limb may shrink in volume

Finally, acrosclerosis should be differentiated from diffuse progressive scleroderma (O'Leary and Waisman 1943) and poikilodermatomyositis (Bamber 1936) The salient points of difference between these four diseases are as follows

Acrosclerosis	*Diffuse progressive scleroderma*
(1) Occurs predominantly in females never attacks children	(1) Occurs equally in both sexes may occur in children
(2) Is always confined to the extremities and face and characterised by slow course and tendency to regress	(2) Often starts on the trunk and the whole body may be affected within three years
(3) Vasomotor phenomena are a prominent accompanying feature	(3) Vasomotor phenomena insignificant
(4) Trophic changes in distal phalanges and ulceration of skin are common	(4) Trophic changes incon stant
(5) Much muscle wasting and weakness uncommon	(5) Much muscle wasting and weakness may occur

Poikilodermatomyositis	*Rheumatoid arthritis*
(1) Occurs in both sexes may occur in children	(1) Predominates in females may occur in children
(2) Whole body may be affected may run a rapid course	(2) Affects the joints rather than the skin but can produce total immobilisa tion within three years
(3) Vasomotor phenomena especially in early stages of the disease inconstant	(3) Vasomotor phenomena inconstant.
(4) Trophic changes in distal phalanges uncommon	(4) Trophic changes uncom mon
(5) Much weakness and muscle wasting are a feature of the disease	(5) Weakness and muscle wasting are common

ÆTIOLOGY

Autonomic Nervous System

The vasomotor phenomena, together with the œsophageal dysfunction, have led many workers to discuss the autonomic nervous system as a factor in the cause of acrosclerosis (O'Leary and Waisman 1943, Olsen et al 1945, Castle 1923, Leriche et al 1937, Sequeira 1916, Robinson 1917) In support of this hypothesis is the occurrence of tachycardia, sweating, and trophic changes Collier and Wilson (1913) found that the cells of the intermediolateral tract were undergoing degeneration, and it is from these cells that the sympathetic fibres arise Knapp (1911) reports lesions in the anterior horn of the spinal cord, and Howell (1914) points out that the distribution of the lesions tends to be segmental, the bilateral symmetry of the lesions is particularly noticeable in acrosclerosis

Endocrine System

Dysfunction of the ductless glands has long been associated with sclerodermatous changes in the integument "Lymphorrhages" and atrophy of muscle fibres are found in thyrotoxicosis and myasthenia gravis Circumscribed scleroderma has been associated with both exophthalmic goitre and myxœdema (Sequeira 1916) The thyroid gland varies enormously in different cases, but thryoid atrophy appears more common than hypertrophy Cases are on record in which Addison's disease and acromegaly have occurred in patients also presenting sclerodermatous skin lesions Osler (1898) found treatment with thyroid extract in no way specific and giving no real benefit to the patient Trauma, mental shock, and infectious disease have all been incriminated as the cause of sclerodermatous skin changes The parathyroid glands have also been under suspicion (Cornbleet and Struck 1937), and Selye (1932) has produced scleroderma like lesions in young rats by injecting parathyroid extract In man calcium is apparently mobilised from the bones and deposited in the soft tissues, and hypocalcæmia may ensue

A widespread endarteritis has been held to be responsible for the skin lesions, emphasis being laid on the changes in the digital arteries in the accompanying Raynaud syndrome It should be recalled, however, that œsophageal disturbances and scleroderma like skin lesions are never found in a pure Raynaud syndrome, the skin over the fingers may ulcerate and be ischæmic, but the changes of acrosclerosis are not seen

Castle (1923) considered that the essential underlying cause was a combination of a disordered function of the internal secretory glands and an affection of the nervous system He felt that the balance between the different members of the endocrine system was so delicate that, if any particular gland failed, the remainder acted so as to minimise that failure He was therefore of the opinion that it was impossible to fix the responsibility for scleroderma and acrosclerosis on any one gland

We are of the opinion that, of the ductless glands, the suprarenal is the one that falls chiefly under suspicion Hyperpigmentation is an almost constant accompaniment of acrosclerosis and scleroderma Winfield (1904) recorded two cases which rapidly improved after the administration of desiccated adrenal gland Barlow (1939) reported a case of scleroderma associated with adrenal neoplasm

There is an important interrelation between the sympathetic nervous system and the ductless glands The connecting link is the chromaffin tissue, which is widely distributed in the medulla of the suprarenals, sympathetic ganglia and plexuses, ovaries, &c This chromaffin system is intimately related to the sympathetic system in embryological derivation and location (Foerster 1916) The medulla represents about 10% of the total volume of each suprarenal gland, and is derived, in common with the ganglia of the sympathetic, from the neural tube in early embryonic life It is thus epiblastic in origin, and is intimately related to the sympathetic nervous structures (McEwen 1916) The cortex, which forms 90% of the volume of each suprarenal gland, is mesoblastic, springing from the genital ridge and therefore having a common origin with the sex glands When one considers the considerable vasomotor instability in cases of hyperthyroidism, the frequent onset of acrosclerosis and scleroderma in females approaching the menopause, and the fact that menstruation may be arrested coincidentally with the appearance of such skin lesions, one can appreciate why Castle (1923) put forward the belief that it is difficult to pin the responsibility for this disease on any single ductless gland

The suprarenal glands are well known to be concerned with the metabolism of salt and water, and it is worth while recalling that the earliest histological feature of acrosclerosis is œdema, swelling up and separating the collagen bundles and fibrils Again, clinically, the skin changes of scleroderma are often preceded by œdema, which, as it subsides, heralds the onset of the characteristic "hide bound" skin Further, the suprarenals are linked closely with the sex glands, cessation of menstruation and other sexual changes occur in suprarenal virilism The connecting link between the suprarenals and the sympathetic nervous system is their common origin from the neural tube in early embryonic life

We are therefore of the opinion that dysfunction of the suprarenal glands is the chief ætiological factor in the pathogenesis of acrosclerosis The autonomic imbalance, hyperpigmentation, œdema, sex incidence, and associated sexual disturbances—e g, menstrual—can be explained fairly satisfactorily on this hypothesis, which links up with the ideas of earlier workers that the autonomic nervous system and the ductless glands are in some way responsible for the pathology of acrosclerosis.

TREATMENT

There is no satisfactory treatment for acrosclerosis. As noted above, acrosclerosis may partly regress, even after many years On general principles most workers recommend residence in a dry and equable climate, and a well balanced nutritious diet Protection of the fingers from trauma, including immersion in cold water, and the avoidance of psychological trauma are also advised. Physiotherapy is important, radiant heat and massage, together with active and passive movements, encourage the patient and should be tried in all cases

Surgical Treatment

This has been described by Leriche et al (1937), who have published their results with both sympathectomy and parathyroidectomy Their treatment by sympathectomy follows work done by Brown and O'Leary (1930), who studied microscopically the capillaries in the nail beds in acrosclerosis These workers concluded that there is a significant sympathetic hypertonia of the vessels in acrosclerosis Of 13 cases described by Leriche et al (1937), 5 were much improved and 4 somewhat improved They make it clear that the greatest improvement is to be expected in cases with antecedent Raynaud attacks and in which this phenomenon is a dominant feature

Because certain patients with acrosclerosis have hypercalcæmia, the same workers tried the effect of parathyroidectomy in selected cases. Selye (1932) has shown that the injection of young rats with parathyroid hormone produces a thickening of the skin similar to scleroderma Osteoporosis, calcinosis, hypotonia, and asthenia are said to be due to the hypercalcæmia in acrosclerosis Of another 13 patients subjected to para thyroidectomy 5 showed much improvement and 7 moderate improvement

Opotherapy

Thyroid extract (Robinson 1917), pituitary (Oliver and Lerman 1936), and suprarenal extracts have also been widely used in the treatment of acrosclerosis

Thyroid extract has long been used, although many workers, including Osler (1898) and Sequeira (1916), have been unable to benefit their patients by this means Since both hyperthyroidism and myxœdema have been recorded coincidentally with sclerodermatous skin lesions, it is difficult to postulate the effect of thyroid extract on the course of acrosclerosis

Winfield (1904) described much improvement in a single case given suprarenal extract, and Schwartz (1917) treated 6 cases with pituitary extract and reported improvement in all

Miscellaneous

Gold, anti histamine drugs—e g, 'Benadryl'—neostigmine methyl sulphate, T A B vaccine, thorium X, and calciferol have all been advocated but are only palliative Dysphagia due to œsophageal involvement may be relieved by the passage of sounds

SUMMARY

Acrosclerosis is defined, and its characteristic features are outlined

The literature is reviewed, and a further case reported

The ætiology is discussed, with special reference to the suprarenal glands It is suggested that these glands may ultimately be directly concerned in the pathogenesis of acrosclerosis

Treatment, both medical and surgical, is briefly surveyed

We wish to thank Dr Leslie Cunningham, senior physician to the Birkenhead General Hospital, for permission to publish this case

REFERENCES

Bamber G W (1936) *Brit J Derm* 48 648
Barlow G B (1939) *Arch Derm Syph Chicago* 39 1021
Brown G E O Leary P A Adson A W (1930) *Ann intern Med* 4 531
Buzzard E F (1905) *Brain* 28 438
Castle W F (1923) *Brit J Derm* 35 255
Collier J Wilson S A K (1913) *Proc R Soc Med* (sect neurol) 6 119
Cornbleet, T, Struck H C (1937) *Arch Derm. Syph. Chicago* 35 188
Crocker R (1880) *Trans path Soc* 31 315
Dostrovsky A (1947) *Arch Derm Syph Chicago* 55, 1
Dowling G B (1940) *Brit J Derm* 52 242
Dudgeon L S Urquhart A L (1926) *Brain* 49, 182
Ehrmann S (1903) *Wien med Wschr* 53 1097
Foerster O H (1916) *J cutan Dis* 34 1
Freudenthal W (1940) *Brit J Derm.* 52 289
Howell A (1914) *Practitioner* 93 604
Klemperer, P Pollack, A D Baehr G (1942) *J Amer med Ass* 119 331
Knapp P K. (1911) *Boston med surg J* 164 671
Leriche R Jung A. De Bakey M. E (1937) *Surgery* 1 6
Lewis T (1940) *Brit J Derm* 52 233
Lindsay, J R. Templeton F E Rothman S (1943) *J Amer med Ass* 123 745
McEwen P (1916) *J cutan Dis* 34 15
O'Leary P A (1943) *Canad med Ass J* 48 410
— Nomland R (1930) *Amer J med Sci* 180 95
— Waisman M (1943) *Arch Derm Syph Chicago* 47, 382
Oliver E L Lerman J (1936) *Ibid* 34 469
Olsen A M. O Leary P A Kirklin B R (1945) *Arch intern Med* 76 189
Ormsby O S Montgomery H (1948) Diseases of the Skin London
Osler W (1898) *J cutan Dis* 16 49
Robinson A S (1917) *Amer J med Sci* 154 657
Schmidt R (1916) *Dtsch med Wschr* 42 1023
Schwartz P (1917) *J cutan. Dis* 35 256
Sellei J (1934) *Brit J Derm* 46 523
Selye H (1932) *J Amer med Ass* 99 108
Sequeira, J H (1916) *Brit J Derm.* 28 31
Weigert, C (1901) *Neurol Zbl.* 20 594
Winfield J M (1904) *J cutan. Dis* 22 586

EFFECT OF IMPLANTATION OF TABLETS OF INSULIN ON NORMAL AND ALLOXAN-DIABETIC RABBITS

I C GILLILAND
M D Edin, M R C P,
MEDICAL TUTOR AND
SENIOR MEDICAL
REGISTRAR

M MENCER MARTIN
M B Durh M R C P
FORMERLY LUND RESEARCH FELLOW,
DIABETIC ASSOCIATION RESEARCH
REGISTRAR DIABETIC DEPARTMENT,
KING'S COLLEGE HOSPITAL

From the Postgraduate Medical School of London

THE present practice of giving insulin by injection has many obvious disadvantages, and alternate routes of administration have been repeatedly investigated The introduction of long acting protamine insulin by Hagedorn et al (1936) has helped to achieve a better control in many diabetic patients, without, however, solving the problem of the daily injections Oral, intra nasal, rectal, and vaginal routes, as well as subcutaneous implantation of pellets, have all been tried from time to time but have been abandoned because the insulin effect was either absent or inconstant and unreliable However, Vargas (1949) claims that tablets or pellets of protamine zinc insulin (P Z I), either alone or mixed with equal quantities of cholesterol, act for a long time when implanted subcutaneously

We report here experiments made to test the effectiveness of subcutaneous implants of pellets prepared according to the directions of Vargas (1949) and of two other similar types of pellets, prepared from P Z I and neutral P Z I (Kirkpatrick 1949) The criteria of activity were the effects on the blood sugar level of normal and alloxan diabetic rabbits and on the glycosuria of the diabetic rabbits

METHOD

Animals

Rabbits * were rendered diabetic (Duffy 1945) by giving them alloxan 200 mg per kg of body weight in a 4% solution intravenously, the solution being neutralised with sodium hydroxide immediately before use A 5% glucose drink was offered for the subsequent two days and given by stomach tube if hypoglycæmic symptoms were noted The subsequent progress of the rabbits was studied by estimation of body weight, blood sugar level, urinary excretion of sugar, and amount of urine excreted per twenty four hours After four days 2 5–7 5 units of P Z I was injected to prevent acidosis maintain nutrition, and keep the urinary loss of sugar at less than 10 g per day At intervals this insulin was omitted to assess the severity of the diabetes Both the extent of the uncontrolled glycosuria and the insulin requirements remained fairly stable from three weeks after the administration of alloxan

Preparation of Tablets

(1) Tablets of equal quantities of P.Z I and cholesterol estimated to contain 500 and 1000 units of P.Z.I were prepared for us under aseptic conditions by Burroughs Wellcome & Co according to the directions of Vargas (1949)

(2) Two tablets of P Z.I mixed with calcium carbonate were made by us in a hand tableting machine lent by Burroughs Wellcome & Co The P Z I powder was obtained by centrifuging commercial P.Z.I, passing the product through alcohol and acetone, and drying it in a vacuum desiccator over phosphorus pentoxide 20 mg of powder, the whole from a solution of 400 unit strength, was used for each tablet, mixed with 100 mg of calcium carbonate

(3) Tablets of neutral P.Z I estimated to contain 500 and 1000 units of insulin and tablets of equal quantities of neutral P.Z I. and cholesterol estimated to contain 1000 units of insulin each were prepared for us by Messrs Boots Pure Drug Co

---

* Male rabbits weighing 2000–3000 g were used in all the experiments and kept in metabolic cages They were fed on a standard diet of oats 60 g and bran 60 g moistened with water 200 ml green cabbage-leaves 60 g and carrots 100 g daily They were allowed water ad lib Rejected food was removed and measured at 6 P M each evening Fasting blood sugar levels were obtained before feeding at 10 A.M The fasting blood sugar levels of normal rabbits under these conditions were 91 7–S.D 18 7 mg per 100 ml (range 56–127 mg per 100 ml in 36 observations)

TABLE I—EFFECT OF P Z I -CHOLESTEROL IMPLANTS ON FASTING BLOOD SUGAR OF NORMAL RABBITS

Insulin given	None	P Z I and cholesterol implanted	Daily injections of P Z I (2 0–4 2 units)	None	P.Z.I and cholesterol implanted
Fasting blood sugar (mg per 100 ml) (mean S D or range)	91 7 ± 18 7	87 5 ± 18 8	43 7	74 8 (56–97)	72 9 (50–100)
No of rabbits No of observations	30 56	9 55	3 5	3 5	5 10
Duration of fast	12 hours			40 hours	

Implantation

A small area on the flank of the rabbit was shaved, and an incision was made about 0 5 cm long With sinus forceps the space between the skin and subcutaneous tissue was opened, and a tablet was dropped in In a similar way implantation into the abdominal wall was carried out, and on two occasions into the peritoneal cavity and into muscle The wound was closed with a single stitch This process had remarkably little disturbing effect on the rabbits

TABLE II—FASTING BLOOD SUGAR LEVELS OF 3 DIABETIC RABBITS IN 3 CONSECUTIVE 5 DAY PERIODS

—	First period	Second period	Third period
Insulin given	None	P Z.I and cholesterol implanted	Implant plus daily injection of P Z I (2 units)
Fasting blood sugar (mg per 100 ml) (mean S D)	367 ± 52 3*	364 ± 56 5	197 ± 77 4
No of observations	15	13	25

* Mean fasting blood sugar of another 15 diabetic rabbits—342 ± 62 2 mg per 100 ml (93 observations)

Estimations

Blood sugar levels were estimated according to the Harding modification of the Schaffer Hartman method (King 1947) on 0 1 ml of blood from the rabbit s ear vein Urinary sugar was estimated by the Meyer modification of Benedict s method (King 1947) on twenty four hour samples of urine

RESULTS

P Z I Cholesterol Tablets

Nine *normal rabbits* (table I) were implanted with tablets of 500–2500 units Further implants of 500 and 1000 units were given to two of these rabbits, and the rabbit which had been given 2500 units was given 10,000 further units after ten days' observation from the initial implant Neither in these rabbits nor in controls was any fall in fasting blood sugar noted over periods of thirty to a hundred days By contrast, daily injection of P Z I solution of 2–4 2 units of P Z I per kg of body weight about halved the fasting blood sugar

Tablets of 500, 1000, and 1500 units were implanted in three *diabetic rabbits* (table II) thirteen days after withdrawal of their maintaining daily insulin injections of 2 5–5 0 units The 1000 and 1500 unit tablets should, according to Vargas, provide absorption equivalent to more than any of the maintaining doses After five days without apparent response daily injections were resumed, and an immediate effect was observed on the glycosuria and fasting blood sugar levels (fig 1)

Of the 26 tablets used, 21 were recovered apparently intact three months after implantation Their weight was found comparable with that of unimplanted tablets (table III) An acid saline extract of one of these tablets crushed lowered the rabbit's blood sugar dramatically However, no insulin effect was demonstrable after implanting a crushed tablet, or after subcutaneous injection of a sterile water extract from a crushed tablet Burroughs Wellcome & Co assayed other tablets of the same batch and reported that three months after manufacture they still contained at least 80% of their stated insulin content They made an acid saline extract of the tablets and assayed its effectiveness by their standard mouse convulsive procedure with comparison with a known dose of insulin

P Z I and Calcium Carbonate Tablets

Observations were made with two of these tablets estimated to contain 400 units of P Z I., and a control tablet of calcium carbonate of equal weight in three diabetic rabbits Implantation was made after twelve hours' fast, which was continued for a further seven hours The standard régime was then resumed. The blood sugar levels observed are shown in fig 2 A fall is shown maintained for about four days

Tablets of Neutral P Z I

Six normal rabbits were implanted subcutaneously in the dorsal region with tablets of neutral P Z I Three rabbits were implanted with 500 units, and three with 1000 units each They were made to fast for seven hours, by which time the blood sugar level of all of them had fallen below 30 mg per 100 ml One rabbit was lost at this point, but five recovered after being fed After forty eight hours the morning blood sugar levels had returned to within normal limits

Three normal rabbits were implanted with 1000 unit tablets, one intraperitoneally, one into the abdominal wall, and one intramuscularly into the thigh Their blood sugar levels fell to below 30 mg in seven hours. The

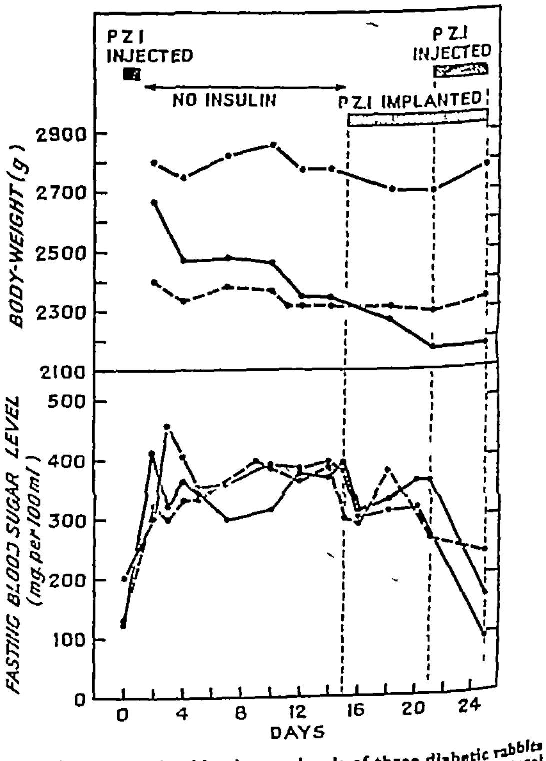


Fig 1—Weights and fasting blood-sugar levels of three diabetic rabbits on insulin, off insulin and after implantation of P Z I.-cholesterol tablets

rabbits were then fed The one which had had the tablet implanted into the abdominal wall died in hypoglycæmia The other two survived, and their blood sugar levels returned to normal in forty eight hours

Seven diabetic rabbits were implanted—three with 500 units each, and four with 1000 units each There was a pronounced effect on the blood sugar levels, which dropped to 70–130 mg per 100 ml within twenty four hours, with a corresponding improvement in the glycosuria After forty eight hours this effect was no longer apparent

All the tablets were removed ten days after implantation, but owing to their friable state only 3 were removed intact These showed on weighing an average loss of 4 6 mg , equivalent to a loss of 90 units of insulin

Histological examination of the site from which the tablets were removed confirmed the impression that these tablets had been “ encapsulated ” A considerable foreign body cell reaction was found round the tablets (fig 3)

One tablet was reimplanted into the same rabbit from which it had been removed, and it again showed a well marked insulin effect lasting for forty eight hours as before Saline extracts made from other removed tablets were also found to cause hypoglycæmia

Tablets of Neutral P Z I and Cholesterol

Three diabetic rabbits were implanted with one tablet each of the mixture of neutral P Z I and cholesterol estimated to contain 1000 units of insulin After implantation the rabbits were made to fast for seven hours, by which time the blood sugar levels of all three had fallen to below 80 mg per 100 ml The rabbits were then fed on the standard diet Within two days the fasting blood sugar levels were back to the original diabetic levels

TABLE III—WEIGHT OF IMPLANTS OF P.Z.I. AND CHOLESTEROL 2 MONTHS AFTER IMPLANTATION

Tablet size	Mean initial weight of 14 implanted tablets (mg)	Mean weight of tablets 3 months after implantation (mg)	
500 unit	91	83 3	(7)*
1000 unit	182	182·6	(14)*

* No of tablets

Two further implants of 1000 units each were given to these rabbits at weekly intervals with similar transient effects

After one to three weeks' implantation the tablets were removed and they were found to be 3–15 mg heavier than when implanted

Histological examination of the tablets removed showed encapsulation by a foreign-body reaction similar to that observed round the tablet of neutral P Z.I mentioned above

DISCUSSION

Parkes and Young (1939) experimented with rabbits, using 5 mg pellets of crystalline or low-zinc insulin containing 100 units each and found that they were absorbed within twenty four hours Mark and Biskind (1940) showed that pellets of crystalline zinc insulin with protamine effectively lowered the blood sugar of depancreatised dogs for as long as a hundred hours Their tablets, however, produced local reactions and they found a great variation in the rate of absorption of insulin from the tablets They found that the dried powder from commercial P Z I was ineffective Cutting et al (1941), also working with depancreatised dogs, found that pellets of zinc insulin with cholesterol, and pellets of zinc insulin with cholesterol and lecithin gave up their insulin slowly for as long as thirteen days

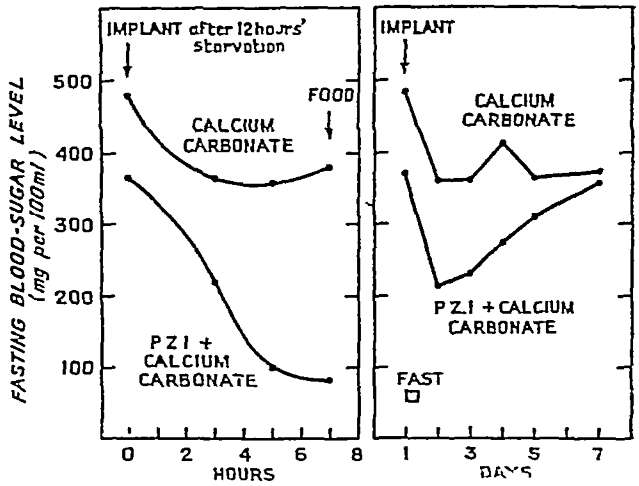


Fig 2—Fasting blood-sugar levels in diabetic rabbits after implantation of P Z.I and calcium carbonate and after implantation of calcium carbonate alone.

The irregularities of absorption, however, were too great, in their opinion, to justify clinical trials of such pellets Further experiments along the above lines were carried out by Parkes (1942) and McCullagh and Lewis (1942) confirming the above results and the fact that subcutaneous implants of insulin seemed too unreliable for clinical use

Vargas and Koref (1949) claimed that tablets or pellets of P Z I , either alone or mixed with an equal quantity of cholesterol were absorbed so slowly as to produce an insulin effect on the blood sugar levels of normal rabbits for as long as fifty days In alloxan diabetic rabbits the diabetic and associated metabolic changes were said to have been controlled for about a hundred days The same technique was then claimed to have been applied with success to human diabetes (Vargas 1949)

Such an important claim, even though it seemed to lack supporting data, nevertheless warranted testing We implanted tablets prepared according to the directions of Vargas (1949), but found no evidence of absorption, although the amounts implanted were in some cases considerably greater than those implanted by Vargas Our preliminary results with tablets of commercial P.Z.I alone were not very encouraging, for though the effect lasted for several days it was entirely out of proportion to the great number of units of insulin used Neutral P Z I was next tried in view of its stability and its better solubility at the pH of the body, but we could only show evidence of adequate absorption up

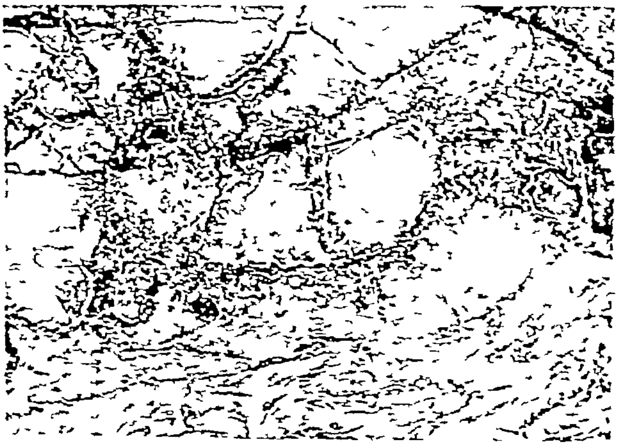


Fig 3—Neutral P Z.I tablet removed ten days after implantation The tablet is surrounded by macrophages. Note absence of new blood-vessels in surrounding tissues.

to two days Since we found insulin in the removed tablets and histological evidence that the tablets had been encapsulated, the problem clearly is to find a sufficiently insoluble insulin which will not be treated as a foreign body We were not able to do this

SUMMARY

Observations have been made of the effect of four types of insulin tablets implanted subcutaneously in 39 normal and 25 alloxan diabetic rabbits tablets of P Z I and cholesterol prepared according to the method of Vargas (1949), tablets of commercial P Z I powder mixed with calcium carbonate tablets of neutral P Z I, and tablets of neutral P Z I mixed with an equal quantity of cholesterol

No metabolic effects were noted from the P Z I and cholesterol tablets, whose weight three months after implantation had not altered Vargas's (1949) claim was thus not substantiated

After the implantation of P Z I tablets containing 400 units some insulin action was noted, lasting up to four days, but less than that obtained from the daily injection of 2 5 units of P Z I

An insulin action was noted from implanted tablets of neutral P Z I either alone or mixed with an equal quantity of cholesterol, but lasting only for about 2 days

Histological examination of the removed tablets showed encapsulation by a tissue reaction, which was evidently the reason for the short duration of their effects

We wish to thank Dr Russell Fraser for his help and advice, and Miss Shirley Looker, B SC, for her assistance with the biochemical estimations We are also indebted to the Diabetic Association for the grant of a Lund Research Fellowship to one of us (M M M) to do this work

REFERENCES

Cutting W C Morton M C, Cohn, R B (1941) *Endocrinology*, 28 679
Duffy F (1945) *J Path Bact* 57 199
Hagedorn H C Jensen B N Krarup N B, Wodstrup, I (1936) *J Amer med Ass* 106 177
King E J (1947) Micro Analysis in Medical Biochemistry London
Kirkpatrick N R (1949) *Proc Mayo Clin* 24 365
McCullagh, E P Lewis L A (1942) *J clin Endocrinol* 2 435
Mark J Biskind G R (1940) *Endocrinology* 26, 444
Parkes A S (1942) *J Endocrinol* 3 220
— Young, F G (1939) *Ibid*, 1 108
Vargas L (1949) *Lancet* i 598
— Koref O (1949) *J clin Endocrinol* 9, 818

LIVER FLUKE REMOVED FROM THE HUMAN COMMON BILE-DUCT

J S Ramage
M B Glasg, F R C S E
SURGEON, ROYAL INFIRMARY, STOKE ON TRENT

HUMAN infection with *Fasciola hepatica* is relatively rare The present case seems to be the second recorded instance of removal of a liver fluke from the common bile duct at operation * Manson Bahr and Walton (1941) reported the first case

A farmer's wife, aged 64, who lived in the country between Leek and Buxton, began in 1947 to have attacks of pain in the right upper abdomen Her doctor diagnosed subacute cholecystitis Between these attacks she was jaundiced on three occasions without much abdominal discomfort

Cholecystography revealed a large number of gall stones in the gall bladder A blood count showed no abnormality Eosinophilia was 1%

At *operation* in September, 1949, the gall bladder was found to be packed with stones the largest being about 1 in in diameter Cholecystectomy was performed The common duct appeared somewhat dilated, though palpation of it revealed no stones In view of the numerous attacks of jaundice, however, the common duct was incised to make certain that no stones were present Immediately a flat dark object, about 1 in long, escaped It was picked up on the end of a glass sucker and proved to be an adult *Fasciola hepatica* The liver was not enlarged The common duct was washed out with sterile water, but no more liver flukes were seen A gum-elastic bougie passed without obstruction into the duodenum. A medium sized T tube was left in the common duct

Convalescence was uneventful The bile from the T tube and fæces were frequently examined, but no adult or immature flukes were found The T tube was removed at the end of three weeks The patient has since remained in excellent health.

Dr A C Hallowes, M O H for Leek, has provided the following figures obtained from the local abattoir over a period of a year

Animals inspected	
Cattle	2359
Sheep	3498
Total	5857
Bovine livers affected either wholly or in part by liver fluke	1150
Sheep livers affected by liver fluke	392
Total	1542

Livers affected = 26 3 %

These figures reveal a relatively high proportion of infected animals in this area, and it is not surprising that a case of human infection should be encountered Yet, so far as I can ascertain, this is the first case observed in North Staffordshire

The source of infection in this case was probably watercress or lettuce Beds of both exist at the patient's farm

REFERENCE

Manson Bahr P, Walton, J (1941) *Brit J Surg* 28, 380

---

* Since this note was submitted for publication a further case has been published by F D Murphy and K G Pascall (*Brit. med. J* 1950, i 647)

SUBACUTE BACTERIAL ENDOCARDITIS CAUSED BY COAGULASE-NEGATIVE STAPHYLOCOCCUS ALBUS

Henry Matthew
M B Edin, F R C P E
ASSISTANT PHYSICIAN, EDINBURGH ROYAL INFIRMARY

COAGULASE is an enzyme, elaborated by certain potentially pathogenic organisms, which can bring about rapid clotting of blood Its production by staphylococci is commonly employed in the laboratory to differentiate pathogenic from non pathogenic organisms of that group

Since at least twelve different techniques can be used to demonstrate an organism's ability to produce coagulase, it is not surprising that results vary considerably (Williams and Harper 1946) Despite this discrepancy the test is now generally regarded as the best single method of determining the pathogenicity of a staphylococcus (Cruickshank 1937, Fairbrother 1940, Jordan and Burrows 1941, Smith and Hale 1944) Topley and Wilson (1946) stated that the production of coagulase had not yet been established as a certain indicator of potential pathogenicity, but Browning and Mackie (1949) hold that one of the most constant properties of pathogenic staphylococci is their power to coagulate citrated blood

Bacterial endocarditis is rarely caused by *Staph albus* An incidence of 1% is given by Thayer (1931) and Perry (1936), who do not say whether the *Staph albus* produces coagulase or not When it is pathogenic, that organism would be presumed to be coagulase positive For a coagulase negative organism to give rise to subacute bacterial endocarditis is, though not unknown (Cunliffe and Gillam 1943), very uncommon

Two consecutive cases of subacute bacterial endocarditis admitted to a medical charge both had a coagulase negative *Staph albus* as the infecting organism They were also remarkably alike clinically The method used for testing for coagulase was that of Fisk (1940)

FIRST CASE

A boy, aged 18, admitted to hospital on Nov 24, 1948, gave a history of acute rheumatic fever in 1946, when he had been off work for fourteen weeks He had made a full subjective recovery and had been working as an electrician in the mines and playing football energetically Three weeks before admission he had developed an influenza" like chill over the course of three days This had been manifested by flitting joint pains sore back, and pyrexia. The only other symptom has been the sudden onset of severe pain from time to time in the pulps of his fingers and toes The acute features of the illness had only lasted three days but had been followed by asthenia and general pallor, which had caused him to be referred to hospital for blood examination There was no recent history of acute staphylococcal skin infection although he had a chronic acneiform eruption of the face shoulders, and back.

On *examination* he was a well built pale youth with acne of the face and shoulders pulse rate 86, respirations 18 per min., temperature 99 4°F moderate clubbing of the fingers and toes Osler s nodes in two fingers The enlarged heart showed very free aortic regurgitation and mitral stenosis blood pressure 150/10 mm. Hg The tender spleen was enlarged to two finger breadths below the costal margin. A recent retinal hæmorrhage was evident and red blood-cells were found in the urine The sternum was tender Hæmoglobin 70% erythrocyte-sedimentation rate 40 mm in 1 hour

During *observation* for two weeks following admission, further pain of sudden onset in the finger pulps was complained of, and one more Osler s node appeared Red cells were found in the urine without any casts or significant quantity of albumin. The spleen extended a further two finger breadths below the costal margin

Blood-cultures—During this period seven blood-cultures were done, and all grew a coagulase negative *Staph albus*, not unexpectedly reported as a contaminant No other organisms grew the blood was withdrawn by four different operators using different cleansing agents for the skin Superficial and deep skin cultures did not grow organisms similar to the *Staph albus* repeatedly isolated from the blood However, pus from an acne pustule and blood obtained from sternal marrow puncture both gave a coagulase-negative *Staph albus* similar if not identical to that obtained by blood-culture The organism was penicillin sensitive with a coefficient of resistance of 1

Serological reactions suggested that the patient's serum had a higher antibody titre for this particular *Staph albus* than had pooled serum, and that the staphylococcus in question was more readily checked in its growth by the patient s serum than were a random selection of staphylococci

Diagnosis and Treatment—The clinical diagnosis of subacute bacterial endocarditis was self-evident It was considered that seven peripheral blood-cultures and one sternal marrow blood-culture all producing the same organism, together with the raised antibody titre indicated that despite the absence of coagulase production the organism was pathogenic and had secured a hold on the heart valves Treatment with penicillin 250,000 units three hourly (Christie 1949) was started. Two days later the blood-culture became negative and it remained so thereafter

The *clinical course* was not so straightforward. Three days after the start of treatment the patient complained of pain and tightness behind the sternum spreading up to the left shoulder The pain, persistent and crushing was accompanied by dyspnœa and aggravated by coughing or taking a deep breath It lasted with diminishing intensity for five days, during which time he was gravely ill The pulse rate rose to 120 but there was no alteration in the blood pressure Electrocardiographic recordings over this period suggested posterior myocardial infarction in the subepicardial layers On the fifth day after the onset of pain while the patient was still gravely ill pericardial friction became audible to the left of the sternum and was soon evident all over the præcordium With the appearance of the friction, his general condition improved, and he was soon free from pain and breathlessness and feeling stronger As friction gave way to muffled heart sounds the improvement continued, the spleen regressed, and the amount of hæmoglobin rose by 15% He experienced the sensation of well being and returning strength characteristic of the successfully treated case of subacute bacterial endocarditis On Jan. 1 1949, the nineteenth day of penicillin therapy he died suddenly while sitting on a bedpan.

Necropsy carried out four hours after death, showed a much distended pericardial sac containing over 600 ml of blood-clot and blood The heart was opened aseptically (Green 1939) and cultures of the heart blood and valves were made The blood was sterile, but the aortic valve yielded a coagulase negative *Staph albus* which proved later to be similar, if not identical to the organism previously isolated The grossly enlarged heart showed on naked-eye examination evidence of old standing rheumatic aortic and mitral disease There were also present acute rheumatic vegetations along with further vegetations suggesting bacterial endocarditis influenced by penicillin therapy

The spleen weighing 700 g was congested but showed no areas of infarction. There was no evidence of congestive heart failure in the liver Section of the mitral valve showed inflammatory changes characteristic of healing subacute bacterial endocarditis together with rheumatic vegetations in which Aschoff nodules of recent formation were demonstrable Organisms were seen beneath the fibrinous layers but it could not be definitely determined whether they were streptococci or staphylococci The myocardium showed a few recent Aschoff bodies in addition to numerous large areas of focal embolic myocarditis placed chiefly immediately below the epicardium This area beneath the epicardium was extremely vascular owing to intensive organisation and formation of new blood vessels The age of the infarcted areas was in keeping with the clinical features It was considered that rupture of certain of the vessels in this highly vascular area had caused the cardiac tamponade which was the immediate cause of death. Section of the kidneys showed focal embolic nephritis Two small areas of infarction of about three and six weeks old were found in the brain.

SECOND CASE

A man, aged 41 had had rheumatic fever at puberty and sustained endocardial damage His activities had not been restricted. and he served throughout the war at Dunkirk and the Malta siege in heavy anti aircraft batteries He had remained well till six weeks before admission when he noticed he was easily tired slightly short of breath and experiencing chills each evening There was associated arthralgia in several joints with swelling and redness of the left ankle Three weeks later he had painful pulps in two fingers which however might have been traumatic He had had no recent dental infection or attention, and no skin lesion.

On examination he was ill nourished and had a temperature of 101 6 F pulse rate 94 respiration 22 per min., slight sacral œdema, moderate fresh pink clubbing of the fingers and toes, no petechiæ and no splinter hæmorrhages His enlarged heart showed a free aortic regurgitation, the spleen was just palpable and there were no red cells in the urine or other evidences of embolic phenomena The sternum was tender electrocardiography showed left-sided hypertrophy, with a very prolonged P–R interval of 0 3 sec The erythrocyte sedimentation rate was 45 mm. in 1 hour, Hb 65% blood pressure 120/50

Blood-culture produced coagulase negative *Staph albus* on five occasions in five days No other organisms were isolated, and no similar staphylococcus was obtained from superficial or deep skin culture The coefficient of resistance to penicillin was 1

Diagnosis and Treatment—The clinical diagnosis was subacute bacterial endocarditis, due to coagulase negative *Staph albus* Treatment with penicillin 250 000 units three hourly was started on the same day because the patient was experiencing tightness in the chest pain in the left shoulder and breathlessness

Course—That evening pericardial friction was audible to the left of the sternum. Electrocardiography showed evidence of subepicardial damage on the anterior surface of the heart After a stormy forty-eight hours during which there was evidence of increasing congestive heart-failure and the pain and breathlessness persisted the patient began to improve and his symptoms lessened Digitalis started cautiously, had to be discontinued after forty-eight hours—6 grains of the powdered leaf had been given—owing to a great increase in the number of dropped beats and further prolongation of the P–R interval. Neptal produced a good diuresis, and as in case 1, the crisis seemed over Cachexia was rapidly dispelled and a feeling of well being induced, despite the persistence of pericardial friction over a wide area Blood-cultures became negative as soon as penicillin was started. The pericardial friction disappeared after twenty six days its place being taken by muffled heart sounds The spleen was no longer palpable after eighteen days penicillin. Improvement was maintained, and œdema was kept in abeyance with neptal 2 ml every third day On the thirty fourth day after starting penicillin the patient died suddenly without warning

Necropsy done twenty hours later showed the pericardial sac to be almost obliterated by old fibrous adhesions, but recent fibrinous pericarditis was also present The heart was opened aseptically, and heart blood and valves were cultured From the heart blood and the aortic valve a coagulase negative *Staph albus* corresponding to that previously isolated during life on blood culture was recovered The mitral valve showed the slight scarring of old rheumatic endocarditis The aortic valves showed long standing rheumatic changes and large vegetations typical of subacute bacterial endocarditis in addition to vegetations suggesting acute rheumatism The myocardium showed no macroscopic infarction The spleen was enlarged, weighing 440 g

Microscopically the place of the aortic valve was largely taken by thrombotic vegetations, but a few coccal organisms were seen their arrangement was quite haphazard, making it impossible to say whether they were staphylococci or streptococci The mitral valve showed old rheumatic scarring but also Aschoff bodies, which were assessed as having been present for about ten weeks—the duration of the present illness The pericardium showed low grade non specific subacute inflammation superimposed on old scarring No *bacteria were seen The myocardium contained Aschoff* bodies, many very old, some recent (about eight weeks old), besides very many areas of focal embolic infarction The infarcted areas were of varying ages, from weeks to 12–24 hours, they were considered sufficiently numerous and extensive to be the cause of sudden death

DISCUSSION

It is generally assumed that the production of coagulase indicates the pathogenicity of a staphylococcus

Two cases of subacute bacterial endocarditis are reported in which a coagulase negative *Staph albus* was repeatedly isolated from the peripheral blood, and in one patient from the sternal blood The cases demonstrated the classical features of subacute bacterial endocarditis, both clinically and post mortem The presence of pericarditis and pericardial effusion, however, calls for comment, because pericardial symptoms and signs are uncommon in endocarditis due to *Strep viridans* Thayer (1931), noting pericarditis in only 5 8% of cases of subacute bacterial endocarditis, draws attention to the importance of this sign in distinguishing bacterial from rheumatic endocarditis Pericarditis was present in 58% of his series of acute rheumatic endocarditis Matthew and Gilchrist (1949) also found pericarditis rare in subacute bacterial endocarditis, it being absent clinically in all 40 of their cases and present post mortem, and that only to a minor degree, in but 1 of 15 cases so examined

In the cases here reported the most striking clinical feature was pericarditis followed by pericardial effusion The pericarditis was demonstrated post mortem not to be rheumatic or infective in origin but the result of very numerous and extensive areas of myocardial infarction in the subepicardial region

Despite apparent improvement under penicillin therapy, both patients died after a remarkably similar clinical course A coagulase negative *Staph albus* was recovered post mortem from the heart valves in each case, and organisms, possibly staphylococci, were seen in the sections of the valves

There can be little doubt that the infecting organism in these two cases of subacute bacterial endocarditis was a *Staph albus*, despite its inability to produce coagulase It is therefore important that, when such an organism is repeatedly isolated from the blood of a *patient suspected to have subacute bacterial endocarditis*, it should not be discounted as a contaminant but regarded as the infecting organism, and its coefficient of resistance to penicillin should be estimated

In such cases a clinical course featuring multiple myocardial infarction with subsequent pericarditis with effusion may be anticipated

The presence of Aschoff bodies of recent formation further supports the view that subacute bacterial endocarditis is often superimposed on a valve in the presence of an active rheumatic carditis (MacIlwaine 1947, Matthew and Gilchrist 1949, Von Glahn and Pappenheimer 1935) rather than on an inactive chronic valvular lesion

The prognostic significance of such a relation between active rheumatic carditis and the superadded infection (Matthew and Gilchrist 1949) is also borne out, a fatal issue being common where the history suggests a concomitant acute rheumatic infection

SUMMARY

In two cases of subacute bacterial endocarditis the infecting organism was a coagulase negative *Staph albus* Pericarditis was a striking feature, being produced in both cases by multiple areas of focal embolic infarction of the myocardium The myocardial damage was sufficiently extensive to be the cause of death

The patients were under the care of Dr A Rae Gilchrist, to whom thanks are expressed for guidance in the preparation of the report *The bacteriological investigations were* made by Dr T B M Durie, and the autopsies by Dr Rhaney

REFERENCES

Browning C H, Mackie T J (1949) Textbook of Bacteriology London
Christie R V (1949) *Brit med J* ii 950
Cruickshank R (1937) *J Path Bact* 45 295
Cunliffe A C Gillam G G (1943) *Lancet* ii 355
Fairbrother R W (1940) *J Path Bact* 50 83
Fisk A (1940) *Brit J exp Path* 21 311
Green C A (1939) *Ann rheum Dis* 1 86
Jordan, E O Burrows W (1941) Textbook of Bacteriology 13th ed Philadelphia
MacIlwaine Y (1947) *J Path Bact* 59, 557
Matthew H Gilchrist A R (1949) *Edinb med J* 56 *Trans med Chir Soc* 128 25
Perry (1936) Bacterial Endocarditis Bristol
Smith W, Hale J H (1944) *Brit J exp Path* 25, 101
Thayer W S (1931) *Edinb med J* 38 237
Topley W W C, Wilson G S (1946) Principles of Bacteriology and Immunity 3rd ed London
Von Glahn W C, Pappenheimer A M (1935) *Arch intern Med* 55 173
Williams R E O, Harper G J (1946) *Brit J exp Path* 27, 7

ACUTE INFECTIOUS LYMPHOCYTOSIS IN AN ADULT

B Malamos
M D, D T M
A Stamatelakis

Most hæmatological textbooks state that lymphocytosis is characteristic of lymphocytic leukæmia and infectious mononucleosis (glandular fever), it also occurs in pertussis, where it may be as high as 145,000 per c mm (Pearson and Newns 1937), in mumps, in some chronic forms of tuberculosis, in convalescence from infections, and in diseases of endocrine origin In most of these conditions pathognomonic symptoms facilitate the differential diagnosis, but when they are not present lymphocytosis suggests either lymphocytic leukæmia or infectious mononucleosis

Smith (1941) described, under the title of "acute infectious lymphocytosis," a benign condition in children, characterised by leucocytosis and a pronounced increase in the number of lymphocytes This condition seems to be distinct from infectious mononucleosis Wintrobe (1946) said that some 52 cases had been reported and added 2 of his own Vomiting, irritability, fever, abdominal signs and symptoms, occasionally signs of involvement of the nervous system, and a morbilliform rash have been observed, but in *many* cases there have been no symptoms whatever In Smith's 1941 experience, infection of the upper respiratory tract has been a common finding Symptoms, when present, have not lasted more than a few days The leucocytosis has persisted, on the other hand, for three or more weeks Leucocyte counts reaching 40,000 per c mm are common,

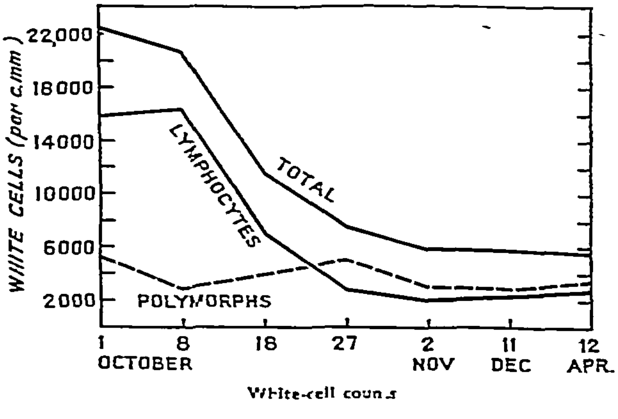
BLOOD CHANGES

Date	Red cells (million per c mm)	Hb (100% =15 g)	Colour-index	Hæmatocrit %	Mean corpuscular volume (c.μ)	Reticulocytes %	Leucocytes per c.mm	Polymorphs %	Monocytes %	Eosinophils %	Lymphocytes %	Plasmocytes %	Basophils %
Oct 1 1948	4·24	80	0·94				22 600	24		2	71		3
Oct 8 1948	4·40	84	0·95				21 000	15	2·5	3	78·5	0·5	0·5
Oct 18 1948	4·25	82	0·96	40	95	7	12 000	33	3	1·5	62		0·5
Oct 27 1948	4·40	85	0·97	37	85	6	7500	53·5	6	3	36·5	0·5	0·5
Nov 2 1948	4·60	86	0·93	38	82	6	5600	56·5	5·5	2	35	1	
Dec 11 1948	4·20	80	0·95	35·5	84	5	5700	48	11	3	38		
April 12 1949	4·38	90	1·03				5700	50	3	2	45		
June 7 1949	4·80	90	0·94	37	77	3	5600	50	12	2	36		
Nov 11 1949							7000	51	4	3	42		

and counts even over 100,000 per c.mm have been reported The great majority of the cells (60–92%) have been "adult" small lymphocytes, not unlike those seen in chronic lymphocytic leukæmia Lymph node enlargement and splenomegaly are generally absent No anæmia or thrombocytopenia has been observed. Wintrobe (1946) reported that the sternal marrow, in the few cases examined, showed an increase in the percentage of the lymphocytes (30–40%), which were of normal type. The lymphocytosis in the marrow reached 86% in Duncan's (1943) case These results were not confirmed by Lorenz et al (1946) and Leitner (1949) thinks that some cases may have been virus pneumonias or that the high lymphocyte percentage was due to an admixture of blood. Biopsy of the lymph nodes revealed degeneration of the lymph follicles, with striking proliferation of the reticulo endothelium (Smith 1944) The heterophil agglutination test has been uniformly negative In 4 cases serological reactions were negative for lymphocytic choriomeningitis and for influenza A and B viruses The disease seems to be both infectious and contagious, with a possible incubation period of 12–21 days The outcome has been uniformly favourable

Most of the cases described have been in children, and only very few were seen in young adults (Duncan 1945, Finucane and Philips 1944, Wintrobe 1946) From Greece only 1 case has been reported, in a girl aged 3½ years (Nimos 1948)

Smith (1944) distinguishes two types of the disease (1) acute infectious lymphocytosis, which is characterised by a transient unexpected hyperleucocytosis, with a relative and absolute lymphocytosis, and not associated with any recognisable symptoms or signs, and (2) chronic infectious lymphocytosis, a more common type which follows infections of the upper respiratory tract and is characterised by low-grade fever and often associated with symptoms, such as anorexia pallor, tiredness, and para umbilical pain Smith considers that both types are separate clinical entities, although there is some evidence that they may be related He believes that the cause is probably a virus



White-cell counts

We report this case of acute infectious lymphocytosis because of the difficulty in diagnosis and the uncommon age of the patient

CASE-RECORD

A woman aged 25, had been married in October 1947 and delivered of a healthy girl on July 16 1948 In the previous year before the onset of her illness, she felt tired which was in contrast to her usual activity She lost her appetite and in a few months her weight fell by 1½ st At the end of her pregnancy it rose again to its original level

Her mother returned from a voyage in the middle of September 1948 and noticed that her daughter was looking pale and tired After thorough questioning the patient mentioned slight abdominal pains on Sept 11 and 12 and lassitude in the last few weeks She had had no fever After delivery she had menstruated normally on Aug 28 and Sept 22 1948 The mother insisted on a medical examination. The obstetrician's findings were negative The specialist in medicine thought that the liver was slightly enlarged No other physical signs were detected A blood-count on Oct 1 1948, showed red cells 4 240 000 per c mm Hb 80% colour index 0·94 white cells 22 600 per c mm (basophils 3% eosinophils 2% polymorphs 24% lymphocytes 71%) Since there had been no pertussis or endocrine disease in the history, this blood-count suggested chronic lymphocytic leukæmia, so the sternal marrow was examined On Oct 5 it was found to be normal except for a slight increase in the proportion of lymphocytes (20%), which were mature and normal On Oct 6 the patient's basal metabolic rate was found to be −1% radiography of her chest was normal and her mediastinal lymph glands were not enlarged

When I saw her for the first time on Oct 8, she still complained of lassitude and looked pale and tired The physical examination was negative No enlarged lymph glands were found The spleen and liver were normal There was no abdominal tenderness Blood pressure 120 60 mm. Hg, pulse rate 60 per min. Weight 58·0 kg No fever

Investigations—A blood-count on Oct 8 showed red cells 4 400,000 per c.mm. Hb 84% colour index 0·95 white cells 21 000 per c.mm (basophils 0·5% eosinophils 3% polymorphs 15% lymphocytes 78·5% monocytes 2·5% plasma cells 0·5%) The lymphocytes were small adult forms with normal nuclei and cytoplasm 30% with azurophil granulation On Oct 18 the white-cell count had fallen to 12 000 per c.mm, and the lymphocytes to 62% The lymphocytes were normal 26% with azurophil granulation. Blood uric acid 9·7 mg per 100 ml Platelets 225 000 per c.mm On Oct 19 a sternal puncture showed bone marrow absolutely normal with 7·5% lymphocytes Further blood-counts are shown in the accompanying table The erythrocyte sedimentation rate (E.S.R.) on Nov 2 was 10 mm in first hour 30 mm. in 2 hours A Paul Bunnel Davidson test was negative

Progress—The patient left in November 1948 for the Côte d'Azur She felt better there complaining occasionally of nausea A blood-count in France showed no increase in the number of leucocytes and the proportion of mononuclear elements was only slightly above normal She returned to Athens in December 1948 feeling less tired

Dec 11 urine normal blood sugar 0·86 g per 100 ml, blood-cholesterol 1·70 g per 100 ml, serum bilirubin 0·56 mg per 100 ml E.S.R. 5 mm in first hour 13 mm. in 2 hours, white cells 5700 per c.mm (lymphocytes 38% 35% with azurophil granulation) Dec 23 no protozoa and no ova in stools Dec 24 Paul Bunnel Davidson test negative (limit 1/14)

Follow up—In a blood count on Nov 11, 1949, the leucocytes totalled 7000 per c mm (lymphocytes 42%) *

Throughout the blood examinations the lymphocytes were found normal in size and shape with normal nuclear and cytoplasmic structure The number of lymphocytes with azurophil granulation was always within normal limits Erythrocytes and platelets showed no abnormal changes

DISCUSSION

The first blood count in the present case was done only because the patient was looking pale and complained of lassitude At the clinical examination the findings were negative The high leucocytosis (22 600 per c mm) with the high relative and absolute lymphocytosis (71%), and the absence of any history of an acute or chronic infectious disease or a disease of the endocrine glands, suggested chronic lymphocytic leukæmia But this diagnosis was improbable because (1) the spleen and lymph glands were not enlarged, (2) the bone marrow contained a normal percentage of lymphocytic cells (in published reports few cases of lymphocytic leukæmia are described without a lymphocytosis in the bone marrow), and (3) only normal adult lymphocytes were found in the peripheral blood and in the bone marrow, without any pathological alterations of the nuclei or degeneration of the cytoplasm Normal azurophil granulation in 26–40% of the lymphocytes is a finding which has not been reported in lymphocytic leukæmia Naegeli (1931) had examined thousands of lymphocytes in such cases without finding any azurophil granules, except in one rather benign case where he found azurophil granules in 14% of the lymphocytes

Infectious mononucleosis (glandular fever) was excluded because (1) all the lymphocytes were small adult forms, and (2) the clinical signs were absent

The diagnosis of acute infectious lymphocytosis was confirmed by the progress and the further hæmatological examinations (see table and figure) In a month the leucocyte count and the absolute and relative lymphocyte counts were again normal

We believe that this case belongs to the type called by Smith (1941) acute infectious lymphocytosis, where clinical pathological signs are absent and the disease starts suddenly, without prodromal symptoms In this type the blood changes are found during a routine blood examination This sudden discovery of the blood changes without clinical signs supports the diagnosis of acute infectious lymphocytosis

Paul Bunnel Davidson tests were negative on two occasions, this result agrees with the findings of other workers The negative Paul Bunnel Davidson test in acute infectious lymphocytosis makes it highly probable that this disease is a separate clinical entity and not a form of infectious mononucleosis (glandular fever)

Acute infectious lymphocytosis is usually seen in children Our case (patient aged 25) is one of the few exceptions in young adults

SUMMARY

Acute infectious lymphocytosis is reported in a woman aged 25 The case was characterised by a high leucocytosis and a relative and absolute lymphocytosis, with no clinical symptoms or signs (no enlargement of lymph nodes, no splenomegaly) The differential diagnosis, especially from lymphocytic leukæmia, is discussed

The outcome of the illness was favourable, the blood picture returning to normal in a month The case was followed for over a year

References at foot of next column

THE "DUFFY" ANTIBODY AND HÆMOPHILIA

J D JAMES
M R C S
DIRECTOR

G PLAUT
M D Heidelberg
SEROLOGIST

NORTH LONDON BLOOD TRANSFUSION CENTRE

THE original antibody anti Fy^a, reported by Cutbush et al (1950), was found after a transfusion reaction in a hæmophiliac who had received previous transfusions the second example (Ikin et al 1950) was found in a patient with a bleeding peptic ulcer who had also had previous transfusions Two further examples of anti Fy^a have since been reported in a hæmophiliac by Van Loghem and Hart (1950), and in a patient undergoing prostatectomy by Rosenfield et al (1950)

We are now reporting this rare antibody in another hæmophilic patient, who had the following history of transfusions

1940 and 1942 Transfused with father's blood

1944 and 1945 Transfused with whole blood from unknown donors (These transfusions stopped the bleeding)

March, 1950 Transfusion with blood from a Red Cross donor produced a reaction

July, 1950 Infusion of fresh plasma and fibrinogen had no beneficial effect

August, 1950 Transfusion of about 300 ml of father's blood produced a reaction

We were then asked to cross match blood from our bank, and in so doing discovered anti Fy^a in the patient's blood, this was only demonstrated by the indirect Coombs reaction Our finding was confirmed by Dr A E Mourant The patient's genetic formula is group O, R$_1$R (CDe/cDE), MN, S + ve, P + ve, Lu − ve, Le^a + ve, Le^b − ve, Kell − ve His father's is group O, R$_1$R$_2$ (CDe/cDE), Fy^a + ve

We have since tested eight hæmophiliacs whose names were kindly supplied by Dr R G Macfarlane and Dr C Merskey, of Oxford, and found that three were Fy^a − ve and five Fy^a + ve, no anti Fy^a antibodies were demonstrated

It is recognised that numerous transfusions may lead to the production of one or more antibodies, but the fact that three of five people in whom anti Fy^a antibodies have been reported were hæmophiliacs suggests that the relationship between this antibody and hæmophilia deserves further investigation

We wish to thank Dr K E Harris for some clinical details and Dr M Maizels and Dr P L Mollison for providing serum for the investigation

REFERENCES

Cutbush M Mollison P L, Parkin, D M. (1950) *Nature Lond* 165 188
Ikin E W Mourant A E Plaut G (1950) *Brit med J* i, 591
Rosenfield R E Vogel P, Race R R (1950) *Rev Hémat* 5 315
Van Loghem J J Hart, M V L (1950) *Ned Tijdschr Geneesk* 11 748

DR MALAMOS, DR STAMATÉLAKIS REFERENCES

Duncan P A (1943) *Amer J Dis Child* 66 267
— (1945) *New Engl J Med* 233, 177
Finucane D L Philips R S (1944) *Amer J Dis Child* 68 301
Leitner S J (1949) Bone Marrow Biopsy London pp 243 40
Lorenz, M Hardy, L M Alt H L (1946) *J Amer med Ass* 131 882
Naegeli O (1931) Blutkrankheiten und Blutdiagnostik. 5th ed., Berlin p 492
Ninios N (1948) *Arch Ellin Paediatr* p 201
Pearson W J Newns G H (1937) *Lancet* ii 254
Smith C H (1941) *Amer J Dis Child* 62, 231
— (1944) *J Amer med Ass* 125 342
Wintrobe M M (1946) Clinical Hematology 2nd ed Philadelphia p 175

---

*In Greece lymphocytes often number 30–40% in healthy persons

SIMPLE AND RELIABLE TEST FOR BILE-PIGMENTS IN URINE

JOHN INGHAM
F.R.I.C.
BIOCHEMIST TO THE MEDICAL UNIT, SCHOOL OF MEDICINE, CARDIFF

FOR ordinary purposes the present tests for urinary bile pigments are satisfactory, but their sensitivity is limited, so they will not detect bile in minute quantities. A simple and reliable test, sensitive enough to detect even a trace of bile pigments, would be helpful to the clinician, especially in the investigation of possible cases of infective hepatitis. Such a test is described here. The principle of this is concentration of the bile pigments by chromatographic adsorption in a gel mat, followed by detection of the pigments in the mat by means of a special reagent.

Stock Colloidal Solution.—Place 1000 ml. of distilled water in a 2 litre conical flask, add 50 g. of alum (ammonium), and heat gently until dissolved. Cool to about 40°C and add, little by little and shaking after each addition, 5% (*v/v*) solution of ammonium hydroxide until the contents are markedly alkaline to litmus. Then add 1% aqueous solution of alum (ammonium) until the contents are slightly acid to litmus. Allow to stand overnight. Next day, pour off most of the supernatant clear liquid, add 500 ml. of distilled water, shake well, and leave overnight. On the following day pour off about two thirds of the supernatant clear liquid. The remaining colloidal solution is ready for use.

Reagent.—Dissolve 26 g. of trichloracetic acid in 100 ml. of distilled water and add 1 g. of pure ferric sulphate $Fe_2(SO_4)_3$. This reagent resembles Fouchet's but contains a little more trichloracetic acid, and the use of ferric sulphate in place of the ferric chloride makes the solution colourless instead of faintly yellow. The reagent is also slightly more sensitive to bile pigments than Fouchet's.

The Test.—Half fill a 2½ inch ribbed glass funnel with absorbent white cotton wool and press this down gently. Shake the stock colloidal solution, to ensure a uniform thickness, and pour some over the cotton wool and allow it to filter through until a smooth gel mat forms on the surface of the wool. Then fill up the funnel with the urine to be tested and as the urine filters through all the pigments will be retained on the gel mat. The filtrate will be colourless if the gel mat has been properly formed and is efficient.

Now add a few drops of the reagent to the gel mat, and if even the minutest trace of bile pigment is present the mat will turn a clear bright emerald green which will not fade for some hours. (The reagent oxidises the bilirubin to biliverdin.) The more bile pigment that is present the more intense will be the green colour. Quantitative estimations, if desired, can be carried out by placing standard solutions of bilirubin on other gel mats similarly constructed, adding a few drops of the reagent, and comparing the colours.

Over 300 specimens of urine containing all kinds of pigments other than bile pigment have been tested by this method and no false positive results have been detected. Comparison with most of the well-known tests for bile pigments—tincture of iodine, Gmelin's nitric acid, Franke's methylene blue, Harrison's barium chloride, Watson's modification of Harrison's, and Murray Franklin's—has shown that the test described here is much more sensitive and therefore reveals the presence of minute amounts which cannot be detected by the others.

" . . . Ether is unpleasant, it is irritating, it is toxic, and it is explosive. . . . And yet ether has one supreme advantage as an anæsthetic agent—it does not depress respiration. Even though a patient may splutter and kick and get full of mucus, he still breathes. For this reason it is my firm conviction that unless a doctor makes himself familiar with the method of controlling respiration, and has available the necessary apparatus, he should not be tempted into using the new easily administered anæsthetics, and he should make old fashioned ether the mainstay of his anæsthetic practice."—H. R. GRIFFITH, *Canad. med. Ass. J.* 1950, 63, 533.

Medical Societies

MEDICAL SOCIETY OF LONDON

Unexpected Death Following Operation

A DISCUSSION on this subject was held on Jan. 8, with Dr A. H. DOUTHWAITE, the president, in the chair.

Dr I. W. MAGILL said it was essential to differentiate between death due to anæsthesia and death occurring from other causes while the patient was under the influence of, or recovering from, an anæsthetic. Modern anæsthetics had not led to a reduction in deaths under anæsthesia, but one reason for this was that with modern techniques many patients who would formerly have been considered inoperable were now given their "only chance" through surgery. A survey of 250 cases showed that abdominal surgery was the chief source of postoperative death, and as a rule more than one grave pathological condition was present. Investigation of the cause of death should be very thorough, and sometimes the anæsthetist was alone capable of giving the answer.

The volatile and gaseous anæsthetics formerly used were, in safe doses, not respiratory depressants, and their action was reversible. The modern solid anæsthetics, on the other hand, did depress respiration. With the volatile anæsthetics there was a time lag before an overdose could be given, but when giving an intravenous injection it was fatally easy to give more than enough. Care of respiration was the first responsibility of the anæsthetist. A recent investigation of 112 cases showed an incidence of nearly 20% of regurgitation and aspiration by which gastric contents entered the lungs, but in the hands of an experienced anæsthetist this should never happen. The endotracheal tube had proved its value. When respiration was depressed or absent, ventilation of the lungs must be taken over by the anæsthetist. Effective control using the rebreathing bag, was easy in the operating-theatre, but care must be taken to ensure that the ventilation was adequate—in other words the young anæsthetist must be taught to concentrate on the patient. Spontaneous respiration must be restored before assistance was ended, but often it was insufficient at first and therefore there was a definite risk in the immediate postoperative period. Other conditions being satisfactory the anæsthetist had a considerable responsibility for the postoperative state of the patient. Pulmonary embolism was preventable, and it was for the anæsthetist to ensure that the patient's posture on the operating-table was such as to ensure an unimpaired venous return. For example, accidental pressure on the calves of the legs in the Trendelenburg position might cause embolism.

The physiological balance of each individual varied and it was essential to assess the patient's ability to withstand the anæsthetics and the surgery. During the operation wide blood pressure variations should be avoided, and blood lost should be replaced concurrently. It was the duty of the anæsthetist to indicate the necessity for this when it arose. A recent development in surgery was deliberate lowering of the blood-pressure by giving pentamethonium iodide. Dr Magill did not know of any fatalities from this, and it might be that the attitude towards the significance of low blood-pressure needed revision. But it seemed fair to infer that a systolic pressure of 50–60 mm. Hg did not enhance the viability of the cerebral centres.

The position of the patient after operation must be such as to ensure respiration and easy expulsion of vomitus. Dr Magill favoured the postoperative recovery room, fully equipped and in charge of a properly qualified person, such as a registrar, to which the patient went for 24 hours. When all anæsthetics were administered by specialists, he concluded, then and only then would there be hope of further reduction in the fatality rate.

Dr C. KEITH SIMPSON pointed out that the coroner had a double duty. He had to see not only that the anæsthetist and surgeon were satisfied, but also that the relatives were conciliated; he was the one man—especially since the change in the administration of medicine—who stood between the public and the ordinance of the law The arrangement whereby the coroner ordered an investigation into the cause of any death before full recovery from an anæsthetic could be satisfactory only if the medicolegal pathologist, the anæsthetist, and the surgeon discussed the matter in detail before the post mortem examination The improvement in the standard of anæsthetics in the last ten years had been remarkable, and of unexpected deaths following operation 75% had little to do with the anæsthetist or the surgeon Of course any operation (however trivial) and any anæsthetic (however well administered) were adverse factors They could not be advantageous except in the occasional (blue) patient who was previously suboxygenated An analysis of 500 cases showed death to be due to natural causes in 279 (56%), to operative shock—resulting from quite restrained surgery—in 149 (30%), to complications of anæsthetic risks in 40 (8%), and to overdosage or bad choice of anæsthetic in 32 (6%) In the latter classes some 85% appeared avoidable

Death from natural causes might be due to cardio respiratory limitations not recognised before the operation A patient who died under a dental anæsthetic had been examined the night before, death was found to be due to a fresh thrombosis which might well have occurred during the night Premedication must not be overlooked as a source of death especially when it was delayed or repeated With some anæsthetic drugs, there was clearly a risk, however skilfully they were used The reaction to a barbiturate varied not only from one person to another but also in the same person at different times, less than 0 5 g of thiopentone might precipitate death Overdosage was largely a matter of the past, but even today a skilled anæsthetist might go on administering an anæsthesia causing considerable suboxia for far too long a period Dr Simpson quoted cases of death which had taken place when the operation was prolonged during teaching The kind of operation most commonly responsible for death was the one undertaken to give the patient any chance of life at all or life in any tenable form Modern intrathoracic surgery, for instance, came into this category there was bound to be a risk of death, which would, however, be recognised by the coroner, and also by the relatives, where the facts had been explained to them

No patient should pass out of the hands of the anæsthetist until fully recovered from the anæsthetic Particularly dangerous was the system, still in force in some hospitals, by which a male attendant or even a porter took the patient back to the ward Quite often a preventable death—e g, after tonsillectomy—occurred on the way

When fat or air embolism was overlooked as a possibility, death might be ascribed to the wrong cause A careful necropsy technique was essential for the discovery of air embolism, and where this condition was suspected the surgeon and anæsthetist should be present and the investigation should start from the point where it was thought that the air might have entered A cause of death which it was impossible for the pathologist to discover on his own was reflex vasovagal inhibition This might arise from the skin, for example the stripping of a dressing might produce a fatal reflex, and this was one reason why some painful dressing should be done under anæsthesia Other sources of reflex vasovagal inhibition were stimulation of sympathetic branches on the cardiac sheath or the aortic bodies, sudden disturbance of large masses in the abdomen, tension on the peritoneum, or urethral and other pelvic instrumentation—especially under light anæsthesia

Dr G S W Organe thought it was important not to attempt too much in operations on old people

Dr E B Strauss reported on the electrical stimulation of respiration in patients where respiratory failure occurred during electroconvulsion therapy or during narco analysis with barbiturates The apparatus devised at St Bartholomew's Hospital consisted of a box condenser with two small round electrodes of the type used in E C T These were applied to the frontotemporal region, giving a steep fixed wave of current of low amperage It was found that a current of 1–2 mA with a pulse width of 50 kilocycles, applied for 2–6 minutes, was very efficacious

Mr Michael Smyth said that a useful means of artificial respiration which the surgeon could adopt was to lean across the table and intermittently compress his chest against the patient's

Mr Zachary Cope had not seen a death during an operation in which there was controlled respiration, but was it possible for controlled respiration to take place for a long period without damage to the constitution of the patient?

Mr E W Riches paid tribute to the older type of anæsthetist who always visited his patient the day before operation He agreed that a skilled attendant must accompany the patient back to the ward, and stressed the importance of proper lighting in the lift, he knew a case in which death took place simply because the lift was ill lit

Mr W McKim McCullagh said that deaths among babies born by cæsarean section under gas and air anæsthesia were 5%, and over half of these were healthy babies He believed that deaths from pulmonary embolism, of which the gynæcologist saw many, could be prevented by a blood-count before the operation If the blood state was good, there was no need for physical exercises, such as having the patient walk about the day after the operation

Dr T Jenner Hoskin said that even a person with a bad heart could stand an operation, provided the anæsthetist knew he had a bad heart to deal with

Mr S M Cohen asked whether there was such a thing as neurogenic shock under anæsthesia, or was death due to blood-loss alone? If a patient with thrombophlebitis had been put to bed, operation might precipitate a blockage, hence, if it was not possible to operate at once, it was better to postpone the operation for ten days. The same applied to fractures of the neck of the femur it was the rule in Edinburgh to manipulate within two days or wait ten days before operating

Mr Guy Blackburn said that controlled respiration made it possible for surgery to go on into the afternoon and evening and he wondered whether that had made some surgeons a little dilatory To reduce the incidence of unexpected deaths it was necessary to pay more attention to the preparation of the patient having an emergency operation Curare had often been blamed for postoperative deaths, but it had enabled the surgeon to do things he could not attempt before There was a general tendency to dispense with spinal anæsthetics because unexpected deaths were more frequent with them than with other anæsthetics

Sir James Walton said that anæsthetics today were so complicated that no one would dare to handle them who was not a specialist He did not accept the contention that old people could stand operations as well as young ones He used to tell his house surgeons that what they had to do was to make the patient comfortable So often, when called out, he had found the patient arrayed in tubes, and had said "Take those things out, and let him have a night's sleep!"

The President thought the artificial distinction between medicine and surgery which was growing up, starting in student days, was wrong He was quite sure that if there was closer collaboration between physicians and surgeons something could be done to reduce post operative mortality

Dr Magill, in reply, said that if a patient did not respond to 1 5g of thiopentone he concluded that any more would be an overdose and he had recourse to other methods Prolongation of the operation was a cause of death, and in that respect there was a certain complacency among young surgeons In some hospitals the bed was brought into the theatre, thus eliminating one lifting of the patient—a possible source of embolism A competent anæsthetist always visited his patient before the operation, or if that was not possible made an assessment on a careful report Dr Magill urged care in the administration of sedatives after operation In his opinion, open ether was not " dead "

Dr KEITH SIMPSON said he had not yet seen a death from C5 or C6 It was some twelve years since he had seen a death from " ether convulsions " possibly because of improved standards of anæsthesia Though there was a decrease in culpable anæsthetic deaths, the number of cases succumbing was maintained by the advent of onerous new surgical procedures The advantages of quick gentle surgery were still quite plain

New Inventions

INSTRUMENTS FOR SUPRAPUBIC EXPOSURE OF PROSTATE AND BLADDER NECK

THE bladder retractor shown in fig 1 (A) has a posterior blade in two parts, so that the lower half can be lengthened or shortened according to the depth of the bladder base The extra-long posterior blade (B) is supplied for use in unusually voluminous bladders

The prostatic-bed forceps (C) has special teeth to enable the surgeon to get a firm grip of any part of the prostatic bed After a wedge resection different parts of the raw surface can thus be brought successively into view and any spurting vessels quickly dealt with

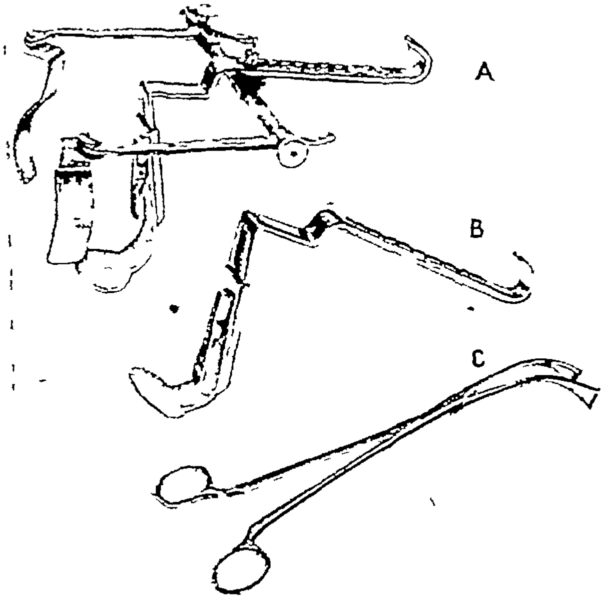


Fig 1

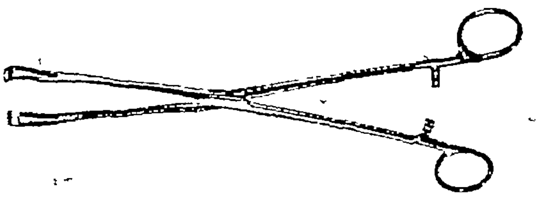


Fig 2

The bladder-neck forceps (fig 2) has the same kind of teeth With this instrument the posterior margin of the internal urinary meatus can be gripped and pulled firmly into view before diathermy resection of a wide portion of a fibrosed bladder neck is undertaken

The instruments were made to my specification by Allen & Hanburys Ltd , of London, W 1

London W 1 H P WINSBURY-WHITE, F.R C S

Reviews of Books

Radiation Therapy in the Management of Cancer of the Uterine Cervix

SIMEON T CANTRIL, M D , director, Tumor Institute of the Swedish Hospital, Seattle, Washington Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 200 36*s*

THIS is a thoroughly good survey of the progress and limitations of radium and X-ray therapy in treatment of carcinoma of the cervix In the midst of an overwhelming mass of work published on this subject, it is refreshing to meet with so clear and concise an evaluation Dr Cantril describes the basic principles which have evolved from the Swedish and French schools of radiotherapy Not all will agree with his statement that the great majority of cervical cancers arise in the endocervical canal, but all will share his view that from the standpoint of curability the cytological differentiation of the growth matters less than the anatomical extent of the disease when the patient is first seen He rightly deprecates any rigid adherence to a routine method of radiation therapy Success is achieved by building up the patient's resistance and adjusting the radiation treatment to suit the individual case The Stockholm, Paris, and Manchester techniques are clearly described, and the section on the role of X rays in the treatment of carcinoma of the cervix gives much useful information on the choice of techniques, and on combinations of radium and X-ray dosage Failures increase with the extent of the disease when treated Parametrial spread to lymph-nodes is the main cause of failure, and presents a problem which cannot be resolved by dosage alone Reviewing the results of surgical treatment of cervical carcinoma obtained by Fauré, Bonney, Taussig, Meigs, and others, Dr Cantril concludes that surgery, even in the best hands, is not likely to increase the survival-rate of patients in the early clinical stage

Radiation dosimetry in terms of " tissue dosage " was introduced by the Manchester school, and expresses tissue dose in rontgens The tissue dose can be added at a selected point, and is contributed by both the intracavitary radium and the external X-ray therapy Dr Cantril compares pelvic dosimetry obtained by other techniques and points out that—though precision is the aim—accurate calculation of dosage has limitations when applied to the patient Not only is it dangerous, but it is often futile, to push the dose in the more peripheral zones of the pelvis to a predetermined " effectual " dose In the living subject measures are at best an estimation precision depends upon the care with which they are made

The Book of the It

GEORG GRODDECK Translator V M E COLLINS London Vision Press 1950 Pp 301 15*s*

Exploring the Unconscious

GEORG GRODDECK. Translator V M E COLLINS London Vision Press 1950 Pp 224 12*s* 6*d*

IT was nothing new in the history of medicine when Groddeck proclaimed his belief that an intangible and unknown force directs everything—physical and mental —that happens in the human individual instead of calling this force the " It," after Nietzsche, he might have called it the Archaeus after Van Helmont, or even the entelechy after a greater predecessor He seems, however, to have had little awareness of the strength and the weakness of his philosophical position, but to have pushed on, after his preliminary work in physiotherapy, with the application of some Freudian tenets to the explanation and treatment of physical disease Naïve in his theorising—and bold, even for a psychoanalyst, in his use of symbolism—he went much further than Freud in attributing somatic disease to unconscious forces The Book of the It," here excellently translated, expounded his views in a series of letters, addressed to a sympathetic woman friend The literary form he chose suited his thought very well there was no need for systematic exposition or argument, and he could pile illustration on illustration, and make frequent use of the personal note This personal note appears also, of course, in the autobiographical fragments reproduced in *Exploring the Unconscious* from these we learn enough to understand his violent repudiation of orthodox medical beliefs, and to recognise his lifelong anti-intellectual bias In these and particularly in his disquisitions on the "belly-mind" he gives the English reader cause to recall D H Lawrence Besides some etymological speculations, there is in *Exploring the Unconscious* a psycho-analytical examination of *The Ring Faust*, and *Peer Gynt*—which is, however, less distinctive than the section on unconscious factors in organic processes His experience here had been heartening "I find that in obstinate organic cases of whatever nature, a psycho analytical examination is always useful and may prove essential to improvement To the best of my judgment chronic organic disease yields to psycho analytic treatment more surely and quickly than do the neuroses " The same however, might be said regarding the response to non psycho-analytical psychotherapy

Principles and Practice of Rehabilitation

Editor HENRY H KESSLER, M D, PH D London Henry Kimpton 1950 Pp 448 63*s*

THE 21 authors of this book are American surgeons, physicians, and psychologists who are engaged in treating the disabled Every branch of their vast subject is covered, and, on the whole, covered well Apart from the surgical and medical aspect, emphasis is placed on the need for a team spirit among all who work to make the handicapped person use fully the powers he still possesses, to place him in employment, and give him independence

The Antihistamines

Their Clinical Application S M FEINBERG, M D, associate professor in the department of allergy, North western University Chicago, SAUL MALKIEL, M D, PH D, assistant, R FEINBERG, M D, assistant Chicago Yearbook Publishers 1950 Pp 291 $4

THIS book sets out all the known clinical uses of the anti-histamines The experimental section has purposely been kept to a minimum, while the clinical application has been well covered Much of the evidence that histamine plays an active part in allergic reactions is inferred A drug which protects a guineapig from a normally lethal dose of histamine could well be called antihistaminic In man, however, these new drugs were found to have many beneficial effects unrelated to their antihistaminic activity The search for a new compound or a new combination of drugs which will give the minimum side effects with the maximum benefits continues An annual business of $100 million in America constitutes sufficient impetus for the manufacturers to look for new cold cures, new seasickness remedies and new cures for many unrelated complaints Written essentially for the American reading public the book does not include all the common English names for the various compounds Nevertheless it can be recommended to all who require a small reference work on the clinical uses of such drugs

Treatment of Uremia by Dialysis and Other Methods with Special Regard to the Principles and Scope of Intestinal Dialysis

E E TWISS physician, Municipal Hospital, Kampen, Holland Rotterdam Drukkerij M Wyt & Zonen 1950 Pp 209

THIS book is the third of a series, published from the Kampen Municipal Hospital, dealing with the treatment of uræmia by dialysis methods Kolff's thesis [1] on the artificial kidney was the first, Kop's thesis [2] on peritoneal dialysis the second, and this is the third The published work on dialysis methods in general is reviewed briefly and that on intestinal dialysis in detail After considering the anatomy and physiology of the intestine in this context, Dr Twiss deals with his own experiments, made on dogs, on the composition of dialysing fluids and the efficacy of dialysis through the intact intestinal wall The technique of intestinal dialysis in humans is described, including the method in which an isolated intestinal loop is used The results in 11 patients are evaluated

Intestinal dialysis seems to be a practicable method of correcting many of the disturbances in uræmia and the technique of dialysis through an isolated intestinal loop shows some promise in patients with severe and irreversible renal lesions It is of interest that Twiss was able to keep a virtually anuric patient alive for 46 days by this method

My Life in Three Counties (London Christopher Johnson 1950 Pp 247 15*s*)—Dr Pooler's roving mind and eye find ample scope in his latest venture, and he writes in his usual straightforward and unaffected style revealing his warmhearted humanity and wholesome sense of humour. The story of his early days in his own county of Shropshire is particularly delightful, and the numerous illustrations add a charm to the book

Urological Surgery (2nd ed London Henry Kimpton. 1950 Pp 855 £4 15*s*)—Prof Austin Dodson's book is already known as one of the finest expositions of operative urological surgery Several experts in particular fields—among them Dr Leon Howard on renal tuberculosis—have shared in this edition, and the work has benefited Illustrations are good and clear But as earlier criticisms have been met, it is a reviewer's duty to offer new ones Many would wish for a more detailed account of the operation of total cystectomy, no mention is made of the simple retropubic excision of congenital valves of the posterior urethra, and retropubic prostatectomy, despite its increasing band of adherents is rather summarily dismissed and poorly described Nevertheless the work maintains its place in the first rank

Practical Neurological Diagnosis (4th ed Springfield, Ill C C Thomas Oxford Blackwell Scientific Publications 1950 Pp 268 37*s* 6*d*)—Prof R Glen Spurling's little book, written for neurosurgeons, naturally has many omissions disturbing to physicians Moreover the structural divisions of the nervous system (as opposed to its function) receive greater attention than in medical texts. But it may be supposed that the neurological surgeon is interested in the diagnosis of conditions which do not require ventriculography if only to minimise the use of that distressing aid to diagnosis Dr Spurling says that ' lateral hemisection of the cord (Brown Séquard syndrome) occurs most frequently as a result of stab or gunshot wounds, a view which must be based upon highly selected material Again, the whole question of double vision as it affects neurological diagnosis is confined to 17 lines of print, while a chapter on radiological diagnosis is long, full and excellently illustrated There can surely be no neurosurgeon who needs such an elementary treatise on diagnosis, and yet it is clearly not intended for anyone else

Lehrbuch der Röntgendiagnostik (5th ed Stuttgart Thieme 1950 Parts 1 and 2 Pp 426, 452 D.M 66 70)—Before the war this textbook in German, by H R Schinz and others, had a wide international circulation It consisted of two fairly large volumes compiled by radiologists in Switzerland, Germany Austria, Italy, and Scandinavia During the war, the whole of the standing type was destroyed by bombing, and a number of the contributors died, so that the editors have had to start from scratch The new edition, in 6 parts will appear in 3 volumes This first volume deals with the physics of radiation methods of production of X rays, and crystallography and with normal and abnormal radiological appearances of the skeleton An average of $1^1/_2$ illustrations appear to a page, and the pages measure 11 × 8 in The introductory section on the physics of radiation is unnecessary, being too advanced for the average radiologist, it might prevent him from exploring the good things to come Every conceivable variation is described in detail and liberally illustrated with beautiful drawings and radiographs, there are 90 sketches of fractures of the humerus alone Part 2 describes avascular necroses, inflammations and hereditary disorders, with the same detail The main emphasis throughout is on anatomical and pathological changes as compared with the X ray findings Clinical findings are not adequately correlated, but this is otherwise a superb work The printing, the quality of paper, and the illustrations excel the best pre war German standards

---

[1] Kolff, W J Die Kunsmatige Nier Thesis Groningen 1946
[2] Kop, P S M. Peritoneaal Dialyse Thesis Groningen 1948

THE LANCET
LONDON SATURDAY, JAN 20, 1951

Dental Ancillaries

FACED with the breakdown of the school dental service, and armed with an unexpectedly unanimous and favourable report[1] on the use of school dental nurses in New Zealand, our Government may well be inclined to create an ancillary body of dental nurses in this country But the visiting mission agreed that the New Zealand system might need modification before it would be suitable here As the dental and medical professions will be directly concerned with any such scheme, they should be ready to consider critically and constructively whatever version may be officially proposed

Here in England we have so far had little experience of the work of dental ancillaries During the war the Royal Air Force trained a few "oral hygienists to clean and scale teeth and 20 of these are now working for local authorities or in hospitals Civilian training courses, lasting a year, began at the Eastman Dental Hospital in November, 1949, since when 30 students have been enrolled , and a subcommittee of the standing dental advisory committee of the Central Health Services Council is watching this experiment The work of the New Zealand dental nurse, however, differs from that of the English oral hygienist both in scope and in responsibility The New Zealand nurse receives two years intensive training and becomes something of a specialist in minor dental operations for children, such as filling and simple extractions certainly she is more experienced in this work than most recently qualified dental surgeons On the other hand, so that she shall not feel frustrated in the day-to day routine of children s dentistry, or feel that she has acquired knowledge she cannot use, her training is limited and practical and no attempt is made to stimulate a scientific attitude of mind Nevertheless when she has finished her training and is posted to a clinic in one of the six administrative districts into which New Zealand is divided, she becomes virtually an independent dental practitioner The principal dental officer who is responsible for the dental nurses of his area has about 80 of them in his charge, and cannot closely supervise their work In practice he seldom visits each clinic more than once in a school term, and a good deal of responsibility is thus placed on a nurse who has been deliberately trained as an ancillary worker Many dentists who might otherwise approve of having a similar scheme for this country regard this degree of supervision as inadequate But this is not an objection in principle to using nurses in children's dentistry, and it could be overcome by different administrative arrangements For instance, if a qualified dentist were at the head of a team of 6 dental nurses, the situation would be very different , for their supervision would then be as close as that of students during their training in conservative dentistry in dental schools The dental surgeon in charge of the team would examine patients, and allocate each child to one of his nurses for treatment, reserving for himself the more complex and difficult cases He would probably give all injections for block anæsthesia, and he might have time for orthodontic treatment

Many dentists are now deterred from entering the school dental service because so much of children s dentistry consists in repetitive routine Many are also discouraged by a sense of helplessness in face of this colossal problem Freed from much of the routine work by the ancillaries in his team, the dental surgeon, as MACGREGOR[2] lately suggested, could give time to the specialty for which he has been trained, and in so doing need no longer blame himself for neglecting the urgent attack upon dental caries In the United Kingdom at present there are probably nearly 5 million children needing some form of continuous dental treatment In New Zealand each nurse looks after 500 children , but fortunately the incidence of caries is somewhat less in Britain, and a nurse here ought to be able to look after at least 750 On this basis we should need about 6000 nurses to build up a satisfactory service There are at present about 825 school dental officers, and with their number raised to about 1000 they could undertake the administration of the scheme and the supervision of its ancillary members To organise and equip a children's dental team would be relatively straightforward in towns and also in those country districts where children can go to central clinics In sparsely populated districts, where mobile units would be needed, the organisation would no doubt have to be more rudimentary , but it should be possible to provide each team with one fully equipped mobile surgery, for the use of the dental surgeon in charge, and folding chairs, foot engines, and portable cabinets of instruments for the dental nurses When visiting an outlying village, the team might take over the village hall or transform the schoolroom into a temporary clinic, for a day or two of intensive treatment Though perhaps not entirely satisfactory, such arrangements would be infinitely preferable to the absence of dental treatment of any kind

The recruitment of so many dental nurses will not be easy nor can it be done quickly The training will be costly, and as LITTLEFIELD[3] has pointed out, so long as facilities for training are limited, we must ponder how far it is wise to train dental nurses at the expense of fully qualified dentists Because of these difficulties even a modified ancillary service will be a long-term remedy But unless the dental profession accepts and uses a great deal of help, most of the children of the country can never hope for any but emergency dental treatment Dentistry will remain a "breakdown service ' destined to go on providing dentures for most of the population indefinitely

---

[1] See *Lancet* 1950 ii 491

[2] MacGregor A B *Ibid* i 505

[3] Littlefield W H *Ibid* p 1010

Analgesics Compared

THE drugs used to relieve pain are of two main classes—narcotics, such as morphine, its derivatives, and the newer synthetic compounds like pethidine and amidone , and antipyretic analgesics, which include aspirin, phenacetin, acetanilide, phenazone, and amidopyrine In general, only a narcotic will relieve the severest pains—from a major fracture, myocardial infarction, renal or biliary colic, or inoperable malignant disease Whereas aspirin and others of its class are often effective in other types of pain, such as headache, and especially so in "rheumatic" conditions of the muscles, fasciæ, or ligaments , their action is said to be potentiated by small amounts of codeine (as in tab codein co) but accurate information on this point is scanty

Among the narcotics morphine is still supreme, for none of its substitutes, whether built from the morphine molecule (diamorphine, codeine, dilaudid, and metapon) or synthesised on a different pattern (pethidine and amidone), has overcome its disadvantages and retained its efficacy Pethidine is less liable than morphine to cause nausea and vomiting or constipation, and it is also the least depressant of the narcotics to respiration , hence its extensive use in obstetrics where avoidance of neonatal asphyxia is vital But it is clearly a drug of addiction, and the same applies to other piperidine compounds, such as bemidone and particularly ketobemidone [1] Amidone ('Physeptone,' 'Methadon,' or '10820') is much more powerful an analgesic than pethidine and even a little more potent than morphine, but it is almost as depressant to respiration as morphine and often causes nausea and vomiting if given by mouth It has hardly any of morphine's sedative action, which is a disadvantage before operations but a valuable feature for patients who want to be relieved from chronic pain while retaining their mental clarity It must be regarded as a drug of addiction, though withdrawal symptoms are slower to develop and less severe than with morphine In small doses amidone effectively relieves useless coughing, and it is widely prescribed in linctus form for children with whooping-cough The need for special precautions in prescribing pleasant tasting syrups containing such potent drugs is well illustrated in the case reported by Dr ROXBURGH and Dr MUNRO FAURE in their letter on p 174 Here a girl of $4^{1}/_{2}$ years with whooping cough was prescribed a proprietary linctus containing 2 mg of physeptone, and gr $^{1}/_{12}$ of phenobarbitone in each fluid drachm A safe amount for her to take would have been not more than 2 4 mg of physeptone four hourly But in fact, because her coughing continued, she was given 12 drachms, containing 24 mg of physeptone and gr 1 of phenobarbitone, over six hours After a day's coma and two further days of somnolence the child recovered The makers of the linctus (Messrs Burroughs Wellcome & Co), in a circular letter, say there have been 3 fatal cases of this kind , they therefore advise doctors prescribing for children to order not more than 2 fl ounces of the linctus, suitably diluted, at a time and to impress on the parents or other attendants that the dose on the bottle must in no circumstances be exceeded Phenadoxone ('Heptalgin') belongs to the same chemical group as amidone and has much the same analgesic action, though of briefer duration

In all the modifications of the morphine molecule hitherto investigated analgesic potency runs roughly parallel with habit formation Thus diamorphine (heroin) is the most powerful and codeine the weakest in both respects The same tendency is seen in the newer synthetic compounds In 1946 GREWE [2] synthesised a new compound, containing 4 of the cyclic rings present in morphine, and a derivative of this, 3 hydroxy-N methylmorphinan hydrobromide ('Dromoran'), is a more powerful analgesic than morphine [3] , but once again it is now regarded as a potential drug of addiction [4] One begins to wonder whether it is basically impossible to dissociate the morphine like capacity to relieve pain from the liability to cause addiction HARDY and his colleagues [5] suggested that morphine relieves pain in three ways

(1) By raising the pain threshold and interfering with pain perception

(2) By detaching pain perception from the usual reaction pattern to pain , though still perceived and recognised as such, pain now seems to be a remote happening which occasions no anxiety This effect resembles that of leucotomy—it might even be said that morphine produces a reversible "pharmacological leucotomy"

3 By inducing lethargy and sleep

The second mechanism appears to be the most important in relieving pain, and since this state of detachment may be very pleasant (euphoria) it is not surprising that predisposed people readily become morphine addicts But does it necessarily follow that no centrally acting analgesic can possibly relieve severe pain without inducing euphoria and causing addiction ? At any rate, no such drug is yet known.

The antipyretic analgesics act quite differently from the narcotics Presumably their antipyretic effect in feverish conditions is brought about through the temperature regulating centre in the hypothalamus heat loss being increased by sweating and cutaneous vasodilatation Their analgesic action is more difficult to explain [6] They are usually said to depress the pain centre, but if so they must act at a different site, or by a different mechanism, from the narcotics, since they do not produce euphoria or addiction Furthermore, morphine can be shown to increase the strength of any stimulus required to elicit pain, but it is very difficult to demonstrate that aspirin has any such action on the pain threshold SONNENSCHEIN and IVY [7] have found that aspirin (as well as amidopyrine, acetanilide, and phenacetin) has no greater effect than lactose on the pain threshold of a tooth stimulated by an alternating current or the skin stimulated by radiant heat COBURN [8] drew attention to the action of salicylates in reducing joint effusions in rheumatic fever , MEYER and RAGAN [9] suggested that gentisic acid, a metabolic product formed in the body from salicylates, may inhibit inflammatory processes and so relieve pain , BARBOUR and HERMANN [10] showed hat these drugs alter fluid and electrolyte balance so s to cause hydræmia, **Sonnenschein** and **Ivy** herefore suggest that the antipyretic analgesics relieve pain through their local actions on the pathological processes causing pain All that can yet be said is hat this possibility deserves further study

---

[1] Isbell H J *Pharmacol* 1949 97 182

[2] Grewe R *Naturwissenschaften* 1946 33 333

[3] Zager, L L Sawtelle W W Gross E G , Nagty, S F Tidrick R T *J Lab clin Med* 1949 34 1530

[4] Isbell H Fraser H F *J Pharmacol* 1950 99 (*Pharm Rev* 2) 355

[5] Hardy J D Wolff H G Goodell, H *J clin Invest* 1940 19 649

[6] Goetzl F R *Permanente Found med Bull* 1946, 4 49 Smith P K *J Pharmacol* 1949 97 part 2, 353

[7] Sonnenschein, R R Ivy, A C *Ibid* p 308

[8] Coburn A F *Bull Johns Hopk Hosp* 1943 73, 435

[9] Meyer K., Ragan, C *Science*, 1948, 108 281

[10] Barbour H G Hermann J B *J Pharmacol* 1931, 18, 166

Biochemistry of Old Age

The next major advance in human biology, comparable to the last half century's work on nutrition, endocrinology, and infectious diseases, may well be the elucidation of the mechanisms of ageing This is a field where even the groundwork has yet to be done Between the fatalists who regard any attack on ageing as "against Nature" and, at the other extreme, the rejuvenation fanatics with their exaggerated claims, until lately no attempt has been made to find out what senescence is and what are its primary and subsidiary causes One important discovery in this field could easily activate a whole new train of research The immediate tasks for the biologist are descriptive and experimental, the geriatrician has plenty to do in applying existing medicine to old people and in remedying by exposure the disgraceful conditions under which some of them live From the social side, much has already been achieved by the survey work of **Sheldon** [1] at Wolverhampton and **Thomson** [2] in Birmingham The theoretical background is still confused and confusing It has long been suspected that the factors which limit somatic growth also play a part in the induction of ageing, and **McKay's** [3] experimental study of growth-delay and longevity in rats fully supported this view Useful results may come from Russian work being done at Kiev on the relation of ageing to the reticulo endothelial system Now that the Notre Dame laboratory has succeeded in raising germ free mammals, it should be possible to dispose experimentally and for good and all of the bacterial toxic theory The endocrine approach, after being seriously discredited by over optimism, looks far more hopeful now that it is generally agreed that no single hormone or organ is likely to provide a complete explanation of age processes as a whole

In Birmingham an investigation now in progress is based on **Albright**'s concept of a human "adreno pause"—a steadily diminishing production of adreno cortical hormones starting at various ages between 60 and 90 The idea draws support from the known decline in urinary excretion of 17-ketosteroids after the age of 50 Preliminary results published by **Marson** [4] show that, among 100 women over 60 the axillary hair was absent in 40 and reduced to under fifty hairs per axilla in 87 Potassium and chloride serum levels were normal, but half of the 57 serum-sodium estimations done were significantly low, and the range was 296–340 mg per 100 ml, compared with the normal 320–350 mg Insulin sensitivity was in general reduced, and both the fall and recovery of the blood-sugar levels were sluggish by comparison with younger adults The series is too small for the findings to be more than pointers, but they confirm **Albright's** own figures and support the general hypothesis of a cessation or reduction in adrenal activity The low levels of serum-sodium with no corresponding fall in chlorides, if the findings are confirmed, may throw new light on tissue dehydration in old age The sodium levels again fit in with the view that the adrenal is involved in the age process The rôle of the pituitary is not yet so clear A C T H is a powerful inhibitor of protein synthesis, and **Mayer** [5] has pointed out that senescence is characteristically a "reorientation of metabolism towards nitrogen equilibrium and fat synthesis" **Findley** [6] has suggested that decreased tissue sensitivity to pituitary stimulation is a factor in ageing, which would make the process largely peripheral **Parkhon** [7] has studied the effect of thyroid on the fat-nitrogen ratio in senescence and experimental thyroidectomy Thyroid function certainly declines with age, both clinically and as judged by I^{131} uptake,[8] and much work has lately been done on the relation between thyroid activity and atheroma, by way of the blood level of cholesterol

The vast mass of publications on sex hormone effects in ageing is confusing and largely unreliable, but some tangible relation between œstrogens, androgens, and metabolic processes in senescence have emerged It seems certain that old age is a general failure of homœostasis, though the origin of the process, and the possibility of attacking it at any one point, remain in doubt But the term "adrenopause" is doubly unfortunate, for it suggests a landmark akin to the true menopause, rather than a gradual decline, and by emphasising the adrenal at the expense of other hormonal degenerative changes it begs a question which should at all costs be kept open Little real progress is likely until some essential experiments on tissue biology are done which show exactly how and where the internal environment and the response of cells to it vary with age What is needed is an extension of the brilliant work of the chemical embryologists to cover the end as well as the beginning of the growth process This may tell us what chances there are of delaying or otherwise modifying the degenerative changes of old age

The Displaced Registrars

The continuing concern over the position of registrars threatened with dismissal, and of the hospitals that are to be denied their help, is reflected in a letter to an M.P from the Secretary of State for Scotland (see p 164) and in a memorandum by the Fellowship for Freedom in Medicine (summarised on p 178) In the first report of the Newcastle upon Tyne Regional Hospital Board, Dr W G Patterson, the senior administrative medical officer, suggests that senior registrar posts should be tenable, on an improved salary scale, for 6–7 years, with a promotion barrier half way through this period, and that full consultant status should normally not be reached before the age of 35 and until twelve years after qualification Whatever its merits in the present crisis, as a persisting feature of our hospital organisation such a scheme would have the defect of leaving the doctor until his middle thirties in ignorance of whether he was to gain a permanent hospital post Hence we prefer the idea of establishing junior consultant posts, carrying the title of specialist, as discussed in our issue of Dec 9

---

1 Sheldon J H Social Medicine of Old Age London, 1948
2 Thomson, A P *Proc R Soc Med* 1950 43 929
3 McKay C M. In Cowdry's Problems of Ageing Baltimore 1942
4 Marson F G W *Proc R Soc Med* 1950 43 935
5 Mayer J *Growth* 1949 13 7
6 Findley T *Amer J Med* 1949 7, 70
7 Parkhon C I *Byull eksp Biol Med. Moscow* 1946, 22, 3
8 Perlmutter M P Riggs D S *J clin Endocrinol.* 1949, 9 430

Annotations

CHOICE OF CAUSES IN HODGKIN'S DISEASE

THE histological picture of Hodgkin's disease in the lymph glands and other organs is more like an infectious granuloma than a neoplasm, and there have therefore been many attempts to find the infective agent Ewing was dramatising a fairly common observation when he remarked that tuberculosis follows Hodgkin's disease like a shadow , but the evidence that Hodgkin's disease is either an atypical reaction to *Myco tuberculosis* infection or a manifestation of avian tuberculosis does not carry conviction , nor do the claims to have implicated diphtheroid or brucella organisms In 1932 Gordon[1] demonstrated, in an extensive research, that when material from lymph gland tissue in Hodgkin's disease was inoculated intracerebrally into rabbits they developed an encephalitic reaction leading to paralysis, ataxia, and sometimes death Later, in these columns,[2] he identified the encephalitogenic agent as a virus and even demonstrated elementary bodies in affected cells Unfortunately subsequent work showed that intracerebral injections of some normal tissues, such as bone marrow and spleen, can produce the same reaction in rabbits , and eventually it became clear that the responsible agent, whether obtained from healthy tissue or from the lymph glands in Hodgkin's disease, is derived from the eosinophil cells[3]

The virus theory has lately been revived in Sweden, where Lofgren and Lundbäck[4] have isolated a virus from ground lymph glands or pleural exudate in 2 out of 6 cases of Hodgkin's disease They have also cultivated it from 1 of their 2 cases of lymphosarcoma, though only after the gland material had been stored at – 70°C for five weeks Material from the negative cases was taken through 5 allantoic and 5 amniotic passages without result After 3–5 egg passages the agent developed agglutinins for the red cells of several animals, and it was shown to fix complement in the presence of serum from 2 out of 5 patients with Hodgkin's disease This work, which follows their demonstration of a closely similar agent in sarcoidosis,[5] is still experimental and clearly requires further investigation

A different approach has been explored by Gendel and colleagues,[6] who had noted an apparent association between Hodgkin's disease and cryptococcosis, or torulosis, a systemic infection with the fungus known as *Cryptococcus neoformans, Torula histolytica, Debaryomyces neoformans, Cry meningitidis*, &c[7] The infection most commonly attacks the central nervous system, though in many cases the lungs and skin are also involved Gendel et al have collected 163 published cases and add 2 of their own , 14 of these 165 cases (8 5%) were associated with Hodgkin's disease—a proportion unlikely to occur by chance In 13 of the 14 cases Hodgkin's disease was diagnosed before cryptococcosis In the 14th case, one of the new cases reported by Gendel et al , both diagnoses were made at necropsy This patient had had Hodgkin's disease for about four years and X ray treatment for about a year He developed bilateral pleural effusion and ascites, with chylous fluid He did not respond to nitrogen mustard treatment and began to complain of headache, and the cerebrospinal fluid yielded a growth of *Cry neoformans* The patient died, and post mortem studies revealed cryptococcal infection in the pleural but not the peritoneal fluid, the organisms were also demonstrated in areas of caseous degeneration in the lungs, periaortic lymph glands, spleen, brain, and elsewhere The normal structure of the periaortic glands was replaced by pleomorphic tumour cells and hyalinised fibrosis, a picture distinct from the Hodgkin's disease areas , similar tumour-like cells were found at other sites The most likely explanation is that Hodgkin's disease weakens the patient's resistance to infection and allows the cryptococcus to win a foothold and spread But it is also possible that the fungus can produce a histological picture simulating Hodgkin's disease or one of the other reticuloses This would support the view that Hodgkin's disease is a response to infection by a variety of micro organisms

BIRTHMARKS AND MOLES

ANGIOMATOUS nævi (birthmarks) and pigmented soft nævi (moles) are by far the commonest congenital defect of the skin Dilatations of blood and lymphatic vessels sometimes also affect the subcutis, muscles, and bone, causing enlargement of part or the whole of a limb Rational treatment of these anomalies depends on a knowledge of their natural history, and this subject was discussed at a meeting of the section of surgery at the Royal Society of Medicine on Jan 3, when Mr D N Matthews described the following clinical types spider nævus , neonatal staining , superficial capillary hæmangioma , port wine stain , cavernous (mixed) hæmangioma , arterial hæmangioma , diffuse hæmangiomatous giantism , and multiple familial telangiectasis, in which lesions may also occur in internal organs and in the mucous membranes, causing epistaxis, hæmoptysis, or hæmatemesis

The spider or stellate nævus is simply dealt with by diathermy, the galvanocautery, or electrolysis to its central vessel and any conspicuous branches Neonatal staining clears up on its own As for the others, the port wine stain is usually a lifetime possession, because unlike the superficial capillary hæmangioma or strawberry mark, it is not associated with proliferation of the endothelial cells but only with a static dilatation of the vessels in the corium Its treatment consists either in excision and plastic repair, or in cosmetic coverage Before deciding on surgery it is well to attempt the latter, because cosmetic technique today has reached a stage where even dark purplish stains can be rendered much less noticeable, while even after operation cosmetic assistance may still be necessary to conceal scars

Three ways in which hæmangiomata may enlarge were mentioned by Mr Matthews they may grow by budding of new endothelial tissue, by canalisation of existing vasoformative tissue, or by tapping an additional blood supply from neighbouring blood vessels The third method may lead to very rapid growth Upward growth may lead to ulceration, which may be followed by fibrosis and slow healing, but often with a ring of residual hæmangioma Growth downwards may in some cases lead to erosion of vital organs, such as the eye Hæmorrhage following ulceration may be a serious complication with hæmangiomata mainly composed of arterial or cavernous tissue, whereas with capillary hæmangiomata it is not a serious matter Mr Matthews believes that spontaneous shrinkage of hæmangiomata is uncommon compared with extension—a view with which many would disagree Fading without treatment may occur by thrombosis and infarction, or by infection, fibrosis, and strangulation Mr Matthews said that excised hæmangiomata may show no sign of fibrosis, and he thought this made it improbable that they often clear on their own He did not, however, discuss their possible disappearance y natural processes which are not yet understood t seems significant that whereas the scars of surgical rocedures and irradiation for nævi are commonly bserved in later childhood and in adult life, one very arely sees a strawberry mark nævus after the age of ive years This suggests that spontaneous disappearance s common, for only a small proportion are excised W A Lister[1] followed up many cases of this sort and noted rapid growth during the first year or so, followed by a static phase, after which the great majority began to fade and disappeared without trace before the end of the fifth year A useful routine scheme is to measure the lesion accurately at the first attendance, or photograph it beside a rule The mother is advised of the probable subsequent progress, disabused about folk lore and the gratuitous advice of the woman next door regarding "male and female nævi," and asked to bring the child for periodical inspection If at about eight or nine months the lesion seems to have stopped growing, it can be safely left to run its natural course Surgical interference is necessary chiefly in the cavernous type, for hæmorrhage, rapid extension, and deep erosion and in cases with severe disfigurement or involving the mouth, ears, or orbital or perianal regions—sites at which rapid extension and disfigurement, or interference with functions, such as deglutition, may occur

---

[1] Gordon, M H Studies on the Ætiology of Lymphadenoma (Rose Research on Lymphadenoma) Bristol 1932

[2] *Lancet* 1936 ii, 65

[3] McNaught J B *J Amer med Ass* 1938 111 1280 Edward D G ff *Lancet* 1938 i 936

[4] Lundbäck H Löfgren S *Acta med scand* 1950 138, 460

[5] Löfgren, S Lundbäck, H *Ibid* p 71

[6] Gendel B R Ende M Norman S L *Amer J Med* 1950 9 343

[7] In recommending *Cryptococcus neoformans* the Medical Mycology Committee of the Medical Research Council remark that they do so without prejudice to any change of name becoming necessary later (M R C memo no 23 London, 1949 p 6

Mr Matthews described surgical treatment by the use of sclerosing agents, or excision, or a combination of the two methods Sclerosing agents are effective particularly in the cavernous (mixed) type, in which this form of treatment most often becomes necessary Suitable methods include heat, cold, irradiation, and the injection of sclerosing solutions Diathermy is preferred to cautery Carbon dioxide snow is used by many, but may leave a disfiguring ring of angioma around the scarred area Mr Matthews strongly deprecated the use of γ irradiation for these benign lesions of childhood—an opinion which should receive wide support Sir Stanford Cade, who presided at the R S M meeting, spoke of possible stunting of limb growth from its use and said that if it was applied to the mammary region in young girls it might lead to non development of the breast at puberty with the ugly scarring of atrophic radio dermatitis, the result might resemble that of a complete mastectomy with subsequent irradiation The treatment of port wine stains by γ irradiation is also contraindicated, but α irradiation by thorium X paint containing 1500 electrostatic units per cubic centimetre, applied at fortnightly intervals, has been recommended as safe, and is sometimes followed by improvement in cases of nævus flammeus, where the individual vessels are not too obvious before treatment is begun Sclerosing fluids include boiling water, 40% saline solution, and 'Ethamolin' froth These, Mr Matthews said, may cure or may lessen the extent of surgery afterwards necessary The best results are obtained by first applying transparent adhesive tape under pressure over the lesion and then injecting through this Mr D F E Nash recommended the use of an all metal dental syringe with a fine flexible needle for easier and safer injection procedures

Turning to moles, Mr Matthews recommended excision in toto and grafting if necessary sometimes only partial excision is possible and in these circumstances a central plaque graft, subsequently stretched, gives the best results He did not deal, however, with the vexed question of the relationship of moles and malignancy The removal of moles about the face is usually requested for cosmetic reasons, and apart from removal of the hairs by electrolysis, their simple excision gives most satisfactory results Some believe that any handling of these lesions may initiate malignant changes, but histological findings suggest that this is unlikely, for the nævus cells are of the intradermal (resting) type Confusion has arisen with junction (active) nævi in which the nævus cells are situated at the junction of the epidermis and the dermis These are usually hairless, more intensely pigmented, and bluish black, and the patient may come for treatment not for cosmetic reasons but because the lesion has lately been enlarging or bleeding In cases of this sort careless manipulation, or even a biopsy, may lead to the grim results which have placed something of a hoodoo on the treatment of moles Nevertheless it is a wise precaution not to subject *any* mole to forceps pressure during its removal, and to refer all moles for histological study Moreover, they should be widely and deeply excised Probably all pigmented moles on the hands or feet or in the axillæ or groins, ought to be excised as a prophylactic measure, because of the risks of trauma at these sites Malignant melanomata tend to arise in the parts of the body more distant from the head, and lesions on the soles and in the paronychial regions are especially suspect, even if pigmentation is inconspicuous or absent

CLASSIFICATION OF CANCER OF THE CERVIX

THE classification of cancer of the cervix uteri adopted by a League of Nations committee and published in 1937 was enthusiastically adopted by many countries and marked a big advance in the presentation of results of radiotherapy in this form of cancer Indeed it gave a lead which might well be followed by all doctors seeking to evaluate the results of treatment of their patients

The committee's aim was to provide a classification that would be accepted everywhere, so as to secure a common basis of understanding and comparison of the results obtained by radiotherapy centres throughout the world In the United States, however, this classification of carcinoma of cervix into four well defined stages has not been used exclusively, and at the fourth American Congress of Obstetrics and Gynæcology, held last year, an international committee was appointed to find a classification that would be acceptable to all centres treating cancer of cervix This new committee has now recommended that the League of Nations classification of carcinoma of cervix should in all essentials be retained, with the one exception that cases of carcinoma in situ should henceforth be removed from stage I and placed in a new category, stage O As thus revised, the stages will be

Stage O —Carcinoma in situ—also known as pre invasive carcinoma intra-epithelial carcinoma, and similar conditions

Stage I —The carcinoma is strictly confined to the cervix

Stage II —The carcinoma extends beyond the cervix, but has not reached the pelvic wall The carcinoma involves the vagina, but not the lower third

Stage III —The carcinoma has reached the pelvic wall (On rectal examination no cancer free " space is found between the tumour and the pelvic wall) The carcinoma involves the lower third of the vagina

Stage IV —The carcinoma involves the bladder or the rectum, or both, or has extended beyond the limits previously described

The committee resolved that "this Classification should be termed the International Classification of the Stages of Carcinoma of the Uterine Cervix, and that all organisations concerned with the problem on hand be approached to consider its adoption "

With the introduction of stage O, pre invasive or intra epithelial carcinoma of cervix—the so called carcinoma in situ—is placed in a stage by itself Technically, pre invasive carcinoma is within stage I, but its prognosis is not the same, the growth being still confined within the basement membrane and therefore likely to be much more amenable to treatment The usefulness of this modification in staging will largely depend on the acceptance by pathologists and other specialists of a diagnosis of cancer based on the cytological study of the cervical epithelium This is a method of diagnosis that enjoys much popularity in America, where cancer-detection centres are widely established and great numbers of examinations by the smear technique are made in laboratories with trained staff concentrating on this study The position in many other countries, however, is different, and this method of diagnosing cancer has so far been less generally accepted outside the U S.A If, with greater experience, the method becomes a routine procedure for all patients undergoing gynæcological examination, a welcome advance, not only in earlier diagnosis but also in the results of treatment, should follow For this reason in itself, apart from the clearer basis for comparison of results of treatment offered by the addition of a stage 0, the new classification deserves adoption

---

[1] *Lancet* 1938 i 1429

PROSPECTS IN THE TUBERCULOSIS SERVICE

Pulmonary tuberculosis still needs—and doubtless gets—more beds and more outpatient hours than any other disease, even so, it does not get enough of either Dr G E Godber, deputy chief medical officer of the Ministry of Health, remarked at a conference of the public health section of the Royal College of Nursing, on Jan 13, that we cannot be satisfied with conditions which do not enable us to treat the early case, or isolate the infectious case, *at once* These, indeed, are the prime necessities in the public health management of any infectious disease, but the difficulties of achieving them for tuberculosis are of course formidable lack of money is possibly the chief of them, but lack of nursing staff for beds, and lack of houses also tell against the tuberculous Probably nothing tells so heavily, however, as the awkwardness of human nature Dr Godber admitted, cautiously, that he did not feel sure that the chest physicians and the medical officers of health were everywhere working well together, and other speakers must have encouraged his doubts There is much to be said for his view that the preventive aspect of tuberculosis has rightly been left in the hands of the local authorities, since the M O H has our preventive machinery constantly in use under his hand The health visitor, being primarily a dealer in prevention, has been left on his staff But this division of responsibility is certainly giving rise to trouble in some places Dr Philip Ellman, who took the chair, felt strongly that the health visitor must be present when the patient is attending the clinic, but in some areas she is not allowed to attend sessions at the chest clinic or is not able to attend all sessions She thus loses an important chance to understand the cases and keep continuous touch with them while the chest physician loses a valuable lieutenant A nurse sent in from the local hospital—perhaps a different nurse each week—cannot give him the same informed help as the health visitor, who knows the patient's home

That this kind of friction is quite unnecessary was made clear by speakers from regions where collaboration between the health department and the chest clinic is good At Southend, Dr E G Sita Lumsden said, the M O H, the assistant M O H (who is also the school medical officer), the superintendent health visitor, the home help supervisor, the superintendent of nursing, the chief sanitary inspector, the children's officer, and the chest physician all meet weekly to discuss the cases of tuberculosis under treatment and to arrange what each shall contribute to their care This plan works well The committee so formed are in touch with the housing authority and advise about patients who need rehousing, taking care to propose only those for whom a change is really necessary Dr Sita Lumsden has also encouraged the general practitioners to send all suspected cases and contacts to the clinic for X ray examination, and this has favoured early diagnosis to such an extent that a mass radiography survey detected only a very small number of new cases Such an example of successful collaboration may be contrasted with the experience of a sanatorium physician who said that while they had found it possible, in her area, to form good relations with the thoracic surgeons and general practitioners, they had not succeeded in interesting the medical officer of health—or indeed the entire local authority The sanatorium of 220 beds has no almoner Many lung resections are done there, and it has been her experience that patients who before admission had high priority for housing, after lung resection—when their need of good quarters is often very high—are taken off the priority list This sanatorium, which employs reabled nurses, is never short of staff, and indeed sometimes has a surplus; but there is no room for more beds in the existing building Yet there is a long list of patients awaiting admission in the region

Dr Marc Daniels reminded the meeting that the allocation of beds for tuberculosis in general hospitals is the one thing which can act immediately on waiting lists Here again progress depends on good feeling In some places, he said, there is considerable opposition from regional hospital boards and hospital management committees Domiciliary treatment can be successful only if the chest physician can use hospital beds for short term measures of treatment, but these measures can be used only if they are supplemented by a good clinic service, and some of the clinics are quite inadequate Dr Godber mentioned a recent Ministry of Health survey, unfortunately still confidential, which has shown that "a surprisingly large number" of chest physicians now have hospital beds at their disposal—news whose value must depend on the surprise threshold of the Ministry

A question about the pool of infection in London's common lodging houses brought Dr William Hartston to his feet in defence of the London County Council. What goes on in Rowton Houses, he implied, is not the council's affair the 200 cases in common lodging houses, which the L C C inspects, represent no more, he thinks, than the incidence in the general population At three of the best houses (where every man has his own cubicle and can cough to his own satisfaction) the L C C has arranged that cases recommended by a chest physician should have priority of admission, and that they should be allowed to lie down on their beds in the afternoons. A hostel has been opened in the country for homeless tuberculous patients who are not fit for work, and another is to be opened in London in March for working men This is not much, but it is something Only money—a great deal of money—can put everything right, and at the moment we cannot afford so much That is all the more reason for pressing forward with measures which cost nothing but good will—the allocation of beds in general hospitals, and a closer collaboration between the chest physician and the M O H Whatever happens, Dr Godber believes we should never again allow the tuberculosis service to work in isolation, out of the stream of general medicine It offers plenty of work for everyone concerned—the chest physician, the M O H the general practitioner, the health visitor—if they will agree to share it

---

Dr J **Eastman Sheehan**, professor of plastic reparative surgery at New York Polyclinic Medical School has died in New York During the late war he worked in London for some time and he contributed to our columns papers on skin grafting and on facial paralysis

Special Articles

THE ADRENOCORTICOTROPIC HORMONE (A.C.T.H.) OF THE PITUITARY GLAND

C. J. O. R. MORRIS
Ph.D. Lond., F.R.I.C.
READER IN CHEMICAL PATHOLOGY IN THE UNIVERSITY OF LONDON
From the endocrine and medical units, the London Hospital

THE intimate connection between the pituitary gland and the adrenal cortex was first satisfactorily demonstrated by Philip Smith in 1928–30. Using his newly developed technique of hypophysectomy in the rat, he showed that the removal of the pituitary caused a relatively rapid atrophy of the adrenal cortex, which could be repaired by transplants of anterior pituitary tissue. The active principle was later called pituitary adrenocorticotropic hormone (A.C.T.H.). Shortly after Smith's work H. M. Evans (*1933*) showed that pituitary extracts could also bring about adrenal repair in the hypophysectomised rat.

CHEMISTRY

Many attempts were then made to isolate the hormone, but little real progress was made until the rapid development in protein chemistry produced the modern techniques for separating and characterising proteins.

In 1943, Li, Evans, and Simpson, at Berkeley, California, working with sheep pituitaries, and Sayers, White, and Long, at Yale, using pig pituitaries, independently isolated proteins with high adrenocorticotropic potencies. These preparations, which were very similar in chemical and physical properties, seemed to be homogeneous in sedimentation, electrophoresis, and solubility studies. Their molecular weight was 20,000.

The preparation of a protein of similar biological potency from beef glands has been cited by White (1944), but no physicochemical data have been published, and efforts in the London Hospital laboratory, and in that of Dr. C. H. Li (personal communication), to isolate a homogeneous beef A.C.T.H. preparation have so far been unsuccessful.

The amounts of A.C.T.H. present in the pituitary glands of different animals vary widely. Astwood and Tyslowitz (1942) showed that pig glands contained most, sheep glands rather less, and beef glands least A.C.T.H. Sayers et al. (1949) estimated that the human pituitary may contain A.C.T.H. equivalent to 20% of the dry weight. The yields of homogeneous protein hormone obtained from animal glands have been lower than these estimates would suggest. Fishman (1947), by a modification of the earlier methods, obtained 1 g. of homogeneous protein hormone from 1 kg. of pig pituitaries (about 5000). Li et al. (1943) originally obtained 60 mg. from 1 kg. of sheep pituitaries, but Li has obtained much higher yields from these glands by a modified procedure.

Though the evidence for the homogeneity of sheep and pig protein A.C.T.H. preparations appears to be satisfactory, there is now much evidence that the active principle may be of relatively small molecular size. Li et al. (1943) reported that about 60% of the protein could be digested with pepsin without loss of biological potency. Li (1947) showed that a similar effect was observed after partial hydrolysis with hydrochloric acid, and from a study of the digestion products he concluded that the active fragment is a polypeptide with a molecular weight of about 1200.

Evidence of another type comes from ultrafiltration experiments. Anselmino et al. (1934) and Tyslowitz (1943) claimed ultrafiltration of A.C.T.H. activity through membranes impermeable to protein, but neither was able to prepare the hormone in more concentrated form.

Work at the London Hospital began in 1938 (Crooke et al. 1947). Cortis Jones et al. (1950) have shown that by ultrafiltration of beef A.C.T.H. concentrates under suitable conditions it is possible to prepare a mixture of polypeptides which is 1.5–2.0 times as active as homogeneous pig A.C.T.H. and contains about half the biological activity initially present in pituitary glands. A polypeptide (A.C.T.P.) isolated from this mixture seems to be homogeneous and is ten times as active as homogeneous pig A.C.T.H. (Morris and Morris 1950). It thus seems certain that, unlike that of most protein hormones, the biological activity of the adrenocorticotropic protein resides in a small molecular grouping. Experiments in the London Hospital laboratory suggest that the beef and pig protein hormone molecule is made up of a group of peptides held together by relatively weak forces. This complex can be dissociated and reassociated by changes of pH and salt concentration. The variation in biological activity in A.C.T.H. from different sources, and also the fact that certain heterogeneous protein preparations are more active than the homogeneous protein A.C.T.H., can be explained on this basis. The active peptide seems to have all the different biological properties associated with the protein hormone.

The implications of the idea of a relatively small active grouping are very important for our understanding of the action of A.C.T.H. Since the space occupied by this group at its site of action is about the same as that occupied by many synthetic drugs, such concepts as that of competitive inhibition, which have played an important part in modern pharmacology, may also be relevant here. Work in this direction must of course await the elucidation of the amino acid sequence in the active grouping and the determination of the chemical specificity of the biological action.

Lesh et al. (1950) have recently announced the preparation of material having 120 times the potency of Armour standard from pig pituitaries. This material had a molecular weight greater than 2500 and contained at least twelve different amino acids. If this preliminary report is confirmed, the concept of A.C.T.H. as a component of the protein hormone of Li et al. (1943) and Sayers et al. (1943) must be abandoned.

BIO-ASSAY

Valid assays of A.C.T.H. can be made only on hypophysectomised animals in which the endogenous source of the hormone has been removed. Many erroneous reports of the presence of A.C.T.H. in blood and urine have been made through neglect of this principle. Three main methods are now generally used for bio-assay of the hormone.

(1) *Adrenal Repair.*—Hypophysectomised rats are kept for 10–14 days after operation. The adrenals then weigh 25–30% of those of controls. The material to be tested is administered in divided doses and adrenal repair estimated by increase in adrenal weight or by histological examination.

(2) *Adrenal Maintenance.*—Administration of the material to be tested is begun *immediately after* hypophysectomy, and the amount of test material necessary to maintain the adrenals at the normal level is estimated.

(3) *Adrenal Ascorbic acid Depletion.*—Sayers et al. (1945) observed that injection of A.C.T.H. leads to depletion of adrenal cholesterol and ascorbic acid, and that this depletion coincides with the liberation of glucogenic hormones from the adrenal cortex. They suggested that these are synthesised from cholesterol in the adrenal cortex by some process involving ascorbic acid. Sayers et al. (1948) have used the depletion of adrenal ascorbic acid by A.C.T.H. in the hypophysectomised rat as a sensitive and specific bio-assay method for the hormone. As little as 0.5 μg. of pig A.C.T.H., or 0.05 μg. of beef A.C.T.P., produces a 20% depletion. This method is probably the best now available.

PHYSIOLOGY

The various biological effects produced by A C T H are mediated *solely through the adrenal cortex* In laboratory animals adrenalectomy abolishes all these effects, and in many cases they have also been duplicated with pure adrenocortical steroids The chief physiological actions of the hormone are

Production of Adrenal Hypertrophy

It has been stated that the adrenals of the rat can be increased in weight from about 30 to 400 mg by continuous intravenous infusion of A C T H Bergner and Deane (1948) show that in the rat this hypertrophy is confined mainly to the zona glomerulosa, but the existence of a species difference does not warrant the extension of this conclusion to man

Synthesis of Adrenocortical Hormones in the Adrenal Glands

As mentioned above, injection of A C T H causes depletion of adrenal ascorbic acid and adrenal cholesterol Sayers et al (1943) showed that this process was accompanied by the increased deposition of liver glycogen typical of the action of adrenal glucocorticoids (" S hormones ") The characteristic decrease in the number of circulating eosinophils brought about by these substances has also been demonstrated in man, mouse, and rat after administration of A C T H Estimations of " 11-oxysteroids " (which give a rough indication of the excretion of glucosteroids) in patients receiving A C T H also confirm these conclusions Since the administration of A C T H causes an increase in 17-ketosteroid excretion in man, it has been concluded that the hormone also stimulates production of " N " (nitrogen-retaining) hormones by the adrenals, contrary to the earlier suggestion of Fuller Albright (1947) that these substances were controlled by the pituitary luteinising hormone However, certain glucocorticosteroids can give rise to urinary 17-ketosteroids, and as the direct effect of A C T H on the nitrogen balance in man seems to be variable, the question of production and control of " N " hormone must await further investigation Most workers now agree that administration of A C T H in man is followed by marked retention of $Na^+ + Cl^-$, similar to that produced by deoxycortone It may therefore be concluded that the adrenal mineralocorticoids (" Na " hormones) are also under pituitary control in man This conclusion, however, is not valid for mouse and rat

It will therefore be seen that all the known types of adrenocortical hormones can be produced by the adrenal glands under the action of A C T H , and that the over all effects of this hormone will depend on the ratio of the various corticoids produced by the stimulation

Sayers and Sayers (1947) have shown that this mechanism is self regulating injection of certain corticoids—e g , ' Cortisone '—inhibits production of A C T H by the pituitary They have also shown by the adrenal ascorbic acid depletion method that a state of stress elicits increased production of A C T H by the pituitary, and that this effect can be inhibited by injection of corticoids This relation is quantitative, in that a severe stress necessitates a large dose of corticoids to inhibit production of A C T H The glucocorticoids —e g , cortisone and 17 hydroxy corticosterone (Kendall's compound F)—are much more effective in this inhibition mechanism than are the mineralocorticoids Sayers and Sayers conclude that the pituitary secretes A C T H at a rate which is adjusted to the corticoid requirements of the peripheral tissue cells The operation of this mechanism has been reviewed by Sayers (1948)

The physiological effects produced by A C T H , indirectly via the adrenocortical hormones can be summarised as

Inhibition of Protein Synthesis

A C T H inhibits the action of the pituitary growth hormone which regulates the rate of protein synthesis in the organism with a consequent increase in the amount of amino acids in the blood and increased excretion of nitrogen

Increase in Rate of Gluconeogenesis

The carbon chains derived from fats and amino acids are used in the synthesis of carbohydrates This process is mediated by the glucocorticoids, which also increase the storage of glycogen in the liver In rats on a high-carbohydrate diet, or with insulin-deficiency induced by alloxan, A C T H can induce glycosuria Similar effects have been observed in persons with abnormal sugar tolerance curves

Involution of the Thymus Gland and Lymph nodes

Dougherty and White (1945) have shown that involution of these tissues follows administration of A C T H. in the normal but not in the adrenalectomised animal. They have also shown that there is a corresponding fall in the lymphocyte-count Forsham et al (1948) found a striking depletion of the circulating eosinophils after the injection of A C T H This effect can also be produced by the glucocorticoids, 17-hydroxy corticosterone (compound F), and cortisone (compound E) Forsham et al. have suggested a test for adrenal function based on this response The extent of the depletion following administration of a standard dose of A C T H may be regarded as a measure of the amount of functional adrenocortical tissue When adrenal function is impaired—e g , in addisonians—the administration of A C T H produces little or no change in the eosinophil count

Dougherty and White (1945) stated that the titre of certain antibodies in the blood rose after the administration of A C T H and suggested that these were liberated as a result of a breakdown of lymphocytes In view of later negative findings, however, this work requires further corroboration

Changes in Electrolyte Balance

These changes, mediated by the mineralocorticoids, may be summarised as retention of sodium and chloride and excretion of potassium, calcium, and phosphate The latter changes may perhaps be correlated with the retardation in chondrogenesis and osteogenesis in the rat tibia and in the decrease in plasma alkaline phosphatase following administration of A C T H (Li et al 1949). The effects of A C T H on calcium and phosphate metabolism in man, however, require confirmation owing to contamination of preparations used with posterior pituitary hormones

A C T H IN BLOOD AND URINE

Several claims have been made for the detection of A C T H in normal human blood and urine None of these, however, are convincing, because of the bio assay methods used

Taylor et al (1949) were unable to demonstrate A C T H in normal blood by the sensitive and specific ascorbic acid depletion method of assay They were, however, able to detect the hormone in the blood of patients with adrenal deficiency We have recently recovered about 2 5% of the amount administered from the urine of a nephrotic receiving peptide A C T H , and 5% has been recovered from the urine of a rheumatoid arthritic

Greenspon et al (1950) have shown that A C T H injected intravenously in the rat disappears completely from the blood stream in about 20 minutes, with a half life of 5 minutes It thus seems very unlikely that appreciable quantities of the hormone persist in normal blood The need for multiple divided dosage in A C T H treatment is also emphasised by this work

CLINICAL ASPECTS

The preparation of pig protein A C T H on a relatively large scale by the Armour Company in Chicago has made it possible to study the effects of the hormone in man in both normal and pathological states

The results of such studies have in general confirmed the above mentioned work on laboratory animals—with the notable exception of the effect on mineral metabolism As already mentioned, it is clear that in man, unlike the rat, considerable retention of sodium and chloride follows administration of A C T H The original studies of J S L Browne, Fuller Albright, Mason, Li, and Evans and their co workers are collected in the Proceedings of he Josiah Macy Conference in 1948 on Metabolic Aspects f Convalescence (Reifenstein 1949)

The most striking clinical application of ACTH has undoubtedly been provided by Hench et al. (1949a and b), who have shown that it produces dramatic remissions in otherwise intractable rheumatoid arthritis The details of this work, which has been completely confirmed, are now so well known that little further discussion is needed t may perhaps be pointed out that no striking abnormalities of pituitary or adrenal function are known in rheumatoid arthritis and that, as the doses used are far above the physiological levels, the defect in such cases may be in impaired utilisation of the glucocorticoids by the peripheral tissue cells However, Sommerville et al (1950) have shown that the conversion of progesterone into pregnanediol is greater in the rheumatoid arthritic than in the normal person Since deoxycortone s also converted into pregnanediol in man, this observation suggests that abnormal steroid metabolism may also be a factor in rheumatoid arthritis It must be emphasised that the sequence from administration of ACTH to relief of arthritic symptoms must involve many biochemical processes, one or more of which may be defective in rheumatoid arthritis Such considerations may explain the conflicting findings in combined administration of deoxycortone and ascorbic acid It must not be assumed that the essential biochemical defect is the same in all cases

The results produced by ACTH in rheumatoid arthritis have led to an examination of its effects in many diseases, which can be grouped into three main classes the so-called collagen diseases, the allergic diseases, and the lymphatic diseases

Collagen Diseases

In rheumatic fever ACTH produces effects as striking as those in rheumatoid arthritis The hormone seems to suppress the symptoms and in many instances shortens the course and severity It also seems to alleviate acute endocarditis and pericarditis Diets very low in salt are advisable during treatment of patients with acute cardiac involvement, so as to reduce retention of water Reports on this condition have been published by Hench et al (1949b) and by Massell and Warren (1949) Striking results in disseminated lupus erythematosus have been claimed by Elkinton et al. (1949) and Grace and Combes (1949) ACTH promptly alleviates symptoms but there is an equally rapid relapse when it is discontinued.

Periarteritis nodosa has been studied by Shick et al (1950) The effects are similar to those observed in other diseases of this group—i.e , relief of symptoms, with recurrence of the condition when ACTH treatment is stopped

In this connection it is interesting that the skin and vascular reactions produced in rats by injection of horse serum have been shown by Berthrong et al. (1950) to be inhibited by ACTH Rich (1946 47) believes that these vascular changes are identical with those in periarteritis nodosa

Other diseases of this group where a temporary alleviation is produced by ACTH are scleroderma, dermatomyositis, and psoriasis , but only a few cases have been studied

Allergic Diseases

ACTH. exerts a well marked effect on bronchial asthma and allergic rhinitis (Rose 1949) It was previously known that during acute asthmatic attacks the patient excretes histamine and histidine in the urine During protracted ACTH treatment these substances are still intermittently excreted, but no bronchial symptoms are observed. The circulating eosinophils, which disappear from the circulation on ACTH treatment, have a relatively high histamine content

Lymphatic Diseases

These have been studied by Rawson and his colleagues A very remarkable effect on acute juvenile leukæmia has been observed. Even in extremely ill patients ACTH relieves the symptoms promptly and the blood picture is restored almost to normal within fourteen days but, when ACTH treatment is discontinued, a relapse to the original state occurs Less dramatic changes have been observed in chronic lymphatic leukæmia, acute and chronic myeloblastic leukæmia, lymphosarcoma, and Hodgkin's disease (Pearson et al 1949)

Gout

Injection of ACTH during a quiescent period of gout induces an attack of gouty arthritis, but injection during an acute attack immediately alleviates the attack (Hellman 1949) The mechanism of the process is not understood but it seems to have no connection with the elimination of uric acid produced even in normal persons by ACTH

Myasthenia

Torda and Wolff (1949) studied cases of myasthenia gravis during ACTH treatment They observed a partial remission in so far as the patients could reduce the daily level of neostigmine necessary for reasonable activity They also observed improved muscular activity and decrease of the specific cholinesterase inhibitor usually present in the serum of patients with myasthenia gravis The improvement was maintained in one case up to a year after the end of treatment

It will be seen that, in almost all the conditions studied, ACTH may produce a more or less striking suppression of symptoms but does not seem to alter the essential course of the condition or to affect the fundamental cause

Ophthalmological Disorders

Gordon and McLean (1950) and Olson et al (1950) have studied the effect of ACTH in a number of ophthalmological disorders Amelioration of inflammation was observed in several of them, and these workers believe that ACTH will be of value in such cases because the improvement seems to be maintained after the end of treatment, in contrast to the other conditions described previously

Virus Diseases and Carcinoma

ACTH seems to have no effect in virus diseases —e g , poliomyelitis (Coriell et al 1950)—or in various forms of carcinoma

The somewhat optimistic hopes which the prompt relief of symptoms in many conditions aroused thus have very little basis A promising line for future work would be to treat the causal factors by other methods while the symptoms are controlled by ACTH

However, the fact that the symptoms of many otherwise intractable conditions have been shown to be reversible is of great importance, and it is evident that ACTH is a physiological tool of great potency, capable of producing fundamental changes in metabolic processes

REFERENCES

Albright F (1947) *Rec Prog Horm. Res* 1 293
Anselmino K. J Hoffmann F Herold L (1934) *Klin Wschr* 13 209
Astwood E Tyslowitz R. (1942) *Fed. Proc.* 1 4
Bergner G E Deane H W (1948) *Endocrinology* 43 240
Berthrong M. Rich A. R Griffith P C (1950) *Bull Johns Hopk Hosp* 86 131
Coriell L L Siegel A C. Cook. C D Murphy L Stokes J jun (1950) *J Amer med Ass* 142 1279
Cortis Jones B Crooke A C Henly A. A. Morris P Morris C J O R (1950) *Biochem J* 46 173
Crooke A C Henly A A. Morris C J O R (1947) Abstr Int Physiol. Congr p 139
Dougherty T F White A (1945) *Endocrinology* 36 207
Elkinton J R Hunt A D jun Godfrey, L McCrory W W Rogerson A. G Stokes J jun (1949) *J Amer med Ass* 141 1273
Evans H M. (1933) *Ibid* 101 425
Fishman J B (1947) *J biol Chem* 167 425
Forsham P H Thorn G W Prunty F T G Hills A G (1948) *J clin Endocrinol* 8 15
Gordon D M. McLean J M. (1950) *Amer med Ass* 142 1271

(continued overleaf)

THE REGISTRARS' CUT

SCOTTISH MINISTER'S EXPLANATION

WRITING to Lady Tweedsmuir, M P, Mr Hector McNeil, the Secretary of State for Scotland, says that he and his officers have been much concerned about the proposed reduction in the number of medical registrars in Scotland, " and I am anxious to persuade you and the public in general as well as the registrars that we have been handling the subject most carefully, without haste, and justly " He continues

" Now I should want to make it emphatically clear at the outset that the changes contemplated are not dictated as an economy measure and that, further, I am concerned, at least as much as anyone else, to see that the standard of medical services in the hospitals is maintained and not impaired by these changes

" It has been apparent for some considerable time that there were far too many registrars under training in hospitals in relation to the number of specialist posts likely to be available in the foreseeable future Now, plainly it was unfair that these young men and women should be left to entertain quite unjustifiable expectations of a specialist career So as long ago as December, 1949, an assessment of the situation by the Department of Health was sent to regional boards for their consideration It was also quite deliberately published in the medical press[1] and elsewhere So I hope that you will agree that we have not acted precipitately and that everyone concerned has had fair and timeous warning of the situation and all its implications

" Further, in June, 1950, a more detailed examination of the numbers in the registrar grades and the optimum number required to meet the needs of the National Health Service for specialists was published[2] and again sent to the regional boards

" The broad conclusion of these studies, i e, that the number of registrar posts would have to be reduced if the training establishment were to be brought into balance, has been generally accepted by the medical profession and the regional boards Consequently, a few weeks ago the Department issued a memorandum to boards specifically asking them to put in hand the necessary adjustments in the hospital staffs so that the number of registrars is reasonably related to specialist prospects in general and, in particular, to the prospective needs for the several types of specialists

" The main cause of the present difficulties is that although the registrar grade was intended to be for doctors training to be specialists it has been used far beyond this purpose and large numbers of registrars are at present unfortunately being employed without any clear idea whether they will be needed later as specialists or whether they are needed now for hospital work which is above the level of a house-officer but below that of a consultant Indeed, there are further irrationalities Although this is exceptional and not at all general, some are being employed in posts (both in teaching and non teaching hospitals) which do not really afford training at all and are virtually a dead-end I hope that you will agree that such situations have to be remedied.

" The Department's memorandum to regional boards attempts to make provision for the maximum number of registrars who can be trained with a reasonable expectation that they will be, if they make the grade, ultimately employed as specialists From the medical staffing point of view it provides in addition for the recruitment of ' clinical assistants who should be able to take over some of the work now being done by registrars and at the same time engage in general practice It also, I should make clear, permits boards to make a case for any other additional posts that they think may be necessary to maintain the essential services of the hospitals

" I must also mention the question of the level of teaching in our medical schools which must not of course be impaired by these changes As you will know, it is the existing practice for some of the doctors who are training to be specialists to be employed to a limited extent during their training on duties connected with clinical teaching How far it is necessary to provide additional registrar posts in the hospital service because of this will be for each regional board to work out in consultation with the university concerned[3]

" We must, I think bear in mind that at present the medical schools can produce only an approximately fixed number of doctors each year This output has to cover all branches of medicine and of course a regular supply of men and women must be made available for the general practitioner service which, it must be admitted, is the backbone of the whole service I am afraid, therefore, that while we shall of course endeavour to see that the specialist service is developed where necessary, we cannot look to that service to provide unlimited opportunities for the registrars

' Naturally, we have had very much in mind the effect of this policy on the existing registrars and I am personally much disturbed that some of them are bound to be disappointed However, even if their expectations suffer, there are several points which I think they might reasonably expect to bear in mind (1) The recent memorandum from the Department is not a bolt from the blue For more than a year it has been manifest to everyone taking an intelligent interest in the subject that the number of registrars proper would have to be reduced (2) Long before the inception of the National Health Service it was customary that the training for specialist status should be highly competitive and the weeding out process consequently was severe What has happened recently is that the increase in the number of trainees has risen in an excessive disproportion even to the increased number of specialist posts provided by the National Health Service (3) Doctors, like all of us cannot always expect to find posts which give them exactly the kind of career they would prefer Individual preferences must be related to the needs of society and this to some extent must always determine the particular branch of medicine which doctors are to follow Even now there are some specialties in which the opportunities are better than in others and in which so far, there has not been heavy competition for appointments I might mention psychiatry and radiotherapy where there has been some difficulty recently in filling some of the senior posts (4) There is no escaping the fact that many of those registrars now in posts will find sooner or later that there is not a specialist post for them either generally or in their chosen specialty It is, I think, in their own interest that this situation should be faced frankly now (5) We have also to consider the position of the younger doctors now approaching registrar status. It is important that we should preserve for the abler doctors of each medical generation a fair chance to train for the higher posts To bar them simply because of their age in favour of senior men who may not be of the same promise would be unfair both to these individuals and to patients and sufferers whom they would eventually treat

---

[1] *Lancet* 1949, ii 1193

[2] *Ibid*, 1950, i, 1165

[3] In Scotland the teaching hospitals are administered by the regional boards —ED L

DR MORRIS REFERENCES (*continued*)

Grace A W Combes F C (1949) *Proc Soc exp Biol , N Y* **72** 563
Greenspan F S Li, C H Evans, H M (1950) *Endocrinology*, **46** 261
Hellman L (1949) *Science* **109** 280
Hench P S Kendall E C Slocumb C H , Polley, H F (1949a) *Proc Mayo Clin* **24**, 181
— Slocumb C H , Barnes A R Smith H L , Polley H F , Kendall E C (1949b) *Ibid* p 277
Lesh, J B Fisher J D Bunding I M , Kocsis J J Walaszek L J , White W F , Hays E E (1950) *Science* **112**, 43
Li C H (1947) *Ann Rev Biochem* **16** 201
— Evans, H M., Simpson M E (1943) *J biol Chem* **149** 413
— Kalman C Evans H M Simpson M E (1946) *Ibid*, **163** 715
Massell B F Warren J E (1949) Proceedings of 1st Clinical A C T H Conference Chicago London p 405
Morris P Morris C J O R (1950) *Lancet* i 117
Olson J A Steffensen E H Margulis R R Smith, R W , Whitney, E L (1950) *J Amer med Ass* **142** 1276
Pearson O H Eliel L P , Rawson R W (1949) Proc 1st clin A C T H Conf p 318
Reifenstein E C jun (1949) Proceedings of Conferences on Metabolic Aspects of Convalescence New York Josiah Macy, Jun Foundation
Rich A R (1946–47) *Harvey Lect* **42** 106
Rose B (1949) Proc 1st clin A C T H Conf p 491
Sayers G (1948) *Rec Prog Horm Res* **2** 81
— Sayers M A (1947) *Endocrinology* **40** 265
— — Burns T W Merkin M (1949) *Ibid* **44** 439
— — Liang T Y Long C N H (1945) *Ibid* **37**, 96
— White A Long C N H (1943) *J biol Chem* **149** 425
Sayers M. A , Sayers G Woodbury L A (1948) *Endocrinology*, **42** 379
Shick P M. Baggenstoss A H Polley, H C (1950) *Proc Mayo Clin* **25** 136
Smith P E (1930) *Amer J Anat* **45** 205
Sommerville I F Marrian G F Duthie J J R Sinclair, R J G (1950) *Lancet* i 116
Taylor A B Albert, A Sprague R G (1949) *Endocrinology* **45**, 335
Torda C , Wolff H G (1949) *J clin Invest* **28** 1228
Tyslowitz R (1943) *Science* **98** 225
White A (1944) Chemistry and Physiology of Hormones Washington p 1

"I am sure that regional boards, who recognise the needs f the specialist service in their areas and know the personal osition of individual registrars, will make the necessary eductions not only with full consideration for the needs of the ervice but seeking also, as far as it is possible, to mitigate ardship for the doctors involved It is perhaps relevant hat I should say to you (without criticism of the excellent nd arduous work overtaken in the other areas) that the uthorities in the North Eastern Region, both before and ince the inception of the new service, have exercised such a degree of caution and restraint in this subject that the difficulties there are much less severe than those in other parts of the country That the hospitals in the North East have continued their work at a high standard with a relatively small number of registrars is worth the closest study "

Reconstruction

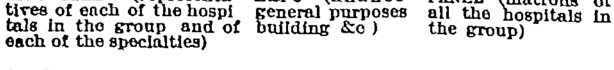
THE PRESENT STATE OF THE HOSPITALS

FROM A CORRESPONDENT

WITH a colleague, I have been visiting hospitals in several regions What follows is an attempt to summarise our impressions

Let me say at once that, from the standpoint of some of the more progressive hospital management committees (H M C), the new set-up is a success Anyone who visits a series of group headquarters as we have done, will find himself approving the outright unification of the hospital services and the broad plan of local administration by bodies constituted solely for this purpose, combined with a wider regional control of the higher flights of medical affairs The British genius for government by committee, backed by the old sentiment towards the hospitals, has proved its capacity to fuse into a new entity the diverse elements that go to make up the H.M C Continually we were told "the committee is working well, there have been teething troubles, there are still many differences of opinion but it is all right" There is a general, and strong, sense of responsibility for the welfare of the hospital services of the area *as a whole* This is a new thing in hospital affairs, and its emergence is a great achievement, the credit for which can be widely shared The revolution that is actually taking place in the hospital services of Great Britain is placing this country ahead of anything that is happening on the Continent or in the United States

In many groups there is clear recognition of the partnership between the administration on the one hand, and the medical and nursing authorities on the other, in the conduct of hospital affairs Diagrams are produced showing variants on the pattern


HOSPITAL MANAGEMENT COMMITTEE
GROUP MEDICAL ADVISORY COMMITTEE (representatives of each of the hospitals in the group and of each of the specialties)
Subcommittees of H.M C (finance general purposes building &c)
MATRON S ADVISORY PANEL (matrons of all the hospitals in the group)

Such a system may, it is true, often throw a heavy load on the chief officer and his staff, for they may have to attend five or six *main committees or subcommittees* in the month, often meeting in the evening, not to speak of numerous minor subcommittees Some are more successful in delegating it than others, but even where the load is heavy there can be felt a sense of something achieved, clearly traceable to the fundamentally sound pattern that has been laid down Practice with regard to house committees varies In some groups they have been abolished, as a hindrance to "group mindedness" In others they have become in effect, and sometimes in name, welfare committees, controlling the amenity funds of the hospitals and sometimes minor staff appointments

SOME BENEFITS

The reorganisation has resulted in, or greatly accelerated, many tangible benefits to the patients Apart from the spread of consultant services—on which more is said below—many examples have been quoted to us of improvements on the old arrangements Hospitals of any size which do not employ a catering officer and maintain a tolerably good standard of feeding are becoming rare—though of course there is still much to be done in this field A new conscience has developed over arrangements for admission and in regard to medical records, prompted and greatly assisted by the King's Fund publication of 1948 In almost every hospital one is shown how the authorities are grappling with the ancient tradition that it does not matter how the patient is received provided he or she somehow hobbles into the ward The large old outpatient waiting halls have given way to more or less successful systems of appointments for outpatients The old institutional brown or green dado of passages and corridors is being replaced by cream and light pastel shades, over which a great deal of trouble is plainly being taken Many of the wards in out of the way places—even those in war time huts and other converted buildings—reach a standard of friendly comfort which can challenge comparison with the leading hospitals in cities All this is being done despite the discouraging heritage of buildings dating back to the poor law of a hundred years ago, and sometimes including the workhouses of earlier days still These latter are often empty their former inmates have been moved to homes for the elderly In fact hospital administration is well and truly on the move

The spread of consultant and specialist services from the larger centres over other units has been the responsibility of the regional boards Working out an establishment for each area and granting contracts on a whole time or sessional basis—the latter has so far been by far the most popular with the consultants—has been a protracted process, and the resulting pattern is only now becoming apparent

The H M C must have been glad to be passive partners in these somewhat personal proceedings, sometimes, it seems, contracts have been granted and payment begun although there were not yet facilities for the necessary beds or clinics

Often the new plan has meant development of consultant staffing which leaves no room for the former medical superintendent of the local authority hospitals Many superintendents have been glad to avail themselves of the opportunity to become consultants and to resign their administrative functions, but in other cases agitated discussion is still going on It seems to be agreed that in many such hospitals there do remain some semi administrative semi medical functions which can best be performed by a medical superintendent, probably under some different title In one case the former medical superintendent of a large local authority unit spoke enthusiastically of the advantages of the present set up, remarking upon the fact that he felt that he was now in closer touch with his committee than under the old county régime Where there are cottage hospitals the general practitioners are naturally apprehensive lest the coming of the consultant services will mean that they are eventually squeezed out, and it is difficult to get a clear picture of exactly what is happening The consultants are being called on increasingly for domiciliary visits, for which they receive fees under the National Health Service additional to their sessional remuneration Though occasionally abused, these visits are of great value, and many patients who would never have seen a consultant in former times if they could not go to the hospital are to that degree better served today

MEDICAL ADVISORY COMMITTEES

Group medical advisory committees (C M A C) are now an established institution in all groups we visited, and relations with the H M C appeared to be almost uniformly good The medical men on the H M C itself do seem to act, as of course they should, as representatives of the G M A C Sometimes the secretary of the group acts also as secretary to the G M A C, and this seems to have worked well in nearly all cases where it has been given a fair trial It provides an important link between the H M C and its medical staff, now that the staff is largely appointed regionally, and functions in hospitals which are geographically far from group headquarters, it can easily happen that the members of the H M C and their lay officers do not even know by sight the medical staff of their own hospitals

NURSES

While medical staffing is mainly a matter for the regions, the responsibility for nursing rests squarely upon the H M C itself Numbers are going up, and though there is still a shortage there is a good deal of confidence among the authorities Two main trends may be discerned First, efforts are being made to develop existing (or establish new) general nurse training schools in the most important secondary hospital centres in the group It seems to be not uncommon to find the old training school at the former voluntary hospital still blessed with ample student nurses, and stress being laid on upgrading one or more of the larger ex local authority units to constitute a second—perhaps numerically larger—general training school Such schools seem to have a fair prospect of recruiting enough staff, because of the increase of surgical and other acute work being undertaken in their wards But there is also a movement for the establishment of "assistant nurse" training schools, under the revised General Nursing Council regulations, to take care of the miscellaneous units—chiefly chronic sick—which are still excluded from the purview of the hospitals with the general training schools There is, as yet, no sufficient body of experience to tell us whether these assistant nurse training schools are likely to be a success or whether it would have been better to allocate all the beds in the group among the general training schools

This is a matter on which the new General Nursing Council will need to keep its ear close to the ground A wrong decision might compromise the new hospital service at this its weakest spot It would be a tragedy if once again the upgrading of some were achieved at the cost of downgrading of others

Two factors were frequently mentioned which tend to make the nursing situation more difficult than it need otherwise be First, the long standing social distinction between different hospitals Though social distinctions are beginning to disappear and members of the medical staff are, here and there, sending their own families to what were formerly poor law hospitals, the feeling is still strong among the nurses Second, the poor quality of much of the accommodation is a sad handicap Some of it is so incurably "institutional" as to defy all modernisation Large houses are being bought to supplement the accommodation—often in beautiful surroundings but somewhat distant from the hospitals Comment may also be made upon the state of the sanitary annexes in many of the hospitals It is now generally agreed that modern bedpan sluices are a distinct asset from the point of view of the nurse, but they are by no means universal Often they are said to be "in the programme," but this is said without much conviction as to when they will materialise This seems mistaken policy at a time when availability of nursing care is, in every group we visited, the final decisive factor in developing the service

DIFFICULTIES

Are there any serious snags ? It is encouraging to be able to say, so far as the hospitals are concerned, No (The impact of all this on general practice is another matter) With the obvious exception of the need for large scale capital development, which now seems to be deferred indefinitely, there are no really important snags Impatience with regional boards for delays and lack of comprehension of local conditions is much less evident than it was a year or so ago

The provision that "savings" must be returned to the Exchequer is regarded by all intelligent H M C personnel with whom we spoke as sheer folly[1] There is surprisingly little anxiety about the restriction of maintenance expenditure to present levels most H M C s seem to feel that with care they can manage pretty well Attention is focused rather on minor capital items, which have little chance of going through in present circumstances An example would be the extension of a staff dining room which would save half its capital cost in a single year by permitting reduction in staff There seems to be no evidence of regional officers visiting and going into such matters with the thoroughness which alone would justify taking this kind of thing out of the hands of the local committee the contrary is the case In one instance we heard of representatives of the H M C having been given "ten minutes" before a subcommittee of the regional hospital board to press the claims of its extensive capital programme Some extension of management committee powers to cover minor capital items—perhaps if they could be met out of "savings" ?—would go some way to relieve such tension as does exist between H M C and the regional authorities An alternative—or possibly supplementary—remedy would be to permit or indeed to encourage the use of "free" monies for these purposes In some areas free money is piling up, and there is indecision as to whether it may be used in support of projects which could theoretically be met from Exchequer funds

The lack of an accessible summary of hospital statistics is felt acutely to quote from the observations of one finance officer appended to an elaborate set of financial statistics covering an expenditure of a million pounds a year—"No information is available at present which would enable me to say how these percentages compare with other groups, but it is hoped that the board will one day find it possible to meet this need and thus afford some guidance to the committee on the matter"

The regions have not—so far—published their programmes of capital developments, and the management committees lack information about the general plan They do not know why the claims of other hospitals are placed before their own, or what steps the regional board is taking to press on the Ministry, and on public opinion generally, the need for a more liberal attitude to capital expenditure upon the hospital services[2] Some few items are given a "first priority," but these are apt to be the larger projects and it seems that many minor but nevertheless highly desirable improvements may never succeed in getting to the front of the queue

H M C AND ADMINISTRATION

Our visits made us aware of the immense importance of the right approach to the administrative work in the H M C In the H M C the administrators are being thrown into positions of great responsibility covering the whole of the hospital services of wide and populous areas, with budgets in some cases running at a million pounds a year and equal in size to those of the largest teaching hospitals The men have been kept on their toes, they have to struggle with the problems of introducing consultant staffing among hospitals primarily staffed by general practitioners, and with finding nurses and other staff for large and somewhat intractable blocks of chronic sick, tuberculous, and other patients Obviously some have been more successful than others but it is encouraging to find, so soon after the revolutionary changes of 1948, numerous examples of real progress and solid achievement

---

[1] See *Lancet* 1950 i, 962

[2] The Ministry has recently announced a two year programme for capital developments in the Metropolitan regions This shows the following figures
N W Metropolitan 1951–52 £700,000 1952–53 £800 000
N E Metropolitan 1951–52 £700 000, 1952–53, £500 000
S E Metropolitan 1951–52 £700 000 1952–53 £800 000
S W Metropolitan 1951–52 £1 000 000 1952–53 £1 200 000

Public Health

RESULTS OF SANATORIUM TREATMENT IN THE MIDDLE-AGED AND ELDERLY

M B PAUL
M.A., M.D Camb
LATELY ASSISTANT MEDICAL OFFICER, LIVERPOOL SANATORIUM, FRODSHAM

THE present shortage of sanatorium beds makes it imperative to use them to the best advantage As things stand, many patients seem to derive very little benefit from their stay in a sanatorium

The bad prognostic significance of a persistently positive sputum was demonstrated by Thompson (1942), who found that of 406 patients with positive sputum 42% died within twelve months of diagnosis, and only 1 in 8 survived ten years Sputum-conversion is in fact the most important single objective of treatment Unfortunately, however, the collapse therapy which is so useful for this purpose is seldom applicable to patients in the older age groups, and the prospects of obtaining sputum-conversion are thus considerably reduced as age increases The only treatment for most of these patients is routine sanatorium care, with the main emphasis on rest and graduated exercise—measures designed to increase general resistance to the disease Such treatment seems to be of doubtful value unless indefinitely prolonged, and the question arises whether the results at present obtained justify the use of beds for this type of case

CLINICAL MATERIAL

This paper is based on 107 consecutive admissions to the Liverpool Sanatorium since Jan 1, 1946, of patients aged 45 and upwards whose stay in the sanatorium has ended.

Of these 107, 86 were men and 21 women, these figures roughly corresponding to the higher incidence of the disease in men in these age groups found by Hebbert (1948) The age range was 45–70 years, and the duration of treatment 5–375 days, with an average of 124 The type and extent of disease as shown by radiography was as follows

In 68 cases there was bilateral tuberculosis with cavitation, in the majority the disease seemed to be predominantly fibrocaseous, while in a few the appearances were of softer more recent disease In 20 cases the disease was unilateral though in some the lung was extensively affected Carcinoma of the bronchus was diagnosed in 2 cases upper lobe bronchiectasis in 8 and inactive tuberculosis in 8 In the remaining case the X ray film was normal though the sputum was said to have been positive before admission

Tubercle bacilli were found in the sputum in 64 cases, in 30 the sputum was negative, and 2 patients had no sputum In the remaining 11 cases the sputum was persistently negative while the patients were in the sanatorium, but tubercle bacilli had been found shortly before admission Most of the cases of tuberculosis were classified as moderately advanced, but 14 were far advanced on admission A few had coexisting disease which further worsened the prognosis 2 had diabetes mellitus, 3 had severe basal emphysema, 1 had silicosis, and 1 had tuberculous pericarditis

TREATMENT

In this series it was seldom possible to apply measures designed to control the local lesion conservative treatment with the object of improving the general condition was the most that could be given Nevertheless, artificial pneumothorax treatment was tried in 19 cases

In 12 of these it was either impossible to induce a pneumothorax, or the pneumothorax was abandoned—either at once, as being contraselective, or later after an effusion had formed One patient died after a coronary thrombosis while undergoing artificial pneumothorax treatment In the remaining 7 the artificial pneumothorax was maintained 4 of these cases were thoracoscoped and 2 had adhesions divided In 1 case in order to control a ' dorsal lobe cavity, the pneumothorax was supplemented by pneumoperitoneum This was the only case in which sputum conversion was obtained, the criterion demanded being three consecutive negative smears and one negative culture

The majority of the remaining cases in the series were given short periods of bed rest of one to two months and were then allowed up on hours in graduated stages A few did not improve sufficiently to be allowed up, and these remained in bed until death or transfer elsewhere A few cases that showed a good response to the preliminary period of bed rest were given more prolonged rest up to six or nine months The cases of doubtful activity were allowed up at once and intensive sputum tests were carried out meanwhile

One case of bronchiectasis of the left upper lobe was treated by lobectomy One patient, whose X ray film showed soft infiltration in the middle and lower zones of the left lung and whose sputum was positive before admission, was given a ten weeks course of streptomycin and *p* aminosalicylic acid with almost complete clearing of the infiltration.

RESULTS

Of the 107 patients 22 discharged themselves, 9 died, 2 were discharged for infringement of the rules, and the remaining 74 completed the prescribed course of treatment The results, assessed according to clinical condition, are as follows

Clinical condition	*Cases*
Unchanged	40
Slight improvement	39
Considerable improvement	14
Worse	5
Died	9

These results are based on objective findings such as gain in weight, diminution in quantity of sputum, lowering of the erythrocyte sedimentation rate (E S.R), temperature, and pulse rate, and on the subjective findings of a reduction of lassitude and feeling of ill health, and a reduction in cough and dyspnœa

Judged by changes in the radiological appearance, the results were

Radiological appearance	*Cases*
Improved	21
Worse	11
Unchanged	55

The cases classed as improved showed a clearing of infiltration or a diminution in cavitation or both Only 87 cases are included, because the other 20 cases were not radiographed again, owing to death or premature discharge

Assessment of the results on the incidence of sputum-conversion shows that this was achieved in only 1 case—in the patient treated by artificial pneumothorax supplemented by pneumoperitoneum In a few cases, however, intermittent negative smears were obtained where previously all had been positive, and it is possible that the degree of infectivity of some cases was temporarily reduced

DISCUSSION

These results show very clearly how little the individual patient unsuitable for active treatment benefits from sanatorium treatment It can, of course, be fairly argued that only half—or even quarter—measures have been applied in most of these cases, for none of them had really lengthy treatment such as was prescribed in the earlier days of sanatorium treatment Today, however, *in this age of shortages and of priorities, it does not* seem reasonable to give prolonged treatment to such patients when it means further delay in the admission and treatment of cases more amenable to therapy

If we cannot expect to materially alter the prognosis for these patients, is it logical to admit them to sanatoria at all? The answer to this question depends largely on the temperament and clinical condition of the particular patient, and it behoves the chest physician to assess each patient carefully from all angles before recommending him for sanatorium treatment The large number in this series who took their own discharge shows that many older patients are unable to adapt themselves to the discipline of a sanatorium, and the main desire of many of them seems to be to get back to their familiar haunts and habits—especially when no active treatment is given A secondary objective of sanatorium treatment is the education of the patient in precautionary measures, and in the nature of the disease and the need to lead a regular disciplined life with a correct balance between rest and exercise This objective is seldom attained with older patients, for they are slow to learn and practise precautions The two patients discharged for infringing the rules were both observed spitting in the grounds

Another reason for admitting this type of case to a sanatorium is to prevent the infection of Mantoux-negative contacts at home Actually it is usually found that all susceptible contacts have been infected by the time the diagnosis is made, but there will always be some cases in which protection of contacts is a major consideration This object is defeated if the patient is discharged infectious in some cases, indeed, the result of treatment has been to convert a bedridden infectious case into an ambulant one, thus increasing the risk to the community in general In a few cases beds will have to be provided for seriously ill patients who cannot be nursed at home, but from the point of view of convenience and expense to the relatives in visiting, it is better that such beds should be in a tuberculosis ward in a general hospital

In several cases in this series no evidence of active disease was found The decision as to whether or not an abnormal X ray appearance is due to active disease should be made at the chest clinic and not at the sanatorium, since all necessary investigations—such as gastric lavage, laryngeal swabbing, estimation of E S R, tomography, bronchography, and bronchoscopy—can be performed on outpatients The resources of the sanatorium should be used in treating those cases which are amenable to active treatment

Wynn Williams et al (1950) have given details of a scheme which successfully reduced a sanatorium waiting-list This has the great merit of realism, but it calls for much cooperation between chest physician and sanatorium superintendent Under this scheme, patients who —because of advanced disease, or age, or for other reasons —are considered unsuitable for collapse therapy are not, except in special circumstances, admitted to a sanatorium, instead, they are kept at home under the careful supervision of the chest physician and health visitor This frees many sanatorium beds Tattersall (1949) has pointed out that a coöperative patient can be taught by the health visitor many of the precautions which he would learn in a sanatorium as well as a suitable regimen to adopt

The policy of admitting to sanatoria only those cases which are suitable for active treatment will be impracticable unless there is a sufficient nursing staff But it might, by making the work more interesting, improve the recruitment of nurses for sanatoria

SUMMARY

1 The present serious shortage of sanatorium beds demands that every available bed be used to the best advantage

2 The results of sanatorium treatment in a series of 107 middle aged and elderly patients, most of whom were unsuitable for collapse therapy, suggest that the use of sanatorium beds for this type of patient is not justified at the present time

3 Patients of this class should, whenever possible, be treated at home under the supervision of the chest physician and health visitor, and priority for sanatorium beds should be given to patients who would profit from active treatment

REFERENCES

Hebbert, F J (1948) *Lancet* ii 247
Tattersall W H (1949) *Ibid* ii 957
Thompson, B C (1942) *Tubercle* 23 139
Wynn Williams, N, Shaw, J B, Mashiter W E (1950) *Lancet* i 221

Influenza

Statistics for the week ended Jan 6 pointed to an increased incidence of influenza throughout England and Wales The figures for pneumonia cases and deaths and for influenza deaths in the Great Towns during the six weeks up to Jan 6 were

	Week ended					
	Dec 2	*Dec 9*	*Dec 16*	*Dec 23*	*Dec 30*	*Jan. 6*
Pneumonia						
Cases	282	347	374	364	502	956
Deaths	198	236	289	351	383	578
Influenza deaths	28	34	33	54	102	458

Of the 458 deaths from influenza, 339 occurred in the region north of a line roughly from Crewe through Sheffield to the Humber, and these deaths were largely associated with outbreaks on Merseyside and Tyneside Here the disease was generally mild, though highly infectious, and the deaths, with very few exceptions, were among elderly people

There was some increase in deaths from influenza in all regions, including London and the South East, compared with the preceding week However, in the week ended Jan 6 deaths certified as due to influenza in London County numbered only 40 It seems that, particularly in the North and North-West, the disease is becoming somewhat more severe

The numbers of new claims to sickness benefit also indicate an increased prevalence of influenza Whereas in the week ended Dec 19 claims totalled 128,842, in the week ended Jan 2 they totalled 240,223

In the areas in the North and North-West that were originally attacked the epidemic seems to have passed its peak There is, however, evidence of increased prevalence in areas that so far have not been seriously affected The position in the South up to Jan 10 remained uncertain There was, however, serological evidence of virus-A infections, and virus A was isolated from garglings in one case during the week ended Jan 13

Influenza Abroad —Prevalence is high in Belgium, Holland Denmark, and Greenland, and the disease is probably prevalent in Northern Spain. In Holland the virus is apparently virus A very possibly of the A prime type as in the Swedish outbreak, which was the first in Europe this winter

Smallpox at Brighton

Up to noon on Jan 16 there had been 30 cases of smallpox in the Brighton area 8 patients had died

Cases have come mostly from three foci

1 *Bevendean Hospital*—All the initial cases from here were employed in the ward on which the 2nd case was nursed for ten days 8 of the patients belonged to the day or night nursing staffs and 2 were ward maids Of these, 3 nurses and the 2 domestic workers have died During the past few days 4 other cases have occurred in the hospital These were connected, more or less directly, with the personnel on the affected ward

2 *Laundry*—The clothing of the original case was sent here, and from this 6 employees have contracted the disease, 2 laundry workers have died

3 *Telephone Exchange*—The 2nd case was employed here, and 2 further cases have come from this source

In the past week 4 cases have been notified which do not belong to the three main foci, and these patients were not under surveillance when they developed the disease Rather tenuous circumstances may relate these cases to existing foci, but the position is not clear Other cases of this type have to be expected Only now is the infection which was disseminated from the three foci, before strict surveillance was set up, becoming manifest

Although the disease is confined to the Brighton area and there is no sign of spread to other parts of Great Britain, the strictest vigilance is still imperative throughout the country

INCIDENCE OF VACCINATION

In his report for 1949, Dr I Gordon, acting medical officer of health for Ilford, records an investigation of the incidence of vaccination among children attending infant-welfare centres In fifteen centres the incidence varied from 54 to 22%, and Dr Gordon remarks ' It is apparent that children living in the three districts which contain the higher income groups are protected to a greater extent than those living elsewhere in spite of the fact that vaccination is free "

Poliomyelitis

In England and Wales notifications of poliomyelitis during the week ended Jan 6 were paralytic 37 (36), non-paralytic 10 (17), total 47 (53) Figures for the previous week are in parentheses

Notifications in the corresponding week of the previous four years were 1947, 10, 1948, 58, 1949, 20, and 1950, 54 The figures for this week in 1948, 1950, and the present year are comparable to the extent that in each case the incidence of the disease in the previous year was very high

The Third Quarter

In England and Wales during the quarter ended Sept 30, 1950, the infant-mortality rate was the lowest ever recorded for any quarter, the rate, provisionally corrected, was 24 per 1000 related live births This is reported by the Registrar General,[1] who gives the death-rate for the quarter as 9 3 per 1000 population, compared with 9 2 for the corresponding quarter of 1949 Deaths from acute poliomyelitis numbered 373 (provisional total), compared with 264, 330, 86, and 71 in the four preceding quarters

The birth-rate was 15 4 per 1000 population, compared with 16 6 per 1000 for the corresponding quarter of 1949, and an average of 18 0 for the third quarters of the five years 1944–48 Illegitimate births accounted for 4 8% of the total births registered, compared with 5 1% in the corresponding quarter of 1949 The stillbirth rate was 22 3 per 1000 total live and still births—0 3 higher than for the third quarter of 1949

Births exceeded deaths by 67,323, the corresponding increases for the third quarters of 1947, 1948, and 1949 being 119,400, 90,310, and 82,031

---

[1] Registrar General s Quarterly Return for England and Wales quarter ended Sept. 30 1950 H.M Stationery Office Pp 35 1s

In England Now

A Running Commentary by Peripatetic Correspondents

Stephen Potter has not mentioned doctors in his book *Lifemanship*, either because he did not realise what a vast structure of ploys and gambits we work in, or more probably because he was appalled by its immensity Countless generations of doctors, from Hippocrates with his oath to the men of today with their doctor-patient relationship, have built up such a system of Lifemanship that even the most insignificant physician can guarantee to retain the essential " one upness " with 95% of his patients

Fifty years ago the successful doctor was said to need three things a top hat to give him Authority, a paunch to give him Dignity, and piles to give him an Anxious Expression Now top hats are out of fashion, the paunch has been rationed away, and liquid paraffin has relieved the anxious expression, but somehow our Authority has grown stronger while the other two wilted away I should like to see Frith Morteroy, Odoneda, or even Potter himself survive a consultation with his physician and retain his one upness to the end The initial verbal encounter usually demoralises any but the hardiest spirits, though there have been patients who hit back at this stage You may remember the example recorded in these columns, where a mother, no doubt roused to a cold fury by the pædiatrician's persistent and wholly irrelevant interrogation, began to inquire into his own past history Then there was the rather similar case where a patient was being asked by the surgeon how long he took to pass water and was replying in the usual indefinite manner—" Quite a while Some time About three months " and so forth Finally, stung by the surgeon's insistence on what seemed a wholly unreasonable degree of accuracy, he said " If I may ask, Sir, how long do *you* take ? " Lay Lifemen will be disappointed but not surprised to hear that this ploy had no effect on the surgeon, who replied without a second's hesitation, " Two minutes dead "

Patients who have preserved their equanimity through the questioning regarding their bowels and water, their habits with wine and women, and their incomes, now face Ordeal by Examination Here there falls out of the fight the woman whose secondary sex characteristics are derived not from nature but from Bond Street at 10*s* 6*d* a pair, and the elderly young man whose slim waist-line is preserved not by rugger but by a belt, and, of course, those who only wash for appearances' sake and not for hygiene (*Note* A resistant patient can often be shaken by making him remove his socks.) Those gallant few who possess torsos like Greek gods and silk underwear, and therefore have nothing to hide, are now subjected to indelicate exploratory investigations with the index finger which soon reduce them to fundamentals

Finally there are the weapons of Diagnosis and Prognosis, although these must be used with discretion The doctor who gives his patient six months to live is in a weak position when he meets him two years later But when applied carefully a suitable diagnosis and well-balanced prognosis should fittingly terminate an interview in which the professional Lifeman has held all the trumps

* * *

After Mr Noel-Baker's broadcast appeal for fuel economy the group round the registrars' dining table were discussing what our several departments could do The surgical registrar agreed that the theatre was the greediest consumer, with its lighting and heating, the flood of hot water poured into the drains in the ritual of scrubbing up, and the diathermy apparatus " I'll hand the Old Man a scalpel next time he wants a diathermy cautery," he said hopefully, " it ought to incandesce quite enough in his grasp And the new H S gets so hot and bothered when his retractor slips that he should save a lot on heating " " I suppose your department, Psyche, uses the least electricity," drawled the E N T registrar, " you wrap your patients in blankets on a couch and sit behind them in a dimly lit room so you can snooze in comfort In fact you're pretty well always in the dark " " What about E C T though, and electronarcosis ? " asked the others , " they're enough to cause a nation-wide power cut " The medical registrar did not join in the discussion, his mind being permanently occupied by thoughts of his forthcoming encounter with the Preceptors We had to be content with making him promise not to burn the midnight oil

* * *

There is, I fear, no doubt that My Work has become an obsession and is seriously interfering with My Life I find myself refusing invitations to sherry parties because they interfere with My Work, and I dread the telephone bell lest it interrupts me at it I go shooting, of course, on Saturday afternoons, largely from force of habit, but I always refuse to stay to tea afterwards, hurry home, clean my gun, and settle down to My Work. Worst of all, perhaps, My Work has virtually put a stop to My Serious Reading A reluctant half-hour in bed is all I can spare for that What is My Work, you ask ? Well, if you must know, I am making a wool rug and am determined that—unlike so many others—it shall be finished "*Fecit* 1951" is to be worked tastefully in blue in the top right-hand corner, and if all this is not evidence of senescence I should like to know what is

* * *

In Casualty the other day we were haunted all the afternoon and evening by a lady with an unalterable conviction that we were detaining her husband there or elsewhere in the hospital Like an unhappy spectre she searched under couches, behind curtains, and in even more improbable places, not one whit deterred by the assurances of Sister and the casualty officers She made the life of the admission clerk a misery all day by catechising him on the name of every patient in all our many hundred beds , his solemn declaration that we had no man of her name in the hospital was met with a hostile stare of cold disbelief At midnight, when she had been getting in our way for eight or nine hours, scrutinising each new face myopically, her tune changed—the lost spouse had apparently died of waiting, and while mourning his departure she was now seeking her daughter Firmly shown the door in the small hours, she was yet back with the dawn , and finally she had to be persuaded to continue her search on the guiding arm of a stolid Metropolitan constable

* * *

I can sympathise with my peripatetic colleague of Dec 16 (p 821) who has had to learn the Derbyshire usage of English the hard way, because I spent some delightful and enlightening months as an assistant in the Yorkshire coal-field during the war when I had just emerged from the depths of Central Europe, knowing only the English of the Warner Brothers, augmented by some virile but rarely applicable adjectives picked up on service with the Merchant Navy There was that abdominal emergency, announced by an early morning caller with a terse " It's coming both ways with Mrs X," the nature of which became obvious when I reached the bedside of the old lady Thanks to my long Boy-Scout and military experience, plus a lively imagination, I soon grasped the implications of that common complaint in the surgery, " I cannot go to the ground, Doctor "

* * *

My friend who has not long been in partnership with two doctors in Kansas tells me that on Christmas morning he got a present of a case of beautiful apples from a Mr Grimme He told his partners about it, and asked who Mr Grimme was " Mr Grimme," they replied, " why he is the undertaker in the next block " " I see," said my friend " Did you two get apples too ? " They were a little embarrassed by this question " Why, no," they told him, " we got oranges You do better next year and then you'll get oranges too "

* * *

Aphorism of the Week

Disseminated sclerosis is the orange peel of orthopædics

Letters to the Editor

PROSPECT OF WAR

SIR,—There is an increasingly widespread assumption, both within the profession and elsewhere, that world war is inevitable Concerned by this defeatist attitude we have met together to exchange ideas and now feel impelled to express ourselves publicly

Five years have passed since the Allies achieved a victory of desolation through unconditional surrender and massed bombing Twenty million men, women, and children were killed or maimed , millions were made to suffer greater indignity and mental and physical torture than the human spirit has ever known, and, of these, many were the noblest characters of their day Now, even the perspective of atom warfare fails to arouse horror , the magnitude of threatened disaster paralyses the mind We shrug the terror away and take comfort in resolute preparations to find hospital beds for the survivors But the evils of war long antedate the outbreak £1,000,000,000 spent in preparation for war (to kill before we are killed) are £1,000,000,000 not spent on houses, schools, hospitals, health centres, and research. Each pound spent on bombs means not only bodies burnt to death in the future but more dead babies now, more families broken by tuberculosis, more jaded women old before their time, more young delinquents Food becomes scarce again , old people barely survive on their pensions

" War is an anachronism " " War never achieves the ends for which it is fought " " There are no warmongers nobody wants war " These are truisms, but every day the news comment in the papers and the speeches of responsible men are putting before us a picture of the world in which it seems that war cannot be avoided These voices name the enemy as communist Russia Sooner or later, they say, Stalin will invade us, and it is useless to negotiate till we are ready to fight him , our motives are clear and innocent, his are clear—however much he may attempt to disguise them—and wholly evil If he offers to meet us, it is only that he may seize the opportunity to make a treacherous attack We are told that communist Russia has enslaved or hypnotised the millions within her borders while our peoples are free , that her government is reckless of human life and that we cherish it

Is this so true a picture that we must acquiesce in the headlong drive to war—a war which must come out of the arms race as inevitably as the depression of human standards follows from the preparation for it ? Is it not likely that the " enemy " is given the same picture, but with hero and villain interchanged ? Willingness to cooperate and to understand the other man's rights and needs are hallmarks of civilisation , belligerency and self interest are not " Negotiation from strength " is as good or as bad an axiom as " The best defence is to attack " Both are the slogans of battle, the equivalent of the schoolboy's " I dare you " Above all else, the great issues of peace and war demand dispassionate judgment , yet thought about them has become charged with irrational emotion

We appeal to all our fellow doctors who think there may yet be an alternative to merely providing treatment for casualties , we ask them to join us, in the spirit of our chosen profession of healing, in doing all in their power to halt preparation for war and to bring about a new and determined approach to the peaceful settlement of disputes and to world disarmament

RICHARD DOLL	HORACE JOULES
ALFRED ESTERMAN	DUNCAN LEYS
IAN GILLILAND	MARTIN POLLOCK
	LIONEL PENROSE

24 Lansdowne Road
London W 11

TROPIC OR TROPHIC

SIR,—It matters very little whether the pituitary hormones are called -tropins or -trophins, the meaning of a word depends on usage and not on etymology and few of us are good classical scholars. The main trouble at the moment is that the terms employed are long and clumsy or else are replaced by a group of capital letters which mean little to the uninitiated. What we need are new short, euphonious, and clear names. I am bold enough to suggest a few, though I am certain that many of your readers can do better:

Growth hormone: somatophin.
Adrenocorticotrophic hormone: adrenophin.
Follicle stimulating hormone: folliculophin.
Luteinising hormone: lutophin.
Interstitial cell stimulating hormone: leydophin (but how many people are familiar with Leydig's cells).
Thyroid stimulating hormone: thyrophin.
Lactogenic hormone: lactophin.

Department of Physiology,
Middlesex Hospital Medical School,
London, W.1.

S. WRIGHT.

VACCINATION AGAINST SMALLPOX

SIR,—Dr. Killick Millard's paper last week is of considerable interest to me as the abandonment of infant vaccination in this country was the subject of a discussion at the Yorkshire branch of the Society of Medical Officers of Health last June, and a paper of mine on this subject is now in the press. My arguments, however, are based on the low level of herd immunity attained and not on the grounds that Dr. Millard advocates.

Dr. Millard's main argument is that mild cases of variola major only occur in the vaccinated. In my opinion this is fundamentally wrong, as all types of smallpox, from fulminating to mild, can occur in the unvaccinated. In a series of cases that I reported from Tripolitania 105 cases of types 6 and 7 (discrete and mild) occurred out of a total of 300 cases in unvaccinated patients. A type 6 case occurred as an intra-uterine infection while the mother had a malignant type 2, neither, of course, having been vaccinated. Dr. Millard also minimises the difficulties associated with the diagnosis of the most severe types. Although true hæmorrhagic smallpox, the purpura variolosa of Ricketts's and my classifications, occurs in probably only 1 or 2% of cases, malignant confluent type 2 cases occurred in 73 of this unvaccinated series. As experience in Glasgow has shown, this type of case may be in a general hospital for five days before being diagnosed.

In my experience modification of the virus of variola major does not occur by passage through either unvaccinated or vaccinated persons. Mild cases in unvaccinated or vaccinated persons give rise to all the different types, the proportion depending upon factors in the herd immunity, either inherited or acquired by vaccination. It is impossible to decide the infectivity of severe or mild cases from quoting a few isolated cases. The most bizarre trains of circumstances sometimes occur. There are plenty of examples in the literature of both severe and mild cases being the origin of outbreaks, although the mild case is usually ambulant and, therefore, a considerable danger to the community. The infective period, however, is probably shorter, and experience shows that the maximum risk occurs in close contacts in the family and at work. It should not be forgotten, however, that the malignant case which ultimately dies may be ambulant on the second or third day of the disease, between the pre-eruptive and eruptive phases, and the presence of many lesions in the mouth and larynx increases the weight of droplet infection.

Dr. Millard refers vaguely to "a vast amount of vaccination in India" having no appreciable effect on smallpox incidence. When one considers India's population of some 400 million, the difficulties of vaccination, and the relatively short duration of absolute immunity, it is very doubtful if 5% of India's total population are immune at any one time. One would not expect this to have any appreciable effect on incidence, but the fault is not with vaccination. While all would wish that the immunity produced by vaccination was more lasting, I am surprised to see Dr. Millard suggest introducing variola minor into India as a remedy. Surely this is likely to confuse patient and medical profession alike.

As we have no carriers of smallpox virus it must not be forgotten that if the world ever reaches a stage of peace the United Nations could for a small sum of money, compared with the cost of armaments, carry out a smallpox eradication scheme for the world, by a once-for the last time vaccination.

Department of Preventive Medicine
and Public Health,
University of Leeds.

C. W. DIXON.

MASS RADIOGRAPHY

SIR,—It is not practicable now, or in the foreseeable future, to examine with mass X-ray apparatus all "males and females between the ages of 15 and 25" no matter where they are—in industry, at school, on the land, or anywhere else, be it in urban or rural communities. Why not use the available man-power and machines to X-ray smaller numbers, but in those groups known to have a higher incidence of disease? The local chest physician is more likely to know these groups and the best method of approach than a highly mobile director of mass radiography.

What is the point of examining with mass radiography such a highly unproductive group as school-leavers without also employing the tuberculin test and B.C.G. vaccine?

Isolation Hospital,
Ipswich.

CHARLES J. STEWART,
Chest Physician.

A CENTRAL DEFECT

SIR,—Readers of *The Gathering Storm* will remember that one of the first steps taken by Mr. Churchill when he took over the Admiralty in 1939 was to form a statistical department, consisting of "half a-dozen statisticians and economists whom we could trust to pay no attention to anything but realities." This gave him, he wrote, "my own sure, steady source of information, every part of which was integrally related to all the rest."[1]

The Ministry of Health, which now has to grapple with a task surely as vast and intricate as that of the Admiralty in 1939, still has no statistical department. Although I shall probably be accused of overestimating the importance of my own profession, I would say that many of the shortcomings of the National Health Service can be traced to this one fact. I suggest, for instance, that the present registrar crisis might not have arisen had the problem been entrusted from the start to statisticians trained to collate and analyse quantitative material in such fields as this.

It is not enough for the Minister to be able to call on the services of such eminent medical statisticians as Dr. Percy Stocks and Professor Bradford Hill (great though these services have been). What is needed is a statistical department permanently working on the many problems posed by the N.H.S., for there can be few problems in a nation-wide health service that have not at least a statistical aspect. It should be the function of the administrative statistician to draw the attention of the policy-maker to trends in, for instance, the probable number of jobless registrars in precisely the same way as the medical statistician draws the attention of the doctors to the increase in, say, the notifications of poliomyelitis , but to perform this function he must be an integral part of the administrative machine , he must be in a position, as was Mr Churchill's statistician, to examine and analyse all the departmental papers with "relentless pertinacity "

---

[1] The Gathering Storm. London, 1948, p. 368.

Is it too much to hope that, in the present crisis of the National Health Service, the Minister of Health will act as decisively as the First Lord of the Admiralty in 1939 ?

Department of Medical Statistics
St Bartholomew's Hospital
London E C 1

M P Curwen
Statistician

OCCUPATIONAL THERAPY

Sir,—I agree with Dr Herford (Dec 30) that it may be very desirable for the patient to see "the range and number of small crafts to which his hand may be turned for sheer pleasure and joy in creation, perhaps with the added gratification of gifts for friends or furnishing for his home" But is that the sort of therapy which is usually needed, especially by men, who often are anxious to earn a living ? Is it not somehow a luxury which we cannot afford at a time when every single hand is needed ?

A proper job means much to the man who has been away from his work throughout his illness , with handicrafts many of them feel simply frustrated Return to a "work environment" is what they commonly want

A number of factors have prevented occupational therapy from being converted into industrial therapy (which means being directed more towards the actual future job) the occupational therapist's training would have to be changed , men with practical experience in industrial life, such as the industrial medical officer and the industrial psychologist, would have to be called in, and, of course, positive cooperation from industry itself would have to be the mainspring Here is the crux of the matter The occupational therapy schools have tried to get such help , but on the whole industry has not reacted very favourably To convince industry that industrial rehabilitation—in which the first step is industrial therapy —is really in its own interest will be possible only with the help of the medical profession Vauxhall and Austin in their rehabilitation workshops have given splendid examples of the work which can be done by the creative cooperation of the doctor and the engineer There is no reason why what has been done there should not be done in other industries

London N W 3

R W M Krauss
Industrial Psychologist

"THE LIVER"

Sir,—May we, as the authors, be permitted to comment on your review (Dec 30) of our book ?

Because of the novelty of the views expressed we did not expect approbation, but we had hoped for equitable treatment In view of the fact that our bibliography covers over 300 references to published works, and that no fewer than 12 important experimental and original communications by Blond are quoted, it seems at least unfortunate that strictures criticising the lack of *experimental* proof should be directed at this pioneer work

At the same time we should like to direct attention to recent papers and their accompanying pathological findings and photomicrographs dealing with the histology of tissues "in the area of portal hypertension"[1] The salient features of these papers indicate that the ætiology of the two clinical entities of appendicitis and gastric ulcer is unknown, and that none of the current theories explain their causation in a way universally acceptable Study of the photomicrographs accompanying each article makes it clear that the condition is accompanied in its early stages by hyperæmia, and in its more chronic phases by ischæmia It will be agreed by all that the phases of a pathological process accompanied by venous engorgement follow this pattern To this extent we claim that these papers vindicate our hypothesis that the common cause in these two conditions at least is associated with venous engorgement of the veins of these two areas We have, it is felt, demonstrated beyond doubt that the venous drainage of the areas is in fact normally via the portal system It must be conceded that a sudden thrombophlebitis occurring in the venous roots of an organ already the seat of venous engorgement, will lead to a catastrophic state of the organ concerned (in the case of a hollow viscus, to perforation)

Enough has been said here, we feel, to vindicate our theories, and thus allow us to press for careful consideration of the thesis put forward in our work, and to ask that more than "those who enjoy finding the weak spots in a novel argument" should read and carefully appraise our work We are quite confident that those who do so with an unbiased mind will inevitably come to a better understanding of some hitherto unsolved problems in medicine You, Sir, we feel sure, will not lightly allow an original work of challenging unorthodoxy quietly to fail, from lack of publicity We are confident that what our "novel argument" needs more than anything else is intelligent and unbiased criticism—criticism which will look beneath the surface of our hypothesis, and which will not be hidebound by conventions which do not explain but only serve the examinational mind to amass degrees

Even if we cannot persuade reviewers to accept all our views, surely these are not to be condemned *in toto* for that reason

London W 1

David Haler
Kasper Blond

PURIFICATION OF VACCINE LYMPH

Sir,—I read with great interest McClean's[1] article o purification of vaccine lymph and the subsequent correspondence[2] It is evident that all the methods in vogu are essentially in the nature of a compromise , for eithe the potency is affected or the bacterial contaminatio of the lymph is not reduced effectively In this connection I wish to call attention to a new technique, known as the "streptomycin technique," developed by m at the Government Vaccine Institute, Bangalore

This technique is based on the findings of a detaile study made by me on the effects of penicillin and streptomycin on calf lymph[3] These antibiotics were used i a variety of ways both on the vaccinifers and on th prepared lymph at various stages The local application of streptomycin over the vaccinated area of the ca was found to offer an over all advantage The advantage are a high degree of purity, high potency, and reduce cost Further, the method is simple and by far th quickest

Briefly, the method consists in local application of streptomycin solution (10–20 mg per ml in 50% sterile glycerin of pH 7 6) over the vaccinated area and its neighbourhoo —in fact over the entire shaved area of the abdomen of th calf—twice a day for five days The first application is mad about 6 hours after infecting the animal with the seed viru and the last about 16–18 hours before scraping When th vesicles are ready for collection they are scraped and triturate with 50% glycerin (1 5) in the usual way The lymp thus prepared is found to have a bacterial count of abou 200 or less per ml —most of them belonging to the *Bacillu subtilis* group of organisms The potency of the lymph *is a* high as 10^{-10} This permits the dilution of vaccine furthe by about 20–25 times

We have been using this technique for the last eigh months with extremely satisfactory results - Moreove his technique, by providing a suitable raw material—namely, vaccine pulp of high purity and potency—should be applicable also to the production of dry vaccine

---

[1] Wakeley C Childs P *Brit med J* 1950, ii 1347 Key J A *Ibid* p 1464

[1] McClean, D *Lancet* 1949 ii 476

[2] Sanjiva Rao R *Ibid*, 1950 i 328 McClean D *Ibid* p 42 Greaves A V *Ibid* p 928

[3] Krishnamurthy V N *Nature, Lond* 1950 165 451, *Bri med J* 1950 ii 1035

I should be glad to give further information about his technique to interested persons

Vaccine Institute Bangalore 2
Indian Union
V N KRISHNAMURTHY

CELL EMBOLISM AND METASTASIS

SIR,—Your leading article last week refers to Prof J S Young's ingenious experiments demonstrating the mechanical basis which underlies the entry of tumour fragments into blood vessels[1] Professor Young suggests that the extravascular pressure rises above that within the vessels

In examining histological sections of clinically benign vesical papillomata I have been struck by the frequency with which tumour cells can be seen lying inside the vessels They were noted in 7 of the last 19 such specimens in this department, and yet such tumours are seldom disseminated by the blood stream It is possible that the extravascular pressure in these tumours has been raised by the distension of the bladder during cystoscopic fulguration, and this observation might be regarded as confirmatory evidence of Professor Young's thesis

Department of Pathology
The Guest Hospital Dudley
A G MARSHALL

ENDURANCE FEAT BY A YOGI PRIEST

SIR,—There is nothing in the feat described on Dec 23 by Dr Vakil which cannot be very simply explained. It is well known that under hypnosis there is an extraordinarily increased control over the autonomic nervous system, and all the corresponding functions of the body It is easy, for instance, to slow the cardiac and respiratory rate The yogi feat is achieved by self hypnosis

London W 1
S VAN PELT
President of the British Society of Medical Hypnotists

EXTRAPERITONEAL CÆSAREAN SECTION

SIR,—Mr Stansfield and Mr Drabble are to be congratulated on their interesting paper last week, and on their excellent results from extraperitoneal cæsarean section, but someone should sing again the praises of the orthodox transperitoneal approach

During the last twelve years I have dealt by this operation with 54 true emergency cases admitted with obstruction late in labour, in some cases the mother had pyrexia and foul discharge, and the fœtus was dead and stinking I have also dealt with a much larger number—probably twice as many women—in whom trial of labour had failed or who developed obstruction or inertia while under supervision, and who were delivered by orthodox lower uterine segment cæsarean section after labour lasting for forty eight hours or longer I have not yet seen a patient develop peritonitis and none of the women has died

Surely we cannot accept a maternal mortality-rate of 2 5% as a satisfactory standard when the usual transperitoneal operation is used after two days of labour I have indeed tried the extraperitoneal approach on 5 occasions but since in my experience peritonitis is not to be feared after the transperitoneal operation, I have give up any attempt to perfect my extraperitoneal technique Most people would agree that this, by any method, is a more difficult operation, many accidents and dangers have been recorded, and the additional risk involved seems quite pointless The worst complication I have seen after operation upon infected cases has been no more than superficial wound sepsis

Woking
L G HIGGINS

TUBERCULOSIS BEDS IN NORWAY

SIR,—Why not English patients for empty Norwegian sanatorium beds? This question is prompted by the long waiting lists in England and by the elimination in many cases of such lists in Norway, thanks to the sustained efficiency of the campaign against tuberculosis in this country

With a population of only 3 2 million, Norway is now provided with some 5000 beds in sanatoriums, coast hospitals, and "homes" for the tuberculous There are also many beds for the tuberculous in several of the general hospitals staffed by eminent lung surgeons such as Holst, Semb, and Murstad The turnover in sanatoriums has been greatly speeded up by earlier diagnosis and recent advances in treatment, and also by the shuttlecock circulation of patients between sanatoriums and hospitals in which various operations are performed I am informed that at Mesnalien Sanatorium, where I was fortunate enough to undergo artificial pneumothorax treatment as far back as 1908, this shortening and increased efficiency of treatment have set many beds free Other sanatoriums and hospitals staffed by specialists in lung surgery are also ready to receive patients from abroad at charges which are moderate, partly because the Norwegian currency is "soft"

Inquirers interested in the subject should communicate with the Medical Superintendent, Mesnalien Sanatorium, Lillehammer, Norway, or with the Secretary-General of the Norwegian National Association against Tuberculosis, Nasjonalforeningen mot Tuberkulose, Incognitogate 1, Oslo, Norway

Leitet Sunnfjord Norway
CLAUDE LILLINGSTON

EARLY AMBULATION

SIR,—I was most interested in Dr Goodall's article of Jan 6 I should, however, like to join issue with him on the figures he gives for the estimated increased turnover in antenatal and puerperal patients effected by early ambulation

In antenatal wards the majority of patients are suffering from toxæmia The mainstay of the treatment of this condition is still bed rest Ambulation means, as a rule, a return of the hypertension, œdema, and albuminuria Ambulation can be used as a test of progress, and if improvement is maintained it may become possible to discharge the patient, but whether this is early or late does not depend on the wishes or whims of the doctor so much as on the ups and downs of the toxæmic patients under his care

Two other types of patient though not so numerous, probably are responsible for a large number of "blocked beds" in an antenatal ward The first is the cardiac case needing long periods of rest between the 28th week and term and the second is the case of antepartum hæmorrhage—suspected placenta prævia—in which the patient may be admitted for a month or six weeks before the fœtus is large enough to stand a reasonable chance of survival, and therefore before cæsarean section can be performed In the former case obviously any exercise is contra indicated, and in the latter ambulation may easily precipitate a further loss on account of the likely location of the placenta

We would all gladly relieve the pressure on busy antenatal wards, but I am unable to see how Dr Goodall arrives at his figure of a 15% increase in "throughput" In the puerperal wards the increase is estimated at 20% I am afraid that the length of stay in these wards is much more often determined by such problems as slow gain of weight by babies, breast feeding which takes a long time to establish, cracked nipples, and prematurity Ambulation, early or late, does not often play much part in the speed of discharge

---

[1] Young J S Griffith H D *J Path Bact* 1950 62 293

Early ambulation is practised in the obstetric department of this hospital, and we have found the results uniformly satisfactory, but I cannot substantiate the suggestion that this method increases turnover

Canadian Red Cross
Memorial Hospital
Taplow

JOHN HENDERSON
Obstetric Registrar

ATHEROSCLEROSIS AND CHOLESTEROL

SIR,—In your leading article of Dec 30 I am sorry not to find the name of Borst, one time pathologist in the University of Munich, who first induced atherosclerosis experimentally, by administration of cholesterol to rabbits Mention of this work does not detract from the value of the investigations of Anitschkov and others in this field

Mariánské Lázně
Czechoslovakia

TH OLBERT

STETHOSCOPES

SIR,—Mr Dickinson's letter of Dec 30 overlooks Glasser's *Medical Physics* (pp 1473–1490) May I add the following considerations to that description and to Mr Dickinson's analysis?

Sounds depend for quality on the size of the source and its mode of vibration, on the qualities of the ear, and on the characteristics of the intervening space or instrument Further, noises loud enough to drive the ear or other diaphragm into a non linear pressure displacement relationship produce beat-tones not present at the source

The sensitivity of the ear varies with loudness to produce the well known effect of one tone masking the presence of another This effect explains why stethoscopes which do not transmit low notes apparently accentuate high pitched ones

The effect of the wave pattern on the radiating surface upon the quality of the sound is well illustrated in percussion, where, with air laden tissues beneath the chest wall, a comparatively large area depresses as the finger is struck With liquid beneath the surface the tissues at each side of the blow rise up, producing a series of ripples over the chest surface resembling the disturbed surface of a pool into which a stone has fallen The former produces a low frequency note the latter causes cancellation of low notes at the ear For an equal number of vibrations the higher notes die away sooner and sound dull Friction within the tissues also attenuates high frequencies more rapidly The need with loudspeakers for a large baffle if low notes are to be reproduced also illustrates this point

All stethoscopes have diaphragms An artificial diaphragm is useful on an uneven surface, on a flabby surface which would fill a bell, and for quick application to a nervous child Hairy surfaces produce unwanted crepitations with artificial diaphragms A lax diaphragm may be rendered taut by pressure, with resultant modification to the frequency response, for all stethoscopes are—of necessity—acoustic filters transmitting certain tones with greater efficiency than others No frequencies are amplified for the stethoscope is a passive device

Resonance associated with acoustic leaks may provide remarkably good efficiency—i e, impedance matching of a large source to a small ear drum—at a few selected frequencies The common fœtal heart stethoscope and the Laennec stethoscope with their resonant cavities and ill fitting ear pieces are splendid examples of this principle

The efficiency of the Cammann stethoscope in common use depends upon the diameter of the chest piece, upon the volume of dead space which dilutes the vibration pressures, and upon the damping produced by turbid air flow within small bore tubes Few find the instrument insensitive, but those who do may profit from larger bells, from less dead space, and from using only one patent ear tube The tubes should be short and bifurcate near the chin There seems to be an optimum internal diameter around 3 mm

Frequency response depends upon tube length and is alternately maximal and minimal at multiples of a quarter wave length in air There may thus be advantage in using tubes to each ear of different length A leak in the air path in the form of an open side tube, about 10 cm long, reduces the low note response and can be closed by pinching as required A taut diaphragm, or one rendered taut by pressure upon the skin, modifies the frequency characteristic For equal energy transmission the excursion of the diaphragm is inversely proportional to frequency The displacement (x) depends upon the applied force (F) the mass of the diaphragm (M), its stiffness (S), and its effective viscosity or damping (R) according to the general equation, at any instant (t)

$$F = M\frac{d^2x}{dt^2} + R\frac{dx}{dt} + Sx$$

For a sustained note of frequency (f) this becomes

$$\frac{F}{x} = R + j\left(wM - \frac{S}{w}\right) \quad \text{where } w = 2\pi f, \text{ and } j = \sqrt{-1}$$

Artificial diaphragms add little mass or damping to the chest wall, but when taut may greatly increase the stiffness which term is seen to diminish in magnitude as the frequency is raised This explains the relatively poor low note response of diaphragm instruments and perhaps too of open bells pressed tightly to the skin

Mr Dickinson's remarks on a rug being gradually compressed may have an explanation in the changed viscosity If he were wishing to compare the transmission properties of a rug with a thick sheet of paper the different ratio of density to Young's modulus and the different order of internal friction damping between strands or molecules would provide an explanation on the above lines This letter, with his, may suggest that there is some value in keeping to one's own stethoscope

University College Hospital Medical
School, London W C 1

NORMAN SMITH

AMIDONE OVERDOSAGE IN A CHILD

SIR,—The possible dangers of amidone ('Physeptone') to children were well illustrated by a case admitted to the children's ward of this hospital on Dec 28

A girl, aged $4^1/_2$ years, had been given 'Linctus Physeptone and Phenobarbitone,' as symptomatic treatment for suspected whooping-cough, on the afternoon and evening of Dec. 9, She took altogether gr 1 of phenobarbitone and 24 mg of physeptone over a period of about 6 hours Next morning her parents found her lying comatose in bed at 8 A M The family doctor brought her up to this hospital, where she was admitted

At that time she was very pale, deeply unconscious, with shallow respiration, narrowly constricted equal pupils, temperature 101°F, pulse rate regular at 172 and respirations 34 per min The fundi showed moderate bilateral papillœdema, without hæmorrhages or exudate No abnormalities were detected in the heart and lungs Both arms and thighs were flaccid, deep reflexes being absent, but there was well marked bilateral ankle clonus and the plantar responses were extensor The urine contained a moderate amount of albumin and a few red cells and granular casts, no sugar Lumbar puncture revealed a clear colourless fluid under pressure, normal in cytology and chemistry The total white cell count was 15,000 (polymorphs 12,600, lymphocytes 2100, monocytes 300) per c mm Her blood urea was 38 mg per 100 ml An X ray film of the chest showed no abnormality A pernasal swab did not grow *H pertussis*

We were fortunate in knowing the exact amounts of the drugs consumed so treatment was begun as follows continuous oxygen, hourly intravenous or intramuscular injections of 2 ml of nikethamide for 6 doses, procaine penicillin intramuscularly to avert lung infection, and an enema of 20% magnesium sulphate solution to reduce intracranial pressure Feeds were given by stomach tube

The child remained unconscious for her first 24 hours in hospital and was drowsy and uncoöperative for a further 48 hours after that A coarse intention tremor became evident as recovery set in, but this lasted only a few days A slight increase in tone was noticed in the left arm but this also passed off The papillœdema had disappeared by the 2nd day The urine was normal by the 4th day The temperature, pulse, and respirations gradually returned to normal by the 6th day At the time of writing, 12 days after her admission, the child is apparently normal in all respects

The average dose of physeptone for an adult is said to be 10 mg three hourly or four hourly, though 30 mg has been given at the same intervals without untoward effect On an age/weight basis, ignoring any possible intolerance during childhood, this child should not have ad more than 2 4 mg four hourly Giving the pheno arbitone at the same time may have enhanced the epressant effects of both drugs

The conclusions to be drawn seem to be (1) that if a D.A. preparation made up in a pleasantly flavoured nctus is prescribed for children, strict precautions gainst overdosage must be taken and (2) that physep one and phenobarbitone may be dangerous in combina ion The case demonstrates once again that giving young hildren cough mixtures containing powerful drugs can e a hazardous step We would be interested to hear f any other cases of coma due to overdosage with hyseptone

We are grateful to Dr C F Harris for encouragement and ermission to report this case

St Bartholomew s Hospital
London, E C 1

R C **Roxburch**
D **Munro-Faure**

*** Messrs Burroughs Wellcome the manufacturers f physeptone linctus, have circulated a letter to all loctors suggesting precautions to be taken when pre cribing it for children The properties and dangers of midone are discussed in a leading article on p 156 —Ed L

SMALLPOX AT INFECTIOUS-DISEASES HOSPITALS

Sir,—An account of the outbreak of smallpox at Brighton is given in your issue of Jan 6 Comment is nade upon the poor vaccination state of some members of the staff, and attention is drawn to the memorandum R.H.B (50)75, issued in August, 1950

The occurrence of smallpox amongst the nursing staff of the infectious diseases hospital reflects the deplorable state of the nursing situation in such hospitals at the present time During the past few years infectious-diseases hospitals have been struggling under very grave conditions with the nursing situation in order to admit and care for their patients

As an illustration, figures are given below of the nursing personnel at Lodge Moor Hospital, Sheffield (a similar state of affairs exists, no doubt, all over the country)

Year (December)	*Beds in use*	*Ward sisters*	*Staff nurses*	*Assistant nurses*	*Student nurses*	*Ward orderlies*
1940	378	10	44	11	31	0
1944	460	10	63	2	42	0
1950	360	11	7	9	33	54

7 staff nurses and 54 ward orderlies are performing the nursing functions in 1950 which required 63 staff nurses in 1944 Is this good nursing ? The orderlies are mostly non resident, and are made up of many classes and types of persons, including Germans, Indians, Poles, Austrians, and Italians, supplemented by university students during their vacation Included in the 54 orderlies are 10 males This class of staff is most transitional, the hospital only having their services for short periods—in some instances only for a few weeks—whilst at the same time the hospital is struggling to keep its doors open in order to care for the sick

In order to produce an effective ' iron curtain " around the fever hospital to prevent the spread of smallpox, a more permanent type of staff is required which can be efficiently vaccinated to prevent any spread of the disease should it occur or, unfortunately, be introduced into the hospital

The terms and conditions for nursing staff at fever hospitals are similar to those for staff at general hospitals The latter have the advantages of more attractive work and a more convenient situation , yet no consideration seems to be given to the hardship and risk taken by staff in fever hospitals Surely, there is something radically wrong today in infectious diseases hospitals when we encounter the male adjusting the diapers of the toddler, and when the welfare of our children, stricken with fever, is left to the care of the alien or the ward orderly ?

Lodge Moor Hospital
Sheffield.

Joseph M Kennedy
Medical Superintendent.

CORTISONE AND INFECTION

Sir,—Recent studies on ' Cortisone ' have dealt with the frequency of spontaneous infections in animals [1] and the possibility of enhancing experimental infections [2]

We have studied the effect of cortisone on experimental granulomatous infection of the rat following the sub cutaneous injection of *Coccidioides immitis* Stiles Post mortem the control rats showed a local tubercle like granuloma without any generalised infection, whereas of 5 cortisone treated animals 3 showed a diffuse infection of the spleen and lungs, the production of connective tissue being greatly inhibited everywhere [3]

INCIDENCE OF SPONTANEOUS INFECTIONS WITH ADMINISTRATION OF CORTISONE

Animal	No of animals	Disorder	Cortisone		No of infected animals
			Daily dosage (mg)	Length of treatment (days)	
Rat	8	Nil	1	70	6
Rat	14	Nil	5	15–20	6
Rat	11	Carbon tetrachloride hepatic cirrhosis	1	20–45	3
Rat	2	Alloxan diabetes	5	15	2
Rat	12	Endocrine kidney	10	10–15	8
Rabbit	4	Nil	10	13	2

In other experiments we have also noted that cortisone determined the appearance of spontaneous infections (see table) necrotic exudative foci were commonly found in lungs, heart and/or liver *Pasteurella muricida* (Meyer and Batchelder) has been obtained from the lesions in the rat

Such pathological findings were never observed either in normal animals or in animals treated with deoxycortone acetate or acetoxypregnenolone under similar experimental and environmental conditions

Anatomo Pathological Institute
University of Milan and Farmitalia
Research Laboratories Milan

C **Cavallero**
G **Sala.**

TREATMENT OF PERFORATED PEPTIC ULCER

Sir,—The late Mr A Hedley Visick, of York, like Mr Hermon Taylor, was stimulated by Bedford-Turner's letter and his own repeated finding of sealed perforations to try out the conservative treatment of acute perforated peptic ulcer His conclusion, based on his own admission on a small number of cases, and published two years before his death (the corrected reference is *Brit med J* 1946, ii, 941), was that if the perforation was small and spillage minimal the cases did well, but that it was in precisely this group of cases that operative mortality was lowest

He too emphasised that the management of these cases was far more exacting without operation, and responsibility for this could not be delegated by the consultant until his staff had had considerable experience of the method It became his practice to operate on all obvious and early cases, and to close the perforation without peritoneal toilet or drainage, reserving watchful conservative treatment for cases where the diagnosis was doubtful, or where the patient was definitely unfit or doubtfully fit for operation With a wise combination of the two methods he hoped to reduce greatly the total mortality There was to be one exception , any case of second perforation was to be treated conservatively and given the benefit of a radical gastrectomy during convalescence, thus obviating an extra operation.

---

[1] Antopol W *Proc. Soc exp Biol N Y* 1950 73 262
[2] Spain D M. Molomut, N *Amer Rev Tuberc.* 1950 62 337
Hart P D A. Rees R J W *Lancet* 1950 ii 301
[3] Redaelli P Cavallero C Borasi M. Sala G Amira A. *Experientia* (in the press)

While the decision as to which is the better treatment for the straightforward case is likely to remain unsettled for many years, two points of practical importance emerge now:

1. All cases diagnosed as perforated peptic ulcer should have gastric aspiration carried out in the reception room as soon as they reach hospital. If there is delay in admission or a long journey is necessary it should be done by the first doctor to see them after the occurrence.

2. Our conception of the prognosis of the patient who is not fit for operation is materially changed.

Bristol. K. D. J. VOWLES.

SIR,—Your issue of Jan. 6 contains two more articles supporting, with varying enthusiasm, the adoption of conservative or "aspiration" treatment of perforated peptic ulcer. I would support, as I have done before,[1] the cautious attitude expressed in your leading article.

Sealing of a perforation of any viscus depends on an interaction of a number of unknown factors. Local tissue response to infection, the nature of the infecting organisms, and the individual resistance to these organisms are concerned. This plastic fibrinous reaction with or without the local adhesion of omentum is as difficult to forecast in cases of perforated ulcer as in appendiceal inflammation or perforation. Mr. Stead's case 2 is a perfect example of the failure of this reaction to occur despite the aid of the conservative régime. I have seen this failure of local plastic or other sealing action in early or late perforations. I am sure it is quite common and it will be recognised much more often (and on the post-mortem table) if conservative treatment is widely adopted.

Mr. Hermon Taylor is, I believe, wrong in minimising the risks of incorrect clinical diagnosis. The accuracy achieved by his team is above the average. In a recent series of 351 consecutive acute abdominal conditions submitted to operation I dealt with 40 perforated ulcers. In 4 of these I made the wrong diagnosis pre-operatively. This compares with DeBakey's figure of 14.5%, representing the diagnostic error in a very large series. Acute appendicitis is the commonest mimic of peptic-ulcer perforation, and I cannot agree with Mr. Stead that a 6-hour delay in operating for this condition is acceptable in any age-group.

In my 351 cases I further diagnosed perforated peptic ulcer with confidence in 5 cases—at operation quite different conditions were found. All required urgent surgery. As Mr. Hermon Taylor writes, this is a most important problem; but his unusually fortunate experience in this direction minimises its importance.

To my mind this high rate of diagnostic error condemns the general adoption of conservative treatment. There are many other objections. Perhaps it is wise to re-state what we hope to achieve by operation. Firstly, the diagnosis is confirmed. Secondly, by simple suture of the ulcer one arrests a leakage which might otherwise be continuous for many more hours. Thirdly, one finds in most cases after operation a patient rapidly and dramatically improved and one who in a very high percentage of cases has a smooth convalescence. With all the armamentarium at our disposal I believe the mortality-rate should be kept below 5% and the incidence of complications less than that described in the various series treated conservatively.

I do not know when dangerous organisms get into the peritoneal cavity. Sometimes they may escape in the first gush of gastric or duodenal contents. Sometimes they may appear many hours after perforation. But I do know that the process is a cumulative one and the sooner it is stopped the better. What can aspiration achieve to this end? In gastric perforations I concede that it may on occasion be completely effective. In the more frequent duodenal perforations gastric suction may achieve little; and, as Mr. Stead rightly points out, it cannot decompress the duodenum, which soon fills with fluid welling up from the inevitable small-intestine ileus associated with peritoneal infection. Mr. Stead recognises this factor but in another paragraph suggests that the "barrier" formed by a "spastic pylorus" is beneficial.

Gastric aspiration as an immediate pre-operative measure in cases of perforation is of great value. Post-operative gastric aspiration is an essential adjunct to operative treatment. But the conservative régime is quite clearly shown by both Mr. Hermon Taylor and Mr. Stead to be a ticklish business, and I would deplore its adoption other than in the most exceptional circumstances.

Department of Surgery,
University of Liverpool.

JOHN A. SHEPHERD.

---

[1] Brit. med. J. 1950, i, 438.

Obituary

JAMES SWAIN

C.B., C.B.E., M.D., M.S. Lond., F.R.C.S.

James Swain was for many years one of the outstanding figures in surgery in Bristol and the west of England. Modern surgery in the west may be said to have begun with Greig Smith, who reigned without a rival in hospital and private practice during his too brief career. When Greig Smith died at an early age in 1897, James Swain had already been on the staff of the Bristol Royal Infirmary as assistant surgeon for five years, and for a time there was only one other pure consulting surgeon in the town. It was the moment when doctors and patients were beginning to realise the great possibilities of surgery in general, and abdominal surgery in particular, and Swain, who was thoroughly competent and had the art of getting on with people without quarrelling, soon found his services in demand over a wide area.

[Bright

He came of a Hertfordshire family, and he entered the Westminster Hospital by an entrance scholarship in 1879, qualifying in 1883. Two years later he obtained the London M.B. with honours, proceeding to the M.D. in 1887, the F.R.C.S. in 1889, and the M.S. in 1890. After holding resident appointments at the Westminster he became house-surgeon, and then senior resident officer, at the Bristol Royal Infirmary. Those were stormy days. The students were a particularly turbulent crowd; he was a stranger, small of stature, and an inveterate talker, and he had his work cut out to maintain discipline.

In 1892 he became assistant surgeon and commenced consulting practice in Clifton. After Greig Smith's death it was a nice point who should succeed him as professor of surgery. There were two general hospitals in the town bitterly jealous of one another; so it was thought expedient to have a professor from each, and the duties were shared by James Swain and C. A. Morton. They were both good, but not outstandingly good, teachers, and indeed Swain was really too busy to put in a great deal of time with the students. In 1909, the University College became the University of Bristol, and he was appointed to the university chair. In his earlier years he was a prolific writer; his first paper on perityphlitis appeared in 1885. From 1897 to 1904 he was an associate editor of the *Bristol Medico-Chirurgical Journal*, and he also edited the sixth edition of Greig Smith's *Abdominal Surgery*.

During the 1914–18 war he became consultant surgeon to the Southern Command, and Bristol saw him but seldom. For his services in France as consultant surgeon he was mentioned in despatches and he was appointed C B in 1917 and C B E in 1919 He was one of the British delegates to the inter-Allied congress on the treatment of war wounds which sat in Paris during the later years of the war

He gave up the chair of surgery to Hey Groves in 1920, two years before he reached the age limit, when he retired from practice because of eye trouble He went into the country to live, and became a justice of the peace for Somerset During the past twenty years, he was only occasionally seen at medical functions in Bristol

He married in 1899 Hilda, daughter of Dr A J Harrison, and there is a son and a daughter of the marriage He died on Jan 6, at the age of 88

A R S

GEORGE CLARK CATHCART

M A , M D Edin

Dr George Cathcart, probably the most senior of British otolaryngologists, died at Broadstairs, after a short illness, on Jan 4, at the age of 90 He was born in Edinburgh, the son of James Cathcart, who was the greatest friend of Robert Louis Stevenson's father From Edinburgh Academy and Loretto he went to Edinburgh University, where he graduated M A in 1883 and M B in 1891 After holding a house appointment at Edinburgh Royal Infirmary, he came to London as a resident at the Children's Hospital, Great Ormond Street, later becoming house-surgeon at the old London Throat Hospital In due course he was appointed honorary surgeon to the hospital and after its amalgamation with the Throat Hospital, Golden Square, he was consulting surgeon to that institution He was also appointed consulting laryngologist to the Mount Vernon Hospital, when it was a hospital for pulmonary tuberculosis

Dr Cathcart came of a family of musical enthusiasts He had himself been a pupil at Naples of Scafati last of the teachers of the old Italian *bel canto*, to help to cure a stammer, and his early contributions to medical literature were mainly on problems of voice production He was convinced that the then current English practice of tuning orchestral instruments to the higher concert pitch, instead of French pitch, was one of the chief causes of vocal strain among professional singers, and to prove his point he instituted the famous Promenade concerts at the Queen's Hall, London, with his friend Henry Wood as their conductor He took great pride in the enduring success of the annual series of concerts —though he personally had lost a considerable sum of money in launching them—and of their important influence on musical appreciation in England Particularly while Sir Henry Wood was still alive, he was happy to be an honoured guest at them year after year

In 1926 Dr Cathcart published a revised edition of his friend Hunter Tod's book *Diseases of the Ear* , and as this was then twenty years old, it was largely rewritten It was favourably reviewed, and a year or two later he produced a small book on the *Treatment of Chronic Deafness*, which went into a second edition in 1931 He was convinced of the effectiveness of the electrophonoide method of Zünd-Burguet in the alleviation of deafness In his hands this method undoubtedly achieved good results in many troublesome cases, though treatment had to be repeated once or twice a year He was disappointed that few other otologists persevered with this treatment He was a careful and conscientious surgeon, though his range was not wide, and most of the leading general practitioners in the West End of London reposed their trust in his judgment Freemasonry was almost his religion and he was a past master of the University of Edinburgh lodge and a member of Grand Lodge

“ Cathcart was above all a kindly man,” writes S H , “ and although it is some forty years ago I still remember the warm welcome which he gave me when, knowing little of E N T work, I became an assistant surgeon at the London Throat Hospital He was unquestionably good at his job, but I always looked upon him more as a philosopher than a surgeon He had whimsical inquiring eyes with a sense of humour in them, and a broad outlook with many interests besides his profession Widely read, he was always willing to discuss any new proposals in connection with his work. He was one of the pioneers when otolaryngology was changing from a branch of medicine and taking its rightful place as a surgical specialty ”

PHILIP FRANKLIN

F R C S , Hon F A C S

Mr Philip Franklin, the well-known otolaryngologist, died suddenly in London on Jan 7, aged 70 Two days before his death he was lunching at the Royal Society of Medicine, cheerful and volatile as ever, apparently about twenty years younger than his real age, and looking forward to a voyage to South Africa next week

He had had a varied and interesting career Born in San Francisco in 1880, he was educated at Lowell High School there, at Heidelberg, and in London at King's College, King's College Hospital, and Middlesex Hospital In 1907 he took the Conjoint qualification, going on to take the F R C S in 1913

He began his medical career as a research scholar at the cancer laboratories of the Middlesex Hospital, and he went into otolaryngology almost by accident, through meeting a friend in the street who persuaded him to apply for the vacant post of house-surgeon at the old London Throat Hospital, which afterwards amalgamated with the Throat Hospital, Golden Square Franklin later became assistant surgeon at the Metropolitan Ear, Nose, and Throat Hospital and ear, nose and throat surgeon to the Italian Hospital

In 1925 he arranged a successful meeting in London of the Inter State Postgraduate Assembly of North America, and not long afterwards he was proud to have been elected one of the few honorary fellows of the American College of Surgeons Through a friend in Vienna he heard that the famous Onodi collection of anatomical specimens which threw a new light upon the anatomy of the nasal sinuses, was privately in the market, and he acted as secretary and treasurer of a fund which acquired the collection for the museum of the Royal College of Surgeons

Franklin introduced, with considerable success, in the early '30s, the treatment of hay-fever and vasomotor rhinitis by ionisation, but probably his most important work was that connected with the early education of deaf-mutes, on which he published a paper in this journal in 1935 He was then otologist in charge of the research clinic for deaf-mutes at the Infants Hospital, Vincent Square, and he brought new instruments from America, the audio frequency-amplifier and the teletactor, which conveyed vibration stimuli to the ears and finger-tips He considered that these methods should be begun as early as the second year of life and that they hastened the mental development of the deaf-mute infants, encouraged the acquisition of natural voice production, and might even increase residual hearing It was a great disappointment to him that the outbreak of war in 1939 brought this work to an end He himself—at the age of 60—became a major in the R A M C , acting as otologist to military hospitals in the south of England

In 1903 Mr Franklin married Ethel, daughter of the late Mr Lewis White , she died tragically, together with a guest and members of the domestic staff, in a fire at their house in Wimpole Street in 1935 They are survived by a daughter and by two sons—Dr A White Franklin, the pædiatrician, and Dr J L Franklin, the dermatologist

SIR ARTHUR HALL

S R writes “ At the first meeting of the Radium Commission, Hall put forward an outstanding conception of its purpose which guided the commissioners for the whole of its life The obligations undertaken by the new body could, he affirmed, only be fulfilled if confidence were established between the commission and the principal radiotherapeutic centres in the country The response to action by the commission on these lines was unanimous and within a year an active impulse ran through the newly established national centres, with inestimable benefit to those suffering from cancer ”

Mr Charles West's first wife, who died in 1935, was Miss Esther McCrossan His second wife, whose name we gave incorrectly last week, was formerly Miss Kathleen Thomas

Notes and News

REGISTRARS

In a memorandum on "displaced registrars," the Fellowship for Freedom in Medicine outlines the factors which, in its view, have given rise to the present situation The memorandum states "Although the number of hospital beds has not greatly increased since July 1948, the hospital O P departments have often been overwhelmed by the patients who previously would have been properly doctored by their G P s and would never have sought hospital care At the same time consultants were no longer encouraged to work the long hours to which they had become accustomed because of the system of payments for a definite number of $3^1/_2$ hourly sessions a week Therefore the needs for these trainee consultants was greatly increased" The present situation has been brought about 'by the precipitate introduction of the N H S, the dislocation of the balance of work between G P s and hospitals, and by thoroughly bad planning by the Ministry of Health The Royal Colleges had been misled into thinking the consultant services were to be expanded to a much greater extent than now seems probable, and they must accept some share of responsibility for the present impasse"

Among the steps recommended by the fellowship are the following (1) The position of general practice and of the family doctor should be re established (2) "It must be possible for some of these 'displaced registrars' to enter general practice and still maintain their interest in hospital work The present tendency of hospital Regional Boards to abolish G.P hospitals must cease The present difficulty would, in considerable measure be overcome if the buying and selling of the goodwill of general practices were resumed at the same time private practice should be encouraged, thereby creating a healthy rivalry between the State service and private practice (to the benefit of both)—as has been consistently advocated by the Fellowship" (3) The total number of consultants needed both in the service as a whole and in each specialty should be fixed as soon as possible "It is absurd to suggest, as the Minister has done, that the number of trainee consultants should be fixed first, and the overall number of consultants laid down at a later date It is also important to let the profession know which specialties offer the most vacancies in the future, so that a trainee may change from one branch to another in his earliest years" (4) There must be a review of the needs of the service so that the number of registrars needed can be fixed "Then, over a period of at least two or three years, the present holders of these posts should be encouraged to enter other fields of medicine, if they are not likely to be made consultants in their present field"

The fellowship deprecates the "precipitancy of the Minister's direction that a considerable number of registrars will not have their contracts renewed It is a waste of valuable experience and of money spent in training, and manifestly unfair to the men concerned It should be realised that the average age of the senior registrar is 37, and most of them have wives and children" The memorandum concludes that the Minister should withdraw his directive, and consult with all medical interests concerned

ALL-ROUND HELP

Under the National Health Service responsibility for the care of the patient is shared by different administrative authorities While he is in hospital he is under the possibly remote wing of a regional hospital board, his new teeth are one of the cares of a local executive council, his home help is, when possible, provided by a local authority Administratively this division is perhaps inevitable, but the patient does not obligingly respond by dividing his illness into sharply defined stages The committee set up by the Institute of Almoners, under the chairmanship of Prof A L Banks, F R C P, to consider the patient's care and aftercare wisely point out[1] that the patient still wants the kind of all round help he used to get in less complicated days from his family doctor If the health service is to succeed the patient must go on getting this kind of help, and he can only do so if there is effective coöperation between the different parts of the health service In particular, the almoners consider that the phrase 'care and aftercare must be widely interpreted for the medical and social needs of the patients are often closely related The committee recommend that local consultative committees should be set up, composed of doctors, social workers, and local health authority officers, to consider the coördination of medicosocial care of the patient

MEDICAL SERVICES OF THE U S ARMED FORCES

The United States department of defence has set up an Armed Forces Medical Policy Council under the chairmanship of Dr Richard L Meiling (*New York Times*, Jan 6) The new council is charged with establishing joint programmes among the three Service medical departments and promoting standardisation of technica activities Its members include Major General Raymond W Bliss, Rear Admiral Clifford A Swanson, and Major General Harry G Armstrong, surgeon generals of the three Armed Forces By the medical draft law passed in the last Congress, about 200,000 doctors and dentists under the age of fifty have been arranged in four groups according to their call up priority The defence department has now announced that all in priority no 1 and some in priority no 2 will be called up by July The first priority, about 14,000 men, is composed of men who received their education at government expense and who have had little or no active military service The second priority includes men who received some or all of their education at public expense and who have had comparatively little of active duty

---

University of Oxford

On Dec 16 the following degrees were conferred

D M—J C Pease J F Monk
B M—M J V Bull C G Miller R M Morris Owen W D E Hamilton J G Wallace J G Millar, E F H Murphy, H E Milligan R G Mitchell B S Freeman, D L Hone J K Pearce G M Scott J P Bingle J R Golding G T Smerdon, G P Barr Constance M Ridley Ruth Lister Jane M Robinson Jean McI Smellie Diana L Spencer Gillian Rowe Dutton, *I B Denny, *R H Hill *Barbara Sellman

* In absentia

University of London

At recent examinations the following were successful

M D Branch I (medicine)—D M Abelson Michael Atkinson A G Bearn G A Bedwell, I D Blainey S O Boldy, Leon Brotmacher F G Campbell H E Claremont R S C Couch, J S Crowther Léon Cudkowicz A F Doyle C J Earl T R L Finnegan Philip Freedman C N Grainger, *P C Harris A R Harrison Arthur Hollman Gwyn Howells F E Jackson C L Joiner, D'Almero Kok M J Livera Joseph Luder J C Macaulay, R A Moir C D Routh, Benjamin Schwartz L G Scott, L V Sthyr P P Turner Albert Venner, R L Ward R G Welch Joan C Wells R R Willcox Irvan Yentis
M D Branch II (pathology)—Naomi Datta Deborah Doniach, *C H Gray W J Hanbury A B Hill C R I Hilson J D O'D Lavertine G L Le Bouvier A J M Reese R B H Tierney

* University medal

M D Branch III (psychological medicine)—A J P Oldham.
M D Branch IV (midwifery and diseases of women)—J G Dumoulin D W James J C S Leverton
M D Branch V (hygiene)—D J Davies R A G Smith
M S Branch I (surgery)—Arnold Elton T W Rowntree

University of St Andrews

At recent examinations the following were successful:

M D—K R Keay (with commendation)
M B Ch B—J D Adam W M Anderson A A Brand, V W M Francis, R J D Gibson Elizabeth H Halliday William Kelso, W D Lobban Duncan MacDonald Ida V MacDonald, T G Sprunt R A Yorston

University of Glasgow

On Jan 13 the following degrees were conferred

M D—H F Hutchison (with honours) A G McCarey, A N MacPhail (with commendation), F A Smith
M B Ch B—J I Adam W D Alexander W L Birrell, Phyllis J Bishop, A H Cassels Gerard Church D W Clementson, Betty Cowan I A Cresswell Margaret J Croall G M Davidson Margaret J Devine Kerr Donald I B R Duncan, C P A Evans, A S Ferrie, I H Gardner J M B Garland D H Goold Henry Graham J H Grant Theresa Grant Alexander Harrow J H Henderson T J G Howie G A Jamieson, R D Laing, J D Leonard George Lochrie G Y McCririck R W D Macdonald Malcolm McEwen N P Mackay F D Mackie, Lottie S Macleod J L McPheat Frances I Melrose I A Millar D B Miller M K Mowee John Owens, T G Parker W J Patterson T C Peden Elizabeth Primrose, D J Reilly M J Scott, J D A Shedden D D G Simpson J G Stewart, D H Sutherland, Thomas Taylor N A Todd, G R Veitch Marion M Whitelaw

Memorial to Mr Girdlestone

Lord Nuffield has given £10,000 to the Nuffield Orthopædic Centre, Oxford, to found a scholarship in memory of Mr G R Girdlestone, whose obituary we published last week The scholarship is to enable doctors from overseas to spend some time working at the Wingfield Morris Orthopædic Hospital Details of the scholarship will be announced later

---

[1] *The Almoner*, January, 1951, p 359

Royal College of Surgeons of England

At a meeting of the council on Jan 11, with Sir Cecil Wakeley, the president, in the chair Prof F A R Stammers was admitted to the court of examiners

It was decided to institute a department of pharmacology at an early date

A replica of the master s chair of the Company of Surgeons, which was destroyed by enemy action, was received from Mr V Coppleson and other fellows of the Royal Australasian College of Surgeons

The following diplomas were granted jointly with the Royal College of Physicians

D.A —Frank Alberts B P Armstrong H I O Armstrong Fazlolloh Bakhshayesh Kathleen Blott R C Brown Henry Collier L F G Cruickshank Sylvia Danks Phyllis M de Saram F G Domaingue J R Elliott J R Forsaith Beryl M Goetzee J A Griffiths C C A Jackson P S Jenkin E L Littler P L McGwinn L V Martin Joan C Mason Gordon Mason Walshaw Rustam Ali Nabi Catherine E D Nash H C Neill D M O Donoghue Maureen O Driscoll J J Polland Marjory A Pollock D R Rigg A R Ryan R C O Saunders E R Sinton Elisabeth B Smith Matthew Spence R J Vale Harinandan Prasad Varma G J G M Yourch

D C.H —Emily M. Frazer

D.I H —M. M. Lewis I S Maclean H T Phillips R K Phillips A. W Smith J L Walsh

D.L O —V D Bear Betsy Brown Chulam Nabi Dar James Freeman A E W Gregson A J Gunning H S A Henry D G H Hollis W P F Kearney Isabella Kingan P W E Moore Asghar Nizami K. R Ogilvie P B O Neill Daryao Singh C W Smith J R Watson

D M.R.D —John Adam Chalmers Allen Alec Attwood James Barr Satyabrata Bose A W Box G A Burfield D E Fletcher A. J M. Griffiths K. E Jefferson A W R Jenkins J R Kirby J K McMyn C P Moxon Onkar Nath Saxena Himadri Kumar Sen R M. S Terry P W Wishart

D.M.R T —J W Boland, E T Feldsted A M Goldstein N D M. Harvey Mohammad Ramzan

D.P M —Abdul Aseem Aziz Anne Bolton Stuart Brest T S Davies C C Evans E F B Forster Safa Eldin Hamid H B Jones D M Leiberman A M Shenkin Kirpal Singh C A Storr Reginald Warnecke Joseph Zelmanowits

D T M & H —E G R Butler Abdurrahman Mohammed Khan Ambrosio Reyes, Nivedita Sen C G F Smartt, G A Smith

At the monthly dinner of the college on Jan. 10 brief speeches were made by Sir Godfrey Huggins, F R.C.S (prime minister of Southern Rhodesia), Mr V M Coppleson F.R.C S (Sydney), Prof C A. R Schulenberg F R C S (Pretoria) Dr J L Rowbotham (Boston) and Dr A Bassett (Toronto) An exhibition in the Hunterian Museum had been arranged by Prof Geoffrey Hadfield and the President and Lady Wakeley took a party of guests through the residential college, where some 25 postgraduate students now have temporary homes When the Nuffield College of Surgical Sciences is built on the east side of the college there will be accommodation for 100 postgraduates and visiting surgeons

Society for Cultural Relations with the U S S R

The medical committee of this society is holding a discussion on Monday, Jan 29 at 8 P.M , on Recent Controversies in Soviet Medical Theory based on the work of Pavlov, A. D Speransky, Bykov and O B Lepeshinskaya Dr Leonard Crome is to open the discussion, and Dr J S Horn will also speak. Tickets (1*s* 6*d* members and students 1*s*) may be had from 14, Kensington Square, London W 8

Coördination in the National Health Service

Representatives of local authorities, regional hospital boards, executive councils and the Scottish Health Services Council met in Edinburgh on Jan. 10 for a conference, under the chairmanship of Sir George Henderson, secretary to the Department of Health for Scotland The object was to give those responsible for the day to-day working of the service an opportunity to discuss their experiences and to see whether within the present framework there are any ways in which the local authority services, the general practitioner services and the hospital and specialist service may be better linked. Among the problems discussed were maternity and child welfare the care and treatment of the chronic sick and the tuberculous, the interchange of health records and statistics the reallocation of hospital beds and the relationship of the general practitioner with the hospital specialist It was unanimously agreed that in each area facilities should be provided for convenient and expeditious discussion of all difficulties and problems of coördination at all stages of responsibility for the health service but local initiative should decide how this should best be done—whether by the appointment of special standing committees or otherwise It was also felt to be important that the form of these facilities should be agreed on by the three main partners in the service and that they should be made known to all grades of staff

Superannuation Rights

Medical and dental officers and senior nurses who take a post for not more than three years with the United Nations Organisation or its specialised agencies—such as W.H O or F.A O —or with another intergovernmental organisation may, if they wish retain their superannuation rights under the National Health Service This right will also extend to posts in certain foreign universities and public institutions approved by the Government Further particulars are given in circular R.H B (51)1

Inflation of Practitioners' Lists to be Ended

The Ministry of Health announces that steps are to be taken at once to put on a more accurate basis the records of people on doctors lists National Health Insurance entry cards without National Registration numbers now in the nominal indexes of executive councils are to be matched with the appropriate portion of the local ' live National Registration maintenance registers , and then, by a central clearance operation based on National Registration numbers, duplicate and other redundant entries are to be eliminated Executive councils have been asked to aim at completing this operation by Sept 30 this year While it is being carried out, the Practitioners Fund will be distributed between executive councils according to the number of people on doctors lists at Jan 1 this year

National Dried Milk for Invalids

The Ministry of Food announces that, as supplies of the proprietary brands of infant milk foods are now plentiful, National Dried Milk after Feb 28 will no longer be available to invalids (including patients suffering from steatorrhœa, cœliac disease, and tropical sprue) From that date, national dried milk will normally be reserved for children under 2 years old to whom it is supplied as an alternative to liquid milk at the reduced price of 10½*d* a tin, or free, under the welfare foods service The Ministry will, however, consider granting supplies to children over 2 years of age or to expectant mothers who are normally entitled to liquid milk at 1½*d* a pint or free under the welfare foods service, on presentation of a medical certificate saying that they should have dried milk instead of liquid milk.

Awards for Blood Donors

The Ministry of Health announces that awards are to be made to long service blood donors who have given at least 10 donations of blood since September 1939 Women will receive a brooch and men a lapel badge on which there is a design, which has been approved by the King showing two interlocking hearts surmounted by the crown and resting on a scarlet background There will be three classes of award silver gilt for at least 50 donations, silver for 25 donations, and bronze for 10 donations There are now nearly 400 000 donors in the National Blood Transfusion Service, and it is estimated that about 200 will be entitled to the silver gilt award, 5000 to the silver and 70,000 to the bronze The Princess Royal has consented to present the silver gilt awards on April 3 at the Royal College of Surgeons Forms of application for the award can be obtained from the regional blood-transfusion centre where the donor is enrolled

Community Care Teams

Speaking at the annual meeting of the National Association for Mental Health on Jan. 12 Dr Alfred Torrie the medical director, urged the importance of treating mental illness in homes and factories while still in its early stages This made him regret all the more that since the National Health Service had started the community care teams which the association had previously managed to run in all 12 civil defence regions had been reduced to 2 These teams had put people in touch with social agencies, and by working with the family doctor had often been able to arrange for early help which prevented the development of mental illness They had also halved the relapse rate among people discharged from mental hospitals Field Marshal Lord Montgomery pointed out that morale was a matter of mental health, and that if we had to face grim times the spirit and mind of the nation were weapons which must be kept in good order Sir Otto Niemeyer was able to report that the association had weathered the financial storm which blew up in 1948 when the Ministry of Health s grant of £2000 to local authorities was withdrawn.

International European Society of Hæmatology

A meeting is to be held in Rome in September Further particulars of this society may be had from Dr A Piney, the secretary for Great Britain, 152, Harley Street, London, W 1

Red Cross Unit for Korea

A British Red Cross unit has this month left for Korea, where its tasks will be to alleviate the plight of the homeless by organising the distribution of food and clothing, establishing camps, and planning a medical programme to ensure adequate water and sanitation, to try to prevent disease, and to treat sickness The medical member of the team is Lieut Colonel M C L Smith Similar units are being sent by other national Red Cross societies

French Medical Films

On Tuesday, Jan 30, at 8 15 P M, at the Institut Français du Royaume Uni, 15, Queensberry Place, London, S W 7, the following French films will be shown Patent Ductus Arteriosus (Professor de Vernejoul, Marseilles), Functional Liberation of the Lungs (Dr Warnery and Dr Metras, Sanatorium du Petit-Arbois), Surgical Treatment of Portal Hypertensions (Professor Santy, Lyons), Glosso pharyngo laryngectomy (Professor Portmann, Paris), Psycho surgery—Prefrontal Leucotomy (Professor Wertheimer and Professor Dechaume, Lyons) Cards of admission may be had from the intendant at the institute

---

Dr Chaloem Puranananda, secretary of the Thai medical research council and director of the Pasteur Institute at Bangkok, is spending three weeks in this country from Jan 3 to 24, under the auspices of the British Council, visiting medical research institutions and studying recent British developments in electron microscopy

Births, Marriages, and Deaths

BIRTHS

BIRT —On Jan 10 in London, the wife of Mr St John Birt F R.C.S —a daughter

BLEAKLEY —On Jan 9 at Bangor co Down, the wife of Dr John Bleakley M B E —a daughter

ESSEX CATER.—On Jan 6 at Bath the wife of Dr Antony Essex Cater—a son

HIGGINSON —On Jan 11 in London the wife of Surgeon Lieut Commander J C Higginson R N —a son

MCCONNELL —On Jan 13 at Bristol the wife of Dr Brian McConnell —a son

MCVICKER —On Jan 7 in London the wife of Mr R A M McVicker, F R C S —a daughter

REUBIN —On Jan 8 the wife of Dr Isadore Reubin—a son

ROBERTS —On Jan 3 in London the wife of Mr P A Lane Roberts F R C S —a daughter

RUTTER —On Jan 8 in Cardiff the wife of Dr F W E Rutter —a daughter

SIMPSON —On Jan 10 in London the wife of Surgeon Lieut Commander R W Simpson R N —a son

VLASTO —On Jan 6 the wife of Dr Philip Vlasto—a son

WYMAN —On Jan 12 in London the wife of Dr A L Wyman —a son

MARRIAGES

DIGGORY—MCCONNELL —On Jan 6 in London Peter L C Diggory M B to Patricia McConnell M C.S P

FLEMINGER—JACKSON —On Jan 8 in London John J Fleminger M B to Ruth Jackson M B

DEATHS

ARMSTRONG —On Jan 12 at Surbiton Surrey Pattison Armstrong M A M D Dubl D P H aged 78

AYMER —On Jan 9 at Stonehaven Kincardineshire Charles Aymer M B Aberd

CLARK —On Jan 9 at Dundee, John Macdonald Clark, M B St And D.A

DEWAR —On Jan 10 at Burnham on Sea Henry Steele Dewar M B Edin aged 34

FRANKLIN —On Jan 7 in London Philip Franklin F R C.S

IRWIN —On Jan 4 at Virginia Water Surrey John O Malley Irwin L R C P I aged 75

MASON —On Jan 10 at Cockermouth Cumberland Mary Emmeline Mason (née Joll) M D Lond

READDIE —On Jan 9 Andrew Finlay Readdie M C. L.R C P E, aged 61

SINCLAIR —On Jan 4 at Torquay Francis Howard Sinclair M D R U I aged 90

SWAIN —On Jan 6 James Swain C.B O B E M D Lond F R C.S

WALLACE —On Jan 6 at Filleigh Chudleigh, Devon Lewis Alexander Richard Wallace B.M Oxfd aged 85

WARE —On Jan 11, John Ware B A Camb M D Edin aged 72

Diary of the Week

JAN 21 TO 27

Monday, 22nd

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture demonstration
MEDICAL SOCIETY OF LONDON, 11, Chandos Street Cavendish Square, W 1
8 30 P M Dr Macdonald Critchley, Dr R Bodley Scott Headache

Tuesday, 23rd

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene, Keppel Street W.C.1) Prof E Adrian, O M P R.S Physiology of Sleep.

Wednesday, 24th

HEBERDEN SOCIETY
4 P M (Westminster Hospital Medical School, Horseferry Road, S W 1) Demonstration of Cases Dr L E Glynn Therapeutic Effects of Cortisone (Film)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242 St Vincent Street Glasgow
5 P M Prof L S P Davidson The Malabsorption Syndrome (Finlayson lecture)

Thursday, 25th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M Dr A G M. Weddell Cutaneous Sensibility
MEDICO LEGAL SOCIETY 26 Portland Place, W 1
8 15 P.M Dr Robert Forbes The G M C Hitherto and Henceforth
LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant Liverpool, 3
8 P M Dr H C Moore Renal Cortical Necrosis
UNIVERSITY OF ST ANDREWS
5 P M (Materia Medica Department, Medical School Dundee) Prof W J Tulloch Influence of Adaptation on the Host parasite Relationships in Disease

Friday, 26th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene) Prof A W Downie Infection and Immunity in Smallpox.
ASSOCIATION OF CLINICAL PATHOLOGISTS
9 30 A M (Westminster Medical School Horseferry Road, S W 1) Short communications
4 45 P M Sir Lionel Whitby Whither Clinical Pathology? (Presidential address)
5 30 P M Sir Henry Cohen Limitations of Laboratory Investigations
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES 11 Chandos Street W 1
8 P M Dr W J O Donovan Skin Conditions Simulating Those of Syphilis

Saturday, 27th

ASSOCIATION OF CLINICAL PATHOLOGISTS
9 30 A M Short communications
2 15 P M Dr R E Holling Dr A C Dalziel Dr C K Simpson, Dr F E Camps Dr R Jarman Manifestations of Anoxia
BIOCHEMICAL SOCIETY
10 30 A M (Postgraduate Medical School, Ducane Road W 12) Short papers
KENT PÆDIATRIC SOCIETY
2 30 P M (Farnborough Hospital Farnborough Kent) Clinical Meeting

Appointments

DOUGLAS A D M, M B St And D I H D.P M consultant psychiatrist Saxondale Hospital Radcliffe on Trent Notts.

GRAF K A M D Vienna, D P.M consultant child psychiatrist Towers Hospital, Leicester

HARRIES, E J M D Lond consultant pathologist South Somerset clinical area

LAL KUNDAN M B Punjab D M.R T asst radiotherapist Liverpool Radium Institute

MASON T A B L R C P E, D M R consultant radiologist West Cornwall clinical area

MORTON, T C St C C B O B E M D Edin F R C.P, D.P.H D.P.M D T M & H area pathologist West Cornwall clinical area.

REID SYLVIA M B Dubl D P M consultant psychiatrist Carlton Hayes Hospital Narborough Leics

SMITH A W H M R.C.S D P M asst psychiatrist Rainhill Hospital Lancs

TERRY R B M D Lond M R C P consultant physician Seamen's group of hospitals

TONKIN R D M D Lond M R C P asst physician Westminster Hospital

TOTTEN J W M B Glasg D OBST appointed factory doctor, Dumbarton district Dumbarton

Hospital for Sick Children, Great Ormond Street, London:

CALNAN C D, M A M B Camb, M R C.P senior registrar department of dermatology

CARTER, F S M D Camb M.R C.P D C H house physician.

HAWORTH J C, M B Birm D C H house physician

JONES P G C F R.C S D P.H house-surgeon

MEARA, R H, M B Camb, M.R C.P senior registrar department of dermatology

ACUTE OBSTRUCTIVE LARYNGOTRACHEITIS AND LARYNGOTRACHEOBRONCHITIS

REPORT OF AN OUTBREAK

JOHN O FORFAR
M.C , M.B , B.Sc. St And , M.R C.P , M R C P E , D C.H
LECTURER IN MEDICAL DISEASES OF CHILDREN IN THE UNIVERSITY OF ST ANDREWS , PÆDIATRIC PHYSICIAN, MARYFIELD HOSPITAL, DUNDEE , ASSISTANT PÆDIATRIC PHYSICIAN, ROYAL INFIRMARY DUNDEE

KENNETH R KEAY
M.B St And , M.R C.P E
PÆDIATRIC REGISTRAR, ROYAL INFIRMARY, DUNDEE

JAMES THOMSON
M.B Edin., F.R C.P.E
LECTURER I C DEPARTMENT OF MEDICAL DISEASES OF CHILDREN, UNIVERSITY OF ST ANDREWS , PÆDIATRIC PHYSICIAN, ROYAL INFIRMARY, DUNDEE

FEW reports on non-diphtheritic obstructive laryngotracheitis and laryngotracheobronchitis have appeared in this country, although during the past thirty years an extensive literature on the subject has grown up in America A recent outbreak in Dundee therefore appears worthy of record.

There is considerable variation in terminology Morgan and Wishart (1947) for instance, use the term acute laryngotracheobronchitis in a wide sense and include within it even cases of spasmodic croup, whereas Kayser (1941), Baum (1945), and others suggest that it should be used only for cases of such severity as to require instrumental relief of respiratory distress The former interpretation seems to be too broad, and the latter too restricted and somewhat unsatisfactory in that such a potentially variable factor as a method of treatment is used in defining it With others acute laryngotracheobronchitis implies the presence of tough viscid secretions throughout the respiratory tract (LeJeune and Bayon 1941) Anatomically we could use three terms obstructive laryngitis, obstructive laryngotracheitis, and obstructive laryngotracheobronchitis From a clinical point of view, however, the difficulty of differentiating in young children between obstructive laryngitis and obstructive laryngotracheitis, without laryngoscopy, leads us to use the one inclusive term, obstructive laryngotracheitis where there is acute laryngeal inflammation associated with signs of persisting respiratory obstruction In obstructive laryngitis, moreover, there is usually some inflammation of the trachea as well (MacCready 1944) We reserve the term obstructive laryngotracheobronchitis for these cases in which, in addition to acute obstructive laryngotracheitis, there is auscultatory or other evidence of bronchitis Further, on the basis of clinical assessment we classify cases as mild, moderate, or severe

THE OUTBREAK

All the cases reported were admitted to the children's wards of the two general hospitals in Dundee, a city of 182,000 inhabitants Although these hospitals serve a regional population of 400,000, no case was admitted from outside the city 22 cases diagnosed as acute obstructive laryngotracheitis or acute obstructive laryngotracheobronchitis occurred within the three months from August to November, 1949 The age incidence was from four months to nine years, and the sex-incidence 68% male and 32% female

Acute laryngeal obstruction was present in all the cases reported but they should be considered against a background of prevalent acute laryngitis and acute laryngotracheitis occurring in the same population at the same time, both in adults and in children, in whom signs of respiratory obstruction were absent or of ins cient severity to warrant admission to hospital quently other members of the family were so affe or had been a few days previously In adults the r complaint was of pharyngeal discomfort, the phar being slightly reddened and appearing granular M cases developed septic tonsillitis about the second or later Although sulphonamide eliminated the se pain was not relieved

The accompanying table sets out the main find and treatment in individual cases In 13 of these a obstructive laryngotracheitis was diagnosed, and acute obstructive laryngotracheobronchitis 9 graded as severe, 7 as moderate, and 6 as mild. condition was not therefore invariably an acute alarming emergency although it was always potent so It will be noted that the grade of severity does necessarily correspond to the amount of respira tract involved

CLINICAL PICTURE

In all cases respiratory distress was of sudden o and in no case had it been present for more than twe four hours before admission One child was brough the casualty department because his mother tho that something had stuck in his throat In some c the respiratory distress arose without previous sympt In others there had been a preceding period of a few d and in 2 cases up to two weeks in which coryza a co or some slight hoarseness had been present Sore th and headache were complained of by a few of the c children The onset of respiratory distress was gene associated with a croupy cough.

On admission the two outstanding features respiratory distress and prostration The children struggling for breath , stridor, inspiratory and ex tory, was severe, and in many cases there was the lessness, the constant changing of position, and anxious facies associated with anoxia Sleeplessness pronounced Suprasternal recession and indrawin the intercostal spaces and epigastrium were us present Obvious cyanosis was not a feature, but, es ally in the more severe cases there was an ashen pa to which we learned to attach a grave significance, which was not improved by tracheotomy In add to the respiratory distress there was a severe toxa leading to prostration and exhaustion out of propo to the amount of asphyxia present This was particularly in case 20, who died rapidly despite the that a free airway had been established early by trac tomy and was proved at necropsy to have been pres The temperature and respirations varied from 98 4 104 6°F and from 28 per minute to 66 per minute res tively Tachycardia was invariably present Inspec of the throat revealed either no abnormality or mode injection A considerable amount of mucopus occasionally present Where laryngoscopy was perfor it revealed inflammation and œdema of the larynx or without mucopurulent exudate No membrane seen In the first 3 moderate or severe cases this ex nation was made to ensure that no diphtheritic memb was present in the larynx On each occasion respiratory distress and prostration were worse th after, so much so that we became reluctant to use procedure, and it was only used once more (in case during the outbreak It was felt that with the occurr of many similar cases the withholding of laryngosc was justified We do not consider that in sporadic c doubtful cases this would be so Examination of chest was often difficult because of the restlessness o patient and the stridor In some cases it revealed no breath sounds, in others diminished air entry, bron vesicular or bronchial breath sounds, rhonchi, or n rales The percussion note was usually resonant Ra graphy showed normal lung fields, bronchitic change, or occasionally terminal bronchopneumonia The white cell count varied from 5000 to 33,000 per c mm , it bore no relationship to the severity or the duration of the illness

Swabs were taken from the pharynx on or shortly after admission and later also from the site of the lesion when feasible They revealed a variety of organisms, none of which seemed to predominate in this outbreak *Corynebacterium diphtheriæ* was isolated from the larynx in case 1 in addition to Friedländer's bacillus, streptococci, and staphylococci, this was proved bacteriologically to be avirulent The child had been previously immunised against diphtheria and had received diphtheria antitoxin without improvement, nor did tracheotomy relieve him There was a profuse mucopurulent exudate in the larynx, trachea, and bronchi We feel justified, in view of these findings and in view of the epidemic occurrence of non diphtheritic respiratory obstruction at this time, in considering that this boy was a diphtheria carrier, and that diphtheria was not responsible for his acute obstructive laryngotracheobronchitis Thomson (1922) has expressed the view that the carrier state may occasionally lead to *C diphtheriæ* being isolated from cases of acute laryngotracheitis of non diphtheritic ætiology Neffson and Wishik (1934) found that in 8% of their cases of non diphtheritic acute laryngotracheobronchitis *C diphtheriæ* was cultured from the laryngeal swab Diphtheria, incidentally, is now rare in this locality

COURSE

The course was short In the 4 patients who died the total duration of illness varied from ten hours to three days, in the patients who recovered, convalescence was established within a week

TREATMENT

Treatment in the main consisted of humidification of the atmosphere and of the administration of oxygen and otherapeutic and antibiotic drugs, with attempted ental relief of respiratory obstruction in 3 cases atmosphere in a small side room was humidified with an open steriliser, a relative humidity of 80% being achieved with a room temperature of 75°–80°F Increase in the temperature beyond this level only added to the patient's discomfort Oxygen was supplied through an oxygen tent or on one occasion through a B L B mask The use of these devices had to be limited in certain cases to short periods only, because the patient tended to become very restless and intolerant of them, so much so that in these cases their continued use was likely to add considerably to the exhaustion already present Adequate fluids were given and these were taken well, particularly by the younger children The chemotherapeutic and antibiotic agents used and the dosage given are shown in the table With severe cases later in the epidemic the dosage of penicillin was increased, and in addition 'Aureomycin' was given Cases 12 and 13, both of whom were so severely ill that they did not seem likely to recover, did so on this régime Following the report of Moncrieff and Weller (1949) we had the opportunity to use chloramphenicol in 2 cases, one moderate, the other mild The former patient (case 17) recovered uneventfully, and the latter (case 21), a mongol, died of bronchopneumonia during convalescence from acute laryngotracheitis while still under treatment with chloramphenicol Tracheotomy was done in cases 1 and 20 In case 1 it was done sixty four hours after the onset of symptoms and was followed by intubation through the tracheotomy tube to suck out secretions In case 20 it was done fourteen hours after the respiratory distress first began In case 5 laryngeal intubation with attempted removal of secretions by suction was done seventeen hours after he became acutely ill. These 3 patients died

NECROPSY FINDINGS

Necropsies were done on cases 1, 5, 20, and 21

Macroscopically, inflammation and œdema of the larynx were the outstanding features The inflammation extended to various degrees downwards to the trachea or the bronchi, and upwards into the epiglottis, pharynx, and tonsils The larynx was partly or, in one case, almost completely occluded Mucopurulent exudate was present in various amounts, in the pharynx only, or extending down the respiratory tract even to the bronchioles. In 2 cases areas of purulent necrotic membrane were present in the subglottic region and in the trachea The lungs were involved to a greater or lesser degree, showing either areas of bronchopneumonic consolidation, patchy collapse, and compensatory emphysema, or little change beyond basal congestion Other abnormalities, noted in some cases but not in others, were enlargement of the cervical and tracheobronchial lymph nodes, pallor and flabbiness of the myocardium, and fatty change in the liver

Histologically, there were œdema, hyperæmia, loss of epithelium, and cellular infiltration These changes were maximal in the larynx but occurred also in the trachea, main bronchi, and epiglottis Case 5 had gross necrosis and denudation of the laryngeal mucosa The submucous glands showed catarrhal change only The appearances in the lung indicated aspiration bronchopneumonia, with little interstitial inflammation Where the heart was examined it showed interstitial œdema, without evidence of focal necrosis or of cellular infiltration.

ILLUSTRATIVE CASE RECORDS

Case 3 (moderate) —A boy, aged 22 months On the morning of the day of admission this boy had been noted to be hoarse That evening his breathing had suddenly become laboured and noisy, and stridor had developed He had refused all food He was admitted to hospital four hours later

On admission there was respiratory embarrassment with struggling noisy respiratory efforts and indrawing of the lower part of the chest Stridor was severe, but cyanosis was not present The respirations were 30 per minute The fauces were injected, but no membrane was visible There was uniform expansion of the chest, with a resonant percussion note The breath sounds were diminished and partially obscured by the stridor Radiography showed no abnormality in the lung fields The white cell count was 17,400 per c.mm., the pulse rate 120, and the temperature 99°F

Treatment and Progress —The patient was kept in a steam moistened atmosphere in an oxygen tent and given penicillin and sulphadimidine (see table) After twenty four hours his stridor and respiratory distress were less and his temperature was settling After forty eight hours only hoarseness and occasional cough remained A throat swab showed the presence of hæmolytic streptococci and was negative for *C diphtheriæ* The boy returned home symptom free after nine days in hospital

Case 5 (severe) —A boy, aged 7 years, had first complained of sore throat and malaise twenty four hours before admission He had gone to school the previous day, but that evening had become hoarse and had difficulty in breathing Throughout the night dyspnœa had gradually increased. He had become cyanosed and vomited once or twice

On admission next morning, fifteen hours after the onset of respiratory difficulty, he was extremely pale and appeared toxic His expression was anxious, his intellect clear He was struggling for breath, and although stridor and intercostal indrawing were present they were not extreme His respirations were 45 per minute, temperature 102 4°F, and pulse rate 174. His pharynx was injected and full of mucopurulent secretions.

Treatment and Progress —The patient's colour improved a little after treatment with continuous oxygen through a B.L B mask and with 1 ml of nikethamide intramuscularly Two hours after admission, however, his condition was deteriorating Laryngoscopy showed an inflamed œdematous larynx The vocal cords were seen, and mucopurulent secretion was present Tracheal intubation and aspiration produced no benefit Breathing subsequently became weaker, and the boy became exhausted and apathetic and died six hours after

SUMMARY OF CASES

Case no	Sex	Age	Duration of (a) symptoms (b) respiratory distress before admission	Bacteriological findings	Diagnosis	Severity	Treatment	Duration of acute illness
		Yr mos.						
1	M	1 3	(a) 8 hr (b) ,,	Pharynx *Staph aureus*, Friedländer's bacillus Larynx and bronchus *Staph aureus*, Friedländer's bacillus *C diphtheriæ* (var *mitis*) (avirulent)	Laryngo tracheo bronchitis	Severe	Pen 50 000 u I M 8 hrly for 3 days S/dim 2 2 1 g q q h for 3 days Ephedrine gr 1/4 8 hrly for 3 days Diphth antitox 15,000 u I M (Laryngoscopy) Tracheotomy	3 days Died*
2	M	5 0	(a) 24 hr (b) ,,	Pharynx Staphylococcus	Laryngo tracheo bronchitis	Moderate	S/dim 1 1 0 5 g q q h for 7 days Ephedrine gr 1/4 t d s for 1 day Diphth antitox 20,000 u I M (Laryngoscopy)	7 days
3	M	1 10	(a) 24 hr (b) 4 hr	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Moderate	Pen 100 000 u I M 8 hrly for 2 days S/dim 2 2 1 g q q h for 5 days Diphth antitox 20 000 u I M	3 days
4	F	3 0	(a) 4 hr (b) ,,	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Mild	Pen 100 000 u I M 8 hrly for 6 days S/dim 2 2 1 g q q h for 6 days	2 days
5	M	7 0	(a) 24 hr (b) 15 hr	Pharynx *Staph aureus* *Strep viridans* Blood *Staph aureus* Lung *Staph aureus*	Laryngo tracheo bronchitis	Severe	Pen 250 000 u I M Oxygen Nikethamide I M. (Laryngoscopy)	30 hours Died*
6	M	2 4	(a) 36 hr (b) 26 hr	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Moderate	Pen 200 000 u I M q q h for 7 days S/dim 2 2 1 g q q h for 6 days S/thiaz 0 5 g q q h for 6 days	4 days
7	F	1 3	(a) 4 hr (b) ,,	Pharynx *Staph albus* hæmolytic streptococcus	Laryngo tracheitis	Mild	Pen 250 000 u I M then 100 000 u I M q q h for 4 days S/dim 2 2 1 g q q h for 4 days	3 days
8	F	3 0	(a) 10 hr (b) 8 hr	Pharynx *Staph aureus* *Staph albus*	Laryngo tracheo bronchitis	Severe		10 hours (admitted moribund) Died
9	F	2 2	(a) 14 hr (b) ,,	Pharynx Staphylococci and streptococci	Laryngo tracheo bronchitis	Severe	Pen 250 000 u I.M. twice S/dim 1 0 5 g q q.h for 5 days Ephedrine gr 1/4 q q h for 5 days	3 days
10	F	2 6	(a) 12 hr (b) 4 hr	Pharynx *Staph aureus* *Strep viridans*	Laryngo tracheitis	Mild	Pen 1 000 000 u then 250 000 u. I M 8 hrly for 5 days S/dim 2 2 1 g q q h for 5 days S/thiaz. 0 5 g q q h for 5 days	3 days
11	F	0 8	(a) 24 hr (b)	Pharynx *Staph albus* *Strep viridans*	Laryngo-tracheitis	Mild	Pen 1 000 000 u then 250 000 u I M 8 hrly for 5 days S/dim 1 1 0 5 g q q h for 5 days	3 days
12	M	2 0	(a) 12 hr (b) 2 hr	Pharynx no growth	Laryngo tracheo bronchitis	Severe	Pen 1 000 000 u then 250 000 u I M 8 hrly for 5 days S/dim 2 g once S/thiaz 1 0 5 g q q h for 4 days S/thiaz sol I M 1 g q q h for 2 days Aureomycin 125 mg 6 hrly for 3 days Ca gluconate 10% 10 ml I M once	3 days
13	M	1 4	(a) 24 hr (b) 2 hr		Laryngo tracheitis	Severe	Pen 1 000 000 u then 200 000 u I M 8 hrly for 4 days S/thiaz sol I M 1 g q q h for 3 days S/thiaz 1 g q q h for 4 days Aureomycin 125 mg 6 hrly for 1 day	4 days
14	M	0 10	(a) 12 hr (b) 2 hr	Pharynx *Staph aureus* *Strep viridans*	Laryngo tracheitis	Severe	Pen 1,000 000 u then 200 000 u I M 8 hrly for 3 days S/thiaz sol I M. 1 g q q h for 6 days S/dim 0 5 g q q h for 6 days Aureomycin 125 mg 6 hrly for 5 days	5 days
15	M	2 6	(a) 24 hr (b) 12 hr	Pharynx *Strep viridans*	Laryngo tracheo-bronchitis	Moderate	Pen 100 000 u then 50 000 u I M q q h for 5 days S/dim 1 1 0 5 g q q h for 5 days Ephedrine gr 1/4 q q h for 5 days	4 days
16	M	0 8	(a) 72 hr (b) 24 hr	Pharynx *Strep viridans*	Laryngo tracheitis	Severe	Pen 1 000 000 u then 200 000 u I M 8 hrly for 7 days S/dim 1 1 0 5 g q q.h. for 3 days S/thiaz 1 g q q h for 4 days Aureomycin 125 mg 6 hrly for 5 days	6 days
17	M	0 4	(a) 24 hr (b)	Pharynx no growth	Laryngo tracheo bronchitis	Moderate	Chloramphenicol 125 mg 6 hrly for 5 days	6 days
18	F	0 7	(a) 24 hr (b)	Pharynx *Staph aureus*	Laryngo tracheitis	Mild	Pen 1,000 000 u then 100 000 u. I M 8 hrly for 4 days S/dim 1 1 0 5 g q q h for 5 days Aureomycin 125 mg 6 hrly for 2 days	2 days
19	M	2 0	(a) 12 hr (b)	Pharynx no growth	Laryngo tracheo bronchitis	Moderate	Pen 100 000 u then 50 000 u I M q q h for 8 days S/dim 1 0 5 g q q h for 8 days	5 days
20	M	2 6	(a) 24 hr (b) 12 hr	Trachea Staphylococcus non hæmolytic streptococcus, *H influenzæ* Pharynx (p m.) *H influenzæ*	Laryngo tracheitis	Severe	Pen 1 000 000 u I M once Oxygen Tracheotomy Nikethamide I M.	1 day Died*
21	M	18 weeks	(a) 5 days (b) 16 hr	Pharynx No growth	Laryngo tracheitis	Mild	Pen 1,000 000 u then 50 000 u I M 8 hrly for 5 days S/dim. 1 1 0 5 g q q h. for 5 days Chloramphenicol 125 mg 6 hrly for 1 day then 250 mg 8 hrly for 3 days	2 days Died* of broncho pneumonia during convalescence
22	M	0 0	(a) 6 hr (b) 4 hr	Pharynx no growth	Laryngo tracheitis	Moderate	Pen 1,000 000 u then 200 000 u I.M. 8 hrly for 4 days S/dim 2 2 1 g q q h for 4 days Aureomycin 250 mg 6 hrly for 2 days	4 days

* Necropsy
Pen Penicillin
S/thiaz sol. Sulphathiazole soluble
S/dim Sulphadimidine (Sulphamezathine)
S/thiaz Sulphathiazole.
All drugs given by mouth unless otherwise indicated

graphy showed normal lung fields, bronchitic change, or occasionally terminal bronchopneumonia The white cell count varied from 5000 to 33,000 per c mm , it bore no relationship to the severity or the duration of the illness

Swabs were taken from the pharynx on or shortly after admission and later also from the site of the lesion when feasible They revealed a variety of organisms, none of which seemed to predominate in this outbreak *Corynebacterium diphtheriæ* was isolated from the larynx in case 1 in addition to Friedländer's bacillus, streptococci, and staphylococci, this was proved bacteriologically to be avirulent The child had been previously immunised against diphtheria and had received diphtheria antitoxin without improvement, nor did tracheotomy relieve him There was a profuse mucopurulent exudate in the larynx, trachea, and bronchi We feel justified, in view of these findings and in view of the epidemic occurrence of non diphtheritic respiratory obstruction at this time, in considering that this boy was a diphtheria carrier, and that diphtheria was not responsible for his acute obstructive laryngotracheobronchitis Thomson (1922) has expressed the view that the carrier state may occasionally lead to *C diphtheriæ* being isolated from cases of acute laryngotracheitis of non diphtheritic ætiology Neffson and Wishik (1934) found that in 8% of their cases of non diphtheritic acute laryngotracheobronchitis *C diphtheriæ* was cultured from the laryngeal swab Diphtheria, incidentally, is now rare in this locality

COURSE

The course was short In the 4 patients who died the total duration of illness varied from ten hours to three days, in the patients who recovered, convalescence was established within a week

TREATMENT

Treatment in the main consisted of humidification of the atmosphere and of the administration of oxygen and chemotherapeutic and antibiotic drugs, with attempted instrumental relief of respiratory obstruction in 3 cases The atmosphere in a small side room was humidified with an open steriliser, a relative humidity of 80% being achieved with a room temperature of 75°–80°F Increase in the temperature beyond this level only added to the patient's discomfort Oxygen was supplied through an oxygen tent or on one occasion through a B L B mask The use of these devices had to be limited in certain cases to short periods only, because the patient tended to become very restless and intolerant of them, so much so that in these cases their continued use was likely to add considerably to the exhaustion already present Adequate fluids were given and these were taken well, particularly by the younger children The chemotherapeutic and antibiotic agents used and the dosage given are shown in the table With severe cases later in the epidemic the dosage of penicillin was increased, and in addition 'Aureomycin' was given Cases 12 and 13, both of whom were so severely ill that they did not seem likely to recover, did so on this régime Following the report of Moncrieff and Weller (1949) we had the opportunity to use chloramphenicol in 2 cases, one moderate, the other mild The former patient (case 17) recovered uneventfully, and the latter (case 21), a mongol, died of bronchopneumonia during convalescence from acute laryngotracheitis while still under treatment with chloramphenicol Tracheotomy was done in cases 1 and 20 In case 1 it was done sixty four hours after the onset of symptoms and was followed by intubation through the tracheotomy tube to suck out secretions In case 20 it was done fourteen hours after the respiratory distress first began In case 5 laryngeal intubation with attempted removal of secretions by suction was done seventeen hours after he became acutely ill These 3 patients died

NECROPSY FINDINGS

Necropsies were done on cases 1, 5, 20, and 21

Macroscopically, inflammation and œdema of the larynx were the outstanding features The inflammation extended to various degrees downwards to the trachea or the bronchi, and upwards into the epiglottis, pharynx, and tonsils The larynx was partly or, in one case, almost completely occluded Mucopurulent exudate was present in various amounts, in the pharynx only, or extending down the respiratory tract even to the bronchioles In 2 cases areas of purulent necrotic membrane were present in the subglottic region and in the trachea The lungs were involved to a greater or lesser degree, showing either areas of bronchopneumonic consolidation, patchy collapse, and compensatory emphysema, or little change beyond basal congestion Other abnormalities, noted in some cases but not in others, were enlargement of the cervical and tracheobronchial lymph nodes, pallor and flabbiness of the myocardium, and fatty change in the liver

Histologically, there were œdema, hyperæmia, loss of epithelium, and cellular infiltration These changes were maximal in the larynx but occurred also in the trachea, main bronchi, and epiglottis Case 5 had gross necrosis and denudation of the laryngeal mucosa The submucous glands showed catarrhal change only The appearances in the lung indicated aspiration bronchopneumonia, with little interstitial inflammation Where the heart was examined it showed interstitial œdema, without evidence of focal necrosis or of cellular infiltration

ILLUSTRATIVE CASE RECORDS

Case 3 (moderate) —A boy, aged 22 months On the morning of the day of admission this boy had been noted to be hoarse That evening his breathing had suddenly become laboured and noisy, and stridor had developed He had refused all food He was admitted to hospital four hours later

On admission there was respiratory embarrassment with struggling noisy respiratory efforts and indrawing of the lower part of the chest Stridor was severe, but cyanosis was not present The respirations were 30 per minute The fauces were injected, but no membrane was visible There was uniform expansion of the chest, with a resonant percussion note The breath sounds were diminished and partially obscured by the stridor Radiography showed no abnormality in the lung fields The white-cell count was 17,400 per c.mm , the pulse rate 120, and the temperature 99°F

Treatment and Progress —The patient was kept in a steam moistened atmosphere in an oxygen tent and given penicillin and sulphadimidine (see table) After twenty four hours hi stridor and respiratory distress were less and his temperatur was settling After forty eight hours only hoarseness an occasional cough remained A throat swab showed th presence of hæmolytic streptococci and was negative fo *C diphtheriæ* The boy returned home symptom free afte nine days in hospital

Case 5 (severe) —A boy, aged 7 years, had first complained of sore throat and malaise twenty four hours before admission He had gone to school the previous day, but that evening had become hoarse and had difficulty in breathing Throughout the night dyspnœa had gradually increased He had becom cyanosed and vomited once or twice

On admission next morning, fifteen hours after the onse of respiratory difficulty, he was extremely pale and appeare toxic His expression was anxious, his intellect clear He wa struggling for breath, and although stridor and intercosta indrawing were present they were not extreme His respiration were 45 per minute, temperature 102 4°F, and pulse rate 174 His pharynx was injected and full of mucopurulent secretions

Treatment and Progress —The patient's colour improved little after treatment with continuous oxygen through B.L B mask and with 1 ml of nikethamide intramuscularly Two hours after admission, however, his condition wa deteriorating Laryngoscopy showed an inflamed œdematou larynx The vocal cords were seen, and mucopurulent secretio was present Tracheal intubation and aspiration produced n benefit Breathing subsequently became weaker, and the bo became exhausted and apathetic and died six hours afte

SUMMARY OF CASES

Case no	Sex	Age Yr	Age mos.	Duration of (a) symptoms (b) respiratory distress before admission	Bacteriological findings	Diagnosis	Severity	Treatment	Duration of acute illness
1	M	1	3	(a) 8 hr (b)	Pharynx *Staph aureus* Friedländer s bacillus Larynx and bronchus *Staph aureus* Friedländer s bacillus *C diphtheriæ* (var *mitis*) (avirulent)	Laryngo tracheo bronchitis	Severe	Pen 50 000 u. I.M. 8 hrly for 3 days S/dim 2 2 1 g q q h for 3 days Ephedrine gr 1/4 8 hrly for 3 days Diphth antitox. 15 000 u I.M (Laryngoscopy) Tracheotomy	3 days Died*
2	M	5	0	(a) 24 hr (b)	Pharynx Staphylococcus	Laryngo tracheo bronchitis	Moderate	S dim. 1 1 0 5 g q q h for 7 days Ephedrine gr 1/4 t d s for 1 day Diphth antitox. 20 000 u I.M (Laryngoscopy)	7 days
3	M	1	10	(a) 24 hr (b) 4 hr	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Moderate	Pen 100 000 u I.M 8 hrly for 2 days S/dim 2 2 1 g q q.h for 5 days Diphth antitox 20 000 u I.M	3 days
4	F	3	0	(a) 4 hr (b)	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Mild	Pen 100 000 u. I M 8 hrly for 6 days S/dim 2 2 1 g q q h for 6 days	2 days
5	M	7	0	(a) 24 hr (b) 15 hr	Pharynx *Staph aureus* *Strep viridans* Blood *Staph aureus* Lung *Staph aureus*	Laryngo tracheo bronchitis	Severe	Pen 250 000 u. I.M Oxygen Nikethamide I.M. (Laryngoscopy)	30 hours Died*
6	M	2	4	(a) 36 hr (b) 26 hr	Pharynx Hæmolytic streptococcus	Laryngo tracheitis	Moderate	Pen 200 000 u I M q q h for 7 days S/dim 2 2 1 g q q.h for 6 days S/thiaz 0 5 g q q h for 6 days	4 days
7	F	1	3	(a) 4 hr (b) ,	Pharynx *Staph albus* hæmolytic streptococcus	Laryngo tracheitis	Mild	Pen 250 000 u I.M then 100 000 u I M q q h for 4 days S/dim 2 2 1 g q q h for 4 days	3 days
8	F	3	0	(a) 10 hr (b) 8 hr	Pharynx *Staph aureus* *Staph albus*	Laryngo tracheo bronchitis	Severe		10 hours (admitted moribund) Died
9	F	2	2	(a) 14 hr (b) ,	Pharynx Staphylococci and streptococci	Laryngo tracheo bronchitis	Severe	Pen 250 000 u I.M. twice S dim 1 0 5 g q q.h for 5 days Ephedrine gr 1/4 q q h for 5 days	3 days
10	F	2	6	(a) 12 hr (b) 4 hr	Pharynx *Staph aureus* *Strep viridans*	Laryngo tracheitis	Mild	Pen 1 000 000 u then 250 000 u. I M 8 hrly for 5 days S/dim 2 2 1 g q q h for 5 days S/thiaz 0 5 g q q h for 5 days	3 days
11	F	0	8	(a) 24 hr (b)	Pharynx *Staph albus* *Strep viridans*	Laryngo-tracheitis	Mild	Pen 1 000 000 u then 250 000 u I M 8 hrly for 5 days S/dim 1 1 0 5 g q q h for 5 days	3 days
12	M	2	0	(a) 12 hr (b) 2 hr	Pharynx no growth	Laryngo tracheo bronchitis	Severe	Pen 1 000 000 u then 250 000 u I M 8 hrly for 5 days S/dim 2 g once S/thiaz 1 0 5 g q q.h for 4 days S/thiaz sol I.M 1 g q q h. for 2 days Aureomycin 125 mg 6 hrly for 3 days Ca gluconate 10% 10 ml I.M. once	3 days
13	M	1	4	(a) 24 hr (b) 2 hr		Laryngo tracheitis	Severe	Pen 1 000 000 u then 200 000 u I M 8 hrly for 4 days S/thiaz sol I.M 1 g q q h for 3 days S/thiaz 1 g q q h for 4 days Aureomycin 125 mg 6 hrly for 1 day	4 days
14	M	0	10	(a) 12 hr (b) 2 hr	Pharynx *Staph aureus* *Strep viridans*	Laryngo tracheitis	Severe	Pen 1 000 000 u then 200 000 u I M 8 hrly for 3 days S/thiaz sol I.M. 1 g q q h for 6 days S/dim 0 5 g q q.h. for 6 days Aureomycin 125 mg 6 hrly for 5 days	5 days
15	M	2	6	(a) 24 hr (b) 12 hr	Pharynx *Strep viridans*	Laryngo tracheo-bronchitis	Moderate	Pen 100 000 u then 50 000 u I.M q q h for 5 days S/dim 1 1 0 5 g q q.h for 5 days Ephedrine gr 1/4 q q h. for 5 days	4 days
16	M	0	8	(a) 72 hr (b) 24 hr	Pharynx *Strep viridans*	Laryngo tracheitis	Severe	Pen 1 000 000 u then 200 000 u. I M 8 hrly for 7 days S/dim 1 1 0 5 g q q h. for 3 days S/thiaz 1 g q q h for 4 days Aureomycin 125 mg 6 hrly for 5 days	6 days
17	M	0	4	(a) 24 hr (b)	Pharynx no growth	Laryngo tracheo bronchitis	Moderate	Chloramphenicol 125 mg 6 hrly for 5 days	6 days
18	F	0	7	(a) 24 hr (b)	Pharynx *Staph aureus*	Laryngo tracheitis	Mild	Pen 1 000 000 u then 100 000 u I.M 8 hrly for 4 days S/dim. 1 1 0 5 g q q.h for 5 days Aureomycin 125 mg 6 hrly for 2 days	2 days
19	M	2	0	(a) 12 hr (b)	Pharynx no growth	Laryngo tracheo bronchitis	Moderate	Pen 100 000 u then 50 000 u. I.M q q h for 8 days S/dim 1 0 5 g q q h for 8 days	5 days
20	M	2	6	(a) 24 hr (b) 12 hr	Trachea Staphylococcus non hæmolytic streptococcus, *H influenzæ* Pharynx (p.m.) *H. influenzæ*	Laryngo-tracheitis	Severe	Pen 1 000 000 u I.M once Oxygen Tracheotomy Nikethamide I.M.	1 day Died*
21	M	18 weeks		(a) 5 days (b) 16 hr	Pharynx No growth	Laryngo tracheitis	Mild	Pen 1 000 000 u then 50 000 u I.M 8 hrly for 5 days S/dim. 1 1 0 5 g q q h. for 5 days Chloramphenicol 125 mg 6 hrly for 1 day then 250 mg 8 hrly for 3 days	2 days Died* of broncho pneumonia during convalescence
22	M	9	0	(a) 6 hr (b) 4 hr	Pharynx no growth	Laryngo tracheitis	Moderate	Pen 1 000 000 u. then 200 000 u. I.M. 8 hrly for 4 days S/dim. 2 2 1 g q q.h for 4 days Aureomycin 250 mg 6 hrly for 2 days	4 days

* Necropsy

Pen., Penicillin

S/thiaz. sol. Sulphathiazole soluble

S/dim. Sulphadimidine ('Sulphamezathine')

S/thiaz Sulphathiazole.

All drugs given by mouth unless otherwise indicated.

admission A laryngeal swab yielded a growth of *Staph aureus*, which further investigation showed to be resistant to penicillin and to streptomycin in concentrations attainable therapeutically in the blood and to sulphanilamide, sulphapyridine, sulphadiazine, sulphathiazole, sulphadimidine, and sulphacetamide

Necropsy (Dr H B Goodall) showed an intensely inflamed œdematous larynx partially covered by a cream coloured necrotic membrane The trachea, particularly at the upper end, was involved in a similar inflammation, it contained thick tenacious mucopurulent exudate which extended into the bronchi The larger bronchi were acutely inflamed, and the intermediate ones showed a few areas of catarrh The lungs were the seat of widespread bronchopneumonic change, especially in the posterior parts of the lower lobes Patches of collapse and of compensatory emphysema were a feature The tracheobronchial lymph nodes were enlarged and inflamed The heart showed terminal engorgement of the right chambers *Staph aureus* was also isolated from the heart blood and from the lung in pure culture

Histologically the larynx showed œdema and hyperæmia The mucosa was almost completely necrosed, and there were areas of purulent infiltration into the submucosa, with catarrhal changes in the submucosal glands Even the intrinsic muscles showed dense purulent infiltration The trachea and main bronchi showed changes similar to those seen in the larynx, but less severe Some of the bronchioles were blocked with pus The inflammation in their walls, however, was not sufficiently developed to have caused this degree of purulent exudation, indicating that pus had been aspirated from the upper respiratory tract

Case 12 (severe) —A boy, aged 2 years, had had a slight cough for two days before the sudden onset of severe respiratory distress at 9 P M

On admission two hours later dyspnœa was extreme The respirations were 48 a minute There was obvious indrawing of the suprasternal notch and of the lower anterior half of the chest Breathing was noisy and harsh, with much inspiratory stridor The facies was anxious, and the skin ashen pale The child was restless and, although exhausted, could not sleep His entire energy was concentrated on the effort of respiration, and he seemed oblivious of his surroundings and of those attending him He appeared to be in extremis The fauces were injected, but there was no membrane The expansion of the chest was poor and equal on both sides, with a resonant percussion note and bronchovesicular breath sounds There were scattered coarse crepitations over both lungs Physical examination was otherwise negative The boy's temperature was 100 8°F, pulse rate 150, and white cell count 17,900 per c mm

Treatment and Progress —Continuous oxygen was given in an oxygen tent, and the room atmosphere was moistened with steam Penicillin, sulphadimidine, sulphathiazole, and aureomycin were given as indicated in the table The boy's condition remained unchanged throughout the first twenty four hours During the next twenty four hours some improvement was manifest, although he was still critically ill Thereafter improvement was rapid, with disappearance of all signs of respiratory distress by the fourth day A throat swab taken shortly after admission, but after drug therapy had been started, revealed no bacterial growth Radiography five days after admission showed normal lung fields The patient was discharged home well after seven days in hospital

DISCUSSION

The fact that obstructive laryngotracheitis and laryngotracheobronchitis tend to occur in epidemic form and in association with a high incidence of infection of the upper respiratory tract in the general population has been noted by many workers (Baum 1928, Kayser 1941, Loza 1941, Crooks 1947), and specific epidemics have been described by Smith (1936) and Jeffrey (1945) Gittins (1942), however, states that in twenty two years' experience of acute laryngotracheobronchitis, he has never seen it in epidemic form We have not been able to find any published report of a previous outbreak in Britain

Ætiology

The view has recently gained ground that acute laryngotracheobronchitis is due to a virus, and that secondary invaders follow this (Morgan and Wishart 1947, Neffson 1949) The virus responsible for the acute laryngotracheobronchitis of fowls has been grown when inoculated into the amniotic sac of the chick embryo (Burnet and Foley 1941) When cultured in this manner the virus does not behave in the same way as the influenza virus, which has been suggested as the ætiological agent in human acute laryngotracheobronchitis because of the frequent association of epidemic influenza and this disease Arden and Duhig (1944) suggest that the pathological changes are more in keeping with viral than with bacterial infection Earlier reports favoured particularly the streptococcus as the ætiological agent (Jackson and Jackson 1936), although the disease has been attributed to the staphylococcus (Neffson 1942), *Hæmophilus influenzæ* (Sinclair 1941, De Navasquez 1942, Alexander et al 1942), and other organisms (Neffson 1944) In the 10 cases described by Sinclair (1941), in which *H influenzæ* was isolated from the blood in every instance and from the pharynx in 8 out of the 9 occasions on which a pharyngeal swab was taken, the clinical features and course were very similar to those of this outbreak In our cases the absence of any predominating organism and the short course suggest that a virus was the cause, and the organisms isolated seem likely to have been secondary invaders, which were controlled in most instances by chemotherapy and antibiotic therapy It is noteworthy that in case 5, where *Staph aureus* was cultured from the throat, larynx, pneumonic lung, and blood, this organism was resistant to all the drugs used It will be observed that throat swabs occasionally yielded no growth

Incidence

In this country cases of obstructive laryngitis and laryngotracheobronchitis have been reported by De Navasquez (1942), Thomson (1949), Moncrieff and Weller (1949) and Garson (1950), but they seem to be not so infrequent as the paucity of these reports suggests Age seems to be a predisposing factor to the severer forms, related no doubt to the small size of the infant larynx and to the readily yielding nature of its tissues. The age incidence of the cases reported here follows closely that noted by others (Baum 1928, Smith 1936), as does the sex incidence in its preponderance of males (Bradford and Leahy 1930, Neffson and Wishik 1934, Smith 1936, Bonham Carter 1949)

Clinical Features

The mode of onset and course over the first 24–48 hours were similar to those of many of the American reports A feature of this outbreak, however, was the occurrence in the cases who survived of what almost amounted to a crisis within 24–72 hours, followed by a rapid abatement of symptoms Another feature was the relative absence of complications The combination of these two features made the course of the illness short In many of the reported cases of acute laryngotracheobronchitis, however, the duration of the illness has been measured, in weeks Perhaps the specificity of the infecting agent in this outbreak was responsible for the short course, or perhaps chemotherapy modified the primary agent or as already suggested, controlled secondary invaders The patients who died seemed to do so as much or more from an overwhelming toxæmia as from the asphyxiation associated with respiratory obstruction with its attendant restlessness and exhaustion Saphir (1945) attributes the sudden death in these cases to acute toxic myocarditis and has produced supporting histological evidence

Diagnosis

The sudden onset, the characteristic symptoms, the pyrexia, and the epidemic occurrence made diagnosis of little difficulty in these cases Diphtheria, obstructive laryngitis associated with the exanthemata, laryngitis stridulosa, retropharyngeal abscess, and the possibility of a foreign body in the larynx had to be considered

Jackson and Jackson (1936) state that fulminating acute laryngotracheobronchitis with rapid death may simulate acute bronchopneumonia Neffson (1949) has pointed out that in laryngeal diphtheria the sequence of symptoms tends to be cough, hoarseness, and dyspnœa, whereas in non diphtheritic acute laryngotracheobronchitis it tends to be cough, dyspnœa, and hoarseness The same worker believes that laryngoscopy should be done in every case In 8 of our 22 cases a history of hoarseness preceding or accompanying the onset of respiratory distress was given Like Jackson (1938) we found that a feature of most of our cases was persisting hoarseness after the respiratory distress had gone

Treatment

The development of sudden and severe respiratory distress in a child who has appeared perfectly well a few hours previously presented an urgent and obvious therapeutic problem Owing to the lack of agreement on what constitutes acute obstructive laryngotracheitis and laryngotracheobronchitis, and to the variation of severity in different outbreaks, no close comparison of percentage mortality figures and methods of treatment between one series of cases and another would be valid Different methods of treatment are therefore difficult to compare On certain measures, however, there is general agreement the necessity for a high humidity of the respired air to prevent the secretions from drying and becoming viscid and crusted, the use of oxygen, the giving of adequate fluid, and the contra indication to atropine and to sedatives which are respiratory depressants Regarding humidity Davison (1940) has described the use of a mechanical humidifier rather than the use of steam Brenneman et al (1938) attribute an improvement in their mortality figures after 1935 to the fact that from that date the services of a skilled bronchoscopist were available They advocate tracheotomy in all cases in which it is warranted by the severity of the illness as judged by the general condition of the patient and the findings on laryngoscopy and bronchoscopy Most workers agree that tracheotomy is the most effective method of relieving respiratory distress, either alone or combined with intubation and suction through a tracheotomy tube, or bronchoscopic suction through the tracheotomy wound, to remove tracheal and bronchial secretions Baum (1945) and Neffson (1942), however, favour intubation through the larynx as the method of choice in the first instance, reserving tracheotomy for cases in which this fails Baum (1928) believes that tracheotomy may act adversely by causing drying and viscidity of secretions McEntee (1949), commenting on early tracheotomy, states "Delay will save some tracheotomies and avoid some deaths" We have already referred to the fact that in our cases laryngoscopy, where this was done, was followed by an increase in the respiratory distress, and we have also noted that the two cases where tracheotomy was done and the one case where laryngeal intubation was done were not improved thereby This failure to respond as expected to tracheotomy is in accord with the experience of Sinclair (1941) In most of our cases we relied mainly on the supporting measures already mentioned, combined with chemotherapy and antibiotics This entailed 24–48 hours of anxious conservatism, but we feel that the results justified this course Certainly some of the patients who recovered on conservative treatment appeared to be as severely ill as those who died and on whom instrumental relief of respiratory distress was attempted Rebatta and Martin (1948) state that the introduction of penicillin and sulphonamides has rendered the avoidance of tracheotomy possible in many cases where previously it would have been done Garson (1950) has used streptomycin successfully in one case and aureomycin with similar success in another Of the 5 severe non fatal cases in our series it will be noted that one patient received penicillin plus sulphonamide and the others received those drugs with aureomycin in addition Published reports show considerable divergence of view about the value of sulphonamides and penicillin in this condition The differences in type and in drug sensitivity of the organisms found has to be borne in mind, however Be they primary agents or secondary invaders, they play an important rôle in the disease, and wide variability in the effect of sulphonamides and of penicillin could only be expected The newer antibiotics aureomycin and chloramphenicol with their wide range of activity seem promising weapons requiring further assessment However, in view of our ignorance about the true ætiology of acute laryngotracheobronchitis, and in view of the rapidity with which the condition may prove fatal, a combination of chemotherapeutic and antibiotic drugs seems to offer, for the present at least, a moderately effective if empirical line of treatment

Mortality

The over all mortality in this series was 18%, the mortality among cases classified as severe being 44%

Pathology

The pathological appearances were similar to those usually described in this condition Only 1 of our cases (case 20) was shown at necropsy to have almost complete occlusion of the larynx, and in this case an early tracheotomy had been done In the others there was a reduced laryngeal lumen, which still, however, showed considerable patency There was also evidence of toxic effects on the liver and myocardium These facts seem to emphasise that, although laryngeal obstruction was an important factor, toxic effects were equally so Regarding the nature of the laryngeal obstruction Brenneman et al (1938) and others have laid particular emphasis on the importance of œdema of the loose subglottic tissue Neffson (1949) has drawn a clinical distinction between cases in which this occurs and those, less frequent, in which supraglottic œdema is the main pathological finding The formation throughout the respiratory tract of a membrane consisting of mucopus, desquamated epithelial cells, necrotic mucosa, and later fibrin, is not uncommon (Neffson 1949)

SUMMARY

An outbreak of 22 cases of acute obstructive laryngotracheitis and laryngotracheobronchitis is described

This seems to be the first outbreak of this kind reported in Britain

The epidemiology, ætiology, clinical features, pathology, and treatment are discussed

Chemotherapeutic and antibiotic drugs may, in many cases at least, supplant the surgical measures which have in the past been considered essential in treatment

We wish to thank Prof W J Tulloch and the staff of the department of bacteriology, Prof A C Lendrum, Dr H B Goodall, Dr H G Morgan, and Dr G Nelson of the department of pathology, Mr G I Henderson and Mr J F Mowat of the ear, nose and throat department and Dr W M Jamieson of King s Cross Hospital, Dundee, for their help with investigation and treatment, and Sister Ansell, Sister Crichton, and Sister Wilson for the care and nursing of these patients

REFERENCES

Arden F Duhig J V (1944) *Med J Aust* i, 145
Alexander, H E Ellis C Leidy G (1942) *J Pediat* 20, 673
Baum H L (1928) *J Amer med Ass* 91 1097
— (1945) *Arch Otolaryng Chicago* 41 175
Bonham-Carter R E (1949) *Practitioner* 163, 504
Bradford W L Leahy A D (1930) *Amer J Dis Child* 40 298
Brenneman J Clifton W M Frank, A Hollnger P (1938) *Ibid*, 55, 667
Burnet F M Foley M (1941) *Aust J exp Biol med Sci* 19 235
Crooks, J (1947) in Paterson D Moncrieff A Diseases of Children 4th ed London vol i p 549
Davison F W (1940) *Arch Otolaryng Chicago* 32 321
De Navasquez S J (1942) *Brit med J* ii 187
Garson J Z (1950) *Ibid*, i 578
Gittins T R (1942) *Arch Otolaryng Chicago* 36, 491

References continued overleaf

ORTHOPÆDIC SIGNS IN THE DIAGNOSIS OF DISC PROTRUSION

WITH SPECIAL REFERENCE TO THE STRAIGHT-LEG-RAISING TEST

JOHN CHARNLEY
B Sc, M B Manc, F R C S
ASSISTANT ORTHOPÆDIC SURGEON, MANCHESTER ROYAL INFIRMARY, LECTURER IN ORTHOPÆDICS, UNIVERSITY OF MANCHESTER

FROM a practical point of view it is possible to distinguish two clinical types of sciatica (1) cases with severe disability, in which the sciatic pain is accompanied by deformity and limited mobility, and (2) cases with only moderate disability, in which mobility is limited only slightly and there is no deformity

In the first type a protruded disc can be diagnosed with certainty by simple clinical tests alone, and the diagnosis can be confirmed by operative findings In the second type a firm diagnosis often cannot be made even with the aid of elaborate radiological techniques, and, even if a protruded disc is found at operation, the result of removal may not show that this was the sole cause of the symptoms

It is an irony of fate that in the first type, where an unequivocal protrusion can almost always be demonstrated, with a nerve root stretched tightly over it, the signs of root pressure are often absent, and even if present are immaterial to the diagnosis, while in the second type, where neurological signs are often the main factor in establishing the diagnosis, surgical exploration of the affected roots often gives disappointing results

The investigation reported here was made to decide to what extent the various signs of deformity and limited mobility might be related to each other

AXIS OF FLEXION AND EXTENSION OF SPINE

Without knowledge of the axis of movement between each pair of vertebral bodies it is impossible to predict the condition of the spinal theca and extradural nerve roots during flexion and extension of the spine When the spine moves from the flexed to the extended position, the space between the vertebral bodies enlarges anteriorly, and that between the spinous processes diminishes posteriorly Though it seems fairly obvious that the axis of movement between each pair of vertebræ must lie near the spinal canal and in the posterior part of the disc, the researches of anatomists have not yet been promulgated in such a way as to convince the practising surgeon that the site of the axis has been conclusively settled, indeed from some reports—e g, Wiles (1935)—it might be concluded that no fixed axis exists, and that the centre of movement changes position in the flexed and extended positions Fick (cited by Steindler 1935), Poirier and Charpy (1926), and Quain (1915) evade direct mention of this point in the course of elaborate descriptions of the mechanics of spinal movement

In investigating the movement of the lumbar spine, with special reference to the movement of the associated dura and extradural roots, the essential feature is not so much the location of an axis of movement *between each pair* of vertebral bodies, if such movement does indeed occur at an axis, but rather the determination of what might be called the "bending axis" for the spine *as a whole*, *this is a longitudinal axis which experiences* the minimal change in length during transition between the extreme positions of flexion and extension

In the light of this conception of the "bending axis," a new attack was made on the problem by a method which is described here in detail because of its extreme simplicity The procedure is to determine the linear distance between corresponding points on all the vertebræ, measured on X ray films of the spine taken in flexion and in extension Those points situated at a distance from the "bending axis" will either separate from or approximate to each other as the spine moves from flexion to extension, and vice versa, *those points* which neither separate from nor approximate to each other will therefore lie on the "bending axis" (fig 1)

Method—A fresh lumbar spine was removed from a cadaver, and lateral radiographs were obtained in positions of extreme flexion and extension at a 6 ft tube distance to minimise distortion of measurements To increase the clarity of definition the lumbar spine was bisected in the sagittal plane, only the right or left half being used, with the flat surface laid on the film This bisection did not seem to alter the behaviour of the spine in flexion and extension as compared with the intact specimen The two dry films so obtained, one in flexion and one in extension, were next cut to give curved strips in the following manner to start the first strip, the scissors were carried through corresponding points along the anterior surfaces of the vertebral bodies, the second cut was made by passing through corresponding points in the substance of the vertebral bodies, midway between the front and back surfaces, the third cut passed through corresponding points at the junction of the anterior three quarters with the posterior quarter of the bodies, the fourth cut passed through the posterior surfaces of the vertebral bodies, and the fifth, and last, cut was made through the estimated position of the posterior wall of the spinal canal This produced two series of curved strips of film, one series taken in flexion and the other in extension there being five strips in each series It was now possible to compare, quite accurately, the exact

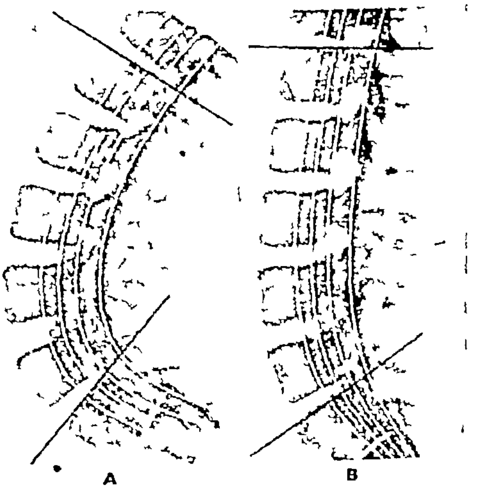


Fig 1—Bending axis of spine A cadaveric spine is radiographed in extension (A) and flexion (B), and lines are drawn through corresponding points in the vertebræ The variation in length of these curved lines can be compared in the extended and the flexed positions. Those lines which show the greatest variation in length lie furthest from the bending axis, whereas those which vary least lie nearest to the axis In this specimen the axis of flexion lies about 5 mm anterior to the posterior surfaces of the vertebral bodies

---

DR FORFAR AND OTHERS REFERENCES—*continued*

Jackson, C Jackson C L (1936) *J Amer med Ass* 107, 929
Jackson C L (1938) *Med Clin N Amer* 22 1581
Jeffrey F W (1945) *Canad med Ass J* 53, 562
Kayser R (1941) *Arch Otolaryng, Chicago* 33, 795
LeJeune F E Bayon P J (1941) *J Amer med Ass* 117 1316
Loza M G (1941) reviewed by Persky A H (1943) *Amer J Dis Child* 65 814
MacCready, P B (1944) *Ann Otol &c, St Louis* 53 65
McEntee J C (1949) *Lancet* ii, 910
Moncrieff A A Weller, S D V (1949) *Ibid* p 748
Morgan E A Wishart D E S (1947) *Canad med Ass J* 56 8
Neffson A H (1942) *Arch Otolaryng Chicago* 36, 773
— (1944) *Amer J med Sci* 208, 524
— (1949) Acute Laryngotracheobronchitis New York
— Wishik S M (1934) *J Pediat* 5 617
Rebatta J Martin H (1948) *Ann Oto laryng* 65 542
Saphir O (1945) *Amer J med Sci* 210 296
Sinclair, S E (1941) *J Amer med Ass* 117 170
Smith W J (1936) *Arch Otolaryng, Chicago* 23 420
Thomson C A (1922) *J Amer med Ass* 78, 1456
Thomson I S (1949) *J Otol Laryng* 63 411

lengths of the convex edges by rolling them against the edge of a ruler, in this way two measurements were obtained for each curve, and the difference in lengths of the same curve in flexion and extension was thereby ascertained The following figures were obtained from a very mobile spine in a person aged 18 and represent maximal figures

Difference in lengths over five lumbar vertebræ of longitudinal parallels passing from flexion to extension

Anterior surfaces of the vertebral bodies increased 12 mm
Mid points of the vertebral bodies increased 3 5 mm
Posterior quarter of the bodies increased 1 mm
Posterior surfaces of the bodies decreased 5 mm
Posterior limit of spinal canal decreased 11 mm

From these figures it is seen that movement was least on a line passing somewhere through the posterior quarter of each intervertebral disc, and therefore this line is to be regarded as the " bending axis " of the spine It will be found from measurements on a vertebra that the bending axis lies about 5 mm anterior to the front surface of the spinal theca

EFFECTS OF FLEXION AND EXTENSION ON SPINAL DURA AND NERVE ROOTS

Attempts to measure relative movement between the dura and spinal canal in the lumbar spine by *direct* observation on the cadaver are unsatisfactory because of the depths of the wound, the difficulty of moving the spine as a result of rigor mortis and body weight, and the small extent of the movements to be expected And, even if these mechanical difficulties could be overcome, such observations would still only concern movement between the dorsal surface of the lumbar theca and the laminæ of the canal The spinal roots emerge from the dura in an anterolateral direction and can be observed only with difficulty in the depths of the canal The plane of the roots lies nearer the posterior surface of the bodies of the vertebræ than the dorsal aspect of the theca, and is thus nearer the bending axis of the spine In the maximal figures obtained in the case described above there was a change in length, between flexion and extension, of 5 mm over the whole length of five lumbar vertebræ measured on the anterior aspect of the theca, whereas corresponding movement measured over the posterior wall of the spinal canal was 11 mm

This difference in mobility of the anterior and posterior surfaces of the lumber theca is reflected in the different anatomical arrangements of these two membranes Being an inelastic membrane, the dorsal dura is lax and relatively redundant, whereas the ventral dura is closely applied to the posterior surfaces of the vertebral bodies without the intervention of any fatty areolar tissue and is rendered immobile by the nerve roots which O'Connell (1943) aptly describes as ' guy ropes which hold the anterior dura against the vertebral bodies "

If the anterior dura is inelastic, as there is every reason to believe, one might wonder how in the lumbar spine it accommodates itself to a change in length of 5 mm between extreme flexion and extension Two possibilities exist either this 5 mm is equally distributed over the whole length of the five lumbar vertebræ, in which case each extradural root has only to accommodate itself to 1 mm of movement in relation to the adjacent bone (in a maximal estimation made on a youthful spine), or, the dura being fixed in the upper reaches of the spine, the range of movement between dura and bony canal becomes cumulatively greater as the distal end of the theca is reached This second possibility is highly unlikely, both on theoretical and anatomical grounds, because this amount of movement would be detectable on gross examination in the cadaver My own observations support the idea that the theca and extradural roots only experience local changes in length corresponding to the adjacent segment of the spinal canal, this behaviour of the theca is therefore quite different from that of the spinal cord and the nerves of the cauda equina, which, as is well known, move a considerable distance in relation to the bony canal during flexion and extension of the spine, and this relative movement becomes cumulatively greater in passing from the foramen magnum to the conus, hence the laxity of the cauda equina

With the theca and nerve roots inelastic, it seems a logical deduction that in the normal spine the total length of dura must equal the length of the anterior surface of the spinal canal when the whole spine is in full flexion, if this is so, all ordinary movements of the spine will take place with a relaxed dura, there is no reason to suppose that the normal dura is ever stretched beyond its maximal length The calculations already mentioned show that the linear changes experienced by the anterior surface of the spinal theca, even for extreme movements, are remarkably small (being near the bending axis) *This therefore explains why a protruded disc can produce more local stretching of the adjacent dura and nerve root than can the local stretch resulting from normal movement between the extreme positions of flexion and extension*

REVERSED LUMBAR LORDOSIS

It is well known that in a severe case of disc protrusion the normal lumbar lordosis is often obliterated, and may even be replaced by a lumbar kyphosis The reasons for this obliteration of the normal hollowing of the lumbar spine offer a most interesting field for speculation

If sciatic pain is caused by *stretching* of the extradural portion of the nerve root (O'Connell 1943) rather than by simple *compression*, a lumbar kyphosis will increase the pain by increasing the tension on the dura One would have expected from the preceding mechanical analysis that the natural protective reaction to stretching of the dura would be to increase the lordosis rather than to abolish it

O'Connell (1943) has attempted to explain reversed lumbar lordosis as a mechanism for relaxing tension in the sciatic nerve and extradural roots in the following words (p 243)

> " If a normal individual is asked to obliterate his normal lumbar lordosis it will be seen that what takes place is a tilting upward of the anterior portion of the bony pelvis with a depression of the sacrum so that the upper portion of the trunk is lowered relatively to the fixed lower limbs Such a movement would have the effect of producing relative relaxation in the roots of the sciatic nerve—the opposite effect to that which follows flexion of the hip or spine "

To the orthopædic surgeon this explanation is untenable In the standing position it is impossible for the normal adult to flatten the lumbar lordosis by backward rotation of the pelvis on the hips, *without at the same*

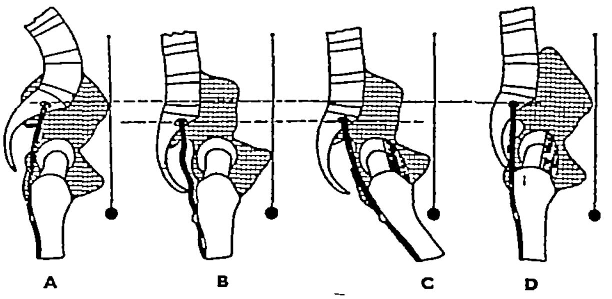


Fig 2—A normal standing position showing pelvis hip-joints, and sciatic nerve in relation to a vertical plumb-line B O Connell s explanation of flattening of the lumbar spine In this theory backward rotation of the pelvis is stated to relax the sciatic nerve C shows the impossibility of the preceding mechanism the pelvis cannot rotate backwards on the hip-joints because of the ligament of Bigelow Flattening of the lumbar spine by backward rotation of the pelvis can only take place if the patient stands with flexed knees. D flattening of the lumbar spine arising locally in the spine as a direct result of altered disc mechanics on this theory flattening of the lumbar spine is not compensatory but tends to stretch the sciatic nerve even further

time flexing the knees, because in the standing position the powerful Y shaped ligaments of Bigelow, which lie in front of the hip joints, are in tension and prevent backward rotation of the pelvis by more than a few degrees (fig 2)

This criticism of reversed lumbar lordosis in disc protrusion as a compensatory mechanism can be further illustrated in a rather different way In a lateral view of the skeleton in the standing position the fifth lumbar vertebra lies almost vertically above the hip joints The sciatic nerve, emerging from the vertebral foramina descends in almost a straight line, through the pelvis posterior to the hip joint If we look on this anatomical arrangement as the face of a clock, with the hip as the centre and the sacrum towards nine o clock, it is apparent that tilting of the pelvis either backwards or forwards on the hip joints so as to move the fifth lumbar vertebra between ten o'clock and two o clock will alter the tension in the sciatic nerve only very slightly (because this region of the clock face, in relation to the direction of the sciatic nerve, corresponds, if one may mix analogies, to a dead centre in the movement of a crank and its connecting rod) If O'Connell s view were correct, it would be necessary for the fifth lumbar vertebra to occupy a position between ten o'clock and eight o'clock if small angles of pelvic tilt were to produce significant changes in the tension of the sciatic nerve It is quite certain that a stance with 10° of hyper extension in the hips, if such a position could be achieved in the adult, would be detectable on clinical inspection

Further evidence that lumbar kyphosis is not a compensatory mechanism to relax the sciatic nerves is suggested by the frequency with which it is associated with pronounced degrees of limitation of straight-leg-raising (S.L.R.) as follows

In 9 cases with *complete reversal* of lumbar lordosis

7 had S.L.R. under 40°
2 had S.L.R. under 60°
0 had S.L.R. under 80°,
0 had S.L.R. full

In 48 cases with mere *flattening* of the lumbar spine

37 had S.L.R. under 40
1 had S.L.R. under 60
8 had S.L.R. under 80°
2 had S.L.R. full

In 13 cases with normal *hollow* lordosis

5 had S.L.R. under 40
2 had S.L.R. under 60°,
2 had S.L.R. under 80 ,
4 had S.L.R. full

Thus with lumbar kyphosis in all cases the S.L.R. was less than 60°, when the lumbar spine was merely flattened there were nearly four times as many cases with S.L.R. less than 60° as there were greater than 60°, and with a normal lumbar lordosis the distribution of limited S.L.R. showed no special trend

Another attempt to explain reversed lumbar lordosis as a compensatory mechanism points out that in the flexed position of the spine the intervertebral foramina are increased in size, and therefore any extradural root which is compressed by a protrusion encroaching on the intervertebral foramen would be relieved of pressure by this mechanism This is a tempting speculation, but it has never been convincingly established that compression of a nerve root in the foramen is more than an occasional complication of disc protrusion, and O'Connell's view that tension, rather than compression, is the source of pain is most in keeping with the general clinical picture In compression of the first sacral root by a protrusion from the fifth lumbar disc the first sacral foramen cannot be at fault, because it has no relation to a disc being an intact bony aperture which cannot be encroached on, yet in involvement of the first sacral root there often exists a reversed lumbar lordosis

For these reasons it seems certain that flattening of the lumbar spine in sciatica is not a reflex mechanism evoked to *reduce* tension or pressure in the affected root, and that it is most probably a primary deformity of the lumbar spine resulting directly from altered disc mechanics When the disc protrudes posteriorly, the interval between the posterior margins of the vertebral bodies seems almost to be "jammed open" by the protruded disc, assisted in this by some loss of turgidity of the nucleus pulposus, causing slight collapse anteriorly between the bodies

EFFECT OF FLEXION AND EXTENSION ON DISC PROTRUSION

The effect of flexion or extension on the prominence of a posterior disc protrusion is not generally known In theory the flexed position should increase the protrusion because in this position, anatomists state, the nucleus pulposus moves backwards Begg and Falconer (1949) showed that a protrusion was better revealed by myelography, and therefore was presumably more prominent, when the spine was extended On the other hand, some surgeons operate with the spine in strong flexion (in the knee elbow position) whereas others have the spine almost straight, yet both seem satisfied with their ability to reveal a protrusion It might seem an easy matter to test the effect of flexion and extension at operation, but in practice this observation is very difficult to make unless the movements of flexion and extension can be repeated several times, which is impossible in the operating theatre

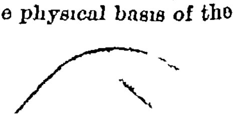
It appears, on the whole, that neither flexion nor extension has any great effect on the size of a protrusion, and very few surgeons seem to have observed the so called "concealed disc" of Dandy In all probability, once a disc has been protruded, there is no cavity left for it to retreat into, and the protruded material, being tough and fibrous like boiled lobster and quite unlike the pasty centre of a normal disc, remains stuck in its abnormal position The correct mental picture of a protruded disc is therefore better that of a wedge of solid material driven between the posterior margins of the vertebral bodies rather than that of a fluid hernia which is reducible like a hernial sac in the inguinal canal

Variations, if any, in the size and shape of the protruded disc in flexion and extension, will therefore be direct local effects on the protrusion and not indirect effects communicated to it from the nucleus On extension of the spine the posterior margins of the vertebral bodies will tend to "pinch off" the protrusion, and by relaxation of the overlying annulus fibrosus the protrusion might appear slightly more prominent On flexion of the spine, separation of the vertebral bodies posteriorly might accommodate more protruded material within its own track, and, the overlying annulus fibrosus being rendered tense, might possibly make the prominence seem slightly less obvious Whatever the mechanism, it seems safe to say that moderate variations in the position of the spine make only slight differences to the size of a protrusion and certainly not enough to determine whether a disc will be found at operation or not

STRAIGHT LEG RAISING TEST

Mechanism

Limitation of S.L.R. is well known in sciatica and not uncommonly is recorded in the laconic phrase "Lasègue's sign positive" The tendency to regard this test merely as one of equal significance with four or five other physical signs, from which the final diagnosis is made as an arithmetic sum, is one which needs challenging In its correct perspective the S.L.R. test, when recorded quantitatively in degrees, is of such importance in the diagnosis of disc protrusion—and more particularly in deciding which cases are likely to be benefited by operation—that its value should be regarded as being greater than that of all the other clinical or radiological signs put together To justify this bold statement it is necessary to review our knowledge of the physical basis of the S.L.R. test



Mechanical Basis of Test

The limitation of S.L.R. can be observed in the cadaver by removing the vertebral bodies from a lumbar spine through the posterior wall of the abdomen until the spinal theca is exposed and the fifth lumbar root is laid bare in its intervertebral foramen It will then be found that if a straight leg is raised to its full extent (after rigor mortis has been broken down) the nerve root will be seen to move in its foramen as a result of increased tension in the lumbar plexus, and will move by a distance which varies in different cadavers from 0·4 to 0·8 cm Inman and Saunders (1942) estimated this range at 0·2 to 0·5 cm and Falconer, McGeorge, and Begg (1948) reported it as 0·2 to 0·6 mm It will be observed during this experiment that the sciatic nerve behaves as though it were devoid of elasticity, and general experience of the great nerve trunks supports this

The point I wish to emphasise is not so much that the nerve root moves, or the amount by which it moves, but the *timing* of the movement of the root in relation to the movement of the leg If movement in the root is closely scrutinised during slow elevation of the extended leg, it will be observed that the root remains quite stationary until the leg has reached an angle of 30° or 40° above the horizontal plane, after which it starts to move quite suddenly and quite briskly and goes on moving with the leg until an elevation of about 70° is reached Beyond this point further movement of the root is sluggish, and by the time the leg has been raised to 90° the root will have been stationary for some time This movement of the nerve root in relation to the S.L.R. has been recorded cinematographically by means of a lever recording on a sheet of paper and attached at the other end to the nerve root The most impressive feature in this direct observation of the movement of the extradural roots in the cadaver, particularly when demonstrated cinematographically, is the suddenness with which the roots start to move

The sudden start of movement after an initial lag can easily be explained by the taking up of slack in the sciatic nerve during the first arc of S.L.R., but it is not at first clear why the movement, after being brisk during the middle arc, should thereafter tail off again as the leg reaches 90° The first explanation that comes to mind is that the nerve roots move briskly until the extradural nerve roots become taut, and thereafter no further movement of the root is possible But this simple explanation is unlikely, because it implies that the nerve-roots in the normal subject are exposed to tension before the completion of S.L.R., and it seems unlikely that normal roots should experience tension except at the most extreme limit of a normal range of movement The tailing off of movement *without a very pronounced rise of tension* can be explained on the principle of "simple harmonic motion" if the following model is constructed

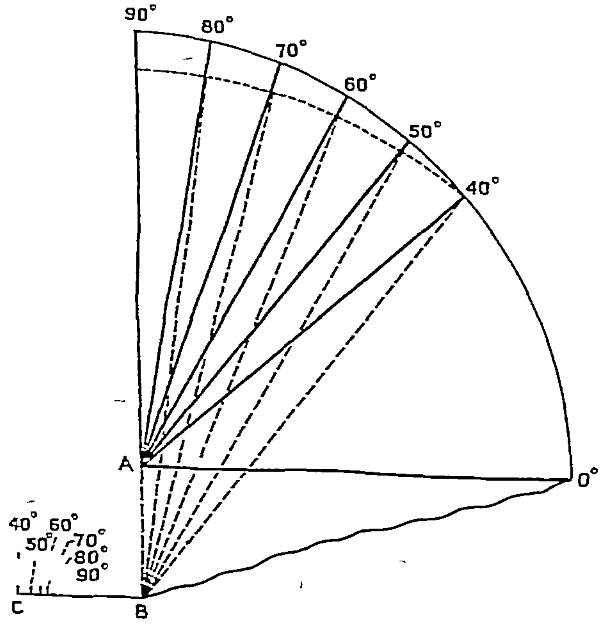


Fig 3—Straight-leg-raising: solid radii from A leg in different positions interrupted radii from B sciatic nerve in corresponding positions. When leg is raised to 40 sciatic nerve is taut. Point C, taken in the nerve at the spine, will move towards B as the leg is raised past 40 Successive positions of C show that movement is fairly rapid from S L.R. 40 to S L.R. 60 but slows up for the later positions of the leg

Experimental Model (fig 3)—A lath of wood is nailed by one end to a board so that it can pivot on the nail and thereby imitate the pivoting of the straight leg at the hip joint A second nail is driven into the board near the first nail but separated from it by a distance which represents the separation of the sciatic nerve from the axis of the hip A piece of string is now tied to the 'foot' end of the wooden lath to represent the nerve and carried behind the second nail to end at a point which represents an intervertebral foramen It is now necessary to arrange a little slack in the string so that, when the wooden lath is raised to imitate S.L.R., the string becomes tight when the 40° position is attained The interest now lies in the behaviour of the end of the string representing the nerve root while the wooden lath is raised to 90° In the working model, as soon as the slack is taken up, the "root" moves rapidly during the middle arc of movement and less briskly when the lath is reaching the end of the S.L.R.

This simple model thus demonstrates that the tailing off of movement in the nerve root is mainly due to the mechanical arrangement of the structures involved in S.L.R. on the principle of simple harmonic motion and that it is unnecessary to suppose that in the normal subject it is caused by a progressive building up of high tension in the root

Clinical Observations on S.L.R.

It is instructive now to examine the frequency and degree of limitation of S.L.R. in relation to the discovery of a protruded disc at operation

Of 88 patients operated on the S.L.R. was limited to less than 40° in 63 (The only significance of this preponderance is that it reflects my selection of cases for operation) Of these 63 patients with such limited S.L.R., 58 (92%) had protruded discs, whereas of the 25 patients with S.L.R. not so limited 16 (64%) had protruded discs Thus with S.L.R. under 40° exploration proved negative in the proportion of 1 to 11·6 cases, whereas when S.L.R. was over 40° the proportion of explorations proving negative was 1 to 1·8

Significance of Slight Degrees of Limitations of S.L.R.

The significance of *slight* degrees of limitations of S.L.R. in the diagnosis of disc protrusion needs considerable thought, because it may ultimately prove of the greatest importance in our understanding of sciatic pain

The observations on the cadaver described above make it difficult to understand the pathological state of the nerve root in a case where S.L.R. attains 90° on the normal side and 80° on the affected side, because in this type of case *the nerve root has already passed its range of greatest excursion without evoking pain or hamstring spasm* It is conceivable that the involvement of the nerve roots in cases with only slight limitation of S.L.R. might not be of the same direct mechanical origin, caused by a space occupying lesion, as in cases with gross degrees of limitation It is not impossible that mild degrees of limitation of S.L.R. may be associated with *referred* sciatic pain—i e, pain which originates in the disc itself even in the absence of a protrusion—and in these cases surgery directed to the removal of pressure *time flexing the knees*, because in the standing position the powerful Y shaped ligaments of Bigelow, which lie in front of the hip joints, are in tension and prevent backward rotation of the pelvis by more than a few degrees (fig 2)

This criticism of reversed lumbar lordosis in disc protrusion as a compensatory mechanism can be further illustrated in a rather different way In a lateral view of the skeleton in the standing position, the fifth lumbar vertebra lies almost vertically above the hip joints The sciatic nerve, emerging from the vertebral foramina, descends in almost a straight line, through the pelvis posterior to the hip joint If we look on this anatomical arrangement as the face of a clock, with the hip as the centre and the sacrum towards nine o clock, it is apparent that tilting of the pelvis either backwards or forwards on the hip joints so as to move the fifth lumbar vertebra between ten o clock and two o'clock will alter the tension in the sciatic nerve only very slightly (because this region of the clock face, in relation to the direction of the sciatic nerve corresponds, if one may mix analogies, to a dead centre in the movement of a crank and its connecting rod) If O Connell s view were correct, it would be necessary for the fifth lumbar vertebra to occupy a position between ten o'clock and eight o'clock if small angles of pelvic tilt were to produce significant changes in the tension of the sciatic nerve It is quite certain that a stance with 10° of hyperextension in the hips, if such a position could be achieved in the adult, would be detectable on clinical inspection

Further evidence that lumbar kyphosis is not a compensatory mechanism to relax the sciatic nerves is suggested by the frequency with which it is associated with pronounced degrees of limitation of straight leg raising (S L R) as follows

In 9 cases with *complete reversal* of lumbar lordosis

7 had S L R under 40°
2 had S L R under 60
0 had S L R under 80
0 had S L R full

In 48 cases with mere *flattening* of the lumbar spine

37 had S L R under 40
1 had S L R under 60
8 had S L R under 80°
2 had S L R full

In 13 cases with normal *hollow* lordosis

5 had S L R under 40
2 had S L R under 60°
2 had S L R under 80 ,
4 had S L R full

Thus with lumbar kyphosis in all cases the S L R was less than 60°, when the lumbar spine was merely flattened there were nearly four times as many cases with S L R less than 60° as there were greater than 60°, and with a normal lumbar lordosis the distribution of limited S L R showed no special trend

Another attempt to explain reversed lumbar lordosis as a compensatory mechanism points out that in the flexed position of the spine the intervertebral foramina are increased in size, and therefore any extradural root which is compressed by a protrusion encroaching on the intervertebral foramen would be relieved of pressure by this mechanism This is a tempting speculation, but it has never been convincingly established that compression of a nerve root in the foramen is more than an occasional complication of disc protrusion, and O'Connell's view that tension, rather than compression, is the source of pain is most in keeping with the general clinical picture In compression of the first sacral root by a protrusion from the fifth lumbar disc the first sacral foramen cannot lie at fault, because it has no relation to a disc being an intact bony aperture which cannot be encroached on, yet in involvement of the first sacral root there often exists a reversed lumbar lordosis

For these reasons it seems certain that flattening of the lumbar spine in sciatica is not a reflex mechanism evoked to *reduce* tension or pressure in the affected root, and that it is most probably a primary deformity of the lumbar spine resulting directly from altered disc mechanics When the disc protrudes posteriorly, the interval between the posterior margins of the vertebral bodies seems almost to be "jammed open" by the protruded disc, assisted in this by some loss of turgidity of the nucleus pulposus, causing slight collapse anteriorly between the bodies

EFFECT OF FLEXION AND EXTENSION ON DISC PROTRUSION

The effect of flexion or extension on the prominence of a posterior disc protrusion is not generally known In theory the flexed position should increase the protrusion because in this position, anatomists state, the nucleus pulposus moves backwards Begg and Falconer (1949) showed that a protrusion was better revealed by myelography, and therefore was presumably more prominent, when the spine was extended On the other hand, some surgeons operate with the spine in strong flexion (in the knee elbow position) whereas others have the spine almost straight, yet both seem satisfied with their ability to reveal a protrusion It might seem an easy matter to test the effect of flexion and extension at operation, but in practice this observation is very difficult to make unless the movements of flexion and extension can be repeated several times, which is impossible in the operating theatre

It appears, on the whole, that neither flexion nor extension has any great effect on the size of a protrusion, and very few surgeons seem to have observed the so called "concealed disc" of Dandy In all probability, once a disc has been protruded, there is no cavity left for it to retreat into, and the protruded material, being tough and fibrous like boiled lobster and quite unlike the pasty centre of a normal disc, remains stuck in its abnormal position The correct mental picture of a protruded disc is therefore better that of a wedge of solid material driven between the posterior margins of the vertebral bodies rather than that of a fluid hernia which is reducible like a hernial sac in the inguinal canal

Variations, if any, in the size and shape of the protruded disc in flexion and extension, will therefore be direct local effects on the protrusion and not indirect effects communicated to it from the nucleus On extension of the spine the posterior margins of the vertebral bodies will tend to "pinch off" the protrusion, and by relaxation of the overlying annulus fibrosus the protrusion might appear slightly more prominent On flexion of the spine, separation of the vertebral bodies posteriorly might accommodate more protruded material within its own track, and, the overlying annulus fibrosus being rendered tense, might possibly make the prominence seem slightly less obvious Whatever the mechanism, it seems safe to say that moderate variations in the position of the spine make only slight differences to the size of a protrusion and certainly not enough to determine whether a disc will be found at operation or not

STRAIGHT LEG RAISING TEST

Mechanism

Limitation of S L R is well known in sciatica and not uncommonly is recorded in the laconic phrase "Lasègue's sign positive" The tendency to regard this test merely as one of equal significance with four or five other physical signs, from which the final diagnosis is made as an arithmetic sum, is one which needs challenging In its correct perspective the S L R test, when recorded quantitatively in degrees, is of such importance in the diagnosis of disc protrusion—and more particularly in deciding which cases are likely to be benefited by operation—that its value should be regarded as being greater than that of all the other clinical or radiological signs put together To justify this bold statement it is necessary to review our knowledge of the physical basis of the S L R test

Mechanical Basis of Test

The limitation of S.L.R can be observed in the cadaver by removing the vertebral bodies from a lumbar spine through the posterior wall of the abdomen until the spinal theca is exposed and the fifth lumbar root is laid bare in its intervertebral foramen It will then be found that if a straight leg is raised to its full extent (after rigor mortis has been broken down) the nerve root will be seen to move in its foramen as a result of increased tension in the lumbar plexus, and will move by a distance which varies in different cadavers from 0 4 to 0 8 cm. Inman and Saunders (1942) estimated this range at 0 2 to 0 5 cm and Falconer, McGeorge, and Begg (1948) reported it as 0 2 to 0 6 mm It will be observed during this experiment that the sciatic nerve behaves as though it were devoid of elasticity, and general experience of the great nerve trunks supports this

The point I wish to emphasise is not so much that the nerve root moves, or the amount by which it moves, but the *timing* of the movement of the root in relation to the movement of the leg If movement in the root is closely scrutinised during slow elevation of the extended leg, it will be observed that the root remains quite stationary until the leg has reached an angle of 30° or 40° above the horizontal plane, after which it starts to move quite suddenly and quite briskly and goes on moving with the leg until an elevation of about 70° is reached Beyond this point further movement of the root is sluggish , and by the time the leg has been raised to 90° the root will have been stationary for some time This movement of the nerve root in relation to the S.L R has been recorded cinematographically by means of a lever recording on a sheet of paper and attached at the other end to the nerve root The most impressive feature in this direct observation of the movement of the extradural roots in the cadaver, particularly when demonstrated cinematographically, is the suddenness with which the roots start to move

The sudden start of movement after an initial lag can easily be explained by the taking up of slack in the sciatic nerve during the first arc of S L R , but it is not at first clear why the movement, after being brisk during the middle arc, should thereafter tail off again as the leg reaches 90° The first explanation that comes to mind is that the nerve roots move briskly until the extradural nerve roots become taut, and thereafter no further movement of the root is possible But this simple explanation is unlikely, because it implies that the nerve-roots in the normal subject are exposed to tension before the completion of S L R , and it seems unlikely that normal roots should experience tension except at the most extreme limit of a normal range of movement The tailing off of movement *without a very pronounced rise of tension* can be explained on the principle of "simple harmonic motion" if the following model is constructed

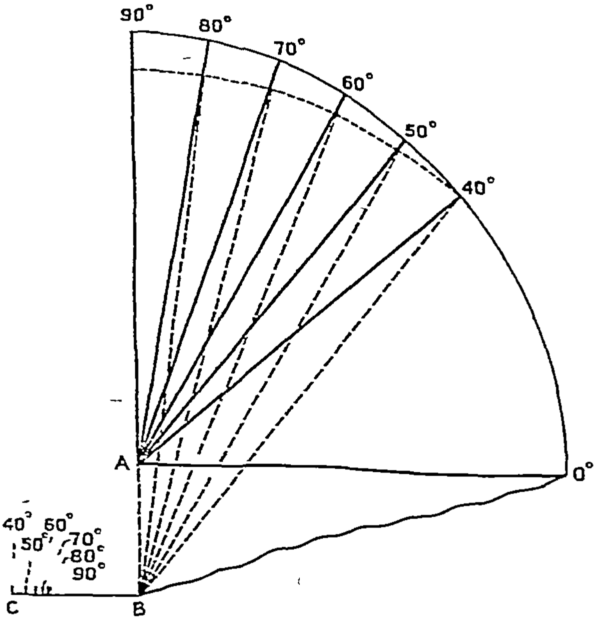


Fig 3—Straight leg-raising solid radii from A leg in different positions Interrupted radii from B sciatic nerve in corresponding positions. When leg is raised to 40 sciatic nerve is taut. Point C, taken in the nerve at the spine will move towards B as the leg is raised past 40° Successive positions of C show that movement is fairly rapid from S.L.R. 40 to S L.R. 60 but slows up for the later positions of the leg

Experimental Model (fig 3)—A lath of wood is nailed by one end to a board so that it can pivot on the nail and thereby imitate the pivoting of the straight leg at the hip joint A second nail is driven into the board near the first nail but separated from it by a distance which represents the separation of the sciatic nerve from the axis of the hip A piece of string is now tied to the foot end of the wooden lath to represent the nerve and carried behind the second nail to end at a point which represents an intervertebral foramen It is now necessary to arrange a little slack in the string so that when the wooden lath is raised to imitate S.L.R , the string becomes tight when the 40° position is attained The interest now lies in the behaviour of the end of the string representing the nerve root, while the wooden lath is raised to 90° In the working model as soon as the slack is taken up, the "root" moves rapidly during the middle arc of movement and less briskly when the lath is reaching the end of the S.L.R.

This simple model thus demonstrates that the tailing off of movement in the nerve root is mainly due to the mechanical arrangement of the structures involved in S L R on the principle of simple harmonic motion and that it is unnecessary to suppose that in the normal subject it is caused by a progressive building up of high tension in the root

Clinical Observations on S.L.R

It is instructive now to examine the frequency and degree of limitation of S.L.R in relation to the discovery of a protruded disc at operation

Of 88 patients operated on the S L.R. was limited to less than 40° in 63 (The only significance of this preponderance is that it reflects my selection of cases for operation) Of these 63 patients with such limited S L.R , 58 (92%) had protruded discs , whereas of the 25 patients with S.L R not so limited 16 (64%) had protruded discs Thus with S.L.R under 40° exploration proved negative in the proportion of 1 to 11 6 cases , whereas when S.L.R. was over 40° the proportion of explorations proving negative was 1 to 1 8

Significance of Slight Degrees of Limitations of S.L.R

The significance of *slight* degrees of limitations of S L R in the diagnosis of disc protrusion needs considerable thought, because it may ultimately prove of the greatest importance in our understanding of sciatic pain.

The observations on the cadaver described above make it difficult to understand the pathological state of the nerve root in a case where S L.R attains 90° on the normal side and 80° on the affected side, because in this type of case *the nerve root has already passed its range of greatest excursion without evoking pain or hamstring spasm* It is conceivable that the involvement of the nerve roots in cases with only slight limitation of S.L.R might not be of the same direct mechanical origin, caused by a space occupying lesion, as in cases with gross degrees of limitation It is not impossible that mild degrees of limitation of S.L.R. may be associated with *referred* sciatic pain—i e , pain which originates in the disc itself even in the absence of a protrusion—and in these cases surgery directed to the removal of pressure from the nerve root is likely to be followed by disappointing results

From our general knowledge of pain arising in deep structures it is not unreasonable to believe that such pain would be evoked on an "all or none principle" and would partake of that quality known in the past as epicritic With pain arising only at 70° or 80° of S L R one can presume that the nerve roots are not already stretched by a protruded disc, the pain is probably evoked in this case by the root being abnormally sensitive to stretching The cause of the increased sensitivity is not necessarily removed by curetting out the adjacent intervertebral disc In other words, I am tempted to suggest that limitation of S L R has two different mechanisms severe limitation to less than 40° implies a mechanical cause extrinsic to the root and evoked by the start of *movement* between the root and the skeletal structures, slight limitation, to not less than 70°, implies a cause of pain intrinsic to the root and evoked by *tension*, because it is not evoked during maximal movement of the root but only when rising tension is to be expected towards the end of S L R

FORWARD FLEXION AND S L R COMBINED

Limitation of forward bending of the spine is a very obvious feature of sciatica To investigate forward bending it is convenient to distinguish five grades of flexion from the erect to the fully flexed position

Grade 1, finger tips reaching 3 in short of the knee caps
Grade 2, finger tips reaching the knee-caps
Grade 3 finger tips reaching 3 in. below the knee-caps
Grade 4, finger tips reaching to mid tibiæ
Grade 5, finger tips reaching to ankles or toes
(Measurements made with knees straight.)

Of the 88 patients operated on, 73 had limitation of forward flexion within the first three grades, of these 73 patients a protruded disc was found in 63 (86%) whereas of the remaining 15 patients with good forward flexion a protruded disc was found in 11 (73%), 4 cases were negative Thus cases with bending limited to the first three grades had a negative exploration in the proportion of 1 to 6 3 cases, whereas cases with bending limited only in the last two grades had a negative exploration in the proportion of 1 case to 2 7 Evidently, therefore, bending alone is not quite so reliable a test for protruded disc as is S L R alone

Further reflection will show that it is impossible to attribute any significance to forward bending without at the same time correlating it with S L R, because forward bending is in fact nothing more than S L R done in the standing position (although certain theoretical differences are superadded by the possibility that the spinal dura is in a different mechanical state, because, when S L R is elicited on a couch, the spine is extended, whereas in forward bending S L R is combined with a flexed spine)

It is perhaps not obvious, unless one has made observations specially with this point in view, how large a part of the movement of forward bending takes place at the hips and how small a part takes place in the spine With a normal person lying supine in the position for the S L.R test the following correlations will be found

20° S L R is roughly equivalent to finger tips reaching 3 in short of knee caps

30° S.L.R. is roughly equivalent to finger tips reaching knee-caps

40° S.L.R. is roughly equivalent to finger tips reaching 3 in below knee-caps

60°–80° S.L.R is roughly equivalent to finger tips reaching mid tibiæ

To touch the ankles or the toes from the supine position is impossible unless the person flexes the neck and raises the shoulders These correlations between S L.R and forward bending are referred to later as being "anatomically consistent"

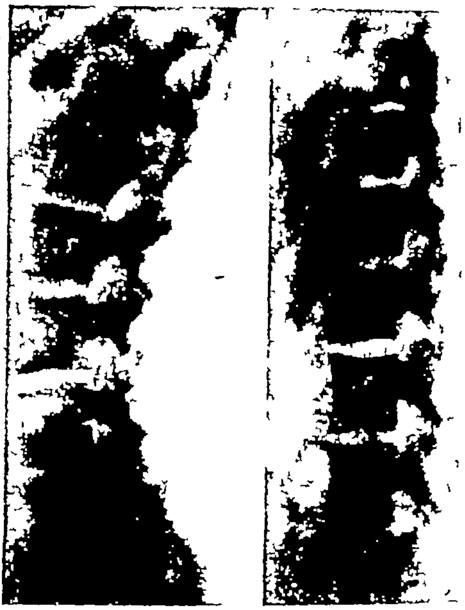


Fig 4—Radiographs showing the relatively small amount of movement which takes place in the lumbar spine between erect stance (A) and full forward bending (B)

Contribution of Spinal Flexion to Total Range of Forward Bending

If a spine is radiographed first in the erect position and next in full forward flexion, a surprisingly small range of movement is shown in the lumbar region In full flexion the lumbar spine never achieves an anterior concavity, at the most the lumbar spine merely becomes straight by the obliteration of the normal lordosis (fig 4) The full range of movement in the lumbar spine probably accounts for only about 20° of forward flexion in an adult without acrobatic powers

This very limited range of movement in the spine is not at first obvious when a patient is seen bending forward to touch his toes, because the strongly flexed position of the head and neck, and the forward drooping of the shoulder blades, reveals the almost fixed curvature of the thoracic spine, which in the erect position is concealed from view It is a common experience to find patients, after fusion of the lumbar spine, whose finger tips reach to the mid tibiæ on forward bending

In the normal person who can easily touch his toes it is not unreasonable to suppose that in this position the sciatic nerves, extradural roots, and spinal dura are at their greatest length and under no abnormal tension

Clinical Observations on Combined S.L.R and Forward Flexion

To decide whether any diagnostic or prognostic significance in sciatica might be extracted from a combined S L.R /flexion relation, it is instructive to construct a chart as in fig 5

In this chart the five grades of forward flexion and the four grades of S.L.R are combined so as to give twenty S.L.R./flexion "boxes", each "box" can be dubbed by the grade of flexion and S.L R it represents in terms such as 90/1, 40/2, &c (meaning 90° S L.R. in a patient with inability to touch his knee caps, 40° S.L.R in a patient able to reach his knee-caps, &c)

By representing each case on the chart as a dot, it is possible to see the distribution of patients in the various "boxes" and by using different symbols to indicate the cases in which a protruded disc was found at operation and those in which it was not, it is possible also to see simultaneously the distri

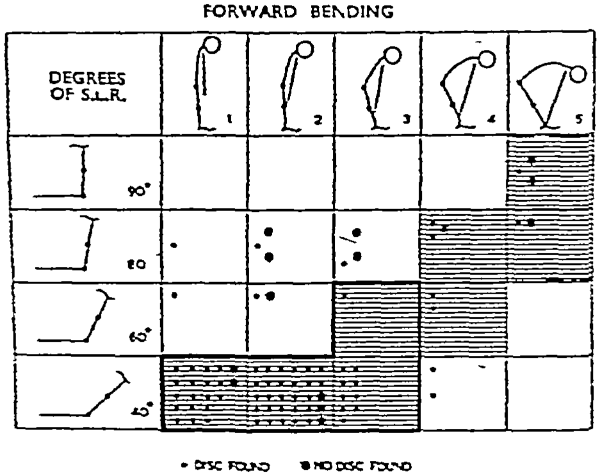


Fig. 5—Incidence of protruded discs in relation to S.L.R. and forward bending in 68 cases (see text)

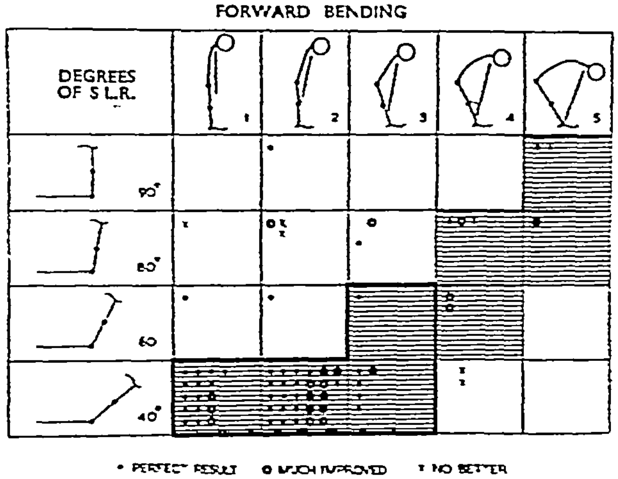


Fig. 6—Outcome of surgery in relation to S.L.R. and forward bending in 72 cases (see text)

bution of findings at operation in relation to S.L.R. and forward flexion.

The shaded boxes represent the combinations of S.L.R. and forward flexion which are anatomically consistent as previously described.

It will also be observed that the first four shaded boxes on the left side of the chart—i.e. 40/1, 40/2, 40/3, and 60/3—have been further distinguished by being enclosed with a heavy black line. These enclosed boxes denote the combinations of S.L.R. and forward flexion which in addition to being anatomically consistent also denote pathological limitation of movement. The remaining boxes which have been shaded but which are not included in the heavy black line denote cases which are anatomically consistent but not necessarily pathological because 90/5 is full flexion in the normal supple young person and 80/4 is normal forward flexion in most middle-aged or stocky patients.

After mastering these conventions in the S.L.R./flexion chart it is now possible to review the distribution of cases. Disregarding at this moment whether a protruded disc was found at operation or not we can see several broad features:

1. On the left side of the chart the physical signs in all the cases were broadly consistent in that there were no cases in which full S.L.R. occurred in combination with very marked limitation of forward flexion—i.e., there were no cases in boxes 90/1, 90/2, and 90/3, except for an isolated case in 90/2.

2. Similarly, on the right side of the chart the physical signs were broadly consistent in that there were no cases in which full flexion was present in combination with very severe limitation of S.L.R.—i.e., there were no cases in boxes 40/5 and 60/5.

3. Most of the cases in the chart fell into the 40° S.L.R. group and it is interesting to observe that most of these showed anatomically consistent degrees of S.L.R. and flexion in that they mainly fell into the 40/1 and 40/2 boxes.

4. The rest of the cases (except those concentrated in the 40/1, 40/2, and 40/3 boxes) are more or less evenly distributed across the chart without any significant trend though avoiding the boxes denoting extreme inconsistency enumerated in paragraphs 1 and 2.

S.L.R./Flexion Relation in Diagnosis

As regards the diagnosis of protruded disc it can be seen that this S.L.R./flexion chart, though raising many interesting features worthy of future study, perhaps does not yield any diagnostic evidence superior to the information gained from the S.L.R. test alone; it is in relation to negative evidence and the results of operation that the S.L.R./flexion chart is most significant.

In the four boxes in the top right hand corner of fig. 5—i.e., 90/4, 90/5, 80/4, and 80/5—where minimal limitation of S.L.R. was combined with minimal limitation of forward flexion, no protruded disc was found in 4 cases out of 9.

In fig. 5 the boxes lying to the left of the "consistent" (shaded) boxes represent those cases in which forward flexion was *less* than might have been expected from the degree of S.L.R. discovered in the supine position. Though the figures in the chart are numerically inadequate to prove the point, it seems that when forward flexion is limited more than one would expect from the degree of S.L.R., a protruded disc is unlikely to be found. Possibly these patients may be more apprehensive of forward flexion, which they understand, than they are of the S.L.R. test, which they do not understand, and possibly this anomaly implies a psychoneurotic element which disturbs the consistency of the clinical picture.

S.L.R./Flexion Relation in Prognosis

It is conceivable that the relation of S.L.R. and flexion to the *results* of operation might reveal the most significant connection, because the results of surgery in the psychoneurotic would probably be poor, whereas on the other hand, "negative" cases, in which a protruded disc was exposed but not recognised, might reveal themselves as good results because the correct mechanical treatment was employed. I believe that this is in fact what is found. In S.L.R./flexion chart no. 2 (fig. 6), it will be seen that out of a total of 49 cases in the "consistent and pathological boxes"—i.e., 40/1, 40/2, 40/3, 60/3, and 60/4—only 1 case was 'no better' for the operation. It is significant that after operation this patient revealed herself as a gross hysteric, and, though she was known to be psychoneurotic before the operation, the gravity of her neurosis was not suspected until her behaviour after the operation made it certain.

Out of 14 cases outside the "consistent boxes" plus the 7 cases in the "consistent but not pathological boxes"—i.e., 90/4, 90/5, 80/4, and 80/5—making a total of 21 cases, there were 7 cases no better for the operation. Thus the proportion of failures to good results was 1 to 49 in the "consistent and pathological" boxes and 1 to 3 in the "inconsistent" boxes and the "consistent but non-pathological" boxes.

Though the numbers in this series are not great their distribution seems significant, and they suggest that the best results of disc surgery are to be obtained when the limitation of forward flexion is anatomically consistent with the amount of S.L.R. elicited passively in the supine position.

Possibly inconsistencies in the S.L.R./flexion relation are objective demonstrations of psychoneurosis; but without invoking this too easy explanation it is difficult to explain how a patient should have gross limitation of S L R , less than 40° in the supine position, and still be able to reach to the mid tibiæ on forward flexion (of the 3 patients in this condition, box 40/4, 2 were no better for the operation) On the other hand, several possible explanations can be offered for the mechanism by which a patient can have S L R on both sides to 80° and yet on forward flexion be only able to reach the knee caps , 4 cases in this category showed three results no better for operation This inconsistency could be explained on psychoneurotic grounds on the theory that the patients' experience in the past has been that forward flexion will cause pain, whereas the S L R test is unknown to them and not associated with apprehension An organic explanation is also possible that in some patients in the standing position the prominence of the protruded disc might be increased by body weight and the root pressure made worse

In the cases which had a consistent S L R /flexion relation, but in which only slight limitation of either was present—i e boxes 90/4, 90/5, 80/4, and 80/5—a high incidence of poor results is perhaps not unexpected, because these boxes contain all the cases within the limits of " normal ' physical signs

SCOLIOSIS

Lateral deviation of the spine is a characteristic feature in the clinical examination of many cases of protruded disc, but an analysis of 82 cases, in which scoliosis was found in 39, did not indicate that any particular significance could be attached to scoliosis in rendering certain the subsequent discovery of a protruded disc at operation Of 43 cases without scoliosis, a protruded disc was not found at operation in 9—i e , 1 case in 4 8, or 20%—whereas of the remaining 39 cases with scoliosis a protruded disc was not found at operation in 5—i e , 1 case in 7 8, or 13%

Scoliosis was usually associated with limitation of S L R but it did not yield information as reliable as that obtained from S L R alone, because scoliosis seemed to vary from day to day according to the amount of rest the patient had taken before examination No case of " alternating " scoliosis was encountered in this series, but cases were often seen which had scoliosis one day and none at all the next Scoliosis appeared to subside on rest in bed much more quickly and more completely than limitation of S L R , even though one knew that the protrusion was still present and likely to cause further symptoms if activity was resumed , for this reason, taken by itself, scoliosis is not to be regarded as a reliable sign

SUMMARY

Two clinical types of sciatica are distinguished (1) those with severe limitation of straight leg raising (S L R) which almost always reveal a protruded intervertebral disc and respond well to surgery , and (2) those with slight limitation of S L R which often do not reveal a protruded disc and often show poor results after surgery

The mechanism of S L R test is examined The suggestion is made that where S L R evokes pain under 40° it indicates the *movement* of the root against a protruded disc , and that, when S L R is limited to only 70° or 80° the pain is caused by the start of *tension* on a root which is abnormally sensitive, from causes intrinsic to the root, and not necessarily accompanied by a demonstrable lesion of an intervertebral disc

I am indebted to Sir Harry Platt for reading my manuscript and for enabling me to concentrate on this type of case during the past four years in the orthopædic department of the Manchester Royal Infirmary

References at foot of next column

SEASONAL INCIDENCE OF CONGENITAL MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM*

THOMAS McKEOWN
M D Birm , D Phil Oxfd, Ph D McGill
PROFESSOR OF SOCIAL MEDICINE

R G RECORD
M D Birm , D Obst , D P H
LECTURER IN SOCIAL MEDICINE

UNIVERSITY OF BIRMINGHAM

ATTEMPTS to relate the incidence of congenital malformations to the season of birth or conception have so far been unconvincing The relevant literature on man scarcely merits detailed comment , it consists of conflicting reports in which numbers are small (Dittrich 1929) or in which insufficient account is taken of seasonal fluctuations in the total numbers of related births (Petersen 1934, Murphy 1936) There have been few observations on experimental animals Landauer (1943) noted seasonal variations in the proportion of malformed chick embryos , and Holt (1948) referred to a similar report by Wright on polydactylism in guineapigs

We have restricted our inquiry to malformations of the central nervous system, which have three advantages for investigations requiring statistical evidence (1) they usually lead to death of the fœtus in utero or shortly after birth and are therefore notified as stillbirths or deaths in the first year of life , (2) they can usually be recognised on external examination, even by persons with no specialised knowledge , and (3) they are common enough to give reasonable numbers—of all malformations notified as stillbirths or first-year deaths about 70% and 40% respectively involve the central nervous system

For investigation of seasonal incidence we have information from two sources (1) the annual reports of the Registrar General for Scotland, which give the causes of stillbirths since 1939 , and (2) observations on 930 consecutive children born in Birmingham in 1940–47 with malformations of the central nervous system

SEASON OF BIRTH

Stillbirths Only

Table I gives for Scotland in 1939–46 the monthly stillbirth rates attributable to fœtal defects The rates for hydrocephalus, spina bifida, and anencephalus are shown separately, and the remaining six subdivisions of fœtal defect included by the Registrar General have been grouped as " other " All but anencephalus show no consistent relationship between incidence and month of birth The group " other " is in any case unsuitable for investigation , and, since many babies with hydrocephalus and spina bifida survive birth, statistics restricted to stillbirths are also unsatisfactory We may therefore turn our attention to anencephalus, which as a cause of stillbirth more nearly satisfies the three criteria of accurate diagnosis, complete returns, and adequate numbers

---

* This research was assisted by a grant from the Birmingham University Students Social Services Fund

MR CHARNLEY REFERENCES

Begg, C A Falconer M A (1949) *Brit J Surg* 36 225
Falconer M A McGeorge M Begg, A C (1948) *J Neurol Neurosurg Psychiat* 11, 13
Inman, V T Saunders J B de C (1942) *Radiology* 38 669
O Connell J E A (1943) *Brit J Surg* 30 315
Poirier P Charpy A (1926) Traité d anatomie humaine Paris, vol I 69
Quain J (1915) Elements of Anatomy London vol IV, part 1
Steindler A (1935) Mechanics of Normal and Pathological Locomotion in Man London
Wiles, P (1935) *Proc R Soc Med* 28, 647

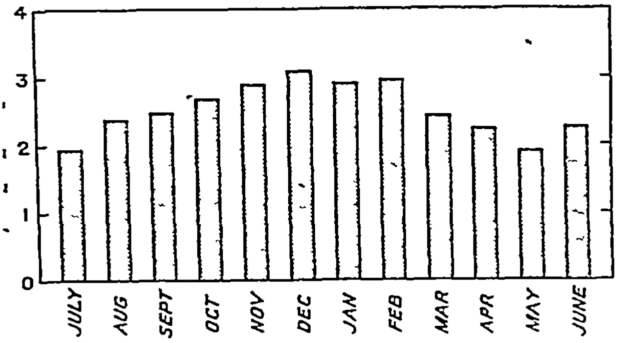


Fig 1—Monthly stillbirth rates attributed to anencephalus in Scotland in 1939–46

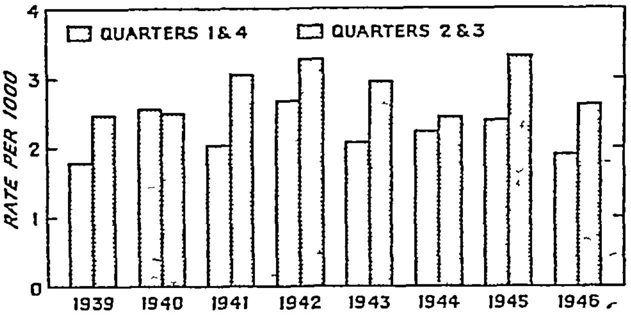


Fig 2—Half yearly stillbirth-rates attributed to anencephalus in Scotland in 1939–46

The stillbirth rate for anencephalus is lowest in May (1 91) and highest in December (3 09), between these two months the rate increases and decreases fairly regularly (see also fig 1) Subsequent comparisons are based on quarterly rates, and on half-yearly rates obtained by grouping the second with the third quarter, and the fourth with the first This choice of groups is arbitrary but was guided by the fact that our data for Birmingham were only available by quarters †

Table II gives quarterly and half yearly rates for 1939–46 (see also fig 2) For the whole eight-year period the rates for the half years are 2 20 (second and third quarters) and 2 83 (fourth and first quarters), the difference being 0 63 ± 0 12 With a single exception (1940) each year shows the same result, but because of the smaller numbers the errors of the differences are greater than for the whole period

Stillbirths and First year Deaths

The Birmingham material has already been fully discussed (Record and McKeown 1949) Briefly, data were recorded for 930 consecutive malformations of the central nervous system certified as the causes of stillbirths or of first-year deaths in the City of Birmingham in 1940–47 Our sources of information were (1) records of the City maternity and child welfare department (available for all 930 malformations), and (2) additional data elicited by field inquiry from 742 mothers who gave birth to 755 children with these malformations A control group of 876 mothers of children who were not malformed was obtained by selecting every two hundredth name from the registers of live births and stillbirths of the same years and interviews were completed with 742 of these mothers Table III shows the way in which the 930 malformations have been classified

Table IV gives for anencephalus, spina bifida, and hydrocephalus quarterly and half-yearly deaths (stillborn and live born) per 1000 births Since they include first-year deaths, the rates for spina bifida and hydrocephalus may be examined with more confidence than could be justified for the stillbirth rates shown in table I, they show no significant variation The half yearly rates for anencephalus again show a substantial difference (0 76 ± 0 24), and the examinations which follow of season of conception and of the effect of birth rank are therefore restricted to this malformation The quarterly rates for Scotland and Birmingham are illustrated in fig 3

SEASON OF CONCEPTION

The month of conception is not given for Scottish stillbirths, and, since many of the children with malformations are born before term, it would be wrong to assume that conception took place, on the average, nine months before birth In the Birmingham inquiry mothers were asked the duration of gestation in months, and the month in which the last menstrual period had occurred was then readily determined from the month of birth Because the same information was not avail-

TABLE I—MONTHLY STILLBIRTH-RATES (PER 1000 TOTAL BIRTHS) ATTRIBUTED TO FŒTAL DEFECTS (REGISTRAR-GENERAL FOR SCOTLAND 1939–46)

Malformation	Jan.	Feb	Mar	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Total	
													No	Rate
Hydrocephalus	1 43	1 44	1 37	1 22	1 34	1 36	1 35	1 51	1·40	1 41	1 48	1 33	1057	1 38
Spina bifida	0 56	0 48	0 48	0 55	0 53	0 47	0 28	0 40	0·43	0 40	0 43	0 53	352	0 46
Anencephalus	2 92	2 98	2 44	2 27	1 91	2 29	1 94	2 37	2 48	2·69	2 90	3 09	1916	2 51
Other	1 75	2 09	1 92	1 87	1 67	1 63	1 93	1 97	1 95	1 78	1 91	2 00	1427	1 87
All defects	6·65	6 99	6 20	5 91	5 45	5 76	5 50	6 26	6 26	6 28	6 72	6 95	4752	6 22
Total births	63 027	57 793	65 216	65 661	70 040	65 494	66 863	62 342	60 542	65 761	58 630	62 419	763 788	

TABLE II—QUARTERLY AND HALF-YEARLY STILLBIRTH-RATES (PER 1000 TOTAL BIRTHS) ATTRIBUTED TO ANENCEPHALUS (SCOTLAND 1939–46)

Quarter	1939		1940		1941		1942		1943		1944		1945		1946		Total	
	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year	Quarter	Half year
Second	1 99	1 78 (*a*)	2 19	2 55 (*a*)	1 85	2 05 (*a*)	2 59	2 68 (*a*)	2 32	2 08 (*a*)	2 08	2 23 (*a*)	2 53	2 40 (*a*)	1 72	1 91 (*a*)	2 15	2 20 (*a*)
Third	1 55		2 95		2 25		2 78		1 82		2 40		2 27		2·08		2 26	
Fourth	2 22	2 48 (*b*)	2 89	2 51 (*b*)	3 15	3 05 (*b*)	3 49	3 28 (*b*)	2 73	2 96 (*b*)	2 49	2 45 (*b*)	4·02	3 33 (*b*)	2 33	2 63 (*b*)	2 89	2 83 (*b*)
First	2 73		2 16		2 96		3 06		3 18		2 41		2 64		2 99		2 77	
*	0 70 ± 0 31		−0 04 ± 0 33		1·00 ± 0 33		0 60 ± 0 36		0 88 ± 0 32		0 22 ± 0 31		0 93 ± 0 36		0 72 ± 0 29		0 63 ± 0 12	

*Difference between half years (*b*) — (*a*)

---

† For 1940–47 Birmingham total births were known by quarters but not by months hence quarterly but not monthly rates could be calculated

TABLE III—CLASSIFICATION OF 930 CONSECUTIVE MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM RESULTING IN STILLBIRTHS OR INFANT DEATHS (BIRMINGHAM 1940–47)

Classified as	Type of malformation	No	
Anencephalus	Anencephalus alone	332	366
	Anencephalus and spina bifida	34	
Spina bifida *	Spina bifida alone	255	380
	Spina bifida and hydrocephalus	120	
	Spina bifida and encephalocele	4	
	Spina bifida, hydrocephalus, and encephalocele	1	
Hydrocephalus	Hydrocephalus alone		150
Other	Encephalocele alone	11	25
	Other central nervous malformations †	14	
Total			930

* Spina bifida includes spinal meningocele, meningomyelocele, and myelocele

† Include microcephaly (8) unspecified congenital cerebral defect (4), and occipital meningocele (2)

able for all related births, seasonal rates cannot be given for conception, and we rely on a comparison of quarterly and half yearly percentage distributions based on the month of the last menstrual periods preceding births of 363 anencephalics and preceding births of 741 controls free from deformities (table v) The proportion of conceptions in the half year from April to September is substantially greater for children with malformations than for controls Once again it must be emphasised that the choice of quarterly and half yearly figures is arbitrary For example, the differences revealed in table v would be slightly exaggerated by comparing the half years from March to August and from September to February We have preferred, however, to preserve the groups used in the earlier tables

EFFECT OF BIRTH RANK ON SEASONAL INCIDENCE

Before entertaining any alternative explanation for the observed seasonal fluctuation in the incidence of anencephalus, we should consider the effect of birth rank, since we have found that the risk of anencephalus and spina bifida is associated with parity and is highest for first births (Record and McKeown 1949) By expressing the figures in tables I, II, and IV as rates we have taken account of variation in the numbers of total births, we have not allowed for the possibility of seasonal changes in the proportion of births at different parities

The Scottish data provide no direct evidence on this question The number of marriages, however, is not constant from month to month, this may influence the relative proportions of first and later births at different seasons For 1939–46 the number and proportion of marriages in Scotland in each of the four quarters were as follows

First quarter	81,243	(22 26%)
Second quarter	90 406	(24 77%)
Third quarter	102 842	(28 17%)
Fourth quarter	90 554	(24 81%)
Total	365,045	

The mean interval between marriage and first birth is shorter than nine months, and the fact that the percentage of marriages is highest in the third quarter might have some bearing on the high incidence of anencephalus in the winter months

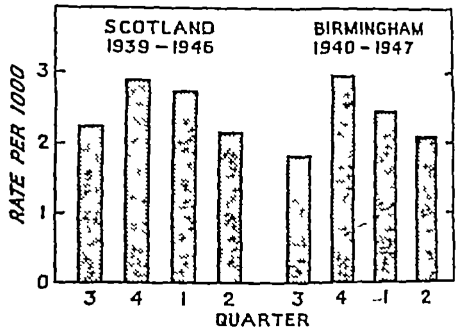


Fig 3—Quarterly stillbirth-rates attributed to anencephalus in Scotland 1939–46 and in Birmingham 1940–47

Birth rank was also unknown for all Birmingham births in 1940–47, but was recorded by field inquiry for 364 anencephalics and 742 controls free from deformities. This information is used in table VI to separate for first and later births the quarterly and half-yearly percentage distributions For first births the proportion of anencephalics born in the fourth and first quarters was substantially greater than the proportion of controls The same difference is also exhibited for later births, but is much less striking

On this evidence it seems unlikely that the seasonal variation in the incidence of anencephalus is explained by changes in the relative proportions of first and of later births One further point supports this conclusion the increased risk of malformation associated with first birth was noted for both spina bifida and anencephalus, yet the quarterly and half yearly rates for spina bifida (table IV) show no seasonal differences

DISCUSSION

There is an interesting difference in seasonal incidence between anencephalus and other malformations of the central nervous system This may provoke the suggestion that the incidence of anencephalus is related to the seasonal incidence of infectious diseases, but no history

TABLE IV—SEASONAL INCIDENCE OF MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM RESULTING IN STILLBIRTHS OR INFANT DEATHS (BIRMINGHAM 1940–47)

Quarter	Total births		Anencephalus			Spina bifida			Hydrocephalus			Other †	Total		
				Rates			Rates			Rates				Rates	
	Quarter	Half year	No *	Quarter	Half year	No *	Quarter	Half year	No *	Quarter	Half year	No *	No	Quarter	Half year
Second	41 036	80 053	85	2 07	1 94 (a)	99	2 41	2 45 (a)	30	0 95	1 04 (a)	7	230	5 61	5·61 (a)
Third	39 017		70	1 79		97	2 49		44	1 13		8	210	5 61	
Fourth	38 871	78 254	115	2 96	2 70 (b)	92	2 37	2 40 (b)	32	0 82	0 83 (b)	4	243	6 25	6·03 (b)
First	39 383		96	2 44		96	2 44		33	0 84		4	229	5 82	
Unknown			0			5			2			2	9		
Difference between half years (b) – (a)			+0 76 ±0 24			–0 05 ±0 25			–0 21 ±0 15				+0 42 ±0 38		

* Stillbirths and infant deaths are added together

† In view of the small numbers rates have not been calculated

ABLE V—MONTH OF LAST MENSTRUAL PERIOD PRECEDING BIRTH OF 363* ANENCEPHALICS AND 741† CONTROLS (BIRMINGHAM 1940–47)

Month of last menstrual period	Anencephalus No		Anencephalus Percentage Quarter (a)	Anencephalus Percentage Half year (b)	Controls No		Controls Percentage Quarter (c)	Controls Percentage Half year (d)	Difference (a)−(c)	Difference (b)−(d)
pril	42	111	30 58	58 13	56	177	23 89	50 20	+6 69 ±2 81	+7 93 ±3 20
May	34				61					
une	35				60					
uly	42	100	27 55		56	195	26 31		+1 24 ±2 84	
Aug	33				69					
ept	25				70					
Oct	23	70	19 28	41 87	68	183	24 70	49 80	−5 42 ±2 69	−7 93 ±3 20
Nov	17				52					
Dec	30				63					
an	19	82	22 59		53	186	25 10		−2 51 ±2 75	
eb	33				57					
March	30				76					
Total	363			100 0	741			100 0		

* For 3 of the 366 anencephalics the duration of gestation was unknown
† See text for discussion of controls in 1 case the duration of gestation was unknown

TABLE VI—SEASONAL INCIDENCE OF ANENCEPHALUS FOR FIRST AND LATER BIRTHS * (BIRMINGHAM 1940–47)

Quarter	Anencephalus No	Anencephalus Percentage (a)	Anencephalus Percentage (b)	Controls † No	Controls † Percentage (c)	Controls † Percentage (d)	Difference (a) − (c)	Difference (b) − (d)
				FIRST	BIRTHS			
Second	38	22 09	38 95	61	24 21	51 19	−2 12 ±4 18	−12 24 ±4 93
Third	29	16 86		68	26 98		−10 12 ±4 15	
Fourth	58	33 72	61 05	65	25 79	48 81	+7 93 ±4 49	+12 24 ±4 93
First	47	27 33		58	23 02		+4 31 ±4 27	
Total	172			252				
				LATER	BIRTHS			
Second	47	24 48	45 83	123	25 10	50 82	−0 62 ±3 68	−4 99 ±4 26
Third	41	21 35		126	25 71		−4 36 ±3 66	
Fourth	55	28 65	54 17	125	25 51	49 18	+3 14 ±3 75	+4 99 ±4 26
First	49	25 52		116	23 67		+1 85 +3 78	
Total	192			490				

* For 2 of the 366 anencephalics the birth rank was unknown
† See text for discussion of controls

TABLE VII—COMPARISON BETWEEN THREE MAIN GROUPS OF CENTRAL NERVOUS MALFORMATIONS (BIRMINGHAM 1940–47)

—	Anencephalus	Spina bifida	Hydrocephalus
Incidence			
Stillbirth rate per 1000 births	2 19	0 76	0 71
Infant mortality rate per 1000 live births	0 12	1 75	0 26
Mortality per 1000 total births	2 31	2 46	0 95
Secular trend in 1940–47	Downward	Downward	Constant
Seasonal incidence of			
Conception	Raised from April to September	—	—
Birth	Raised from October to March	No significant variation	No significant variation
Association of incidence with			
Birth rank	Well marked	Well marked	Slight
Maternal age	Slight	Slight	Well marked
Sex incidence (percentage of males) *	26 7	43 3	50 9
Fertility of mother			
Period of infertility preceding all pregnancies	Slightly shorter than average	Slightly shorter than average	Slightly shorter than average
Period of infertility preceding pregnancy resulting in malformation	Slightly shorter than average	Slightly shorter than average	Longer than average
Results of pregnancies not resulting in recognisable malformations			
Abortion rate per 1000 known conceptions †	117	107	98
Stillbirth rate per 1000 births ‡	52	22	89

* Data given by Registrar General for Scotland (1939–46)
† Abortion rate for mothers of controls = 75 per 1000 known conceptions
‡ Stillbirth rate for mothers of controls = 23 per 1000 births

of a specific fever during pregnancy was elicited from mothers who gave birth to the children with malformations

Data already published (Record and McKeown 1949, 1950a) suggest other biological differences between the three main types of central nervous malformations, and these are summarised in table VII We shall postpone detailed comment until we have presented evidence from a study of 69 pairs of twins exhibiting malformations of the central nervous system (Record and McKeown 1950c) Since attention may be focused on secular trends, we should emphasise that the decline in the annual incidence of anencephalus and spina bifida in Birmingham in 1940–47 may partly be explained by changes in the parity structure of the population of mothers

The evidence obtained in this inquiry suggests that the risk of a later malformation depends to some extent on the type of the first malformation, but numbers do not permit us to speak with confidence on this point, which is therefore omitted from table VII When all malformations of the central nervous system are grouped together, the incidence in later sibs is seen to be about six times greater than the expected rate (table VIII)

TABLE VIII—RISK OF MALFORMATION FOR SIBS BORN SUBSEQUENT TO A CHILD WITH CENTRAL NERVOUS MALFORMATION (BIRMINGHAM 1940–47)

No of sibs	No of malformations		Malformation rate	
	Observed	Expected*	Observed	Expected
470	13	2 12	2 77 ±0 76%	0 45%

*For details of the method used to obtain expected numbers of malformations see Record and McKeown (1950b)

SUMMARY

The seasonal incidence of births with malformations of the central nervous system has been examined in material from two sources (1) the annual reports of the Registrar General for Scotland for 1939–46, and (2) records of 930 consecutive malformations of the central nervous system certified as the causes of stillbirths or of first year deaths in Birmingham in 1940–47

The incidence of anencephalus is significantly higher in children born in the half year October–March than in those born in the half year April–September

There is no evidence of seasonal variation in the incidence of spina bifida or of hydrocephalus

It is unlikely that the seasonal variation in the incidence of anencephalus can be explained by changes in the relative proportions of first and of later births This possibility was explored because the risk of anencephalus is higher for first than for later births

The data for anencephalus, spina bifida, and hydrocephalus are tabulated to show the main differences

The incidence of central nervous malformations in sibs born after the birth of a child with such malformation is about six times the expected rate

We are grateful to Miss Catherine Wall and Miss Eileen Gibson for their careful assistance in the preparation of this paper, and to Dr Jean Mackintosh and members of the Birmingham Maternity and Child Welfare Department who made available to us the records of the department

REFERENCES

Dittrich R J (1929) *Hum Biol* 1, 278
Holt S B (1948) *Ann Eugen Camb* 14 144
Landauer, W (1943) *Anat Rec* 86 365
Murphy D P (1936) *Amer J Obstet Gynec* 31 106
Petersen W F (1934) *Ibid* 28, 70, 443
Record, R G McKeown T (1949) *Brit J soc Med* 3 183
— — (1950a) *Ibid* 4 26
— — (1950b) *Ibid* p 217
— — (1950c) *Ann Eugen, Camb* 15, 285
Registrar General for Scotland (1939 46) Annual reports

INFECTION OF THE DIGITAL PULP SPACE

T G LOWDEN
B M Oxfd, F R C S
SURGEON, SUNDERLAND ROYAL INFIRMARY

IN the last three years many articles on septic hands have been published Most of them have come from the teaching hospitals, have covered a comparatively short period, have illustrated some special investigation, and have been the personal series of individual surgeons or of a team All have included cases of pulp space infection. Some workers (Bolton et al 1947, Webster 1947, Bardin 1949) have classified such cases separately, whereas others (d'Abreu et al 1947) have included them with paronychia Some have illustrated the value of penicillin (Harrison et al 1949), others have shown it to be useless (Webster 1947) All have at least proved that in many centres the septic hand is at last receiving the attention and skill which its impact on industry demands. The *Lancet* (1947, 1949) and the *British Medical Journal* (1949) have emphasised the value of that attention.

But a larger picture should, I believe, be drawn Even with increasing interest and attention, most septic hands are not treated in teaching centres by experienced surgeons, with full teaching centre facilities, inpatient accommodation available, and a comparatively leisured operative ritual Nor is it likely, in the immediate future, that they will be I therefore report three years' work in a casualty department where septic hands are treated as an item (albeit an important one) in the daily round, where the majority are operated on by a junior casualty officer (changed at least once in six months), and where the time spent on each case must be kept at a minimum. It is not a personal series and it includes all cases with adequate records, whether easily classified or not

With advances in chemotherapy, streptococcal lymphangitis in this clinic has been thrust almost into insignificance A few days' penicillin therapy, sometimes with sulphonamides, has suppressed the "streak" which twenty years ago threatened such serious, sometimes fatal, results The incapacitating lesion which concerns us now is a focal necrosis of fibro fatty tissue, usually due to the staphylococcus Most of even these infections become localised quickly and are relieved by incision, and the patients are fit for work again within a fortnight These infections include the volar compartments (mid and proximal) of the fingers, the "web space" infection, the hair follicle on the dorsum, and most of the subcutaneous infections of the palm and the thenar and hypothenar eminences Penicillin therapy in the early stages may lead to resolution or to limitation of spread, but most patients do not attend early, and late chemotherapy does not then reduce the total period of incapacity

The condition causing the longest incapacity, and often permanent disability, is the pulp space infection With persistence of cavitation the period of incapacity for work averages twenty days, and osteitis of the phalanx, when present, increases the period to fifty one days Of the 438 cases of pulp space infection reviewed in this paper, 72 (16%) developed osteitis (14% in 1947, 22% in 1948, and 12% in 1949) In fact osteitis has been so common and important a mishap that an attempt has been made to consider every possible ætiological factor Here, however, I shall discuss only those factors on which, it is hoped, some conclusion can be reached

Kanavel, Iselin, Bunnell, and many others, in standard textbooks, all teach that osteitis is the result of ischæmia of the phalanx caused by the pressure of inflamed tissue on the nutrient vessels passing to the distal two thirds of the bone Bolton et al (1947) and Pilcher et al (1948) question this and regard osteitis as the result of a lymph tic convection, or an infective thrombosis of the vessels tandard textbooks also describe a standard incision for ll cases and casualty officers take up their appointment with this incision as their sole weapon against pulp pace infections All authorities agree that infection of one is established much earlier than X ray evidence ndicates, and it is a short step from there to the comfortable assumption that it is established before treatment t the clinic is begun I am not sure that this short step is a safe one

In 1947 and 1948 at this clinic the Kanavel "hockey-stick" incision (single or bilateral) was used in almost all cases There were 6 (barbarous, mutilating, and outspokenly discouraged) "alligators" The pulp space infection was regarded as an emergency, and an early incision was made in 94% of cases 3 cases (6 6%) treated thus within three days of onset developed osteitis Of the late cases 22% developed osteitis Separate analyses for cases treated with and without penicillin showed no significant difference, though penicillin had been given in what is generally regarded as adequate dosage (250,000–300,000 units in oil, b d)

CONSERVATIVE TREATMENT

More recently an attempt has been made to assess the application of the views of Pilcher et al (1948) and of Harrison et al (1949) to a clinic of this type Conservative treatment, as defined by them, consists essentially in complete rest to the whole hand, local applications of dry heat, and penicillin injections It is indicated in cases seen before there is evidence of pus In this clinic the conditions required are obtained in the minority of cases Only 18% of all pulp space infections treated are seen within four days of onset Moreover, the principle of conservative treatment had to be applied cautiously Early disasters almost certainly due to delay in treatment (either outside or inside the clinic) were vivid memories, and an over all reduction of a few days' attendance would be dearly bought if the incidence of osteitis increased even a little I have seen no serious harm done by Kanavel's incision in early cases, though I am prepared to accept that it may be unnecessary I have seen much harm result from delay

TABLE 1—CONSERVATIVE TREATMENT OF CASES SEEN THREE DAYS OR LESS FROM ONSET

—	1948	1949	Duration of symptoms (days)	Days under conservative treatment	Average incapacity (days)	
					1948	1949
Cases ending in resolution	7 (*21%*)	7 (*27%*)	1–3	2–3	6	7
Cases requiring later incision	4 (*15%*)	5 (*20%*)			10	9

Percentages indicate proportion of cases in which conservative treatment was applicable In 1949 8 cases with longer histories were also treated Their results are included in a later table

I have not found that all cases promptly become painless with absolute rest, elevation, splintage and penicillin, and I am reluctant to deny the relief of a well placed incision in cases which do not respond promptly My practice now is to treat early cases (usually three days or less from onset, but mild cases of longer duration) for twenty four hours conservatively and, if they respond, to continue until localisation or resolution takes place. No conservative treatment is continued for longer than twenty four hours if there is not prompt response, nor is it undertaken if it has been strictly but unsuccessfully attempted outside before the case comes to the clinic Harrison et al (1949) found that delay in operating on cases showing significant swelling (they measured the swelling) was unprofitable, and discontinued this part of their investigation I believe that their group showing over 20% swelling corresponds approximately to our clinical group of those who do not respond to twenty four hours' conservative treatment, and I am therefore in agreement with them If incision is necessary in successful conservative cases, a local incision is made, only the abscess cavity is decompressed, and healing is rapid Incision in those not responding within twenty-four hours is usually a single hockey stick incision, almost but not quite "through and through"

The results of this approach to early cases are set out in table I The percentages indicate the proportion of early cases in which conservative treatment was applicable The majority required immediate incision

OSTEITIS

Osteitis of the distal phalanx resulting from pulp space infection may be divided into three fairly well differentiated types

Type I—Not infrequently a terminal subonychia is associated with necrosis of the adjacent part of the nail bed and pulp This may lead to osteitis of the tip of the phalanx Unroofing the area (the roof includes some nail as well as cuticle) is followed by rapid resolution, and there is no tendency to spread It causes no permanent disability and does not greatly prolong incapacity It accounted for 30% of osteitis cases in the whole period To include these cases in a general analysis of osteitis gives optimistic figures

Type II—Pulp-space infection which does not localise promptly may lead to a superficial osteitis—not merely a periostitis, as often described—in the volar surface of the phalanx Judging by its radiological appearances, this may well be brought about by convection of infection from the pulp space by lymphatics The bone seldom if ever sequestrates, but the osteitis prolongs the incapacity period 21% occurred in the series

Type III—Massive necrosis with the formation of a sequestrum occurs in our series too frequently (45%) Not only does it take the longest time to heal but also it is the only type leaving a permanent bony deformity In some the mechanism is clear The patients come to their first attendance with a bag of pus ' Exploration reveals a thin crust of true skin and nail bed with the phalanx holding up the middle like a tent-pole Vessels are destroyed on all sides, and loss of most of the phalanx is almost inevitable

I further divide all cases of osteitis into those established when first seen at the clinic, and those developing during treatment My criteria for the former are (1) observation, at operation, of destruction (not merely exposure) of bone, (2) X ray evidence, or (3) spontaneous sequestration within the first ten days' treatment I regard all the rest as late cases, for them I blame myself, and in treating them I hope to improve In 1947 we had 4 cases sequestrating late in the course, in 1948 we had 9, and in 1949 we had none Types I and II of osteitis occurring late have shown no sign of improvement yet

CENTRAL SINUS

Iselin (quoting Klapp) states that a central sinus indicates osteitis of the phalanx I have not found this so Only 19 of 59 cases presenting with, or developing, a central sinus had osteitis, 6 had massive necrosis (type III)

I suspect that many cases presenting with a central sinus, developing one under conservative treatment, or having extensive destruction of soft tissues anywhere in the pulp, *develop* osteitis when hockey stick incisions are added to the existing destruction Hockey stick incisions are bound to cut across what few vessels remain between healthy tissue and the volar surface of the phalanx, and I now regard the appearance of superficial pus near the midline as an absolute contra indication to classical drainage In these cases the volar scar is inevitable and, as other workers have already said, the volar drainage is usually adequate Nearly all late cases are now treated by removal of cuticle, evacuation of pus and loose slough, and drainage of all infected spaces through the hiatus I do not excise adherent slough

I suspect, in fact, that any *unnecessary* incision increases the jeopardy in which the phalanx lies—e g , the removal of nail because of redness and swelling of the nail fold—but I have insufficient cases (fortunately) to support me

In this late type of case, which is so common a problem in our department, we consider the Kanavel incision definitely harmful Previous writers have, I think, failed to emphasise this Their condemnation applies to early cases, in which I think it may still have a place My figures were as follows

Condition and treatment	*No of cases*	*Late osteitis*
Central sinus and hockey stick or other incision	47	11 (23%)
Central sinus and local drainage	12	1 (9%)

CAVITATION

The discharge or release of pus, and the separation of slough, leave a cavity in the pulp space which fills with granulations and heals We always have one or two patients attending with infection apparently overcome, and a clean cavity *lined* by granulations but reluctant to fill with them, having overhanging walls and often an area of viable bone also covered with granulations in its base These cavities may persist for two or three weeks

Gibbs (1948) states that delay in the collapse of cavity walls is due to penicillin therapy, which sterilises but does not dispose of the abscess and encourages delay in surgical drainage In the present series by no means all the cases showing this delay had had penicillin The problem is usually mechanical The cavity is often held open by the healthy bone, rather than prevented from healing, as many suppose, by unhealthy bone in its base It is sometimes held open by the nail, and cutting the nail as far back as possible helps in these cases In most there is no answer, short of deliberately undertaking a plastic operation (a miniature " thoracoplasty "), which I hesitate to try Occasionally, however, when first operating on extensive cavitation, or when performing sequestrectomy, such a delay may be anticipated, and, instead of making an incision, a *wedge* of superficial tissue may be excised to allow later collapse to take place It must not be forgotten, however, that by far the greater number of cavities contract rapidly and heal quickly, and I use the word " occasionally " advisedly

OTHER CASES

This series has not included private cases or cases among the nurses Septic hands (except paronychia, which is no respecter of persons) are less common and show fewer complications in the professional than in the working classes Perhaps the hands of professional people are less exposed to trauma (though this is less so nowadays , domestic occupations are common to all) , but greater factors are the thinner horny layer, which allows small infections to swell, and earlier alarm at pain I have not seen a pulp space develop osteitis in this class of patient in three and a half years, and I have not seen a case take longer than sixteen days to heal

DELAY

The greatest single factor preventing further improvement in results is delay in attendance at the clinic Only 18% of these patients attended within three days of onset of symptoms Our records are by no means complete in this respect, but an attempt to find how much delay is due to the patient and how much to treatment, in general practice surgeries, works first aid posts, and in our own clinic, establishes that doctors or nurses are responsible for at least 16% of the delay Some propaganda has been made outside, and more will be, but only the 16% is likely to be affected by it I have noticed a high incidence of the " doctor (or nurse) made a nick " history in the osteitis cases, and blame the method mainly because it encourages further delay before seeking hospital treatment to see if the " nick " has done any good The increasing use of penicillin in practice has the same effect Undoubtedly many cases in general practice resolve successfully on penicillin therapy, but this may lead to longer delay in referring the ones that do not respond, and this is unfortunate

It would be absurd to demand the immediate attendance of every pricked finger end that has pain. Not only would the department be unable to deal with them, but it would lose the respect of the area Yet advice must be precise Any case suspected of early pulp space infection should have a kaolin poultice applied, the whole hand put at absolute rest, and one's favourite " big " dose of penicillin It must be seen again within twenty four hours If it is improved (and a reply from the patient to a question about pain is usually reliable evidence), treatment should be continued, and one should be guided by events If it is no better it should be referred to the clinic forthwith

DISCUSSION

These 438 cases (table II) are taken from a series of about 2700 septic hands seen in the clinic in three years The total number of non orthopædic non dermatological hand conditions seen in this time was a little over 13,000. The pulp space infection has been selected because it is the most important single condition demanding attention, but in such a condition, even with a comparatively large series, where incapacity for work can vary from three days to one hundred and thirty three days, it is almost impossible to draw any reliable conclusions from the figures alone The figures, though care has been taken, are only roughly reliable As an instance, the 3 cases of

TABLE II—AVERAGE INCAPACITIES

Year	Treatment and time after onset	With osteitis		Without osteitis		Total	
		No of cases	Days	No of cases	Days	No of cases	Days
1947	*Prompt incision*						
	Early	2	40	20	20	22	22
	Late	13	53	73	23	86	25
	Unknown	4	56	21	29	25	33
	Conservative ending in resolution						
	Early			1	5	1	5
	Total	19	52	115	23	134	27
1948	*Prompt incision*						
	Early	1	46	22	16	23	17
	Late	32	49	74	24	106	32
	Unknown	1	17	10	23	11	22
	Conservative ending in resolution						
	Early			7	6	7	6
	Conservative with later incision						
	Early			4	10	4	10
	Total	34	48	117	21	151	[illegible]
1949	*Prompt incision*						
	Early	3	43	11	15	14	21
	Late	15	60	93	20	108	25
	Unknown	1	55	10	17	11	20
	Conservative ending in resolution						
	Early			7	7	7	7
	Late			6	8	6	8
	Conservative with later incision						
	Early			5	9	5	9
	Late			2	13	2	13
	Total	19	57	134	17½	153	22

osteitis in 1949 "seen within three days" were almost ertainly late cases. 2 had a central sinus when first een at the clinic, and the 3rd discharged a sequestrum our days after the first attendance. Cases of obvious defaulters have been omitted, though these include many who get a quick response to conservative treatment and do not come back to tell us so. (We lose many splints and slings!) To include them would brighten the picture considerably but unjustifiably. Those who do not attend for their official discharge after a reasonable course of treatment have been counted up to their last attendance. One patient for whom, on his sixteenth day, a dry dressing had been prescribed for three days, next appeared on his thirty-seventh day. He was assessed on the full period, though he had probably been healed a fortnight earlier.

With these sources of error—and they must occur in all clinics if a long enough period is reviewed—I cannot understand how a few days' difference in the results can be attributed to any particular alteration in details of treatment—even including the use of penicillin. Moreover, the descent of a surgical team on a casualty department for a limited period of time, with the consequent renaissance of enthusiasm and supervision of dressing technique, will produce an improvement in results whatever the "object of the exercise."

I do think it significant, however, that there has been a progressive reduction in length of treatment for the non-osteitis cases (from 23 days in 1947 to 17½ in 1949), and that no case of massive necrosis has occurred in the course of treatment since 1948. I attribute these improvements to a tendency to treat each case on its merits instead of all cases by a routine. There is no doubt also that penicillin in the early cases, with an increased adoption of the conservative approach, has contributed; but we have tried intensive penicillin therapy for osteitis cases along the lines laid down by Bolton et al. (1947), with less successful results. All their cases were healed within eight weeks, but every few months we are defeated by an isolated case which jolts our averages far out of their prescribed orbits.

The conservative treatment has a definite rôle, but it applies only to a minority of the cases in this area, and is fraught with danger to the inexperienced. The vast majority of patients attend too late for it, and in these cases, particularly, I believe improvement can be obtained by the abandonment of classical incisions.

I am still concerned about delay (often up to three weeks) in seeking treatment, and I aim at eliminating all cases of osteitis which cannot be directly attributed to this delay. Until this delay is eliminated, there will always be a hard core of refractory cases.

SUMMARY

The results published by various teaching clinics on the treatment of septic hands excite the admiration of surgeons elsewhere, but must be regarded as a goal rather than a standard for the country as a whole.

The results obtained in three years in a provincial casualty department are reported, with particular reference to infection of the digital pulp space. The average delay in seeking treatment is greater than that reported by other workers, and osteitis is a formidable problem. Measures are recommended to reduce the incidence of osteitis of the phalanx resulting from pulp-space infection.

It is suspected that much osteitis is caused by too rigid adherence to classical incisions. The latter is nevertheless recommended for *early* pulp-space infections not responding within 24 hours to conservative treatment.

One acknowledgment makes all others relatively unimportant: it is to the casualty officers and to Sister E. L. Bolam and her staff, quite inadequate in numbers, miraculously adequate in effect. They give over 40,000 services a year in a room 24 ft. square. In the rush of it all they yet find the extra moments necessary to give a septic hand that skilful attention which makes all the difference.

REFERENCES

Barclay, G. A. (1949) *Brit. med. J.* i, 175.
Bolton, H., Catchpole, B. N., Jepson, R. P. (1947) *Lancet*, ii, 608.
British Medical Journal (1949) i, 187.
d'Abreu, F., Flood, C. M., Hewitt, H. B. (1947) *Brit. med. J.* ii, 603.
Gibbs, J. R. (1948) *Lancet*, i, 926.
Harrison, S. H., Topley, E., Lennard-Jones, J. (1949) *Ibid*, i, 425.
Lancet (1947) ii, 622.
— (1949) i, 443.
Pilcher, R. S., Dawson, R. L. G., Milstein, B. B., Riddell, A. G. (1948) *Lancet*, i, 777.
Webster, A. L. (1947) *Ibid*, ii, 610.

ÆTIOLOGY OF CHRONIC GASTRIC ULCER

OBSERVATIONS ON THE BLOOD-SUPPLY OF THE HUMAN GASTRIC MUCOSA WITH A NOTE ON THE ARTERIOVENOUS SHUNT

F. S. A. DORAN
M.D. Camb., F.R.C.S.

LATE SURGICAL CHIEF ASSISTANT, CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE, MANCHESTER, AND CLINICAL DEMONSTRATOR IN ANATOMY, MANCHESTER UNIVERSITY

WHEN, in the last century, Virchow advanced his vascular hypothesis to explain the formation of chronic peptic ulcers he regarded it as being of fundamental importance, although he did not consider it to be the only factor at work in this condition. In his view, the essential feature in the production of these ulcers was a vascular infarction of part of the mucosa, due to thrombosis, arteriosclerosis, spasm, or embolic occlusion, the resulting area of necrosis being then digested by the acid gastric juice. This idea derived some support from the demonstration by Reeves (1920) that in the lesser curvature of the stomach the submucous plexus was composed of very small arteries with few anastomoses, unlike those existing in the rest of the stomach, and that the branches of this plexus supplying the mucosa were arranged in a manner that predisposed to thrombosis. In recent years, however, the importance of this concept of the cause of peptic ulceration has steadily diminished. Now, overshadowed by the neurogenic and chemical hypotheses, it attracts little attention. This decline in the status of Virchow's hypothesis is attributable not only to the increasing mass of evidence in favour of the neurological and chemical factors but also because it is closely linked with the idea that the ulceration is preceded by infarction.

Much experimental work has been based upon this concept of an infarct, as McCann's (1929) review shows, but the results weakened rather than strengthened the idea. A remarkable assortment of substances, including mycotic emboli and tobacco, have been injected into the blood-vessels of the stomach in laboratory animals to produce infarction; but even when ulceration resulted all the lesions healed in about three weeks. Moreover no firm support was produced from the various ligation experiments, or from those which sought to bring about areas of mucosal ischæmia by means of vascular spasm (McCann 1929). More damaging still was the demonstration by Mann and Bollman (1932) that the chronic peptic ulcers which result experimentally from the diversion of the duodenal contents into the terminal ileum (Mann and Williamson 1923), and which are identical with those occurring clinically, begin not as an infarct but as a saucer-like depression on the surface of the mucosa. Nevertheless a modified vascular hypothesis, freed from the concept of infarction, could still be of value in helping to explain the situation of a chronic peptic ulcer, particularly in the stomach, and the recent work of Barclay and Bentley (1949) is a step in this direction.

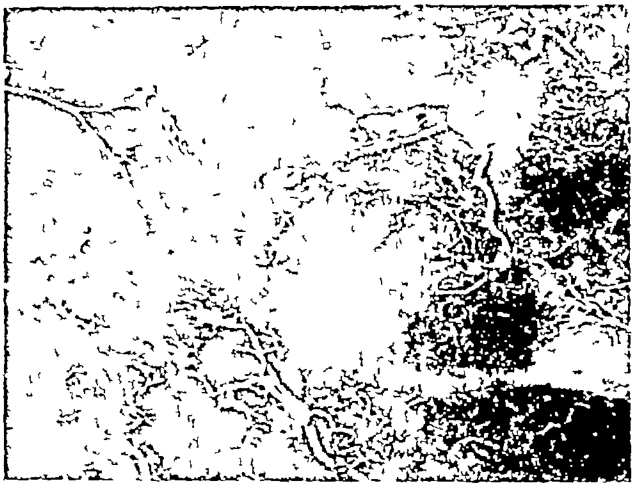


Fig 1—Microradiograph showing the vascular density of the mucosa on the lesser curvature of the stomach

METHOD

The technique employed in the present study was the radiological one devised by Barclay (1947) The contrast medium used to demonstrate the arterioles and finer vessels, with which this investigation is alone concerned, was a colloidal suspension of 10% silver iodide (Barclay and Bentley 1949) injected with a syringe through a hypodermic needle tied into a convenient artery, usually the right gastro epiploic, the small bore of such a needle being found to act as a convenient safeguard against the development of too great a pressure The mercury manometer and pressure chamber used in the preliminary trials were therefore discarded as being unnecessary

The material consisted of portions of sixteen stomachs removed during partial gastrectomy in the treatment of chronic peptic ulceration Ten were done under general and six under epidural anæsthesia In four instances the lesion was a gastric ulcer, the remainder being duodenal ulcers

The injection was always made as soon as possible after the specimen had been removed In most instances the delay was three or four hours, in two instances the injection was performed within an hour, and in a few the delay was twelve hours

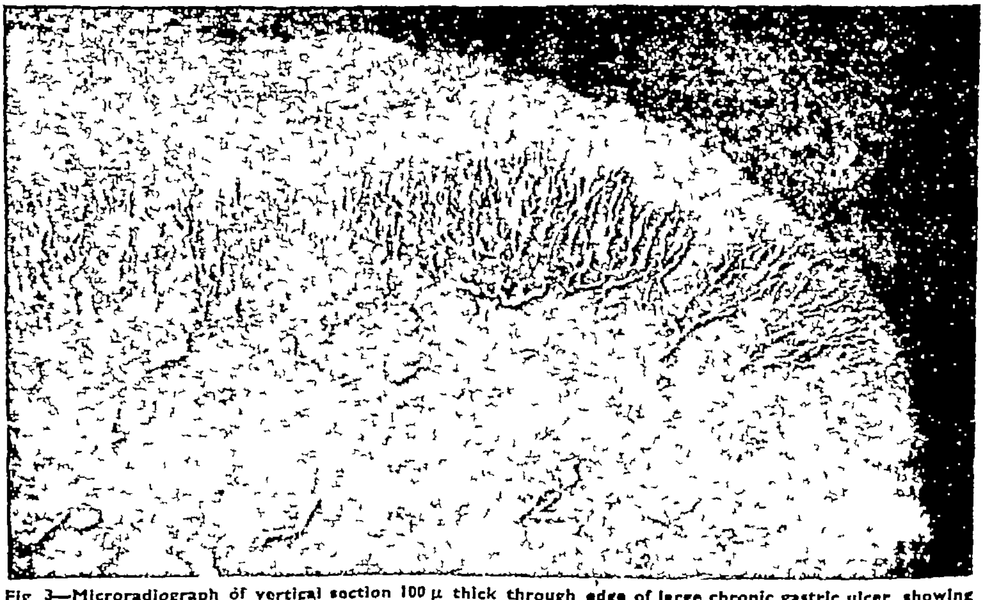


Fig 3—Microradiograph of vertical section 100 µ thick through edge of large chronic gastric ulcer showing vascular pattern

To obtain adequate filling of the arterial system i
found necessary not only to ligature all points of le
along both curvatures but also to oversew the cut e
the stomach from which leakage was otherwise ver
The injection was continued until a slight resi
was encountered Then the specimen was radiogr
to confirm that the filling of the arterial system
satisfactory The next step was to slit the sto
longitudinally down its anterior wall midway be
the greater and lesser curvatures The specimen
opened out flat and radiographed This second fil
then examined with a magnifying glass, suitable
were selected, the corresponding pieces were excisec
the stomach, and microradiographs were made of

Although in the preliminary trials an attempt was
to wash all the blood out of the vessels with saline so
before the contrast medium was injected, this ste
not taken in any of the twelve specimens radiogr
in this series

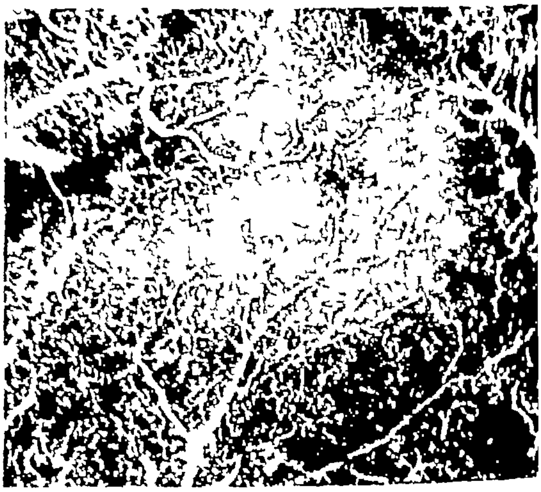


Fig 2—Microradiograph showing the vascular density of the mu
the greater curvature of the stomach

The four specimens used to demonstrate the a
venous shunt, however, were treated in a di
manner, the technique of intravascular hæmat
advocated by Grant (1930b) being used

MUCOSAL BLOOD-S

The vessels whic
ply the gastric m
arise from a rich p
in the submucosa
behaviour as they
towards the sube
lial layer of the m
and their relations
the gastric glands,
been known for a
dred years Th
proved by Arnold'
gram made in 184
reproduced by La
(1931) A good de
tion is given als
Jonnesco and
(1912) These acc
are confirmed by
present study

The vessels origi
from the subm
plexus penetrate
muscularis mucosa
immediately divide
two main branch

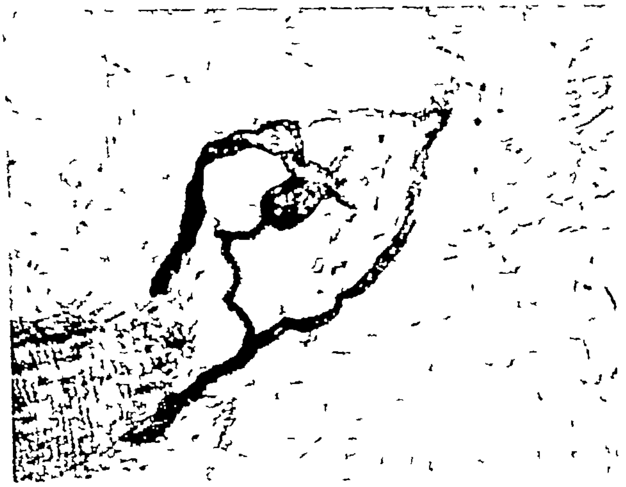


Fig 4—Histological section 100 μ thick showing an arteriovenous shunt with the characteristic sudden enlargement in lumen of the anastomotic channel (Intravascular hæmatoxylin.)

right angles to the parent stem. These branches run longitudinally parallel to the muscularis mucosa which they have just pierced. The extremities of these branches anastomose with those springing from the neighbouring vessels of the same kind. From this longitudinal arcade, lying just on the mucosal side of the muscularis mucosa numerous vertical arterioles arise which penetrate the thickness of the mucosa to reach the subepithelial layer. These arterioles are of three types: (1) long straight vessels varying somewhat in calibre and without branches, (2) vessels showing one primary division, and (3) a short vertical stem which breaks up into a moderately complex series of arborisations.

From the ends and sides of these arterioles numerous capillaries arise which anastomose with similar vessels from neighbouring arterioles to form a rich plexus throughout the whole thickness of the mucosa. The system of vascular anastomoses which exists in the substance of the mucosa, as opposed to the intercommunicating vascular arcade lying on the muscularis mucosa, is composed of capillaries. Anastomoses between the arterioles are not common, a point which has been emphasised by Latarjet (1931).

The relationship of these arterioles and capillaries to the tubular glands of the body of the stomach is a simple one. The arterioles run parallel to, and in between, the glands. Most of the glands, however, are supplied by two or three capillaries originating from the arterioles and placed in the reticular tissue connecting the glandular tubules together; these capillaries also run parallel to the glands and are interconnected by short channels at right angles to the long axis of the tubule.

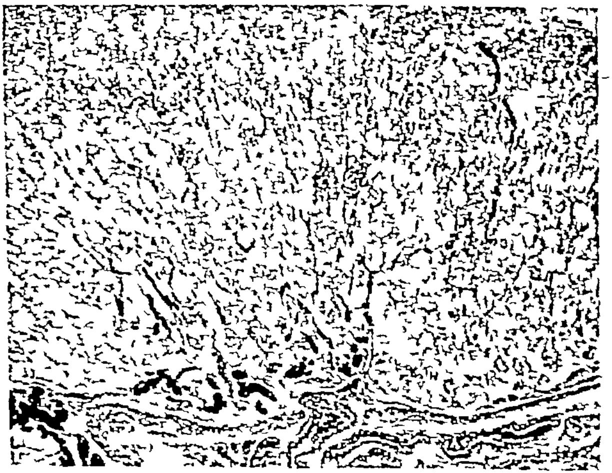


Fig 5—Histological section of injected specimen showing poorly filled area of mucosa (× 33)

DENSITY OF DISTRIBUTION OF BLOOD VESSELS SUPPLYING GASTRIC MUCOSA

Possibly the formation of a chronic gastric ulcer is due in part to the chemical action of the acid gastric juice upon a piece of mucosa whose total vascularity makes it unable to withstand that action. Several specimens in the present series support this idea that the lesser curvature has fewer vessels per square inch of mucosal surface than has the greater curvature. This point is illustrated by figs 1 and 2, which are microradiographs of mucosa from the lesser and greater curvatures respectively of a stomach resected because of a gastric ulcer. In each case the mucosa has been dissected off the muscular coats and spread out flat upon an X-ray plate so that the vascular density in the same plane as the mucosal surface is shown. This lower density is not evident in a section at right angles to the mucosal surface, even at the edge of a large gastric ulcer (fig 3). It is of particular interest to note that in cases of duodenal ulcer the vascular density of the lesser curvature tends to be the same as that of the greater.

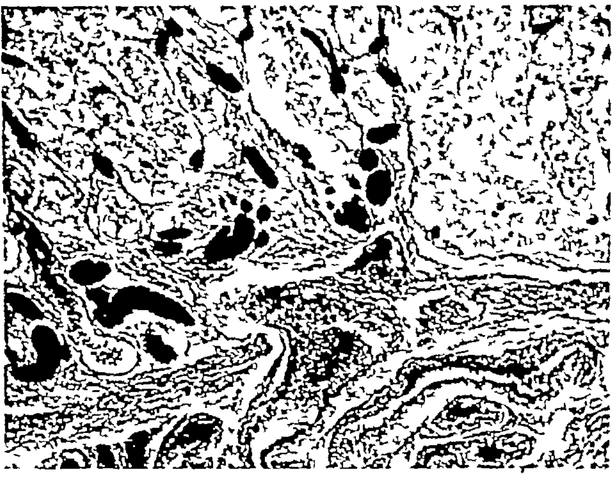


Fig 6—Histological section of the same area as in fig 5 under high power showing that the injection material has not been diverted into the vein passing through the muscularis mucosæ (× 78)

FACTORS INFLUENCING THE MUCOSAL BLOOD SUPPLY
RÔLE OF ARTERIOVENOUS SHUNT

If, in addition to a lower vascular density of the ulcer-bearing area of the stomach, this region is exposed to the operation of other factors tending to diminish its blood supply, the vascular hypothesis would be strengthened further.

It has been suggested (Barclay and Bentley 1949) that the blood supply of the gastric mucosa can be cut off completely by the opening of arteriovenous shunts in the submucosa, the ætiological significance of which has been noted by Alvarez (1949). He even suggested that the correct line of surgical treatment for chronic gastric ulceration would be the denervation of the shunts to prevent them from opening.

The existence of an arteriovenous shunt was doubted for many years, even after they had been demonstrated histologically, as the historical reviews (Clark 1938, Boyd 1939) of the subject show. Now they have been definitely established, and their presence proved in several organs and tissues. They were first seen in vivo by Grant (1930b). Recently, however, they have been found in the stomach wall (De Busscher 1948, Barlow 1950), and an example from the present series is shown in fig 4

If the future treatment of chronic gastric ulceration is to be based upon the denervation of the shunts, the properties of their nervous control must be studied The view has been expressed (Barclay and Bentley 1949) that they are supplied by the sympathetic and opened by its stimulation This opinion resulted from an inference based on the observation that, if the gastric resection was performed under general anæsthesia, leaving the sympathetic pathway open to convey the efferent side of a reflex initiated in the abdominal parietes, the injection material did not enter the mucosa Conversely, if the efferent sympathetic path was blocked by a spinal anæsthetic, the injection medium passed freely into the mucosal vessels This observation, however, has not been confirmed by the present study, in which no definite correlation was found between the mucosal filling and the type of anæsthetic, as follows

Case no	*Mucosal filling*	*Anæsthetic*
1	Good	General
2	Poor	Epidural
3	Quite good	Epidural
4	Good	General
5	Good	General
6	Poor	General
7	Quite good	General
8	Moderate	General
9	Moderate	Epidural
10	Poor	General
11	Quite good	General
12	Moderate	General

The best mucosal filling was obtained in a specimen removed under general anæsthesia Moreover, although the shunt mechanism is known to be under powerful sympathetic control, it has been demonstrated by Grant (1930b) that sympathetic stimulation closes the shunts Another difficulty in the way of attributing mucosal filling defects to the opening of an arteriovenous shunt is Grant's (1930b) observation that, when the shunt opens, a reflux flow of blood to the periphery occurs distal to the opening of the anastomotic channel This is of importance, especially as regards the stomach, because its veins, being part of the portal system, are devoid of valves Some of the injection material might therefore be expected to pass through the shunt and backward up the veins into the mucosa This retrograde pathway could not be detected in a microradiogram It is, in fact, very difficult to differentiate between arterioles and venules even histologically Grant's (1930a) study of the factors determining the calibre of the small peripheral branches of the arterial tree make it more probable that these mucosal filling defects are due to local vascular spasm caused by direct pressure and the action of a product of tissue damage To resect a stomach without bringing these factors, whose effect is independent of the nervous system, into play in various degrees is unlikely Furthermore, technical artefacts are certain to occur If the filling defects were due to a shunt, the diverted injection material should be found in the appropriate veins, but, as figs 5 and 6 show, this evidence was not found

Lastly, the number of shunts needed to achieve an extensive diversion of blood from the mucosa would be large, unless they were of great size The present series, however, suggests that they are neither numerous nor large, and De Busscher's (1948) findings agree with this opinion Nor is there any evidence that they are confined to, or are more numerous in, the ulcer bearing area

CONCLUSIONS

The lower vascular density of the lesser curvature of the stomach is probably one of the factors responsible for the observed localisation of chronic gastric ulceration to this region

The ætiological significance which has been predicted for the arteriovenous shunt mechanism is premature

SUMMARY

The importance attached to the vascular component in the ætiology of chronic gastric ulcer has steadily diminished in recent years, and the reasons for this decline are given

The vascular hypothesis may still be of value if it can be shown that the ulcer bearing area contains certain peculiarities

The material studied, the radiological method used, and the contrast medium injected into the arterial tree are described

Microradiographs show the lower vascular density of the mucosa from the lesser curvature

The technical difficulties inherent in the method are discussed, and it is shown that deductions based on radiological filling defects are open to criticism

An example of an arteriovenous shunt in the stomach wall is given Its ability to divert the injection material from the mucosa is discussed

I wish to thank Prof G A G Mitchell for his help in the preparation of this paper, Prof J Morley, Mr R L Newell, Mr R L Holt, Mr G O Jolly, and Mr W A B Nicholson for an ample supply of specimens, Mr F L Nowell and Mr K Pearson, for their highly skilled technical assistance and Mr H Gooding and Mr P Howarth for the photographs The expenses of the investigation were partially defrayed from a Medical Research Council departmental grant

BIBLIOGRAPHY

Alvarez W C (1948) *Gastroenterology* **10**, 413
— (1949) *Ibid* **12**, 323
Barclay, A E (1947) *Brit J Radiol* **20**, 394
— Bentley F H (1949) *Ibid* **22** 62
Barlow, T E (1950) Personal communication
Bollman J L Mann F C (1932) *Arch Surg* **24**, 126
Boyd J D (1939) *Lond Hosp Gaz* **42** clin suppl
Boyd W (1947) Surgical Pathology 6th ed, London
Brown M E (1937) *Anat Rec.* **69**, 287
Clark, E R (1938) *Physiol Rev* **18** 229
Cushing H (1932) *Surg Gynæc Obstet* **55** 1
Davis F (1949) in Gray's Anatomy 30th ed London
De Bakey M F (1937) *Arch Surg* **34**, 230
De Busscher G (1948) *Acta neerl morphol* **6** 87
Dragstedt, L R (1942) *Arch Surg* **44**, 438
— Harper P V jun, Tovee E B, Woodward E R (1947) *Ann Surg* **126** 687
Edwards H C (1948) Recent Advances in Surgery 3rd ed., London
Eusterman, G B Balfour, D C (1936) The Stomach and Duodenum London
Fauley G B, Ivy A C (1936) *Surg Gynæc Obstet* **63** 717
Flood C A Howes E L (1934) *Ibid*, **58** 136
Grant R T (1930a) *Heart*, **15**, 257
— (1930b) *Ibid*, p 281
— Bland F F (1930) *Ibid* p 385
Hadfield G, Garrod L P (1947) Recent Advances in Pathology 5th ed London
Harkins H N Hooker D H (1947) *Surgery*, **22** 239
Heslop T S (1938) *Brit J Surg* **25** 884
Ivy A C Fauley G B (1931) *Amer J Surg* **11** 531
Jonnesco T Soulié A. (1912) in Poirier P Charpy, A, Traité d anatomie humaine Paris vol IV, part 1
Kapsinow R (1926) *Ann Surg* **83**, 614
Lamarque P (1937) *Brit J Radiol* **11** 425
Lannin B G (1945) *Surgery*, **17** 712
Latarjet A (1931) in Testut Traité d anatomie humaine 8th ed, Paris vol III
Lawson H Ambrose A M (1942) *Amer J Physiol* **135** 650
Lindau A Wulff H (1931) *Surg Gynæc Obstet* **53** 621
Mann F C Williamson C S (1923) *Ann Surg* **77**, 409
— Bollman J L (1932) *J Amer med Ass* **99**, 1576
McCann J C (1929) *Arch Surg* **19** 600
McCrea E d'A (1925–26) *Brit J Surg* **13**, 621
McMaster P E (1933) *Arch Surg* **28** 825
Modell W (1933) *Anat Rec* **55** 251
Morley, J (1946) *Edinb med J* **53** 273
Morton C B (1927) *Ann Surg* **85** 207
— (1928) *Ibid* **87**, 401
Mottershead S (1946) in Jones F W, Buchanan's Manual of Anatomy 7th ed London
Orndorff J R Fauley G B, Ivy, A C (1936) *Amer J digest Dis* **3** 26
Reeves T B (1920) *Surg Gynæc Obstet* **30** 374
Roth J A Ivy A C (1945) *Surgery* **17** 644
Schiffrin M J Ivy, A C (1942) *Arch Surg* **44** 399
Symington J (1914) in Quain's Elements of Anatomy 11th ed London vol II part 2
Woolf, A L (1950) *Brit J*, *Radiol* **23**, 8

THE ELECTROPHORETIC SERUM-PROTEIN PATTERN IN MALIGNANT MALNUTRITION

C. G. ANDERSON
Ph.D. Birm., Dip. Bact., A.R.I.C.
OF THE SERUM DEPARTMENT, SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH, JOHANNESBURG

The late A. ALTMANN
M.D. Berlin, M.D. Witwatersrand, L.R.C.P.E., D.T.M. & H.
OF THE DEPARTMENT OF PÆDIATRICS, BARAGWANATH NON-EUROPEAN HOSPITAL, JOHANNESBURG

WE report here the results of an electrophoretic examination of the sera of patients suffering from malignant malnutrition (kwashiorkor, infantile pellagra), taken at various stages from the beginning to the end of treatment and at various times after recovery. The work is part of a larger study of the clinical, histological, and biochemical aspects of malignant malnutrition which will be reported in due course. The anæmia involved has already been described by Altmann and Murray (1948).

METHODS

The blood samples were drawn from the fontanelle and allowed to clot. The serum was separated, and the specific gravity determined by the copper sulphate method. The protein content was calculated from the specific gravity, using the formula $P = 364\,(G_p - 1\cdot0060)$ where P is the amount of protein in grammes per 100 ml. of serum and G_p is the specific gravity, given by Hoch and Marrack (1945).

Serum samples were appropriately diluted in phosphate buffer, pH 7·5 and $\mu = 0\cdot1$, and dialysed against the same buffer solution until equilibrium (as determined by change in refractive index) was reached; 24–48 hours in the refrigerator at about 4°C was usually adequate. The electrophoresis runs were made in the Tiselius apparatus at 1°C with 10 mA at a potential gradient of approximately 4·5 V per cm. The photographic records were enlarged five times by projection, the curves traced, and the areas corresponding to the different components measured with a planimeter and the proportion of each component in the whole serum was calculated. The averages of values determined for both ascending and descending columns at two or three time intervals were used. The absolute amount of each component was calculated from the proportion and the known total protein content of the serum.

ELECTROPHORETIC COMPONENTS OF SERA FROM CASES OF MALIGNANT MALNUTRITION AND NUTRITIONAL ŒDEMA

Case	Date	Specific gravity (sp gr)	Total protein from sp gr (g /100 ml.)	Proportion of total (%)				Absolute amount of components (g /100 ml.)					Ratio		Notes
				Albumin	Globulins			Albumin	Globulins				Alb glob	Alb γ-glob	
					α	β	γ		α	β	γ	Total			
Malignant Malnutrition															
1	Sept 17, 48	1·020	5·1	50·9	13·0	14·2	22·0	2·60	0·66	0·72	1·12	2·50	1·04	2·32	Discharge specimens
2	Apr 19, 49	1·0265	7·5	53·3	14·6	11·5	20·5	3·99	1·09	0·86	1·54	3·49	1·14	2·59	
3	Dec 15, 48	1·0165	3·8	40·9	15·8	8·6	34·7	1·56	0·33	0·60	1·32	2·25	0·69	1·18	Fatal
	1949														
4	Jan. 26	1·025	6·9	50·8	9·7	14·4	25·3	3·50	0·67	1·00	1·75	3·40	1·03	2·00	Discharge specimens
5	Feb 2	1·026	7·3	45·1	10·1	16·8	28·2	3·30	0·74	1·23	2·06	4·03	0·82	1·60	
6	Apr 25	1·026	7·3	51·3	14·0	14·3	20·3	3·74	1·02	1·05	1·48	3·55	1·06	2·50	
7	Apr 25	1·0315	9·3	34·5	12·5	12·9	40·1	3·21	1·16	1·20	3·73	6·09	0·53	0·86	
8	July 14	1·016	3·6	32·5	16·5	22·0	29·1	1·17	0·59	0·79	1·05	2·43	0·48	1·11	Fatal
9	Jan. 13	—	8·0*	37·2	10·3	13·9	38·2	2·98	0·83	1·12	3·07	5·02	0·59	0·97	—
	July 1	1·027	7·6	46·7	11·1	13·8	28·4	3·55	0·85	1·05	2·06	4·05	0·88	1·72	Follow up
„	Nov 17	1·027	7·6	53·8	9·1	12·6	24·4	4·09	0·69	0·97	1·86	3·51	1·16	2·20	
10	Apr 13	1·016	3·6	29·6	12·5	20·8	35·0	1·07	0·45	0·75	1·26	2·46	0·43	0·85	Serial specimens
	Apr 28	1·020	5·1	39·8	8·3	12·7	39·2	2·03	0·42	0·65	2·00	3·07	0·66	1·01	
	May 9	1·0255	7·1	43·1	11·6	15·5	29·8	3·06	0·82	1·10	2·12	4·04	0·76	1·44	
11	May 3	1·020	5·1	42·9	12·9	15·4	28·9	2·19	0·66	0·79	1·47	2·92	0·75	1·49	
	May 20	1·0275	7·8	47·4	10·5	13·9	28·2	3·69	0·82	1·08	2·20	4·10	0·90	1·68	
12	June 14	1·017	4·0	38·6	17·8	17·5	26·1	1·55	0·71	0·70	1·05	2·45	0·63	1·48	
	June 24	1·020	5·1	36·8	10·9	18·2	34·1	1·88	0·55	0·93	1·74	3·22	0·58	1·08	
	July 20	1·027	7·6	45·9	13·9	16·0	28·9	3·49	1·06	1·22	1·82	4·11	0·85	1·92	
13	June 25	1·017	4·0	44·0	14·0	15·3	26·3	1·76	0·56	0·61	1·05	2·24	0·79	1·67	
„	July 8	1·023	6·2	43·2	9·3	17·0	30·2	2·68	0·58	1·06	1·82	3·52	0·76	1·47	
„	July 26	1·026	7·3	59·0	5·9	11·4	23·7	4·31	0·43	0·83	1·73	2·99	1·44	2·49	
Nutritional Œdema															
14	Feb 28	1·0285	8·2	51·4	10·5	16·6	21·5	4·21	0·86	1·36	1·76	3·98	1·06	2·39	Discharge specimens
15	Apr 12	1·024	6·6	32·7	9·8	19·1	38·4	2·16	0·65	1·26	2·53	4·44	0·49	0·85	
16	Mar 9	1·025	6·9	49·6	10·6	17·6	22·2	3·43	0·73	1·22	1·53	3·48	0·99	2·24	
17	Mar 23	1·0285	8·2	46·8	8·0	19·4	25·8	3·83	0·65	1·59	2·12	4·37	0·88	1·81	
18	Mar 11	1·025	6·9	56·4	4·1	14·9	24·7	3·89	0·28	1·03	1·71	3·02	1·28	2·28	
19	Apr 4	1·027	7·6	45·4	12·9	15·8	26·2	3·45	0·98	1·20	1·99	4·17	0·83	1·73	
20	Apr 7	1·018	4·4	54·6	13·0	10·3	22·1	2·41	0·57	0·45	0·97	1·99	1·21	2·48	Serial specimens
	Apr 20	1·023	6·2	44·9	18·7	14·0	22·4	2·78	1·16	0·87	1·39	3·42	0·81	2·01	
21	Apr 9	1·0165	3·8	46·7	21·7	9·1	22·5	1·78	0·82	0·35	0·86	2·02	0·88	2·07	
	Apr 21	1·022	5·8	39·6	13·0	29·0	18·4	2·30	0·75	1·68	1·07	3·50	0·66	2·15	
	Apr 28	1·026	7·3	50·4	9·7	14·7	25·2	3·68	0·71	1·07	1·84	3·62	1·02	2·00	
22	July 15	1·020	5·1	46·3	17·5	13·4	22·9	2·36	0·89	0·68	1·17	2·74	0·86	2·01	
„	July 30	1·028	8·0	45·3	7·5	17·1	30·1	3·62	0·60	1·37	2·41	4·38	0·83	1·50	
Normal	Mean		7·2	63·1	11·4	11·7	13·2	4·55	0·82	0·84	0·95	2·65	1·72	4·80	
	Range		6·5–8·0	59–72	6·2–15·0	11·3–17·1	8·8–16·0	4·0–5·7	0·4–1·2	0·7–1·4	0·6–1·3	1·7–3·9	—	—	—

* Nitrogen estimated by Kjeldahl method

RESULTS

The values obtained for sera from 13 cases of malignant malnutrition and from 9 cases of nutritional œdema are given in the table The "normal" values quoted are the mean of many such values given in the literature Lubschez (1948) found that the mean values given by electrophoresis of sera from normal children were about the same as those for adults, although the range was considerably greater

DISCUSSION

It can be seen that the serum protein value is low at the time of admission to hospital, as previously reported by Trowell (1944), Gillman and Gillman (1945), and Altmann (1948), and rises during the course of treatment on a diet with a high protein intake A normal total serum protein content is reached in three to four weeks, in which time clinical recovery also occurs The outstanding features of the protein pattern in malignant malnutrition are the low absolute and relative amounts of albumin compared with normal values, and the high absolute and relative amounts of γ globulin Even on admission to hospital when the total protein is at its lowest level the amount of γ globulin is almost always higher than normal As the normal serum protein level is restored both albumin and globulin rise Usually the amount of albumin in the serum at the time of clinical cure is somewhat below the normal average but the amount of γ globulin is almost invariably higher That this abnormal state may persist for some time is shown by case 9 On discharge as clinically cured this patient had 2 98 g of albumin, and 3 07 g of γ globulin, per 100 ml of serum On readmission to hospital six months later for follow up study, the values were 3 74 g and 2 27 g Twelve months after cure the albumin content was 4 09 g, and the γ globulin content 1 86 g, per 100 ml This patient's serum also showed, on all three occasions, the positive thymol turbidity and flocculation reaction often found in cases of malignant malnutrition during the recovery phase,[1] which is normally associated with an increase in the γ globulin content of the serum (Maclagan 1948, Wunderly and Wuhrmann 1947) He was clinically well and had been on a satisfactory diet in an institution during the twelve months since his original discharge from hospital The explanation and significance of these observations are not yet clear, particularly in relation to possible liver damage

The α globulin content of the sera is usually not far from normal and the same applies to β globulin, although here the tendency is for the value to be on the high side of the normal average

These findings are very much like those reported by Martin (1949) for sera from patients with progressive uncomplicated cirrhosis of the liver Here, too, the serum albumin is low and the γ globulin content very high, and accompanied by a strong thymol turbidity reaction In clinically cured cases of malignant malnutrition, however, liver biopsy specimens do not show signs of early cirrhosis

It will be seen from the table that there is no essential difference between the values found for the sera of patients suffering from nutritional œdema and those with the additional signs of the syndrome of malignant malnutrition This similarity affords support for the opinion of Altmann (1948) and of Waterlow (1948) that malignant malnutrition is primarily a result of protein deficiency and that the manifestations of vitamin deficiency are only incidental Further evidence of this is given by Hottinger et al (1948), who state that concentration camp inmates suffering from "hunger disease" had low serum albumin content, approximately normal α and β globulin contents, and high γ globulin content, the values being very similar to those found in the present work These workers go so far as to define "hunger disease" as "hypoalbuminæmia with dysglobulinæmia" The sera from their patients gave a positive Takata reaction, analogous to the thymol tests in this series

SUMMARY

The electrophoretic examination of sera, taken at various stages during treatment, from Bantu children suffering from malignant malnutrition or from nutritional œdema has shown that, although on admission to hospital the total serum protein content is much below normal values, the amount of γ globulin is both absolutely and relatively normal or higher than normal The albumin content is much reduced whilst the values for α and β globulins are about normal After clinical cure the albumin content of the serum is usually still below normal and the γ globulin considerably above normal The abnormal γ globulin content may persist for at least a year with the patient in good condition and on an adequate diet These findings are similar to those found in adults with "hunger disease" and therefore link malignant malnutrition to the hunger œdema of adults

REFERENCES

Altmann A (1948) *Clin Proc* 7 32
— Murray J F (1948) *S Afr J med Sci* 13 91
Gillman T, Gillman, J (1945) *J Amer med Ass* 129 12
Hoch H, Marrack J R (1945) *Brit med J* ii 151, 876
Hottinger A, Gsell O Uehlinger E Salzmann C Labhart A (1948) Hungerkrankheit, Hungerödem Hungertuberkulose. Basle p 130
Lubschez R (1948) *Pediatrics* 2 570
Maclagan N F (1948) *Brit med J* ii, 892
Martin, N H (1949) *Brit J exp Path* 30 231
Trowell H C (1944) *Clin Proc* 3, 381
Waterlow J C (1948) *Spec Rep Ser med Res Coun Lond* no 63
Wunderly, C, Wuhrmann, F (1947) *Brit J exp Path* 28, 86

UNIOVULAR TWINS SHOWING GROWTH DISPARITY DUE TO RENAL DWARFISM

M D MILNE
M B, B Sc Manc, M R C P
CHIEF ASSISTANT, DEPARTMENT OF MEDICINE,
UNIVERSITY OF MANCHESTER

UNIOVULAR or so called "identical" twins are generally very similar both in appearance and size In a biometric study of more than five hundred members of twin pairs Stocks (1930) defined the differences in size to be expected in pairs of uniovular twins, he considered that "a difference in height exceeding the standard deviation of height appropriate to the age of the pair almost certainly excludes monozygotism"

Greater disparity in size is, however, occasionally encountered as a result of chronic disease or deformity in one of a monozygotic pair, but very few such cases are recorded, presumably because disease greatly influencing growth is likely to affect both twins simultaneously The case described here is of interest both because of the considerable disparity in growth and as an example of renal dwarfism of developmental ætiology

CASE RECORD

A boy, aged 13, was referred to the Manchester Royal Infirmary because of polydipsia, polyuria nocturnal enuresis, and dwarfism He was one of a family of five, three boys and two girls, and had a twin brother The parents and siblings all appeared healthy The patient had been considerably smaller than his twin brother at birth, their respective weights being 3 lb and 4½ lb This disparity had persisted throughout childhood, and the patient had always been somewhat retarded in development He had always drunk an excessive quantity of fluid as long as the parents could remember, and had been late in gaining diurnal control of micturition Nocturnal control he had never attained, and he invariably wet the bed at night There seemed to be relatively little intellectual impairment, although he was poor at reading and writing, partly because of intermittent and often half time school attendance

---

[1] A paper describing the correlation of liver function and thymol tests is in preparation (Altmann and Bersohn)

On examination he was clearly dwarfed, his height being 50 in, the mean height for his age being $59^{1}/_{2}$ in (standard deviation 3 1 in.) His weight was correspondingly reduced to 50 lb, the mean weight for his age being 89 lb (S D $16^{1}/_{2}$ lb) There was however, no evidence of rickets or other deformity, and the dwarfing was perfectly symmetrical The heart and lungs were normal, and the blood pressure was within normal limits being 120/70 mm Hg No abnormal masses were palpable in the abdomen, there was no evidence of renal enlargement or vesical distension The urine was pale sp gr 1 010, and contained a moderate amount of albumin The average volume of urine voided in twenty four hours was about 1500 ml there was complete isosthenuria sp gr remaining at 1.010 despite estriction of fluids The average protein content of the urine Esbach) was 1 5 g per litre There was considerable retention of nitrogen. the blood urea level being 114 mg per 100 ml, the urea-clearance was only 13% of the average normal. The urine contained no pus cells or erythrocytes, but a few granular casts were present it was sterile on culture The serum-calcium was 9 mg the inorganic phosphorus 5 mg, the alkaline phosphatase 27 King Armstrong units and the alkali reserve 51 c cm CO_2 per 100 ml Radiography of the epiphyses showed no evidence of rachitic change, and radiography of the abdomen was normal there being no sign of urinary calculus or other abnormal opacity

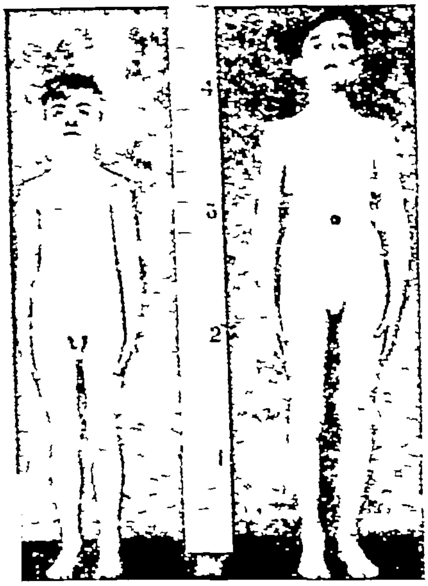


Fig 1—Patient (left) and uniovular twin (right) (Scale in ft.)

DIAGNOSIS

The diagnosis was clearly renal dwarfism due to chronic renal insufficiency without secondary hypertension This may cause the well known triad of dwarfism, renal rickets, and infantilism but in this case there was no evidence of rickets and the boy was too young to decide whether there would be secondary infantilism

This type of chronic renal failure in childhood is usually due either to chronic atrophic pyelonephritis or to chronic urinary obstruction, which may result from a congenital valve in the posterior urethra (Ellis and Evans 1933), rarer causes are latent glomerulonephritis and bilateral polycystic disease of the kidneys (Rule and Grollman 1944) On clinical grounds it was considered that chronic atrophic pyelonephritis was the most likely cause of the renal failure in this patient despite the lack of evidence of urinary infection Such cases of chronic pyelonephritis are often superimposed on some congenital anomaly of the upper urinary tract (Erb and Summerfeldt 1941) Unfortunately this cannot be demonstrated by intravenous pyelography in patients with gross reduction of renal function, because the kidneys do not concentrate the contrast medium sufficiently to give a satisfactory shadow Retrograde pyelography can be used, but it is a comparatively major procedure for an investigation which can only be regarded as of academic interest and can occasionally lead to a serious or even fatal urinary infection in such cases It was therefore regarded as unjustifiable in the present case, especially since relevant information was available from examination of the normal twin

COMPARISON OF THE TWINS

The patient's twin appeared to be a normal boy of 13 although somewhat smaller than the average His height was $56^{1}/_{4}$ in and weight 67 lb He had no polydipsia, polyuria, or nocturnal enuresis, his urine did not contain albumin, and the specific gravity of a morning specimen was 1 026 The blood urea was normal, being 26 mg per 100 ml

Despite the obvious difference in size it was considered that the twins were uniovular They were compared by the method described by Newman (1940) and, except for their unequal growth were found to be strikingly similar (figs 1 and 2) Their hair was of the same colour, texture and distribution, their eyebrows and eyelashes were almost exactly alike, their eyes were of the same colour, both twins had a congenital partial ptosis of the left eyelid, their ears were of the same shape, their teeth were much alike (but the patient's were more crowded because of his smaller jaws), their palm and fingerprints showed considerable points of similarity, the two boys had a livedo reticularis of the legs of identical distribution, and the blood groups of both were O, R 2, MN, S negative, P positive, Lewis negative, and Lutheran negative

There therefore seems to be no reasonable doubt that the twins were uniovular It was consequently a reasonable assumption that if the patient had a congenital renal lesion it would also be present in his twin brother It was readily demonstrated in the twin brother by intravenous pyelography, a method inapplicable in the patient because of his renal insufficiency Dr E D Gray reported on the intravenous pyelogram (fig 3) as follows

> Neither kidney is enlarged and both appear to be excreting diodone normally Both kidneys have a pelvis which is largely extrarenal The left renal pelvis is considerably larger than the right The minor calices are smaller and more numerous than average, and except in the upper poles, arise directly from the pelvis It is difficult to define the pelvi ureteric junction on either side The somewhat unusual appearance of the upper urinary tract can be classed as a variant of the normal

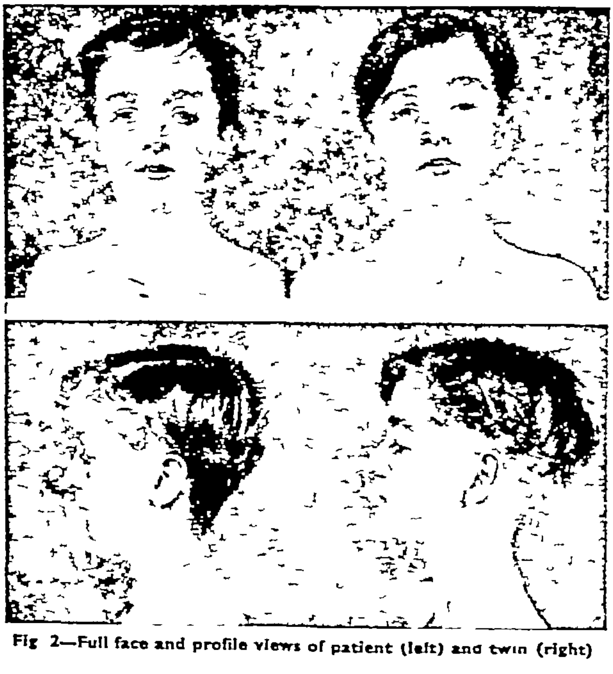


Fig 2—Full face and profile views of patient (left) and twin (right)

It is postulated that a chronic pyelonephritis has been superimposed on similar renal pelves in the patient, but no explanation is offered as to why this has happened in the patient and not in his twin

DISCUSSION

Few examples of such unequal growth in uniovular twins are recorded Siemens (1927) described female uniovular twins very different in height owing to scoliosis in one of them A similar case of kyphoscoliosis in one of male uniovular twins is described by Lehmann (1937) Lewis (1936) described a case of much disparity due to gigantism and acromegaly in one of uniovular twins An interesting example in Japanese male uniovular twins is recorded by Komai and Fukuoka (1934)

One of the twins developed polydipsia, polyuria, and dwarfism at the age of 6 years This was diagnosed as due to diabetes insipidus, but unfortunately the medical details are inadequately described The only evidence given in favour of the diagnosis is a disparity in size between their sellæ turcicæ, but as the smaller sella turcica was in the smaller twin this evidence can hardly be regarded as relevant A diagnosis of diabetes insipidus would not now be accepted without either evidence of satisfactory response to treatment with pituitary extract or a negative response to the intravenous hypertonic saline test described by Hickey and Hare (1944) Neither of these criteria was applied in this case Nor does diabetes insipidus in childhood lead to dwarfing unless it is secondary to cerebral tumour, xanthomatosis, or diencephalic encephalitis (Warkany and Mitchell 1939) No evidence was given of any of these conditions in the affected twin No tests of renal function seem to have been made, and in fact there is nothing in the published description against a hypothesis that the true diagnosis was renal dwarfism as in the present case

The growth disparities recorded in these cases are summarised in the accompanying table

Many cases of renal rickets and dwarfism, or lesions likely to cause this, have previously been described in siblings The cases published before 1930 have been reviewed by Mitchell (1930), who lists 11 instances of renal dwarfism or rickets in which more than one member of the family was affected Davidsohn and Newberger (1933) described twins, presumably uniovular, who died on the seventeenth and nineteenth days of life from uræmia due to congenital valves in the posterior urethra

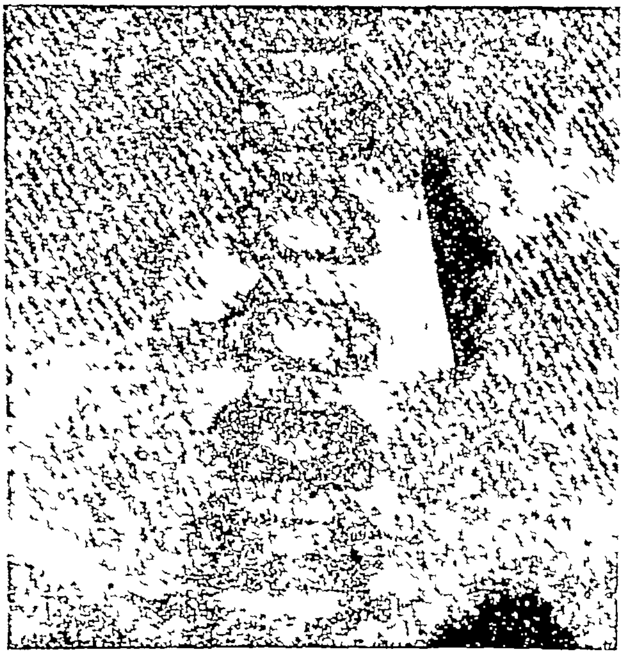


Fig 3—Intravenous pyelogram of patient's twin brother

Reference	Diagnosis	Sex	Age (years)	Height (cm)		S D appropriate to age (cm)	Growth disparity as multiple of S.D.
				Of shorter twin	Of normal twin		
Siemens (1927)	Scoliosis	F	16	142 0	154 0	5 75	2 1 × S.D.
Lehmann (1937)	Kyphoscoliosis	M	14	119 1	149 3	8 50	3·6 × S.D.
Lewis (1936)	Gigantism and acromegaly	M	46	194 3	172 7	6 50	3 3 × S.D.
Komai and Fukuoka (1934)	Claimed to be diabetes insipidus	M	15	140 0	154 8	8 20	1 8 × S.D.
Present case	Renal dwarfism	M	13	127 0	143 0	7 98	2·0 × S.D.

Weill Hallé et al (1939) described a brother and sister both of whom were renal dwarfs Graham and Hutchison (1941) recorded a family in which certainly 3, and possibly 4, of 8 siblings were renal dwarfs Of these, 2 were twins, but they were clearly dizygotic, for they were of unlike sex Danis and Rossen (1941) recorded renal dwarfism and rickets in a brother and sister Mackay (1945) described a family in which 5 siblings had congenital lesions of the kidneys or of the ureters

The importance of congenital lesions of the upper urinary tract causing pyelonephritis is emphasised by Erb and Summerfeldt (1941), who found, in 1148 consecutive necropsies on children, that 4 4% of such congenital anomalies were associated with pyuria during life Hawthorne (1941) describes how such lesions lead to urinary infection which often persists despite therapy Of 95 cases of urinary infection in childhood, 60% proved resistant to treatment owing to a congenital lesion demonstrable by intravenous pyelography In a statistical review of 471 cases of congenital anomalies of the kidney and ureter Smith and Orkin (1945) stated that there is often predisposition to poor function and stasis, with retention and subsequent infection Of this large series 10 seem to be anatomically similar in type to the present case Although this type of pelvis is classed radiologically as a variant of the normal, it would appear to be an undesirable variant in view of possible complicating infection

SUMMARY

A case of renal dwarfism is described together with an apparently normal uniovular twin brother in whom, however, intravenous pyelography demonstrated unusual renal pelves

The published cases of unequal growth in uniovular twins, and the familial occurrence of renal dwarfism and rickets, are briefly reviewed

I am grateful to Prof Robert Platt for permission to publish this case, to Dr E D Gray for the radiological investigation and report, to the Regional Transfusion Service, North West Region, for determination of the blood groups, and to the departments of clinical pathology and of medical photography, Manchester Royal Infirmary, for the pathological investigations and the illustrations respectively

ADDENDUM

Since this paper was written, the following similar case has been studied

A married woman, aged 22, was admitted to the Manchester Royal Infirmary under Dr J F Wilkinson for low back pain, polyuria with nocturnal frequency of micturition and polydipsia, and anæmia She had 3 brothers and 4 sisters, one of the sisters being her twin, all these were perfectly healthy She had had nocturnal and diurnal polyuria and consequent frequency of micturition for as long as she could remember, she had always had to drink more than the average both by day and by night In June 1949 she had become pregnant, and the doctor found that she was anæmic and she had not responded to adequate iron therapy Her pregnancy had terminated at the fourth month in a miscarriage associated with considerable blood loss Since the pregnancy the patient had become breathless on exertion and had frequent attacks of palpitations over the same period she had had chronic aching pain over the sacrum which was made worse by exercise For the last two years she had noticed progressive blurring of vision

On examination she was small but normally proportioned height 55¾ in. weight 84 lb She was obviously anæmic and her mucosæ and skin were rather dry Her heart was enlarged towards the left side the apex beat being 1 in outside the mid-clavicular line her blood pressure was normal 115/75 mm Hg Movement of the lumbar spine was somewhat limited, with pain on extension and tenderness on percussion the urine showed constant albuminuria bilateral radiate cataracts typical of chronic hypocalcæmia were present in both eyes there was, however, no evidence of latent tetany The blood had a hæmoglobin content of 50% of the average normal (7 4 g per 100 ml), the colour index being 0 83 total and differential white cell counts were normal The average protein content of the urine (Esbach) was 0·75 g per litre there was complete isosthenuria, sp gr being constantly 1 010 , some red cells and pus cells were present on microscopy The blood urea level was 190 mg per 100 ml , and the urea clearance 10% of the average normal The serum-calcium level was 6 5 mg per 100 ml serum inorganic phosphorus 7 9 mg per 100 ml , serum alkaline phosphatase 32 King Armstrong units and the alkali reserve 43 vol CO_2 per 100 ml Electrocardiography showed prolongation of the Q–T interval owing to the hypocalcæmia Radiography showed that the epiphyses were normally closed but there was evidence of renal osteodystrophy in that pseudo fractures were present in the right 10th and 11th ribs Radiography of the abdomen revealed no evidence of abnormal calcification or renal calculi In summary this was a case of normotensive uræmia with chronic hypocalcæmia and consequent formation of cataracts but not showing any evidence of tetany because of the severe acidosis due to the renal failure The patient had a refractory anæmia and an early osteodystrophy both of which were secondary to the uræmia

Her twin sister was 2¾ in. taller than the patient and appeared perfectly healthy , she was not anæmic her urine was of normal specific gravity and contained no protein, and her blood urea level was 20 mg per 100 ml. She was however, in the later stages of pregnancy, and therefore intravenous pyelography has had to be delayed until after her future delivery

The twins were considered to be uniovular by the method described above , this was confirmed by the blood groups, these being identical as follows O, cDe/cDe M, S negative, P positive, Lewis a-negative b positive Lutheran a negative, and Duffy a negative

This is, therefore, a further example of growth disparity in uniovular twins secondary to chronic renal failure in one of the pair , the disparity amounted to 7 cm , which is only just above the standard deviation of height appropriate to age and sex—i e 5 95 cm (equivalent to 1 18 × S.D)—and therefore only just outside the maximum variation in normal uniovular twins as defined by Stocks (1930)

I am grateful to Dr J F Wilkinson for permission to publish this case

REFERENCES

Danis P G Rossen J A (1941) *J Pediat* 18 103
Davidsohn I Newberger C (1933) *Arch Path* 16 57
Ellis A Evans H. (1933) *Quart J Med* 2 231
Erb I H Summerfeldt P (1941) *Canad med Ass J* 44 14
Graham, S. Hutchison J H. (1941) *Arch Dis Childh* 16 253
Hawthorne A B (1941) *Canad med Ass J* 44 152
Hickey R C Hare K (1944) *J clin Invest* 23 768
Komai T Fukuoka G (1934) *J Hered* 25 423
Lehmann W (1937) *Z KonstLehre* 20 237
Lewis A (1936) *Ann Eugenics* 7 58
Mackay H (1945) *Proc R Soc. Med* 38 567
Mitchell A G (1930) *Amer J Dis Child* 40 101
Newman H H (1940) Multiple Human Births New York.
Rule C Grollman, A. (1944) *Ann intern Med* 20-63
Siemens H W (1927) *J Hered* 18 201
Smith E. C Orkin L A (1945) *J Urol* 53 11
Stocks P (1930) *Ann Eugenics* 4 49
Warkany J., Mitchell A. G (1939) *Amer J Dis Child* 57 603
Weill Halle B Abaza A., Meunier P (1939) *Bull Soc. Pédiat. Paris* 37 266

THE INVESTIGATION OF SUGAR TOLERANCE

JOHN FRIEND
M.D Lond M.R C P
SENIOR REGISTRAR, PROFESSORIAL MEDICAL UNIT, MIDDLESEX HOSPITAL, LONDON

TESTS of glucose tolerance are designed to reveal a failure to maintain the blood sugar level within normal limits under the stress of a carbohydrate load The test may show normal or reduced tolerance The latter is often termed " diabetic " despite the common finding of such a reduction of tolerance in many conditions other than diabetes mellitus This diabetic type of glucose tolerance curve has been described as high and spread,' although it is recognised that the degree of hyperglycæmia attained is of no significance (Spence 1920, MacLean and de Wesselow 1920, Mosenthal 1947a) Reduced sugar tolerance is shown by protracted hyperglycæmia It is considered that two hours after 50 g of glucose has been taken by mouth the venous blood sugar level should normally fall to below 120 mg per 100 ml and that blood sugar levels above this indicate a reduction of glucose tolerance (Hale White and Payne 1926, Langner and Dewees 1942, Duncan 1947, Mosenthal 1925 and 1947b) Moyer and Womack (1950) allow 125 mg per 100 ml as the upper limit of normal.

As alternatives to complete tolerance tests and to estimation of the 2 hour blood sugar level * certain blood-sugar levels for both fasting and non fasting states have been suggested as reliable indications of reduced sugar tolerance Most workers give about the same figure for the upper limit of the normal range of the blood sugar level in the fasting state Hale White and Payne (1926), Mosenthal (1947a and b), and Moyer and Womack (1950) regard 120 mg per 100 ml. as the highest acceptable figure, whereas Joslin (1946) and Lawrence (1950) regard any fasting blood sugar level above 130 mg per 100 ml as indicating diabetes mellitus In the non-fasting state diabetes may be diagnosed according to Joslin (1946), if the venous blood-sugar level exceeds 170 mg per 100 ml or the capillary blood sugar level is above 200 mg per 100 ml. in the presence of glycosuria Lawrence (1947, 1950) expresses a similar opinion , but Moyer and Womack (1950), investigating 103 normal persons, could not define any postprandial blood sugar level having this significance

With a few exceptions, these standards of reduced sugar tolerance seem to have been suggested as a result of extensive experience over many years They are critically examined here with the 2 hour blood sugar level as the index of glucose tolerance

INVESTIGATION

In the years 1940–49 inclusive 1582 patients were submitted to a glucose tolerance test of the standard type One dose of glucose 50 g was given by mouth after an overnight fast, the venous blood sugar level was estimated at half-hourly intervals for two hours by Benedict s (1928) method until late in 1948, and subsequently by the method of Folin and Wu (1920) and Folin (1928)

In these 1582 tests a fasting blood sugar level of at least 120 mg per ml was found in 431 cases and a 2 hour blood-sugar level of at least 120 mg per 100 ml. in 424 of these 431 (table I) Therefore, if a fasting blood sugar level above 120 mg per 100 ml. had been taken to denote that a diabetic type of tolerance curve would follow, 7 (1 6%) persons would have been diagnosed incorrectly as intolerant of glucose On the other hand, a considerable number of cases of intolerance would have been missed , for, though 1151 cases showed a fasting blood sugar level under 120 mg per 100 ml , only 982 had a 2 hour level under 120 mg per 100 ml Therefore 169 (26 8%) of the curves of diabetic type would have escaped detection

---

* 1 1½ and 2 hour blood sugar levels mean the venous blood-sugar levels at these times after the administration of glucose 50 g by mouth.

When the fasting blood sugar level was 130 mg per 100 ml or higher, the 2-hour blood sugar level was invariably at least 120 mg per 100 ml Of the 593 curves of diabetic type only 378 showed a fasting level of 130 mg per 100 ml or higher , hence the remaining 215 (36 3%) would have been wrongly forecast as showing normal tolerance

The height of the curve produced after the oral administration of glucose had, in this series, no significance Table II shows clearly that blood sugar levels of 170 mg per 100 ml or higher at 1 hour do not invariably denote a loss of tolerance to glucose 607 curves showed a 1 hour level greater than 169 mg per 100 ml 75 (12 35%) of these did not show any reduction of glucose tolerance, since their 2 hour blood sugar level was less than 120 mg per 100 ml 3 patients with a 1 hour hyperglycæmia in excess of 230 mg per 100 ml showed normal glucose tolerance, since the blood sugar level fell to below 120 mg per 100 ml in the course of the second hour of the test (Beckwith 1947) There were 52 patients (8 8%) with reduced tolerance whose blood sugar level did not reach 170 mg per 100 ml at 1 hour , these would have been incorrectly classified as normal from the 1 hour blood sugar level alone Similar, though smaller, errors were found when the 1¹/ hour blood sugar levels were examined (table III) 512 curves showed a 1¹/₂ hour level higher than 169 mg per 100 ml , of these, 16 (3 1%) had fallen below 120 mg per 100 ml in the following half hour Adoption of 170 mg per 100 ml as the critical level at 1¹/₂ hours would also have excluded 47 curves showing reduced tolerance—an error of 3 2% in 1469 tests

TABLE I—TWO HOUR BLOOD-SUGAR LEVELS COMPARED WITH FASTING LEVELS

Fasting blood sugar level (mg per 100 ml)	No of cases	2 hour blood-sugar level (mg per 100 ml)			
		0–119	120–129	130–139	>140
0–119	1151	982	44	27	98
120–129	53	7	1	3	42
130–139	28	0	1	0	27
>140	350	0	0	0	350
Total	1582	989	46	30	517

DISCUSSION

As a result of the examination of 2 hour blood sugar levels in a standard glucose tolerance test reduced tolerance may be revealed No further information may be gleaned from the test In diabetes mellitus there is no relation between the blood sugar levels during a tolerance test and the severity of the diabetes (as judged by daily requirements of insulin) The so called renal sugar threshold can be assessed only with great inaccuracy from the results of an investigation which commonly uses venous blood and makes no allowance for variation of glomerular filtration rate in the kidney (Mirsky and Nelson 1943) Complete standard tolerance tests cannot be justified, since the only information obtained from the five blood and three urine examinations of the test can be found equally well by estimation of a single 2 hour blood sugar level

TABLE II—TWO HOUR BLOOD SUGAR LEVELS COMPARED WITH ONE HOUR LEVELS

1 hour blood sugar level (mg per 100 ml)	No of cases	2 hour blood sugar level (mg per 100 ml)	
		0–119	>120
0–169	954	902	52
170–179	36	23	13
180–189	33	19	14
190–199	47	16	31
200–209	41	7	34
210–219	29	3	26
220–229	31	4	27
>230	390	3	387
Total	1561	977	584

TABLE III—TWO HOUR BLOOD SUGAR LEVELS COMPARED WITH 1¹/₂ HOUR LEVELS

1¹/₂ hour blood sugar level (mg per 100 ml)	No of cases	2 hour blood sugar level (mg per 100 ml)	
		0–119	>120
0–169	957	910	47
170–179	25	9	16
180–189	34	2	32
190–199	20	1	19
200–209	26	2	24
210–219	23	0	23
220–229	30	1	29
>230	354	1	353
Total	1469	926	543

This analysis shows that, if the 2 hour blood sugar level is the index of glucose tolerance, errors occur if fasting or postcibal blood sugar levels are taken in place of the 2 hour level Normal people are included in the group showing reduced tolerance, no matter which criterion is adopted, apart from a fasting level exceeding 130 mg per 100 ml , though Gray (1923) found that 2 3% of 431 normal people showed a fasting blood sugar level higher than this He did not, however, indicate whether or not the 2 hour level in these cases signified reduced tolerance, and distinguished only that these people had not got clinical diabetes mellitus

TABLE IV—ERRORS ARISING WITH DIFFERENT CRITERIA

Blood sugar level used as criterion (mg per 100 ml)	No of cases	No of normal curves wrongly included	No of curves of diabetic type wrongly excluded
Fasting >120	431	7 (*1 6%*)	169 (*26 8%*)
Fasting >130	378	Nil	215 (*36 3%*)
1 hour >170	607	75 (*12 3%*)	52 (*8 8%*)
1 hour >200	491	17 (*3 46%*)	110 (*18 5%*)
1¹/₂ hour >170	512	16 (*3 1%*)	47 (*8%*)
1¹/₂ hour >200	433	4 (*0 9%*)	114 (*19 2%*)

Relying on the fasting and postcibal blood sugar levels as evidence of reduced tolerance instead of the 2 hour blood sugar levels would have caused an omission of cases which did show, in fact, reduced tolerance in their 2 hour levels (table IV) If the fasting blood sugar levels alone had been taken as an index of reduced sugar tolerance, curves of diabetic type, sufficient in number to invalidate the fasting blood sugar level as a diagnostic aid, would have escaped detection Though a fasting level above 130 mg per 100 ml confirms a reduction of sugar tolerance, a normal fasting blood sugar level is of no significance Similarly, table IV shows that adoption of the 1 hour or the 1¹/ hour blood sugar level as a criterion of reduced tolerance will lead to the exclusion of a considerable number of curves of diabetic type

It is concluded that there are no sensitive specific methods of detecting reduced tolerance other than estimation of the 2 hour blood-sugar level

SUMMARY

1582 standard glucose tolerance tests have been analysed

If reduced tolerance of sugar is indicated by a venous blood sugar level higher than 120 mg per 100 ml 2 hours after taking glucose 50 g by mouth, 593 results in this series showed reduced tolerance

The blood sugar levels both fasting and postcibal, suggested as being significant of reduced sugar tolerance, are unreliable

I wish to thank Prof E C Dodds, F.R.S., for his advice and for permission to report results obtained in the S.A. Courtauld Institute of Biochemistry, and Prof A Kekwick and Dr Robert Semple for their advice and criticism in the preparation of this paper

REFERENCES

Beckwith E W (1947) *Amer J Digest Dis* 14 245
Benedict S R (1928) *J Biol Chem* 76 457
Duncan G G (1947) Diseases of Metabolism Philadelphia
Folin O (1928) *J biol Chem* 77 421
— Wu H (1920) *Ibid* 41 367
Gray H (1923) *Arch intern Med* 31 241
Hale White R Payne W W (1926) *Quart J Med* 19 393
Joslin E P (1946) Treatment of Diabetes London
Langner P H jun Dewees E J (1942) *Amer J med Sci* 204 85
Lawrence R D (1947) *Med Clin N Amer* 31 289
— (1950) The Diabetic Life London
MacLean H de Wesselow O L V (1920–21) *Quart J Med* 14 103
Mirsky I A Nelson N (1943) *Arch intern Med* 71 827
Mosenthal H O (1925) *Med Clin N Amer* 9 549
— (1947a) *Amer J digest Dis* 14 245
— (1947b) *Med Clin N Amer* 31 299
Moyer J H Womack, C R (1950) *Amer J med Sci* 219 161
Spence J C (1920–21) *Quart J Med* 14 314

DUODENAL INTUBATION WITH MAGNET-TIPPED TUBES

A H JAMES
M.A., D.M. Oxfd M.R.C.P
ASSISTANT TO THE MEDICAL UNIT, ST MARY'S HOSPITAL, LONDON

INTUBATION of the duodenum, undertaken for diagnosis, treatment, or research, is often difficult Sometimes a tube passed into the stomach and pushed further enters the duodenum at once, more often it becomes coiled in the stomach, the tip being found usually at the pylorus or in the gastric fundus, partial withdrawal and replacement may or may not overcome the hindrance

Various procedures are used to assist passage through the pylorus, the most usual being to lay the patient on his right side and introduce the tube extremely slowly Delay results mainly from ignorance about what is happening to the tube tip, so that manœuvres are often misdirected, for example, a tube coiled in the fundus rarely finds its way into the duodenum however long the patient lies on his side At present this can only be overcome by using radiology, the progress of the tube being watched on the fluoroscopic screen or by means of serial films In practice such methods have many disadvantages if the procedure is lengthy, as it often is it hinders the work of busy radiological departments, if the screen is used the work has to be done in the dark, and the possibility of overdosage with X rays makes it necessary to hurry These difficulties are magnified when the patient is a small child, and very ill patients cannot be taken to the X-ray apparatus

In the course of research requiring duodenal intubation we have developed a method of locating the tube tip without the help of X rays, and have found this of practical value with both adults and children A small permanent magnet is incorporated into the tip of the tube, and its position within the abdomen found by detecting its magnetic field with a small compass needle Magnets of a size which can be used are detectable at a range of about 3½ in and a compass pressed on the abdomen can be brought within this distance of most parts of the stomach and duodenum

CONSTRUCTION

To make sufficiently powerful magnets one of the highly magnetisable nickel-cobalt aluminium alloys must be used in this work magnets were made of 'Ticonal' (Mullard Electronic Products Ltd) This alloy cannot be machined and has to be ground to suitable size and shape on a grindstone For use in adults the magnet should be cylindrical, 2 5 cm long and 6 mm in diameter, and tapered slightly at each end. For children the diameter should be 4 mm and the length 2 cm, or less for small infants The magnet is inserted into suitable rubber tubing (no 3 I R) and the end closed by dipping into crude 'Latex,' which, when dried, makes a satisfactory rounded end Holes are cut as required A plotting compass, measuring ¾ in in diameter and ¼ in in depth, is used

METHOD

When the tube tip is lying horizontally and the compass is placed over it, the needle oscillates more rapidly than it does in the earth's field, and aligns itself in the axis of the tube, one end or other will always point in the direction of the tube tip, and which end does this must be discovered by trial before the tube is passed In this way the orientation as well as the position of the tube tip in the stomach can be determined. If the magnet is "end on" below the compass, the needle will be seen to dip, and according to which end dips it can be decided whether the tube tip is pointing towards or away from the compass A little practice with a compass and magnet will make these points clear Sometimes the polarity of the compass needle becomes reversed during the intubation, under the influence of the strong field of the tube magnet, this causes the needle to point in the opposite direction relative to the tube It is usually obvious when this has happened, and it can be confirmed by a reference magnet, or by observing the orientation in the earth's field.

For duodenal intubation, the tube is passed into the stomach and then sought by pressing the compass on to the abdomen with the patient lying flat The compass must be held horizontally so that the needle can swing freely When it comes near the tube-tip the needle, previously swinging slowly in the earth's field, is seen to swing much more rapidly, and to point in a new direction, the place at which it swings most rapidly is the best guide to the position of the tube

Ideally the tip is found first in the mid epigastrium, pointing transversely to the right, and very superficially as judged by the rapidity of the oscillations When the tube is pushed further the tip is next found slightly above and to the right of the previous position, and pointing away from the compass—that is, backwards through the pyloric canal Finally when it enters the duodenum the tip is found at the outer border of the right rectus, pointing downwards, and much less superficially When this sequence has been observed the tube is almost certainly in the duodenum Often only the first and last positions are seen When the tip is obstructed in the fundus of the stomach it is less easy to localise exactly, but a magnetic field can be detected below the left costal margin or outside the left lower chest In children the findings are similar, the shorter distances in the child compensating for the smaller size, and therefore slighter power, of the magnet

RESULTS IN ADULTS

Duodenal intubation has been attempted with a magnet tipped tube in 17 adults When the tube was thought to have entered the duodenum, as judged by the compass, a radiograph was taken In 14 instances the tube was in fact in the duodenum, and in the remaining 3 it was in the pyloric antrum The compass thus proved correct in 82 5% of cases, and mistakes, naturally more liable to be made with fat patients, became less common with practice None of these patients had distended abdomens from intestinal obstruction, in such cases deep palpation with a compass is more difficult, but at the crucial point—namely, the pylorus—the tube tip overlies the spine and is therefore more easily approached With such patients a larger magnet would have a decided advantage

A magnetic tip is also of value in tubes used for gastric aspiration, particularly where, as in research, it is necessary to be certain that the fluid so obtained is really of gastric origin

INTUBATION IN INFANTS AND CHILDREN

Duodenal intubation of children is necessary for the certain diagnosis of fibrocystic disease of the pancreas, but often has to be abandoned after attempts which may last several hours have ended in failure The magnet tipped tube, enabling the work to be done in the ward, in daylight and at leisure, while providing constant information about the progress of the tube, has greatly increased the chances of success and reduced the time in which it can be achieved

The attempt was made in 21 children whose ages ranged from one month to six years, 8 being one year old or less In 20 the duodenum was reached (X ray confirmation being obtained in each instance), although in 1 case the tube was regurgitated before a satisfactory sample could be obtained, the remaining child, a boy aged 3 resisted so strongly that the attempt had to be abandoned Most samples were got in 15–45 minutes, one took 2 hours The juice was allowed to drip out without the aid of suction

Three procedures were found of the greatest assistance

1 The tube is more easily swallowed and controlled if it can be passed through the nose In 8 cases where it was not possible to do this owing to buckling of the tube, success was achieved with the aid of a piece of copper wire passed in through one of the holes to rest on the back of the magnet By this means it was possible to push the tube through the nose, and the wire was then withdrawn

2 When the tube becomes stuck repeatedly in the fundus of the stomach, it should be withdrawn into the œsophagus and replaced with the child lying face downwards

3 When the tube is in the pyloric antrum and pointing to the right, gentle pushing at the nose combined with intermittent pressure on the epigastrium, has often caused it to enter the duodenum without delay

In palpating a child with a compass it is particularly important to keep the compass level, when the child is crying, reliance can be placed on the behaviour of the compass only during the momentary relaxation accompanying inspiration

CONTROL OF INTESTINAL TUBES WITH A MAGNET

Various workers have tried to pull a tube through the pylorus with a magnet Mayer (1944) inserted a small magnet made of 'Alnico,' an alloy similar to ticonal, into the tip of a Miller Abbott tube, using an electromagnet placed on the right chest wall, he claimed that he was always able to pull the tube into the duodenum under fluoroscopic guidance At the start of this investigation it was hoped that the magnet tipped tubes would have the double advantage that they could be moved with a magnet outside the body as well as detected with a compass A ticonal magnet was made, of the largest size that could be conveniently handled—such a magnet being more powerful than an electro magnet worked by any supply of direct current likely to be available While this magnet could exert a pull on the tube of 100 g at a range of 0 5 cm, at 10 cm the pull was only 6–8 g, and the distance from the pylorus to the lateral chest wall is usually greater than this In practice there was never a convincing instance of a tube having entered the duodenum more rapidly with the magnet's help than without It was often possible to bring the tube out of the fundus and into the pyloric antrum, especially in children, but this can be done by more simple methods, such as that described above For these reasons magnet tipped tubes are of value only for use in conjunction with a compass

My thanks are due to the staffs of this hospital, of Princess Louise Hospital, Kensington, and of the Queen Elizabeth Hospital, Hackney Road, for permission to make observations on patients under their care, and especially to Dr W F Young for assistance with many of the intubations, and to Dr E Rohan Williams and the staffs of the radiological departments of the above hospitals for their kind help

REFERENCE

Mayer, H (1944) U.S Nav med Bull 43, 463

PROCAINE WITH HYALURONIDASE AS LOCAL ANÆSTHETIC

J N Thorpe
M.B, Edin
ANÆSTHETIC REGISTRAR, UPTON HOSPITAL, SLOUGH BUCKS

For the reduction of Colles's fracture and similar injuries, the anæsthetic which is probably most often employed is nitrous oxide This, however, has several drawbacks Its anæsthetic properties are so slight that it is always given with a very small concentration of oxygen, which may be dangerous, particularly where the patient—like so many with Colles's fracture—is elderly and has cardiovascular disease In the young fit adult it is even harder to obtain satisfactory anæsthesia with nitrous oxide, and impossible to obtain adequate muscular relaxation Postoperative vomiting with its attendant risk of aspiration—slight though this may be—is not uncommon with nitrous oxide if the period of anæsthesia is prolonged, and when radiography does not show proper reduction of the fracture, the patient has to have another anæsthetic for correction of the deformity

If general anæsthesia is required, a quick acting barbiturate is preferable (1) for the patient because it is more pleasant than nitrous oxide and does not involve anoxia, (2) for the anæsthetist because quiet anæsthesia is rapidly and simply achieved, and (3) for the surgeon because the patient is immobile with muscles relaxed Its chief disadvantage is that the patient requires a bed and nursing supervision for some time after administration, either or both of which are difficult to provide in a busy and short staffed outpatient department

Brachial plexus block has been used for the reduction of Colles's fracture, but it is time consuming, not without danger, and, in inexpert hands at any rate, often fails.

The anæsthetic of choice in the treatment of this condition appears to be local infiltration anæsthesia But this method, though described in most of the orthopædic textbooks, is not widely practised, because satisfactory analgesia is not attained until the injected anæsthetic agent has diffused into the tissues surrounding the fracture site, which may take a quarter of an hour or more Even then, if diffusion has been insufficient—and this is not uncommon—some pain is experienced during the subsequent manipulation For these reasons most surgeons tend to regard local infiltration analgesia as a last resort where general anæsthesia cannot be used

A modification of this technique[1] has recently been tried at the Upton Hospital with promising results Before injection the local anæsthetic agent (for Colles's fracture 20 ml of 1% procaine) is mixed with 1000 "Benger units" of hyaluronidase ('Hyalase'), which promotes diffusion of injected substances Two injections are made the bulk of the solution is put directly into the fracture hæmatoma from the extensor aspect of the forearm, and 2–3 ml is infiltrated around the ulnar styloid process The anæsthetic solution diffuses rapidly all round the injured area and the fracture can be manipulated as soon as the needle is withdrawn The patient, being ambulant, can at once walk unaided to the X ray department, and, if reduction is found to be incomplete, further manipulation is possible straight away

---

[1] Kirby C K Eckenhoff J E Looby J P *Surgery* 1949 25 101 Moore D C *Anesthesiology* 1950, 11 464

To date, this technique has been used in 22 cases of Colles's fracture and 4 cases of Pott's fracture (using 40 ml of 1% procaine for the latter) Though the series is very small, we have been struck by the rapidity with which analgesia is achieved and by the fact that it has always been complete Despite the rapid absorption of the anæsthetic, the fracture area remains pain free for well over an hour in one of the cases of Pott's fracture, three manipulations were required over a period of 1¼ hours and no pain was experienced during that time

I should like to express my thanks to Mr G P Arden, accident and orthopædic surgeon, for his interest and advice, and to Mr I J Gordon the resident surgical officer, who performed most of the manipulations

A CASE OF

CONGENITAL AFIBRINOGENÆMIA

A I D Prentice
M C M B Camb
ASSISTANT PATHOLOGIST,
ESSEX COUNTY HOSPITAL, COLCHESTER

One of the causes of a hæmorrhagic diathesis is congenital absence of fibrinogen Though the defect can be demonstrated without difficulty, the condition may be overlooked because of its rarity, for only eight or nine cases have been recorded, the first in 1920 by Rabe and Salomon In the following case, which showed all the features of this interesting state, a necropsy was performed.

CLINICAL RECORD

The patient, an architect s assistant aged 19 was admitted to the Essex County Hospital on Nov 19, 1947, complaining of pain in his chest

History —From the time of his birth, when his cord bled profusely, he had lost large amounts of blood from minor injuries and had always bruised easily The main bleeding episodes, previously attributed to hæmophilia, were

Age (years)	Injury sustained	Treatment given
3	Minor crush injury to finger	Three weeks in hospital Treatment unknown
7	Cut finger	Snake venom applied without effect ½ pint of his mother s blood stopped the bleeding
8		Fortnight in hospital Transfusion
10		Bleeding controlled after the second bottle of blood Had a minor operation on his finger immediately after but had no trouble from this
11		In hospital Bleeding controlled by transfusion
13	Perforating injury to foot	Fresh blood applied locally stopped the hæmorrhage

His only other illness was whooping cough in infancy

There was no family history of bleeding His parents came from different parts of the country and there was no known consanguinity in the last three generations A sister and brother are both alive and well

In October 1947, he developed headaches and pain down the back of his neck, sweated profusely, and felt very weak He had a spontaneous epistaxis for which he was admitted to hospital and given 1500 ml of blood This controlled the hæmorrhage and he was again discharged A week later he began to get pain shooting across the right side of his chest, and he was admitted to the Essex County Hospital for the first time

Examination —He was lean, but otherwise normally developed He had a pyrexia of 100–102°F and persistent tachycardia 110–140 per min respirations were 30–35 per min Physical signs indicated a large collection of fluid in the right pleural cavity and this was confirmed radiologically His joints showed none of the changes to be expected in a hæmophilic

Blood Examination —Hæmoglobin 70%, red cells 3,600,000 per c mm, white cells 25 000 per c.mm (polymorphs 96%, lymphocytes 3%, monocytes 1%), platelets 280,000 per c mm Bleeding time 6 min 30 sec (Duke s method) Clotting time no clot after 2 hours (capillary tube method)

Course of Illness —Aspiration of the chest yielded 28 oz of turbid dark-brown fluid containing many polymorphs and red blood-cells and scanty epithelial cells No organisms were revealed by Gram or Ziehl Neelsen staining Aerobic and anaerobic cultures were sterile

As he had been treated with sulphonamides before admission, a provisional diagnosis of pneumonia, sterile empyema, and hæmorrhagic diathesis of unknown ætiology was made During the next few weeks, however, the pleural effusion re formed repeatedly after aspiration The five aspirations all caused considerable oozing from the puncture wound, and the later ones showed increasing proportions of lymphocytes to polymorphs No organisms were seen in direct films all cultures were sterile, and all cultures for tubercle bacilli were negative Two inoculated guineapigs were free from tuberculosis after six weeks Four specimens of sputum were examined and two were cultured for tubercle bacilli with negative results

On Dec 4 it was decided to remove as much fluid as possible and replace it by air After withdrawal of 7 pints, radiography next day showed a completely collapsed right lung and a residue of fluid at the right base During the next two weeks signs of consolidation developed at the base of the left lung and the patient began to cough up heavily bloodstained sputum A transfusion of 2 pints of blood on March 11, 1948 brought temporary improvement and on April 2 a further transfusion with 80 ml fibrinogen solution and 3 pints of blood was given But his clinical condition deteriorated, and on April 6 he became cyanosed and dyspnœic, and died

SPECIAL INVESTIGATIONS

On March 16, 1948, the erythrocyte sedimentation rate had been estimated and it was noted that the fall in 1 hour was 5 mm, an exceptionally low value considering the patient's state This, coupled with the fact that his X-ray films showed a deficient fibrin formation, suggested that the case might be one of congenital afibrinogenæmia A further series of experiments was therefore undertaken

1 A specimen of the patient's fresh whole blood was incubated at 37°C for three days No clot formed

2 His plasma was heated to 60°C No fibrin was precipitated

3 Quarter saturation of the plasma with ammonium sulphate failed to bring down a precipitate of fibrin

From these three tests it was concluded that the patient was completely lacking in fibrinogen

4 Prothrombin time was estimated by Quick s method The control clotted in 12 sec With the patient's plasma, a faint granular precipitate appeared after a few seconds, but no clot or flakes of fibrin Quick s test was again carried out using as a control 50% normal plasma diluted with saline and the patient s plasma to which was added an equal volume of 1 2% solution of fibrinogen The control clotted in 21 sec and the patient s plasma in 6 min.

From this it was deduced that the patient's blood contained some prothrombin

5 *The Bleeding time* —In the eight cases reviewed by Henderson et al (1945) the bleeding times varied between 5 and 30 min and in the case described by Pinniger and Prunty (1946) it was 3½ min In the present case the shortest bleeding time recorded was 1 min. (Ivy s method), using the smallest prick necessary to draw blood, and the longest time was 20 min. Pricks of the finger pulp always stopped

bleeding within 2–3 min , whereas bleeding caused by the aspiration needle in the chest wall went on for several days Bleeding sometimes stopped temporarily and recurred in about 20 min , presumably as the temporary contraction of the capillaries (Macfarlane 1945, 1948) wore off

The bleeding time therefore, even when uncomplicated by clotting, gave results which varied widely according to such factors as the rate and degree of capillary contraction, the support offered by surrounding tissues, the depth of the prick and possibly the speed and completeness with which platelet agglutinates plugged the vessels

6 *Capillary Fragility*—As in most of the previously reported cases, the capillary fragility (as tested by Hess s method) was not increased, and capillary microscopy showed normal response of the capillary to injury

7 *Erythrocyte sedimentation Rate*—An attempt was made to compare the sedimentation of the patient s blood and ' defibrinated " blood (made by adding cells to a serum, which before defibrination sedimented at 50 mm per hour) Measured at fifteen minute intervals over 3 hours the two sedimentation curves showed a similarity, a fact which might be held as doubtful evidence that other globulins were present in the patient's plasma in approximately the proportions that would be expected from his condition Rouleaux formation, though present in wet-blood preparation, was not conspicuous

8 *Agglutination*—Apitz (1937, 1939) postulated a precursor of fibrin which he called " profibrin " and suggested that platelet agglutination depended on the coating of the platelets with this substance It has also been suggested that certain forms of erythrocyte agglutination depend on this factor (Quick 1942) Accordingly, blood grouping and rhesus grouping were carried out under the microscope, but no abnormality was noted in the agglutinated clumps The platelet agglutinates in wet-blood film preparations were also examined but appeared to be normal The fragility of the red cells was normal In this case, therefore, unless the fibrinogen was present in very minute amounts, its product " profibrin ' did not appear to exert any obvious influence on agglutination

9 The platelets were counted twice, and on the first occasion were 280,000 per c mm and the second 420,000 per c mm Of the other eight reported cases, only two showed a temporary thrombocytopenia

10 *Investigation of Relatives*—Two of the cases described previously had relatives showing a hæmorrhagic tendency We therefore carried out fibrinogen estimations and clotting times on all our patient's available living relatives All reports fell within the limits of normal except that a maternal aunt on two occasions had a plasma fibrinogen of 0 12% She had had no ' bleeding incidents " and her blood clotted and retracted normally

POST MORTEM FINDINGS

Necropsy (April 6)

Wasting An ecchymosis in the right forearm surrounding the site of a venepuncture Right chest considerably flatter than left

Cardiovascular System—No clotting was found in any of the vessels or the heart The pericardial cavity contained 3–4 oz clear, serous fluid The heart appeared normal, though the muscle was pale

Respiratory System—The trachea and bronchi were filled with bloodstained mucus On the left side there was 8 oz of clear brown fluid The visceral and parietal pleuræ were studded with nodular thickenings particularly over the upper lobe and along the line of division between the upper and lower lobes Both lobes of the left lung showed confluent tuberculous bronchopneumonia apart from a small area at the apex There was considerable infiltration of fibrous tissue in the lower lobe

On the right side the pleural cavity was completely obliterated by adhesions, the adherent layers which were $^1/_4$ in thick, surrounded a shrunken fibrotic lung The upper lobe was normal

Abdomen—The liver was enlarged (8 lb), its surface was smooth and it showed a normal pattern. The cut surface was firm and the cut edge bulged out below the capsule The lobular pattern was distinct, but the whole organ was paler than normal The spleen (10 oz) was approximately double the normal size, and the cut surface was red and diffluent The kidneys, ureters, and bladder were normal The stomach was filled with altered blood but no other abnormality was found in the alimentary tract

All other organs were macroscopically normal.

Morbid Histology

The *liver* showed slight fatty degeneration at the periphery of the lobules and moderate albuminous degeneration Scattered throughout there were very scanty giant-celled tubercles There was no microscopical cause for the great increase in weight

In the *spleen* the malpighian bodies were enlarged with plasmacytoid mononuclear cells, polymorphs, and round cells with a rim of pale eosinophil cytoplasm and nuclei resembling those in the outer part of the malpighian body Four giant celled tubercles were found in one of these sections.

The *sternum* showed a normal bone structure The marrow was very cellular and a single giant celled tubercle was seen There were, however, groups of hyaline, palely eosinophil masses resembling necrosed bone surrounded by granular debris

All sections of the *lungs* showed confluent giant-celled and caseous tubercles and acute necrotising tuberculous pneumonia The collagen fibres of the visceral pleura were separated by œdema fluid and there were scanty included tubercles Groups of alveoli in the lungs contained eosinophil hyaline coagula (œdema fluid), but none of them showed gram positive fibrin, and no fibrin strands were seen on the pleura Sections of the lung, stained by the Ziehl Neelsen method, showed acid fast bacilli in large numbers

The sections of skin, kidneys, myocardium, and pancreas were normal

DISCUSSION

The rarity of this condition is the only stumbling block in diagnosis, which, when reached, is irrefutable From the eight cases reviewed by Henderson et al (1945) the main features were shown to be

1 A hæmorrhagic tendency from birth.
2 Easy bruising
3 Sometimes consanguinity between the parents
4 A poor prognosis (4 patients died in childhood)
5 A very slow constant sedimentation rate
6 In all cases an absolute afibrinogenæmia and absence of clotting

The present case conforms well with these criteria

With regard to the fibrinogen and blood transfusions given three days before the patient's death, if it is assumed that there was a circulating fluid of $5^1/_2$ litres at the end of the fibrinogen *transfusion* (containing 0 96 g of fibrinogen) his plasma fibrinogen should have been in the region of 0 017 g per 100 ml A specimen of blood was taken at this stage and incubated for twenty four hours, at the end of which time no clot had formed In fact, with only this small amount of circulating fibrinogen, a soft gelatinous clot will form in whole blood

Immediately after the fibrinogen transfusion 1000 ml of whole blood was given, the equivalent of 3 g of fibrinogen This in itself should have raised the patient's plasma fibrinogen to 0 055 g per 100 ml —an amount capable of producing quite a solid clot A blood sample taken after this transfusion, however, again failed to clot *An explanation might* be that because of his multiple tuberculous lesions the fibrinogen was utilised from the circulation as soon as it was put in On the other hand, examination of sections did not reveal fibrin Possibly the amount was too small to detect by this method

Pinniger and Prunty (1946) transfused their patient with 300 ml of a concentrated solution of plasma and took specimens of blood at intervals They were able to show the presence of clotting three days after transfusion, and flakes of fibrin were detected after eight days

The modification of the tuberculous lesions by the lack of fibrinogen is difficult to assess Immunity must depend partly on the localisation of bacteria by fibrin, and indeed this patient had extensive disseminated tuberculosis The fluids aspirated from the chest did not contain clots and it is interesting to surmise how the collagenous pleural adhesions still formed despite the apparent lack of a fibrin scaffold

The significance of the relative lack of abnormality of the enlarged liver is not very clear. It seems that if fibrinogen is indeed manufactured in the liver its absence does not produce any obvious pathological change in the cells, and whether the enlargement is the result or the cause of the afibrinogenæmia is not plain. Certainly the small number of tubercles in it could not be responsible for such a degree of hepatomegaly.

SUMMARY

A case of congenital afibrinogenæmia complicated by tuberculosis is described. The clinical and pathological features are compared with those of previously reported cases.

I would like to thank Dr S. A. Propert for permission to publish this case, and Dr D. J. O'Brien for making the histological examinations.

REFERENCES

Apitz, K. (1937) *Z. ges. exp. Med.* 101, 552.
— (1939) *Ibid*, 105, 88.
Henderson, J. L., Donaldson, G. M. M., Scarborough, H. (1945) *Quart. J. Med.* 14, 101.
Macfarlane, R. G. (1945) *Proc. R. Soc. Med.* 38, 399.
— (1948) *J. clin. Path.* 1, 113.
Pinniger, J. L., Prunty, F. T. G. (1946) *Brit. J. exp. Path.* 27, 200.
Quick, A. J. (1942) The Hæmorrhagic Diseases. Springfield, Ill.
Rabe, F., Salomon, E. (1920) *Dtsch. Arch. klin. Med.* 132, 240.

POLIOMYELITIS AND POLIOENCEPHALITIS WITH OPSOCLONIA FOLLOWING APPENDICECTOMY

M. D. WARREN
M.B. Lond.
LATE RESIDENT MEDICAL OFFICER,
HERTFORD COUNTY HOSPITAL; SQUADRON-LEADER, R.A.F.

THERE is an increasing number of reported cases of poliomyelitis in which a relation appears to exist between previous trauma and the site of maximum paralysis.

As long ago as 1910 Sheppard, in Massachusetts, noticed a relation between tonsillectomy and the onset of poliomyelitis. Reviewing many of the subsequent reports Aycock (1942) concluded that the proportion of cases of bulbar poliomyelitis following tonsillectomy was significant. This observation has been confirmed by Rhodes (1947) and other workers.

McCloskey (1950) and Geffen (1950) have observed an association between prophylactic immunisation and poliomyelitis, the inoculated limb being affected more severely. These observations were noticed particularly after pertussis or combined pertussis-diphtheria inoculations. A similar phenomenon has been reported after injections of T.A.B. vaccine and penicillin (Russell 1949). Possibly some similar cases of poliomyelitis were included among the shoulder-girdle syndrome described as localised neuritis by Spillane (1943) and as neuralgic amyotrophy by Parsonage and Turner (1948).

Many precipitating causes have been suggested, including tooth-extraction. This is a common operation and therefore information about the relationship is more readily accessible. Aycock (1942) summarised the then available evidence as follows: "It would appear that this reported circumstance can be relegated to the category of miscellaneous precedent events of no ætiologic significance." This view still holds.

The association with appendicectomy has only rarely been reported.

CASE RECORD

A boy aged 7 years was referred to the surgical outpatients department of Hertford County Hospital on Aug. 20, 1946, and was seen by Mr W. Donald Bedford. He had had intermittent attacks of epigastric pain during the last year. His doctor had seen him during the attacks and considered that these were due to appendicular colic. The child had had pneumonia three years previously but otherwise, except for the attacks already mentioned, he had been quite well. He had had no headaches, and his bowels had been generally regular. On examination the ileocæcal glands were palpable, and in view of the history the child was admitted for appendicectomy.

Operation.—Mr Bedford removed the appendix on Sept. 5, 1946. The child was premedicated with Nembutal gr. 2 and atropine gr. $^1/_{100}$. He was anæsthetised by Dr H. S. H. Gilmer with thiopentone, gas, oxygen, and 'Trilene.' Through a Battle's incision a long kinked retrocæcal appendix was removed. The wound was stitched up without drainage tubes. For three days after the operation the child had a mild pyrexia in the evening (99·0°–99·8°F). However, the wound healed satisfactorily, the temperature settled, and he was discharged to convalescence at home on the seventh post-operative day.

Readmission.—On Sept. 17, twelve days after his operation, he was readmitted. On Sept. 15 his parents had noticed that he was hot and delirious ('saw envelopes on the wall'). Later on Sept. 15, he had become rational; that night he had vomited. Next morning he had again been delirious and his temperature had been 104°F. He had spent a restless night, and on Sept. 17 he had once more become rational. On admission he complained of a severe basal headache and of pain in the lower abdomen. He had no limb pains or back-ache. Temperature 101°F; pulse-rate 128. His abdomen was grossly distended and tympanitic, and his bladder was distended up to the umbilicus. He was also tender over the right kidney and could not sit up. There was a mild degree of neck rigidity. Further questioning of the parents revealed that the child had passed very little urine since Sept. 16 and had been constipated since the 15th. Mr Bedford suggested the diagnosis of acute poliomyelitis.

Course of Illness.—On Sept. 18 the paralysis had spread to the neck muscles. No urine had been passed since a small amount after admission, and 19 oz. was withdrawn by catheter. Next day the temperature had settled to normal, but there was complete flaccid paralysis of the legs except for some plantar flexion. No tendon jerks could be elicited. Lumbar puncture on Sept. 18 produced clear cerebrospinal fluid containing total protein 90 mg. per 100 ml. and 49 white cells per c.mm. (report by Dr V. Magee). The urine, sp. gr. 1·012, contained nothing abnormal except acetone. Blood-culture was sterile, and a blood-count showed Hb 15 g. per 100 ml., red cells 5,580,000 per c.mm., colour index 0·99, white cells 18,600 per c.mm. (filamented polymorphs 74%, non-filamented polymorphs 4%, lymphocytes 20%, and monocytes 2%).

On Sept. 19 cyanosis and respiratory embarrassment were noted. The accessory muscles of respiration were being used, and by the evening it was necessary to put the child into an "iron lung." At the same time weakness of the shoulder-girdle muscles and wrist-drop developed. During the next three days catheterisation continued to be necessary and the bowels were not opened.

His condition remained much the same, except for restoration of function in the bladder and bowels, until Oct. 2. During this time he was apyrexial, except for an evening temperature of 99°F on Sept. 26, 27, and 28. His pulse-rate was 104–132. On Oct. 2 he was removed from the "iron lung" for an hour, and this period was gradually increased until on Oct. 15 he was removed completely from it. Since Sept. 20 splinting to prevent muscle stretching, and passive movements and massage had been instituted as indicated by the palsies.

On Oct. 11 he had a pyrexia of 99°F and he continued to have a temperature fluctuating between 98·6° and 100°F until his death on Oct. 23. His general condition seemed to remain static until on Oct. 18 he developed twitchings of the right side of his face and his right arm and was incontinent of urine and fæces. This attack recurred on and off during the day. Towards evening the right arm was no longer involved but three new features had developed: he became cyanosed during the attack; he lost consciousness for periods of about an hour; and he had a peculiar oscillation of his eyes which seemed to roll in a circular movement. The attacks continued on Oct. 19, and the child was delirious, disoriented, and hallucinated. Polioencephalitis was diagnosed.

On Oct. 20 he became unconscious and was given intramuscular penicillin 20,000 units three-hourly as a prophylactic against pneumonia. He died on Oct. 23 without having regained consciousness. Permission for a necropsy was not given.

DISCUSSION

The incubation period of poliomyelitis is considered to be 7–17 days and is usually about 14. This lad developed his first symptoms 10 days after his operation and was therefore in or near the incubation period at the time of the operation The first signs—i e, paralytic ileus and a paralysed bladder—occurred in the area of trauma Gaustad (1948) recording a case of poliomyelitis seven weeks after appendicectomy, noted that the muscles near the operation site were paralysed, particularly the right psoas Mills (1947), however, reported that 3 of 33 cases of acute poliomyelitis in which no operation was performed developed paralytic ileus The symptoms of bowel paralysis appeared three days after the first onset of paralyses in the voluntary muscles and in all 3 cases there were absolute constipation and retention of urine Mills advised the use of neostigmine 0 5 ml daily, but in the present case normal function returned after five days, and except for catheterisation no other treatment was thought necessary for the paralytic ileus Critchley (1948) pointed out that in the 1947 epidemic "retention of urine was frequently encountered in the poliomyelitis patients both before the onset of paralysis and after"

The peculiar ocular movements in association with polioencephalitis were first described by Orzechowski (1927), who called them opsoclonia Marmion and Sandilands (1947) described a case in a boy, aged about 3 years, who developed in both cases rapid jerking nystagmoid movements occurring in groups of up to six The movements occurred in horizontal, vertical, and oblique directions and came on with attempts to fix the gaze Their case also showed rapid head-nodding tremors The boy did not develop paralyses and reco completely McAlpine et al (1947) reported a similar Other eye signs reported are diplopia, nyst ptosis, and complete paresis of the occulomotor (*British Medical Journal* 1947)

Finally, the recurrence of symptoms, and the of polioencephalitis, four weeks after the initial s toms of poliomyelitis, appears to be unusual, an encephalitis in this case was also exceptionally widesp

I wish to thank Mr W D Bedford, consulting s to Hertford County Hospital, for permission to publi case record, and Air Marshal P C Livingston, Di General of the medical branch of the Royal Air For permission to publish

REFERENCES

Aycock W L (1942) *Medicine, Baltimore,* 21 65

British Medical Journal (1947) ii 620

Critchley M (1948) In Tidy H L, Short, A R, The M Annual Bristol p 256

Gaustad, V (1948) *Nord Med* 38, 877

Geffen D (1950) *Med Offr* 83, 137

McAlpine D, Buxton P H Kremer M., Cowan, D J *Brit med J* ii 1019

McCloskey B P (1950) *Lancet* i 659

Marmion D E Sandilands J (1947) *Ibid*, ii, 508

Mills J (1947) *Brit med J* ii 507

Orzechowski K (1927) *J Psychol Neurol Lpz* 35, 1

Parsonage, M J Turner, J W A (1948) *Lancet*, i 973

Rhodes A J (1947) *Bull Hyg Lond* 22, 353

Russell, W R (1949) *Brit med J* i 465

Spillane J D (1943) *Lancet*, ii 632

New Inventions

A TIDAL SPIROMETER

ONE of the difficulties in using muscle relaxants in anæsthesia is to know when and how much to give An objective method of determining the patient's requirements is desirable Since respiratory depression is the most easily demonstrable effect of these drugs, an instrument for measuring the tidal volume was considered Harbord[1] described an apparatus consisting of a tap by which a single expiration can be deflected into a 600 c cm bag The tidal volume is obtained by estimating the distension of the bag—e g a quarter full or half-full The apparatus described here (fig 1) is more accurate

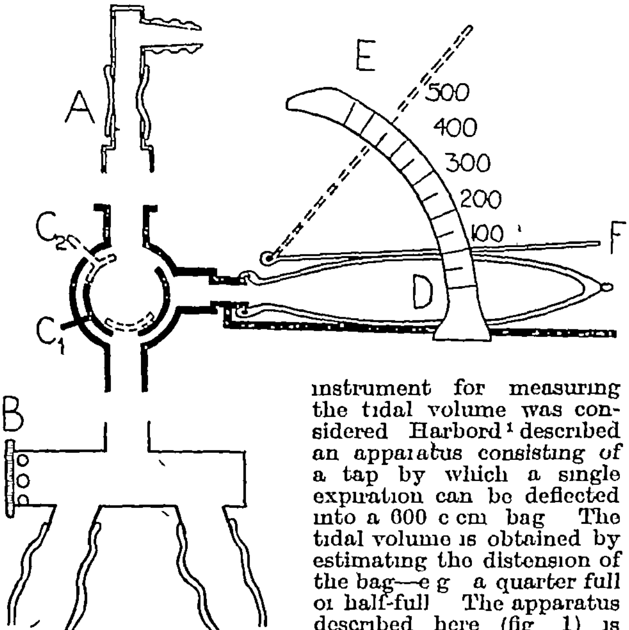


Fig 1—Tidal spirometer : A, endotracheal connection B, expiratory valve mount C rotating drum ; D bag ; E, scale ; F, 'Perspex' plate

A by pass is fitted between the endotracheal connection A and the expiratory valve mount B, it contains a rotating drum moved by a lever C When this is in position 1 the patient s respirations pass to and from the anæsthetic machine, when the lever is in position 2 respiration takes place in and out of a 600 c cm bag D A hinged 'Perspex' plate F re on the bag moves up and down with the respiration, a calibrated scale E is provided along which the move of the plate can be read

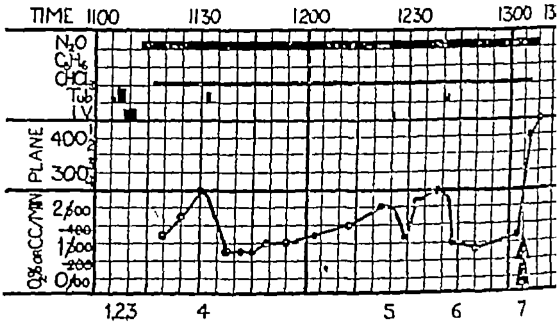


Fig 2—Upper portion of Nosworthy chart. Numbers on left in se plane ' and ' O₂% have been altered to show tidal volu c cm : this is given by lowest curve Injections : 1 tubarine 5 2 tubarine 15 mg 3, thiopentone 0 75 g 4, tubarine 10 m thiopentone 0 2 g 6 tubarine 7 mg 7, prostigmin 2 5 atropine gr 1/75

When in use the spirometer lies beside the pati head, if covered by the drapes these can be raise the short time required Anæsthesia is maintained in usual way, the additional dead space is 50 c cm measure the tidal volume the lever is moved into pos 2 If this is done at the end of inspiration, an expira will be caught in the bag, but it is better to press reservoir bag on the machine while the lever is mo to be sure that the spirometer bag will not collapse du inspiration, for this would give a false measurem It is generally sufficient to observe two or three res tions, the lever is then moved back to position 1 *the anæsthetic is continued* The circuit must be airt and a cuffed tube is best, but the instrument can be with a face piece if this fits closely In this way est tions can be made at the bedside The instrument also be placed on the anæsthetic machine, between reservoir bag mount and the corrugated tubing, wher semi-closed technique is in use

The tidal volume can be measured at regular inte —e g, between blood-pressure estimations The res tory rate should be counted at the same time in ca is desired to know the minute volume The tidal vol can be charted on the Nosworthy card in the sp marked "plane" and "O₂ %" An example (fig given of a record made during a partial gastrectomy, and the effects on the tidal volume of injections of 'Tubarine,' thiopentone, and 'Prostigmin' are shown

---

[1] Harbord, R P *Brit J Anæsth* 1948 21, 94

When this instrument has been used, an increase in the tidal volume has always preceded the return of muscle tone, and can be taken as an indication for a further injection of muscle relaxant The intensity and duration of the effect of the previous dose is of assistance in estimating how much more to give

Thanks are due to Dr John Gillies for his encouragement and assistance, the spirometer was made by Mr J P Morison of the department of anæsthetics, Royal Infirmary, Edinburgh

C T BARRY
M D Paris, D A

Reviews of Books

Virus and Rickettsial Diseases

S P BEDSON, F.R.C P, F R S, professor of bacteriology, London Hospital, A W DOWNIE, M D, professor of bacteriology, University of Liverpool, F O MACCALLUM, M.D, director of the virus laboratory, Central Public Health Laboratory, C H STUART HARRIS, F R C P, professor of medicine, University of Sheffield London Edward Arnold 1950 Pp 383 24s

The Pathogenesis and Pathology of Viral Diseases

Symposium held at the New York Academy of Medicine, Dec 14–15, 1948 Editor JOHN G KIDD New York Columbia University Press London Oxford University Press 1950 Pp 235 32s 6d

An Introduction to the Study of Viruses

K. M SMITH, F.R S, director of the plant virus research unit, Molteno Institute, Cambridge London Pitman & Sons 1950 Pp 106 10s 6d

THESE three books on viruses are all handy volumes, written by experts, and well produced But there the similarity ends

Bedson and his colleagues deal with only the virus diseases of man, and try 'to present a coherent readable account rather than an exhaustive treatise" In this country their book will be by far the most useful of the three The main facts are all there for senior students, bacteriological and public-health workers, and clinicians who want to keep up to date in this subject, and though the book is not primarily intended for those working on viruses it will be helpful to them nevertheless The scene is apt to change between the writing of a book and its publication, and probably the authors would today be less hopeful about the use of ultraviolet irradiation as a means of destroying hepatitis virus in plasma, and would say something about poliomyelitis in relation to inoculation, and more about the Coxsackie viruses. Epidemic keratoconjunctivitis, however, seems to be the only important human virus infection omitted The four introductory chapters, three of them by Professor Bedson, are particularly good

The book on virus pathology edited by John Kidd will appeal to a smaller circle, mainly of laboratory workers but it is full of good things R E Shope discusses the spread of viruses, illustrating his story particularly by references to some of the epidemiological puzzles he has himself helped to solve, T F Anderson gives a stimulating account of adsorption co factors in infection of bacteria by 'phages, and Wyckoff's descriptions and pictures show beautifully developments in the field of virus electron micrography Most of the other chapters are illustrated by well-produced photomicrographs, showing such things as the pathological changes caused by yellow fever, and various neurotropic viruses A chapter on cardiac lesions contains some little-known data, and Kidd himself writes well on proliferative lesions caused by viruses

In the third book Dr Kenneth Smith has had the idea—theoretically sound—of treating side by side the viruses attacking plants, animals, and bacteria He deals adequately with the plant viruses, but his knowledge of animal viruses is sporadic The virus field is now so extensive that no one author can hope to cover the whole of it

Primary Carcinoma of the Vagina

R G LIVINGSTONE, M D, formerly member resident staff, Gynæcological Division, Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 73 15s

IN 20 years, only 110 cases of this form of cancer were collected at the Memorial Hospital, New York—representing a low incidence, as reported elsewhere Clinical findings are well described in this little book, and the relative incidence of genesis from different parts of the vagina is given The notes on treatment by radiotherapy are of little use because of the failure to indicate the dose of irradiation received by the tumour Surgical treatment is now advised, but no long-term results are yet available The 5-year survival was 8 out of 85 cases, a figure resembling that usually quoted for this type of cancer, which for some reason is much harder to treat than cancer in the adjacent cervix

Health and Disease in the Tropics

CHARLES WILCOCKS, M D, F R C P, director, Bureau of Hygiene and Tropical Diseases London Oxford University Press 1950 Pp 200 15s

DOCTORS, whether they are practising in the tropics or not, will find this book useful, but it is written primarily for the lay administrator, the non-medical missionary, and in fact for anyone who lives in or proposes to live in a tropical country The administrator, whether in government service or commerce in the tropics, has to have a much greater knowledge of medical subjects than his counterpart in temperate-zones, partly because he may at any time find himself out of reach of medical aid, and partly because health—his own, his family's, and that of people for whom he is responsible—needs much more care than in a country with a well-organised public health service Dr Wilcocks opens and ends his book with homilies on collaboration all departments must work together, and to do that each must understand the point of view and difficulties of the others After a very simple exposition on the causes of disease, he discusses groups of diseases Treatment is given in outline only, nowhere is the reader encouraged to treat himself, and in some instances special warnings are given of the danger of attempting this There are useful chapters on housing, water supplies, drainage, and public health A section on organisation and personal protection concludes this sensible and informative book.

Therapeutic Radiology

GEORGE WINSLOW HOLMES, M D, former radiologist in chief, Massachusetts General Hospital, MILFORD D SCHULZ, radiologist at the hospital London Henry Kimpton 1950 Pp 347 52s 6d

THE opinions expressed in this book, the authors tell us, are very largely those of the tumour clinic of the Massachusetts General Hospital They have limited the discussion of radium therapy to ancillary procedures where there is a choice between radium and X rays the method using X rays has been described Bearing this limitation in mind, readers will find much to interest them in this description of radiotherapy as practised in a major American centre An early chapter, illustrated by coloured photographs, of the effects of röntgen rays on the living cell, shows the striking effects of excessive dosage—which may seem premature to the reader who has not yet been told the biological dosage recommended at the centre The choice of dose and technique is considered fully later, but the use of dose in air is allowed to confuse the calculation of depth-dose in relation to skin dose The sections on the treatment of tumours in various sites are sound The emphasis is rightly on surgery for cancer of the breast, but the condemnation of preoperative X-ray therapy seems rather sweeping For cancer of the oral cavity X-ray therapy is advocated in sites where radium is probably the better alternative, and in the chapter on diseases of the central nervous system the treatment of medulloblastoma is said to be merely palliative, though this tumour can be cured in the sense that patients have survived ten years without recurrence. The importance of radium therapy for cancer of the female genitalia is recognised, though with the method recommended serious high-dosage effects are likely to follow In general, some first-class accounts of clinical cases and the processes of malignant disease are not supported by good descriptions of radiotherapeutic techniques

Cell Physiology and Pharmacology

J F DANIELLI, professor of zoology, King's College, London London Elsevier, Cleaverhulme Press 1950 Pp 150 24*s*

THIS valuable book gives much information tersely yet readably The author, with considerable success, attempts to integrate biophysics, quantitative biochemistry, and quantitative pharmacology at the cellular level The work is based on a series of lectures delivered at University College, London, and directs attention to factors which are important for students of drug action It is not intended as an exhaustive study of the place of cell physiology in pharmacology

Documenta Ophthalmologica

Editors F P FISCHER, Utrecht, A J SCHAEFFER, Los Angeles, ARNOLD SORSBY, London Vol IV The Hague Uitgeverij Dr W Junk 1950 Pp 362 Dutch guilders 36 (or £3 7*s* 11*d*)

THE present volume is dedicated to Prof Karl Wessely on his 75th birthday It also carries news of the death of F P Fischer, one of the editors, at the early age of 52 It is to be hoped that this loss will not affect the excellence of this series of academic work

Outstanding in this volume are a critical analysis of the quanta theory of vision by M A Bouman, and a detailed record of twin research in ophthalmology by P J Waardenburg An extensive review of fundamental principles involved in the local application of ophthalmic drugs is given by A J Schaeffer, whose contribution is apparently a first instalment of a comprehensive survey of principles of ocular pharmacology Shorter studies on visual purple by Katharine Tansley, on protein deficiency by G B Bietti, on lighting and vision by R G Hopkinson, on tonometry by J S Friedenwald and R Moses, and on protective glasses in welding by G A W Rutgers are all critical reviews

Psychiatric Sections in General Hospitals

PAUL HAUN, M D, assistant professor of psychiatry, Georgetown University Medical School New York Architectural Record 1950 Pp 80 $4

Dr Haun points out that architects in the United States have often treated the psychiatric section of a general hospital as an afterthought He describes the various stages through which the architects and the psychiatrists should consult their way towards a satisfactory, if not ideal, unit

Approaching the matter from a functional rather than a structural standpoint, he considers all the phases of admission, examination, special investigation, nursing, and treatment which a patient will pass through, and then indicates how these purposes can be served The outcome of his way of looking at the architectural problem is a series of clear guiding principles, and considerable flexibility in their application This flexibility is effectively demonstrated in his systematic critical appraisal of eight designs for psychiatric wards in general hospitals, submitted by architects to the Veterans Administration The plan of each of these is shown, and first the desirable and then the undesirable features of the central area (or administrative offices) the "disturbed nursing unit, and the "quiet nursing unit" are listed below it, with reasons It is noteworthy that in these modern designs, reflecting the requirements of the most advanced American psychiatrists, a hydrotherapy unit and a solarium are never lacking a roof garden is also customary though the patients enjoy the use of occupational and similar facilities provided for the orthopædic and other patients on the lower floors The book contains also an interesting set of plans for a complete six floor general hospital, drawn up by two well known New York hospital architects

Though it will be long before we can hope to use these precepts and examples here in any but a few favoured instances, it is valuable to have the book, since it contains much that is suggestive for smaller psychiatric units of the kind that our hospitals will doubtless have to establish before long

A Manual of Cardiology (2nd ed Philadelphia a London W B Saunders 1950 Pp 355 25*s*)—T pocket size book gives clearly and soundly the essentials cardiology Prof T J Dry provides some of the informat in tables or lists, but elsewhere his style is very readab Common conditions get pride of place, but there are sh accounts of such rare conditions as amyloidosis and scle derma One or two small errors have crept in, but in t main the little manual is outstandingly good of its kind.

Whitaker 1951 (83rd annual vol London Whitake Pp 1156 12*s* 6*d*)—This, the largest Whitaker yet printe has recovered its pre-war promptness the new volum appeared before the old year died It casts its net as wid as ever, ranging from stamps to stars, from weights to weathe and from films to high finance The Festival of Britain h an article to itself, and is supported by sections on places historic interest in our chief cities and London's cathedr and churches, too, have found their way back Medical a academic readers will be gratified by the return of a list Oxford and Cambridge professors since 1939 we have be without this convenient inventory Perhaps we may ho that next year the learned clerks of London University w be added

Lipidoses Diseases of the Cellular Lipid Metaboli (2nd ed New York and London Oxford University Pr 1950 Pp 595 96*s*)—The difficulty of making pure p parations of the fats and lipoids, and the chemical similar of the various fatty acids found in them, has always made study of these substances a formidable task Neverthel immense progress has been made, and the chemistry of fats and sterols has largely been elucidated, though ther still much to be learnt about their intermediate metaboli Progress has not been so rapid in the study of the lip dystrophies, though a great deal of work has been done them in the last ten years The second edition of Pr Siegfried J Thannhauser's book reviews this progress in light of older work The opening chapter deals with physiology and chemistry of the fats and allied substanc discusses their absorption from the gut, and summarises steps by which the fats, proteins, and carbohydrates may converted one into the other within the body The grea part of the book is devoted to the problems in lipoid me bolism presented by the xanthomatoses, Gaucher's disea and the Niemann-Pick syndrome Von Gierke's glycog storage disease is also included by virtue of the associat hyperlipæmia and occasional secondary xanthomas fou in the skin Much of the detail is supplied by the autho own case records and chemical investigations The bo a mine of information, is well illustrated by photograp coloured plates and photomicrographs, and the stateme made are supported by numerous references

D D T and Newer Persistent Insecticides (2nd London Chapman & Hall 1950 Pp 632 50*s*)—The fi edition of this handbook was published in 1946 and contain numerous references to work completed in 1945 In the prese edition, however, there are very few references in the text lat than 1946—though the authors, Mr T F West D SC, and M G A Campbell, have appended a bare list of later reference Nevertheless, the book has doubled in size mainly owing thorough revision and numerous new passages The section on the manufacture and chemistry of D D T contain mo useful data on its solubility in various liquids, its chemic and physical stability its chemical estimation, and th composition of the technical grades A valuable list is giv of the various analogues of D D T, with notes on their insec cidal activity The chapter on formulation includes metho and formulæ which did not appear in the first edition, a these data are all set out in a practical way The autho have collected much information on the toxicity of D D to mammals but this would be easier to follow if it had be arranged under subjects Two defects of D D T first noticed 1947 are omitted One is the irritant action on mosquito of D D T treated surfaces, noted by Kennedy, and consider by Muirhead Thomson to interfere with control of *Anophe gambiæ* the other is the appearance, in many countries, house flies highly resistant to D D T There is a useful chapter γ B H C but only rather inadequate information on other n insecticides This subject however, is moving continuous and it is impossible for a textbook to be entirely up to da Criticisms of this new edition fade into the background behi its substantial advantages

THE LANCET

LONDON SATURDAY, JAN 27, 1951

This Influenza

This winter's epidemic of influenza bids fair to be the most extensive Britain has had since 1937—perhaps since 1929 The weekly death-roll in the 126 great towns in England and Wales has risen steeply from 54 in the week before Christmas to 102, 458, and now 890 in the week ended Jan 13 , the figures will presumably go still higher, and the steepness of the recent rise is disturbing So far, however, the fatal cases have been mainly in the over-55 age group and very largely confined to people already suffering from cardiac or other chronic illnesses In Merseyside the death rate is approaching its 1918–19 levels, but there is no suggestion in this epidemic of a high mortality among young adults such as was seen in 1918–19, despite the contrary reports in some newspapers

Thanks to the international studies of the last few years we can understand a good deal about the background of this epidemic Influenza virus A is always apt to cause more widespread trouble than virus B Since 1947 the older A strains have been replaced all over the world by a serological variant called A-prime, which was first detected in Australia in 1946 and in 1947 caused outbreaks in America and to a less extent in Britain and Sweden In 1948–49, information and strains of virus sent to the World Health Organisation World Influenza Centre in London made it possible to trace the spread of a virus right across western Europe This, too, was an A-prime strain, slightly different from that of 1947 Starting apparently in Sardinia in the autumn of 1948, the virus soon reached continental Italy, whence it spread to Austria, Switzerland, France, northern Spain, western Germany, and the Low Countries About New Year, 1949, it reached Britain, and so on to Denmark and Iceland Sweden and Ireland were just touched but hardly affected, and Britain was less affected than most of the Continent, perhaps because of her experience of a similar A prime virus in 1947 In June, 1950, local outbreaks of influenza due to an A prime virus were reported in central Sweden On previous occasions such local summer "flurries" have been followed by an autumn outbreak in the same area , so a special watch was kept and batches of experimental vaccine were prepared against the Swedish strain Sure enough, in November influenza appeared in Scandinavia—first in rural Denmark, then in northern Sweden, and soon in Oslo and all over Scandinavia The fact that the first appearance of the present epidemic in Britain was in Newcastle just before Christmas makes it likely that this had a Scandinavian origin Also in mid December, influenza appeared in Belfast and northern Spain It is still a matter for speculation whether the Merseyside outbreak came from Belfast There seem at any rate to have been at least three foci of origin—Scandinavia, Belfast, and northern Spain The infection is now spreading to Eire, up into Scotland, south to London and (perhaps from Scandinavia) into Germany, Belgium, Holland, and France , also from Spain to southern France Iceland and Greenland are affected, probably again from Scandinavia Since Britain and Scandinavia suffered less than the rest of the Continent in 1949 they might be expected to be relatively harder hit this time It will be interesting to see whether the United States become involved , they had a good deal of influenza last year when we had none, and their herd-immunity may still be valid Practically all the major European influenza this year is of the A type, the viruses isolated up to now being A prime strains No clinical infections of the classical severe type have been reported as yet

With proper perspicacity the newly formed general practitioners' section of the Royal Society of Medicine had planned a discussion on influenza for January 17 It was only too clear there that the vast body of knowledge about the influenza viruses built up in the last eighteen years has done little to solve the immediate problems of general practice Dr E P Scott, who opened the discussion, even brazenly suggested that influenza was "a disease of doubtful ætiology" (but perhaps he was deliberately "trailing his coat") Discussion centred largely on the differential diagnosis of influenza by clinical criteria from other febrile illnesses , for it was generally agreed that during an epidemic almost anything is liable to be diagnosed as flu It still does not seem to occur to clinicians to make use of the specific serological tests for influenza It is true that these tests are not applicable to diagnosis in the first few days of fever , but after ten days, when the doctor may be getting worried, they might well be helpful Considerable argument followed Dr C H Andrewes's plea for the abandonment of the misleading term "gastric flu" , Sir Horace Evans and others agreed that gastro-intestinal symptoms may occur in influenza but that epidemics predominantly gastro intestinal probably have nothing to do with true influenza Speakers differed on the advisability of using antibiotics or a "sulphonamide umbrella" in the more serious cases most were against their indiscriminate use It appears that, as in 1949, penicillin may be disappointing in fulminating cases, especially where staphylococci cause a complicating pneumonia

Current opinion on virus-vaccines seems to be roughly this Where a formolised vaccine against the prevailing type of virus infection is available it will give some, but not 100%, protection With better facilities for following the country-to country course of an epidemic, in future years we should know fairly definitely, as we have this year, what type to expect The problem is then largely economic A monovalent vaccine is likely to be better than a polyvalent one Ideally, manufacturers should keep stocks of vaccines against all the main types so that they can issue the appropriate one as soon as an epidemic threatens

B_{12} as the factor necessary for cure Yet we are not sure whether the most appropriate name for this ailment is not still that which **Pye Smith** gave it in 1883, the "idiopathic anæmia of Addison "[8]

If the numerous references given by **Robb-Smith** are arranged in decennial groups, it will be seen that three of the decades—1840–49, 1870–79, and 1920–29—contain as many papers of fundamental importance as all the others put together They correspond respectively with the high tide of the French clinical school and its repercussions in other lands, with the technical improvements of hæmocytometer and hæmoglobinometer, and with the new light brought by **Murphy**, **Minot**, and **Whipple** to a subject obscured by excessive attention to static morphology It is no new idea that knowledge advances not inch by inch but in sudden and exciting bounds, but nobody can say where the advance will come next It is a matter of opinion whether the next phase in hæmatology will be one of expansion or of mere consolidation We shall not emulate the **Bartlett** brothers in prophecy

---

Annotations

RUSSIAN PSYCHIATRY

The *Journal of the American Medical Association* recently deplored the fact that in the present world situation the publisher of a book on Soviet psychiatry should need to apologise to public opinion for producing it No such apology, one would like to think, is called for with the appearance here of copies of Wortis's collection of facts and documents on the state of Russian psychological medicine[9] English science, and particularly English psychiatry, are undoubtedly concerned to understand both their Soviet counterparts and Russia as a culture pattern, and the too brief period of friendly contact during the war suggested that neither, given the opportunity of contact, would prove incomprehensible The increasingly paranoid character of international relationships—and of international stereotypes—has also made a psychiatric and anthropological picture of the Soviet culture, its standards, and its motivations, highly urgent for all of us, and a study of Russian psychiatry which gave us a full picture of mental health in the Soviet Union, of the cultural attitude of medical science there, of the political background, and of the philosophical and sociological forces involved, would not fall far short of a complete psychosocial study of Marxism Leninism in action

Wortis's book is a heroic attempt to give a just account of the mind and practice of Soviet society as seen through its psychiatry As a collection of documents, bound together by a commentary which might be headed "how life appears to the intelligent Marxist," it is both informative and fairly comprehensive Yet in a society where conscious politicism and (Western sociologists would say) the unconscious forces which underlie it have been pressed so far and so fast, it is virtually impossible to assess psychiatric practice and ideas without wide discursions into general sociology, and without seeing the culture pattern in action The author of this book, though he learnt Russian, was prevented by the Berlin crisis from visiting the U S S R, and his work might therefore have been called "Soviet Psychiatry as Reflected in the Literature" Read as it stands, the picture is naive read, however, against the background of other studies, such as Crankshaw's *Russia and the Russians*, or Prof E H Carr's history of the Russian revolution, the documents at least are highly informative, especially those which deal with the radical change in the Soviet attitude towards marriage, discipline, sexual standards, education, and the validity of psycho analytical concepts, which coincided roughly with the Stalin Constitution Admirable as Wortis's attempt at a strictly factual picture may be, it is difficult to assess Soviet mental health *without reference to its public* manifestations—on the one hand the remarkable endurance of the war years and the hardships and achievements which preceded them, and on the other hand the outbreaks of paranoia against Trotskyists We should be obliged to consider factors like these in any assessment of our own society, and in dealing with one less familiar it is all the more necessary Wortis's own assessment is perhaps indicated by his comment that "a deep conviction in the power of reason is strikingly illustrated by the complete absence of a literature on the psychology of propaganda in the U S S R"

From the documents, a very clear picture of Russian psychiatric thought does nevertheless emerge In general it is Pavlovian, functional, based on a far more definite dogma of the mind body relationship than our own, intensely conscious of its social context Its therapeutics make full use of the integrative effects of work and social purpose, which are the strongest psychological cards of any order based on a strong corporate ideology in one case report we find a child therapist using controlled projection against an outside enemy (the Germans) as a deliberate outlet for fear and hate arising from the experiences of the occupation The Russian attitude to Freudian and post Freudian theory is very close to that of the more sceptical English eclectic, or even the older general practitioner, though it substitutes ideology for "common sense" as a ground for its scepticism The sexual orientation of Communism is an important marker for the social psychologist After a brief period of rather wild experiment this has become increasingly similar to that of the English middle class Homosexuality was made punishable in 1947, divorce by consent was ended earlier Capital punishment, after being abolished, was reinstated "by overwhelming public demand" for offences involving treason and sabotage[10] The interposition of attempts at reconciliation before the courts between would be divorcees may foreshadow a line of development in our own divorce law Giliarovsky's statement on normal sexual development[11] sounds remarkably familiar

> "Because psychological sex interests may often develop before physical sex maturity, precocious sexuality should be discouraged We cannot consider it normal for an adolescent of 14 to 16 to have practical experience in sex matters from the point of view of mental hygiene it may be regarded as generally undesirable for sex practices to begin before the age of 17 or 18 It is desirable that sex relations, as far as possible, take place without contraceptives and with a view to conception It is extremely important that the sex act produce complete psychological as well as physical satisfaction There is no reason to believe that sex abstinence in itself can cause any serious mental disturbance, let alone a psychosis "

The book contains little on the bitterly debated subject of the Soviet penal system

On the credit side, the successes of Russian psychiatry are essentially the successes of Communism The bitter political struggles and economic hardships of the early days, the struggle over collectivisation, the purges of the '30s, and the appalling character of the Nazi invasion have not succeeded in destroying the morale or the dynamic appeal of Communism, and Russian psychiatry can in exploiting the integrative powers of the ideology, can effect a synthesis of medicine and social outlook which is far harder to achieve in any culture that has a less intense sense of social purpose. These successes have been gained at the price of intellectual rigidity, and of the forfeiture of the critical approach to psychosocial medicine and to the dynamics of power on which we in Western cultures today pin much of our hope of social progress. There is no doubt, however, that such an ideology provides, to the young in particular, a source of enthusiasm comparable to that derived from the major proselytising religions, and very similar in structure. Perhaps the rudest shocks to those unacquainted with Soviet scientific polemics (or with the theological debates of the English Puritans) come from the appendices to Wortis's book, containing criticism of psychological textbooks on the grounds of objectivity vis à vis the class struggle.

---

[8] Pye Smith P H *Guy's Hosp Rep* 1883, **47**, 219

[9] Wortis J Soviet Psychiatry Baltimore 1950

[10] Karpinsky, V The Social and State Structure of the U S S R Foreign Languages Publishing House Moscow 1950

[11] Giliarovsky, V A *Psikhiatria* Moscow 1942

Psychiatry in England can learn much, both from the refusal of Marxist psychiatry to dissociate social, political, and mental health, and from the history, successes, and blemishes of Communism in practice. It is on every count essential that we should understand modern Russia, and that we should do so as scientific observers, despite the difficulties imposed by the suspicions and the propaganda of both sides in the present international tension. For this reason if no other, Wortis's book is valuable to all interested either in psychiatry or in political psychodynamics.

FAMILY STUDIES IN CHILD HEALTH

THE increasing emphasis on child health is one manifestation of the importance now attached to preventive medicine. The conception of long-term field studies of the child in his natural environment is fairly new. The most notable are those being conducted in Newcastle upon Tyne by Sir James Spence, and in Luton by Dr. R. M. Dykes, with their respective teams. These projects are already yielding a rich harvest of facts which will prove of great value in framing enlightened health policies. Dykes[1] reviewed the health of the 1498 infants born in Luton in 1945 who could be observed throughout the first year (these comprised 79% of the total births) and showed that constitutional factors greatly influence child health, and also that the infant-mortality rate is a more sensitive index of social standards than the infant morbidity rate.

The carefully planned domiciliary study of the child which is being carried out in Newcastle is probably the most comprehensive of its kind ever to be undertaken. The objects and methods of this investigation were described in Boston last year by Spence,[2] who discussed some of the data yielded by the first year's work. After tracing the evolution of "preventive pædiatrics" and mentioning the importance of medical statistics, hospital pædiatrics, and laboratory research, he emphasised that much further progress can be made by field workers who go outside the hospitals into the community, to study the incidence and spread of disease, the effects of social conditions on disease, and the control of disease and promotion of health by social environment. He deprecated the idea that field work is something entirely divorced from clinical and laboratory medicine, and suggested that a considerable proportion of those who work in social medicine should be clinicians and laboratory workers who follow their problems into the field when necessary. He pointed out that field inquiries are laborious, diffuse, and difficult to control with scientific standards—these are indeed the main reasons for their former neglect. He also asserted that, although research on some aspects of social medicine concerned with family life can best be conducted by a general practitioner who lives in the community as the family doctor and keeps records of each individual from year to year and from one generation to another, the isolated inquiries of a general practitioner are applicable only to limited subjects; moreover, few general practitioners have the time, training or inclination for such work. For particular purposes such as those which the Newcastle workers are pursuing, efficient organisation and team work are necessary.

The Newcastle city health authorities have shown themselves anxious to coöperate with the university department of child health, the children's hospitals, and the laboratory services in field research to improve child health. An initial coöperative investigation into the causes of infant mortality in Newcastle in the year 1939 was directed by Miller.[3] The most notable finding was wide disparity between notified causes of death and actual causes as revealed at necropsy—a finding that indicates the inaccuracy of vital statistics relating to causes of death in infancy. A domiciliary study of morbidity in the first eight years of life was inaugurated in 1947; the work was greatly helped by the team spirit and technique evolved during the earlier mortality investigation. The main object was to observe, against the background of the home, the acute infective illnesses of young children—their incidence, clinical types, and results. Other objects were to bring those working in wards and laboratories into daily contact with field workers, thus broadening their concepts of health and disease; to provide relevant local facts with which to freshen clinical teaching; to guide health programmes; and to create a method for giving a contemporary picture of disease, verified by statistics and direct clinical observation, which would reveal new problems for research. It was decided to study from the day of birth a sample of 1000 infants—one-sixth of Newcastle's annual births. Altogether 1142 infants, born in May and June, 1947, were selected, representing a cross-section of all social groups. The team of investigators consisted of one pædiatrician who devoted most of his time to the research; two more senior pædiatricians for consultation; two clerks; and five specially trained health visitors, who were entrusted with much of the intimate observation and research. Each week's collected material was discussed at a Saturday conference attended by the medical officer of health and others concerned. As Spence aptly remarked, this study of 1000 infants inevitably became a study of 1000 families.

Although this investigation has not yet reached the half-way point it has already yielded much valuable information. The records show in detail how 1000 families drawn from all social classes live, how they react to the problems of life, how they avail themselves of the health services, how the children are nurtured in body and mind, what their activities are, and the relation of these to others in the family. By the end of the first year 967 (85%) of the children remained in the investigation; 44 had died, and 125 had removed from the city. In only 6 instances had coöperation been lacking. The study is now in its fourth year. The main object of pursuing it for eight years is to study the familial pattern of disease, particularly respiratory conditions. It is already apparent that the intrafamilial method of clinical investigation yields a simultaneous view of infectious disease—notably subclinical varieties—in other members of the family which could not otherwise be studied. Regular tuberculin testing is revealing exact information about the tuberculisation of the group.

From this work Spence has already drawn the broad conclusion that over-emphasis on diagnostic medicine diverts attention from the detailed study of the sequence of clinical events that make an illness, and that a scientific study of this sequence of events, minutely observed and carefully recorded, is the method of the natural scientist which becomes a powerful instrument in the training of the young clinician Such a broad approach to the study of life—particularly child life—is like a breath of fresh air in these days of ultrascientific medicine when many students, and their teachers, cannot see the wood for the trees

---

[1] Dykes, R. M. Comparative Study of Infant Sickness and Infant Mortality in Luton. Luton, 1950. See *Lancet*, 1950, i, 453.

[2] Spence, J. C. *New Engl. J. Med.* 1950, **243**, 205.

[3] Miller, F. J. W. *Lancet*, 1942, ii, 269.

BEDPAN EXERCISE

As a labour saving device the bedpan is a total loss Patients have known this all along, and the news is now reaching the doctors, and even a few of the hospitals Dr J G Benton, Dr Henry Brown and Dr H A Rusk[1] have lately been measuring the energy expended by patients on the bedpan and comparing it with that expended on the bedside commode They studied the oxygen consumption of patients in these two situations by means of a closed circuit metabolism apparatus Since there were psychological and other obstacles to the study of patients during actual defæcation, the subjects were asked to "bear down" 10 times when seated first on the bedpan and later, after a rest, on the commode The tests were conducted in a small quiet room and the patient was screened off from the doctor, who could nevertheless observe him through a crack Of the 28 patients studied 15 had cardiac conditions, and the remainder were either normal or had other disorders The tests showed that in all patients there was a consistently greater oxygen consumption for performance on the bedpan than on the commode, and that there was no improvement with practice The rise above resting levels was, in the cardiac patients, 50 7% higher on the bedpan than the commode, and in the other subjects 48 4% This finding confers the blessing of science on the universal opinion of those who have used a bedpan If we wish to spare patients, and especially cardiac patients, we will give them a bedside commode, if we wish them to use half as much energy again we will insist on the bedpan

NEUROLOGICAL COMPLICATIONS OF DISSECTING ANEURYSM

WITH dissecting aneurysms of the aorta neurological *involvement is not uncommon, and its presence may* help in diagnosis In 1944 Weisman and Adams[2] described 11 confirmed cases of dissecting aneurysm with prominent neurological dysfunction This was associated with ischæmic necrosis of the peripheral nerves, the spinal cord, or the brain With necrosis of the peripheral nerves the circulation through the main artery of the limb was impeded, with a pulseless cold extremity, weakness, anæsthesia, and loss of tendon reflexes When the blood supply of the spinal cord was affected a transverse lesion of the cord developed rapidly, with flaccid paralysis, sensory impairment up to a spinal level, and loss of sphincter control Impairment of the cerebral blood supply resulted in hemiplegia often accompanied by confusion, stupor, or coma, and at times a "carotid hemiplegia" with blindness on the side opposite to the hemiplegia Weisman and Adams showed that the cause of the neurological disturbance was either extension of the dissection into one of the major branches of the aorta (such as the common carotid artery) with occlusion of the lumen, or severance of the smaller branches of the aorta by the dissection, this was the commoner cause of interference with the blood supply of the spinal cord Moersch and Sayre[3] have analysed the Mayo Clinic records of 26 verified cases of dissecting aneurysm. Clinical neurological signs were present in 12, but probably this does not truly reflect the incidence of neurological complications, since 9 other patients died so suddenly that neurological examination was impossible. They found ischæmic lesions of the spinal cord and brain but no convincing evidence of peripheral nerve lesions

These studies indicate that dissecting aneurysm of the aorta is a possible diagnosis when a sudden cerebral or spinal disturbance is associated with other symptoms such as severe pain in the chest or abdomen, perhaps radiating to the back It is of historical interest that probably the first recorded patient with a dissecting aneurysm and cerebral involvement was King George II who "was found fallen on the ground, speechless and motionless,"[4] and in whom post mortem examination showed a dissecting aneurysm of the ascending aorta

ANIMAL OR VEGETABLE?

FOR some of us the true tragedy of Kongwa lies not in the sad loss of £36 million but in the harm that the failure may do to other projects which demand something more than a parochial outlook on food problems We are told there is nothing so shy as a million dollars, and a million dollars once bitten can be expected to be twice shy There are others who feel the most recent reduction of the meat ration as another tragedy It is useless to point out to such people that they have available, often quite cheaply, abundant supplies of animal protein in such forms as milk, cheese, fish, and the rabbit or hare. For them "protein" means a pre 1914 steak

Things being as they are, the Nutrition Society could not have chosen a more topical theme for its symposium in London on Jan 20 than the comparative merits of animal and vegetable foods Problems relating to the supply of food have a fascinating complexity As D A Boyd showed, cost in money, man power, and acreage must be balanced against the value of the foods as sources of energy, protein, vitamins, and "waste products" which can be utilised to provide more foods. By setting the balance more correctly, we are now producing for human consumption nearly twice as much vegetable food as before the late war Animal products have also been increased in total amount, despite large reductions in imported feeding materials The dairy cow, which needs little protein in its diet because it can synthesise amino acids in its rumen, is largely responsible for this increase K L Blaxter has calculated that the cow can take, from cereal, residues of which a high proportion are inedible by man, and manufacture from them, and yield in its milk, enough lysine to make up for the shortage of this amino acid in the original cereal The cow needs much attention, but repays the extra *cost of labour by the high value of its produce* Other creatures such as the hen need even more attention, and, as K J Carpenter pointed out, must be provided with rations rich in well balanced protein Such a diet is usually costly, but the cost can be reduced by the skilful mixing of proteins from different sources This is what we do for ourselves when we insist on a "good mixed diet" G R Tristram showed that many plants, if they were eaten entire, would provide at least a good mixture of amino acids It is the specialised organs such as the seed which have the incomplete mixtures

If the protein in the diets of newly weaned children is inadequate the syndrome of kwashiorkor, or malignant malnutrition, may appear Dr Lucy Wills has obtained excellent results by treating this disease with large amounts of the protein of dried skim milk Cow's milk and other agents reported to cure the disease may act by virtue of their specific amino acids or the vitamin B_{12} which all of them probably contain Some experimental and theoretical evidence which supported this concept was advanced by Dr R F A Dean He has fed children with mixtures of soya and various cereals, and is convinced that diets could be constructed exclusively from plant sources, on which young children could grow rapidly and remain healthy His mixtures lacked vitamin B_{12}, he has found that the addition of this improves their nutritive value for rats, and it would probably improve their value for children The mixtures were given their original scientific trials by Miss Harriette Chick, who suggested that many similar mixtures had great possibilities, especially in child nutrition Even protein free extracts of some plants have, it seems, remarkable powers of supplementation when added to plant proteins

---

[1] *J Amer med Ass* 1950 **144** 1443
[2] Weisman A D Adams R D *Brain* 1944 **67** 69
[3] Moersch F P Sayre, G P *J Amer med Ass* 1950, **144** 1141
[4] Nicholls F *Phil Trans roy Soc London* 1761 **52**, 265

The meeting demonstrated the broad range of the modern science of nutrition Scientific knowledge is often many years in advance of its application to human purposes Do our administrators and their financial advisers realise that in nutrition the need to apply our knowledge is urgent ?

TOO FEW BEDS

THE London Local Medical Committee has published a resolution urging "that in view of the amount of illness at the present time, unprecedented since the start of the National Health Service, and the consequent increased need for hospital accommodation in London for acute cases, every step should be taken to provide beds by all possible means" Among the means suggested are exclusion from hospital of normal maternity cases, postponement of non urgent operations, and temporary crowding of wards

Certainly the incidence of sickness is now unusually heavy Dr Frank Gray, secretary of the committee, points out that one in three of the cases offered to the Emergency Bed Service is not admitted to hospital This is a serious matter, though fortunately the chances of getting a patient admitted are better than this ratio suggests, since the doctor commonly makes arrangements directly with the hospital, indeed the service is only provided as a means of helping doctors when direct approach has failed Inquiry of the service shows that in the first week of January applications for admission of acute cases were 32% higher than at the start of last year There were 1792 applications, with 1058 admissions, the number admitted is actually greater than in the same week of 1950, owing, no doubt, to the gradual increase in the number of staffed beds During the same week the service received 571 applications for admission to infectious disease hospitals, and about the same proportion were admitted This is the first time since the start of the N H S that there has been any serious difficulty in gaining admission for patients with infectious diseases This difficulty is due primarily to the unusually high prevalence of infectious diseases, and notably of measles, but probably it is due also in part to the recent appropriation of infectious disease hospitals for general use

Except for the closing of maternity wards to normal confinements, the remedies suggested by the London Local Medical Committee are already being put into operation The regional boards have called for a reduction in the intake of cases from waiting lists, and many hospitals have spontaneously started crowding their wards Whether in the long run this is a wise step remains doubtful In some large hospitals it has an evil reputation, and the gain in the numbers of nursing staff achieved through determination not to overwork nurses should not lightly be endangered Perhaps by next winter criteria for definite stages of emergency could be worked out, at each stage a definite degree of overcrowding would be called for, and this would equally definitely be cancelled as soon as the emergency passed Such a system would ensure that the willingness of nurses was not exploited unnecessarily

RELIEF OF POSTOPERATIVE PAIN

THE anæsthetic used to be the worst part of having an operation, but now the focus of dislike has changed to the postoperative period Pain, particularly after abdominal and thoracic operations, is the worst feature of this period, and its relief must be a first concern The favourite remedies are morphine and its synthetic substitutes (which were discussed in our leading article last week), but their value is sometimes offset by such undesirable side effects as respiratory depression and vomiting Many alternatives have been suggested, two very promising ones are intravenous procaine and intravenous alcohol With each of these two methods, however, careful supervision is necessary if overdosage is to be avoided Now Blades and Ford [1] suggest another rather novel method of relieving postoperative pain, which they have used successfully after thoracotomy —an operation commonly followed by severe pain Fine plastic tubes made of 'Aeroflex' are placed along the edge of each of four ribs bordering the incision The tubes are held in place with a few fine sutures, and the end of each tube is brought out at the anterior angle of the wound Through these tubes, 2 ml of procaine solution is injected every two to three hours At the same time morphine is given, if necessary, for its euphoric effect These workers are convinced that the procaine injections produce very great and hitherto unobtainable relief Pain disappears immediately after the injection, and the patients are able to move about in bed, and earlier ambulation is possible The tubes are left in situ for nine days, and the wounds heal well and without infection

MR BEVAN AND MR MARQUAND

THE new Minister of Health, unlike Mr Aneurin Bevan, will not be a member of the Cabinet Some may welcome this as evidence that the health services are being taken out of politics, but in the next few years, when Defence will demand an increasing share of the national resources, we may have cause to regret the loss of influence that Mr Bevan's departure entails Mr H A Marquand, however, may prove an able advocate of efficient medical care, and he comes to the Ministry at a time when a fresh mind and a conciliatory disposition can do much good His chief task is to improve the balance of the service by giving more weight to the needs of public health and general practice—if only because failure to meet these needs is partly responsible for the strain on the hospitals As will be seen from the brief biography we print on p 243, he brings to these problems a valuable experience not only of economics but of human relations and of social services, and he has won approval at the Ministry of Pensions It remains to be seen whether the N H S will gain or lose by the removal of housing from the control of the Minister of Health when a change of this kind has been debated and resisted for years it is somewhat irritating to have it made overnight, to facilitate a Cabinet reshuffle, and without detailed consideration of the consequences As has been sensibly suggested, a logical sequel to the present changes might be the union of the Ministry of Health with the Ministry of National Insurance in a Ministry of Social Services—over which Mr Marquand (elections permitting) would be well qualified to preside Meanwhile, he has more than enough on his hands without asking for more The medical profession will earnestly wish him success in what he has to do

---

[1] Blades B, Ford W B *Surg Gynec Obstet* 1950 91, 524

Special Articles

A SOCIOMEDICAL STUDY OF TWO HUNDRED HOSPITAL MEDICAL PATIENTS

JOHN PEMBERTON
M D Lond , M R C P
SENIOR LECTURER IN SOCIAL MEDICINE,
UNIVERSITY OF SHEFFIELD

THE following study was undertaken with two general aims (1) to find out how a random sample of teaching hospital medical outpatients and inpatients fared after discharge from hospital, and (2) to assess what part environmental influences had played in the ætiology of their illnesses The wards and outpatient department concerned dealt with all general medical illnesses except diabetes

METHODS

It was decided to try to obtain detailed sociomedical records of 100 outpatients and 100 inpatients To this end, a letter was sent to an unselected consecutive series of 146 outpatients and 144 inpatients, whom I had examined one year previously, asking them to come to the hospital for a follow up examination In the case of inpatients who had died in hospital, the letter was sent to the nearest relative In response to the letter, 100 outpatients, 88 inpatients, and near relatives of 12 inpatients who had died came to the follow up clinic. The distribution of the commoner diagnoses among the 47 outpatients and 43 inpatients who failed to attend was similar to that among the patients who were investigated, except that 9% of the non attenders had cancer compared with 1% of those who attended, and 7% of the non attenders had pulmonary tuberculosis compared with 1 5% of those who came

Each patient who attended the follow up clinic had a consultation lasting about three quarters of an hour The diagnosis was reviewed, the outcome of the illness assessed, and a detailed account of the social environment obtained This included an occupational history since leaving school, details of economic status, diet, housing conditions, leisure activities, and a family history The patient was also asked about his childhood, his married and working life, and an attempt was made to assess the quality of his more important human relationships The interviews were conducted in private, and all but one or two of the patients willingly gave all the information required I was often impressed by the additional light thrown on these medical cases by privacy and adequate time To supplement the case history, a relative was interviewed separately in 29 cases, in 8 cases a visit to the home was made, and in 10 cases the patient's place of work was inspected

TABLE I—DISTRIBUTION OF THE 290 PATIENTS BY AGE AND SEX

—	Years							
	0– %	10– %	20– %	30– %	40– %	50– %	60– %	70 + %
Male (161)	0 6	3 7	13 0	20 0	27 3	19 9	13 0	2 5
Female (129)	0 8	7 7	14 7	26 4	22 5	17 0	8 5	2 4
Total (290)	0 7	5 5	13 8	22 8	25 2	18 6	11 0	2 4

GENERAL PICTURE OF MEDICAL ILLNESS IN A TEACHING HOSPITAL

Age and Sex

For this part of the analysis, the 90 patients who failed to attend because of death or some other reason have been added to the 200 who attended, thus making a consecutive unselected series The whole group contained 144 inpatients and 146 outpatients The age and sex distribution of the group is shown in table I

Diagnosis

Table II shows the diagnoses of the 290 patients. The commonest illnesses found, including cases with multiple diagnoses, were peptic ulcer and non ulcer dyspepsia* 23%, psychoneurosis 13%, pneumonia, bronchitis, and bronchiectasis 8 3%, essential hypertension (including its complications such as cerebral thrombosis) 8 2%, rheumatic heart disease 4 8%, rheumatoid arthritis 4 1%, and pulmonary tuberculosis 3 1% The primary diagnoses were classified under the following headings

TABLE II—DIAGNOSES OF THE 290 PATIENTS

Somatic		Psychosomatic		Psycho neurotic	Psychotic	Multiple diagnoses
Rheumatic heart disease	12	Peptic ulcer	33	28	Schizophrenia 1 Suicide 2	20
Cancer	11	Dyspepsia	33			
Bronchitis emphysema and pneumoconiosis	9	Essential hypertension (including coronary disease 4 cerebral thrombosis 1, malignant hypertension 1)	23			
Pulmonary tuberculosis	9	Rheumatoid arthritis	11			
Nephritis	5	Asthma	8			
Lobar pneumonia	4	Nervous diarrhœa	5			
Bronchiectasis	3	Spastic colon	4			
Pernicious anæmia	3	Rheumatism	4			
Thrombophlebitis	2	Thyrotoxicosis	4			
Hydronephrosis	2	Ulcerative colitis	2			
Tænia saginata	2	Migraine	2			
Cirrhosis of the liver	2 2	Fibrositis	5			
Miscellaneous (single cases)	30	Epilepsy	2			
		Miscellaneous (single cases)	7			

	Somatic	Psycho somatic	Psycho neurotic	Psychotic	Multiple diagnoses
	%	%	%	%	%
146 outpatients	18	57	17	1	7
144 inpatients	46	41	4	1	8
290 all patients	32	49	10	1	8

These categories tend to merge into each other, but it was considered worth attempting to separate them to obtain a clearer idèa of the ætiology of the different illnesses

For grouping the psychosomatic cases, Halliday's classification (1943) was largely adopted and his definition used as a guide "a bodily disorder whose nature can be appreciated only when emotional disturbances—i e., psychological happenings—are investigated in addition to physical disturbances—i e , somatic happenings." The most important diseases included in the psychosomatic group were peptic ulcer and non ulcer dyspepsia, essential hypertension, "rheumatism," spastic colon, nervous diarrhœa, ulcerative colitis, and hyperthyroidism The psychoneurotic group included those patients whose symptoms consisted mainly in a morbid degree of anxiety and who showed no evidence of a physical disorder

The dominating importance of psychosomatic and psychoneurotic illness in current medical practice was confirmed in this series of cases

Duration of Illnesses

Table III shows that approximately four fifths of the 200 patients who attended the follow up had had symptoms of their illness for more than a year before coming to hospital A third had had symptoms for five years or more

---

* Non ulcer dyspepsia covers patients referred to the hospital as possible cases of peptic ulcer in whom there was no radiological evidence of ulcer and no reflex cause of dyspepsia such as chronic cholecystitis

TABLE III—DURATION OF SYMPTOMS BEFORE COMING TO HOSPITAL IN THE 200 WHO ATTENDED

—	Years					
	0–1	1–2	2–3	3–4	4–5	5 +
100 outpatients	17	29	15	1	3	35
100 inpatients	23	31	5	8	3	30

Results of Treatment

It is perhaps inaccurate to describe the health of a patient a year after receiving treatment recommended at a hospital as the result of that treatment. His improvement or deterioration in health is often due to more potent causes. The patient's present condition was assessed mainly on his own and, where possible, a relative's report, unless these conflicted with the results of physical examination. If a new complaint had developed, this also was recorded. The so called results of treatment are tabulated in table IV.

It will be seen that in the whole outpatient group, 17% were assessed as cured, 48% improved, 24% about the same, 7% worse, and 4% dead. In the inpatient group, the figures were 22% cured, 31% improved, 16% about the same, 11% worse, and 20% dead. Perhaps the most significant finding was that about three quarters of all these patients still had their original complaint; they had neither died nor been cured of it. Of the 200 who attended, 36 had developed a new complaint. Three quarters of these 36 patients had passed from one psychosomatic or psychoneurotic complaint to another, a point which was made by Ryle (1939) in the Goulstonian lectures on the visceral neuroses. It seems that in many illnesses the "disease" is a necessary component of the patient's adaptation to his environment and to get rid of the disease either the "patient as a person" or his environment must be changed.

TABLE IV—RESULTS OF TREATMENT IN THE 200 PATIENTS WHO ATTENDED AND THE 53 WHO REPLIED BY LETTER

—	Cured	Improved	Same	Worse	Dead	New complaint
% of 128 outpatients	17	48	24	7	4	16
% of 125 inpatients	22	31	16	11	20	13

RELATIONS BETWEEN ILLNESS AND SOCIAL ENVIRONMENT

The results of treatment of many of these medical illnesses were disappointing. The detailed inquiry into the social history was undertaken to try to ascertain the contribution to the ætiology of the illnesses made by environmental and hereditary influences and the extent to which the illnesses might have been prevented by healthier living conditions.

Often, of course, it was impossible to assign an environmental or hereditary cause to the illnesses with any certainty. In a good many cases a combination of more than one environmental cause, with or without an inherited susceptibility, was no doubt responsible. Environmental conditions to which especial attention was paid were occupation, housing, nutrition, the use of leisure, and human relationships. Table V shows the cases in which one of these factors seemed to be of dominant ætiological importance.

Unhealthy occupational conditions were judged to be the main cause of illness in 5.5%, bad housing conditions in 3.5%, inadequate diet in 0.5%, misuse of leisure in 1.0%, and unsatisfactory human relationships (in which inherited disposition may have been an important factor) in 43.5%. There were no cases of known hereditary disease, but in 9% of the cases hereditary factors were considered important ætiologically. In 46%, there was no *apparent* environmental or hereditary cause of the illness. If anything, the numbers assigned to each main ætiological category have been underestimated, for only the more obvious cases were included.

Occupation

The 11 cases in which the patient's occupation was judged to be the chief cause of the illness are shown in table VI. All but 1 were men. The exception was a woman who developed lead poisoning on taking up war work at the age of 65. There were 4 cases of silicosis or miner's pneumoconiosis, 3 of chronic bronchitis and emphysema, 2 of gastric ulcer, and 1 of dyspepsia.

TABLE V—ENVIRONMENTAL AND HEREDITARY INFLUENCES AS MOST IMPORTANT ÆTIOLOGICAL FACTORS

—	Occupation	Diet	Housing	Leisure	Faulty human relationships	Heredity	No apparent environmental or hereditary cause
100 outpatients	6	0	2	1	52	0	39
100 inpatients	5	1	5	1	35	0	53
Total %	5.5	0.5	3.5	1.0	43.5	0	46

Diet

Only 1 case in the series was obviously due to a deficient diet. The patient was a bachelor, aged 60, who had scurvy. He had given up work about six months before and did his own cooking on a gas ring in the single room where he lived. He did not bother to cook any vegetables.

There may have been other cases in this series where a poor diet was an important ætiological factor; in some of the infective illnesses perhaps, in the 12 cases of rheumatic heart disease, or in the 9 cases of pulmonary tuberculosis. Without an accurate analysis of the diet before the onset of the illness it was impossible to assess its importance. In 2 cases of dyspepsia the rushed conditions under which the meals were eaten seemed to be important.

TABLE VI—OCCUPATION AS CHIEF CAUSE OF ILLNESS

Sex	Age	Diagnosis	Occupation
F	65	Lead poisoning	Painting. Poor cleansing facilities
M	44	Miner's pneumoconiosis	Coalminer (ripper) for 20 years
M	38	Miner's pneumoconiosis	Coalminer (ripper) for 17 years
M	55	Silicosis and bronchitis	Gannister crusher 30 years
M	65	Miner's pneumoconiosis	Coalminer (ripper) for 19 years
M	55	Chronic bronchitis and emphysema	Coalminer for 21 years
M	55	Chronic bronchitis and emphysema	Hot drop stamper. Exposed to dust gases fumes and big temperature differences
M	71	Chronic bronchitis and emphysema	Street hawker
M	34	Gastric ulcer	Foreman responsible for rapid construction of aerodrome runways in early part of the war
M	45	Gastric ulcer	Doing two jobs. Police war reserve 8 hours a day and commercial traveller the rest
M	55	Stress dyspepsia	Doing three jobs. Coalminer small holding and keeps a shop

TABLE VII—BAD HOUSING AS CHIEF CAUSE OF ILLNESS

Sex	Age	Diagnosis	Housing
F	16	Rheumatic fever	7 sleeping in two bedrooms. No bath; outside w.c.; damp ceilings falling
F	14	Rheumatic fever	Shares bedroom with her 5 sisters. No bath; outside w.c. Damp
M	17	Nephritis	12 sleeping in two bedrooms. No bath; outside defective w.c.
M	10	Bronchiectasis following 2 attacks of pneumonia	Condemned back-to-back slum house. 4 in one bedroom. Outside w.c.
F	12	Acute nephritis	Rural slum house. Very damp. 11 share three bedrooms. Outside midden
M	48	Anxiety state and essential hypertension	Living in his mother's house. Wife and mother do not speak to each other
M	25	Nervous dyspepsia	Living in in-laws' house. 10 of them in all

Housing

In 7 (3.5%) of the cases bad housing was considered the chief cause of the illness. The diagnosis and housing of these cases are listed in table VII.

The homes of the 2 patients with rheumatic fever and the 2 patients with nephritis listed in the table were visited. All 4 were overcrowded and insanitary. The families were large and a large proportion of the brothers and sisters had had illnesses of the streptococcal or pneumococcal group (table VIII).

One of the patients, a girl, L.M., aged 14 (rheumatic fever), lived in a house which was one of a terrace of four-roomed slum houses, about eighty years old. The front room opened on to the street and was used as a bedroom by Mr. and Mrs. M. Mrs. M., who had diabetes and a colostomy following an operation for carcinoma of the rectum, was in bed. The floor of the back kitchen had dropped about 2 in. below the wainscot and the rain came in above the lintel of the door. The water supply to the house was through one slow-running cold tap over the kitchen sink and the w.c. was at the back of the house across the yard. In the back bedroom was one bed where the two boys slept. One of these also had rheumatic heart-disease. In the front bedroom, the six sisters, including the patient, slept in two double beds. There were no sheets or pillow cases, no floor coverings, and no furniture in the bedrooms other than the beds. Each of the rooms measured about 10 by 8 ft. The patient and her brother who had rheumatic heart-disease gave a history of repeated attacks of tonsillitis and quinsy.

Most of the illnesses in which bad housing was considered the chief cause resulted from infection, but the last two cases (table VII) showed how the psychological strain of crowded housing conditions can aggravate or cause illness.

Mr. J. N., aged 25 (nervous dyspepsia), was living with his wife and one-year-old baby in lodgings when first seen. The diagnosis was nervous dyspepsia which he had had for about one month. His wife was pregnant, and, because of this, they had been asked by their landlady to find other accommodation. When seen a year later, he was still getting bouts of epigastric pain. The four of them were now living at his mother-in-law's house with her and his brother-in-law's family of five. There were three bedrooms and an attic. He, his wife, and his two children slept in the attic. He and the baby's crying got on his mother-in-law's nerves, and she had told them to leave. He went to bed at 7 or 8 P.M. to get out of the way.

This patient was a sensitive conscientious man whose mother had died when he was 3. It is possible that a more robust personality might have remained well in his circumstances, but it is equally likely that if he and his family could have had a house of their own he would not have become ill.

Leisure

There were two patients with chronic alcoholism, both of whom had had venereal disease. Misuse of leisure might be regarded as the chief cause of their illnesses. In both, however, there were also potent psychological causes.

Mr. W. E., aged 64, lost his mother when he was 10, and his father remarried when he was 17. His father was a heavy drinker. The patient acquired gonorrhœa at 17, resulting in his present urethral stricture. He became a heavy drinker in early adult life and developed delirium tremens during the pneumonia for which he was admitted to hospital.

Mr. W. L., aged 51, had very strict parents. He joined up at 17 in the 1914–18 war and acquired syphilis soon after. Had gonorrhœa and has been treated for urethral stricture. Discharged from the Army with neurasthenia. Has been drinking heavily ever since. He is a steel-painting contractor and says he is spending £3 10s. a day on drink. He was in a state of great anxiety about his heart when seen, although, apart from a systolic pressure of 170 mm., nothing abnormal was found. He produced the following letter which he said a doctor in another town had given him three years before:

> Dear Mr. L.,
> I examined you today. You are suffering from a serious disease of the heart threatening paralysis. You are only fit to do light work if at all.
>
> L.R.C.P.

This letter had, I think, aggravated his anxiety state.

Heredity

There were no cases of known hereditary disease in this series. However, 6 of the 8 patients with asthma, 5 of the 28 patients with peptic ulcer, 5 of the 17 cases of psychoneurosis, and the single cases of mental deficiency and psychosis gave a positive family history.

TABLE VIII—ILLNESSES OF BROTHERS AND SISTERS OF TWO CASES OF RHEUMATIC FEVER AND TWO CASES OF NEPHRITIS IN WHICH OVERCROWDING WAS CONSIDERED THE CHIEF ÆTIOLOGICAL FACTOR

Rheumatic fever			Rheumatic fever			Nephritis			Nephritis		
Family	Age	Illnesses	Family	Age	Illnesses	Family	Age	Illnesses	Family	Age	Illnesses
James	21	Cervical tuberculosis	Barbara	28	Pneumonia	Annie	12	No history	Ronald	14	Rheumatic fever Abscesses Septicæmia Mastoid (twice)
Mabel*	17	Rheumatic fever	Elizabeth	28		Henry	40	No history	Roy	13	Recurrent tonsillitis
Ernest	15	Pneumonia Bronchitis	Violet	23	Pneumonia	Ernest	38	No history	Cynthia*	12	Nephritis
Edna	12	Tubercular abscess	John	22	Erysipelas	Alice	29	No history	Marion	10	Scarlet fever
Mary	8	Asthma	Joyce	18		Fred	27	Rheumatic heart-disease	Mary	8	Scarlet fever
Harry	4	Pneumonia Erysipelas	Roy	17	Rheumatic fever	George	25		Bobby	5	Scarlet fever
Eric	1	Fits	Lilian*	14	Rheumatic fever	Ivy	22	Pneumonia Fits	Irene	4	Pyelitis Bronchitis Otitis media
			Clara	13	Diphtheria	Mary	18		Olive	2	Pyelitis
			Mary	10	Diphtheria	Raymond	17	Mastoid	Baby	4/12	d. bronchopneumonia
			Spencer	3		Eric*	16	Nephritis			
			Kathleen	2							
			Sister	?	d. bronchopneumonia						
			Brother	4/12	d. wasting						

* Patient

suggesting inherited susceptibility. Siblings, parents, cousins, uncles, aunts, and grandparents were included in the family inquiry.

Human Relationships

The data about human relationships and ætiology were of necessity largely derived from the patients' own accounts of their lives and illnesses. Although it is difficult to present data of this sort quantitatively, it seemed to be worth attempting so that some sort of estimate, however rough, could be made of the contribution of unsatisfactory human relationships to the ætiology of the illnesses. A special effort was made to assess the importance of emotional insecurity in childhood and of psychological stress before the onset of the illness.

A control group of 81 healthy people was obtained by interviewing random samples of 47 patients from the fracture wards, 7 from a plastic and burns unit, and 27 normal parturient women in a maternity hospital. They were not an entirely satisfactory control group. The sex and the social class distribution was similar to that of the 200 patients but they were somewhat younger (average age 38 years compared with 42). Also the possibility that a group of accident cases will include more than a normal proportion of psychologically abnormal people cannot be excluded.

Insecurity in Childhood

The factors which were considered most important were persistent quarrelling, drunkenness, unfaithfulness, or violence of one or both parents, and the loss at an early age of father or mother by death or separation. The following cases illustrate relatively clear cut examples of insecurity in childhood.

TABLE IX—HISTORY OF INSECURITY IN CHILDHOOD

Type of illness	No of cases	Loss of one or both parents before age 6	Insecure childhood for other reasons	Total
Somatic	55	13%	11%	24%
Psychosomatic	109	18%	37%	55%
Psychoneurotic	17	18%	59%	77%
Controls	81	12%	11%	23%

Mr G.S., aged 40 (essential hypertension). Father died when he was 2. Mother remarried when he was 8. Parents separated when he was 14. They were never happy. "My stepfather used to sleep with a razor under his pillow. I was terribly afraid of him. If I saw him coming up the street, I would run in and sit quiet as a mouse."

Miss D.S., aged 31 (rheumatoid arthritis). Mother was in mental hospital; father killed in 1914–18 war. "My youth was anything but happy. I was brought up in an orphanage. You live in an atmosphere of fear all the time wondering whether you are doing right."

Table IX shows the incidence of a history of important causes of insecurity in childhood in the main types of illness and in the control series. Loss of one or both parents before the age of 6 was commoner in the psychosomatic and psychoneurotic groups than in the somatic and control groups but the differences were not, by themselves, statistically significant. The other causes of insecurity in childhood were commoner in the psychosomatic and psychoneurotic than in the other two groups and the differences were statistically highly significant.

Psychological Stress before Onset of Illness

A history of mental stress at, or just before, the onset of illness was significantly commoner in the psychosomatic than in the somatic group—61% compared with 16% (table X). The three most important causes of mental stress at or about the time of onset, which were all significantly more common in the psychosomatic than in the somatic group, were serious illness or death in the family, work anxiety, and sexual or marital difficulties (table X).

TABLE X—HISTORY OF MENTAL STRESS AT, OR JUST BEFORE, ONSET

Type of illness	No. of cases	No with stress at onset	Commonest types of stress at onset		
			Family illness or death	Work anxiety	Marital or sexual difficulties
Somatic	55	9 (*16%*)	3	0	2
Psychosomatic	109	67 (*61%*)	15	28	8

EXAMPLES

Family Illness

B.R., aged 11 (recurrent vomiting). Attacks came on, six months previously, during the last illness of his father, and cleared up within three months of his father's death.

Work Anxiety

Miss E.P., aged 42 (nervous diarrhœa). Duration one year, since new job in administrative department of a big store. Dealing with complaints about fuel supplies. Got back to her old job as manageress of a shoe department, and the diarrhœa cleared up.

Mrs L.Z., aged 30 (stress dyspepsia). Mother died at her birth. Adopted. Foster father drank and foster parents quarrelled. Married for ten years, one son aged 7. Husband called up in 1941. She continued to look after their butcher's shop. Dyspepsia came on then. "It was a big strain." Husband came home in January, 1946. When she was seen again in May, 1946 her dyspepsia had gone.

Marital Unhappiness

Mrs E.K., aged 51 (gastric ulcer). Mother died when patient was 3, stepmother at 8. Father died when she was 11. Patient divorced her first husband because he was unfaithful and drank to excess. Her first bout of pain came on at that time. Second attack of pain came on just after she lost her home and furniture in 1940 through enemy action. She now keeps a theatrical boarding house and gets the pain when she "rushes round a lot."

Mrs M.B., aged 51 (toxic goitre). After she had a hysterectomy in 1943, her husband stopped having intercourse with her as he thought her sex life was ended. She suspected that he was being unfaithful and symptoms of thyrotoxicosis began to develop.

On the limited data available, it was not possible to say whether a particular type of stress was associated with a particular type of illness, but some of the figures were suggestive. For example, while only 17% of the 164 patients suffering from psychosomatic or somatic illness gave a history of anxiety arising out of employment at the time the illness began, 46% of the 50 cases of ulcer and non ulcer dyspepsia gave such a history.

Some of the burdens which seemed to precipitate the symptoms in these ulcer and non ulcer dyspepsia cases were not abnormally heavy, and no doubt many adults experience similar strains without becoming ill. Serious cause for chronic anxiety in childhood was three times commoner in the histories of the ulcer and non ulcer dyspepsia group than in the somatic group, and it seems likely that disturbing experiences in childhood had made some of these patients particularly susceptible to stresses in adult life. Davies and Wilson (1937) found that in 84% of 205 patients with peptic ulcer the symptoms began soon after some disturbing event affecting the patient's work or finances or the health of his family. In a control series of 100 patients with hernia, only 22 gave such a history. Davies and Wilson do not mention possible causes of chronic anxiety in the childhood of their patients.

Of the 4 women in this series who suffered from thyrotoxicosis 3 gave a history of marital or sexual anxiety at the time of onset, compared with 8 out of the 109 psychosomatic and 2 out of the 55 somatic cases. The figures, although small, suggest that this type of anxiety may be of importance in the ætiology of hyperthyroidism.

In general the case histories of this survey support the hypothesis that people who experience chronic anxiety in *childhood are vulnerable to psychological stress in* adult life and that they are prone to develop psychoneurotic or psychosomatic illness It is difficult to prove that insecurity in childhood and psychological stress before the onset of illness are important causes of the illness, for we cannot demonstrate the mechanism of such a relationship

Some workers have, however, shown that emotional disturbances can produce abnormal physical changes in the tissues Grant and others (1935) showed that urticaria could be provoked through the efferent peripheral nerves when these were stimulated by emotion, and Wolf and Wolff (1943) demonstrated in a patient with a gastrostomy that abnormal physical changes in the gastric mucosa could occur under the influence of fear and anger

CONCLUSIONS

All the cases studied in this survey were seen in a teaching hospital, and, although they were unselected in the sense that all the available cases in one medical service over a given period of time were included, the group was too small and too heterogeneous to be a basis for conclusions of general validity The study does, however, confirm that most medical illness referred to a teaching hospital is long standing or recurrent and that in only a minority of such cases can a cure be expected

It is therefore pertinent to ask how far these illnesses could have been avoided Better conditions of housing, nutrition, and occupation, and a higher level of popular health education, could probably have prevented most, if not all, of the cases of tuberculosis, rheumatic heart disease, nephritis, scurvy, venereal disease, pneumoconiosis, and lead poisoning, which represented about 10% of the total

The striking feature of the series was the high proportion of psychosomatic and psychoneurotic illness—59% of all cases While the bacterial diseases are becoming less important as causes of morbidity and mortality, diseases in which mental and emotional factors are of primary importance demand our attention more insistently Canby Robinson (1944) in a similar study of unselected cases in the medical service of a teaching hospital concluded that " adverse social conditions cause emotional disturbances in over 50 per cent of the patients and are the major precipitating cause of illness in about 36 per cent of the patients "

Halliday (1948) has produced evidence that the incidence of the psychosomatic illnesses is increasing in Great Britain and the United States and that younger age groups are increasingly affected The reported relative freedom of primitive people from neurotic and psychosomatic illness supports the hypothesis that conditions peculiar to Western civilisation are to some extent responsible Gelfand (1948), for example, states that peptic ulcer and coronary disease are rare in the African in Africa, whereas the incidence of peptic ulcer and coronary disease in negroes in some parts at least of America approximates to their incidence in the white population (Lewis 1942)

While a great deal of ill health can be prevented by further improvements in the physical conditions of life, especially those connected with housing and occupation, it is becoming clearer that further substantial advances in preventive medicine will depend as much, if not more, upon improving the emotional and mental environment, especially in childhood

SUMMARY

Consecutive series of 146 medical outpatients and 144 inpatients who attended a teaching hospital were followed up a year later to assess the results of treatment and to investigate possible social causes of their illnesses

Of the 200 patients who attended the follow-up 17% of the outpatients and 22% of the inpatients had been cured The remainder still had their illnesses or had died of them

In 43 5% of the cases the most important ætiological factor in the social environment seemed to have been disturbed human relationships, in 5 5% unhealthy working conditions, in 3 5% bad housing, in 1% misuse of leisure, and in 0 5% deficient diet In 46% there was no apparent environmental or hereditary cause of the illness The combination of emotional insecurity in childhood and psychological stress in adult life seemed to be a common and potent cause in the cases of psychosomatic and psychoneurotic illness

REFERENCES

Canby Robinson C (1944) *Bull Johns Hopk Hosp* 74, 959
Davies D T Wilson, A T M (1937) *Lancet* ii 1353
Gelfand M (1948) The Sick African Cape Town
Grant R T , Pearson, R S R Comeau, W J (1935–36) *Clin. Sci.* 2 253
Halliday J L (1943) *Lancet* ii 692
— (1948) Psychosocial Medicine London
Lewis J H (1942) Biology of the Negro Chicago
Ryle J A (1939) *Lancet* ii, 297 353 407
Wolf, S , Wolff, H G (1943) Human Gastric Function London

MANAGEMENT OF BATTLE CASUALTIES FROM KOREA

R M Latta
M B Glasg
SURGEON COMMANDER, R N

DURING the first two months of the Korean war, H M Hospital Ship *Maine* carried some 1850 patients to base hospitals in Japan For various reasons this report of the management of these patients has to be based chiefly on impressions detailed statistics are not available

The actual sailing time from Korea to Japan was in the region of forty two hours , and on some of the trips the patients were on board for about forty eight hours On other trips, because sailing was delayed by typhoons in the neighbourhood, they remained on board for up to six days With few exceptions patients had had primary surgical treatment before embarkation, close to the battle zone and/or at an evacuation hospital. In many cases, however, the records were scrappy and some cases had none at all so that it was impossible to learn the time between treatment and admission to the ship, or the kind of treatment given, even if there had been the necessary time and staff to do this on board For obvious reasons follow up of the patients was impossible, but a cross section of similar cases was seen at a base hospital in Japan, and some idea of the probable results of treatment was obtained

Such figures as can be given were obtained from the nominal lists which accompanied each load of patients, and absolute accuracy cannot be assured About 230 cases had major soft tissue wounds without bone involvement, and 180 had major compound fractures , Some 400 had relatively minor wounds for which no special treatment apart from renewal of dressings was required, and no particular mention will be made of this group The figures referring to other types of injuries will be given later under the appropriate headings

In general, the first thing which impressed one was the need of the average patient for food and rest , and considerable improvement was apparent after supplying these two things alone for three or four days Evacuation of the patient from the front line is now organised to such a degree that he gets little chance of resting, and he may even be snatched away from approaching food He goes with little pause from front line to dressing station, dressing station to field hospital, field hospital to hospital train, hospital train to evacuation hospital, evacuation hospital to hospital ship or aircraft, and so, eventually, to base hospital With a fair proportion of patients this itinerary is short-circuited, but those who go through the whole programme arrive travel weary, quite apart from any wound or injury they may have. Moreover, adequate medical supervision is difficult under these circumstances, and it is possible that a small number of patients may suffer as a result—e.g., by the development of gas gangrene.

When admitted on board most patients needed only postoperative supervision, and these did very well; but some cases went wrong, and it is chiefly with these cases that this report is concerned.

SOFT TISSUE WOUNDS

Soft tissue wounds comprised the largest group of cases. All had had surgical treatment, and all had been given routine penicillin (the usual dose was 300,000 units of procaine penicillin daily or twice daily), while in some cases an antibiotic bomb of penicillin, steptomycin, and 'Aureomycin' had been used.

Out of the 410 cases of major soft tissue wounds and wounds in which bone was involved, 51 (12%) required further surgical treatment during the short time they were on board. The indications for intervention were the usual ones: local pain, toxæmia, hæmorrhage, unhealthy smell or appearance of the dressing, evidence of gangrene, and so on; but there was a further group of cases in which primary suture had been carried out. In other words, cases in which the surgical treatment had been inadequate or over optimistic required further intervention.

It was abundantly evident that nothing can yet take the place of the efficiently planned surgical toilet of a wound. The trimming of damaged skin edges, opening up of fascial planes, excision of dead or damaged tissues, removal of foreign bodies (especially those of vegetable origin), and hæmostasis are all essential. Of the value of antibiotic therapy there can be no doubt, but it cannot take the place of surgery in the treatment of war wounds. If surgery is efficient, delayed primary suture or secondary closure with or without skin grafting can become almost a matter of routine in conjunction with antibiotic therapy; and it was possible to follow this procedure on board in a small number of cases. If, however, surgery has not been efficient, with larger wounds where there has been a good deal of tissue damage further intervention is required, usually as a matter of some urgency; with less severe wounds the antibiotics limit the spread of infection and the development of toxæmia, thereby permitting some delay in instituting surgical treatment without serious deterioration in the patient's condition. The general appearance of such a wound is rather like that of a cold abscess. It is highly probable that a number of such cases were overlooked on board because they were relatively asymptomatic, and there were always enough cases with symptoms to keep one busy.

The inclusion here of primary suture among the reasons for further surgical intervention is open to criticism, which is valid as long as the limitations of primary suture are recognised. If the wound is treated efficiently and if it can be kept under supervision for the first few postoperative days, primary suture should certainly be considered. But, under the conditions which war imposes, it is not without danger. Front-line surgery cannot always be done under good conditions, and the necessary evacuation of the patient from the front line through the various staging posts to the base hospital means that he is not under surgical supervision all the time. Because of this, primary suture is not without risk. Two minor tragedies were seen in this series. In both cases wounds of the foot had been closed. Had they been left open both patients would probably have had useful feet; but, as a result of closure of imperfectly excised wounds, there was swelling and tension and spread of infection, and it seemed likely that both feet would eventually have to be amputated. These were the two worst cases seen, but almost every wound which had been closed had to be opened and have further excision done.

GAS GANGRENE

There were 3 cases of clinical gas gangrene in this series, involving the legs in 2 and the arm in 1. All 3 had had routine penicillin therapy from shortly after the time of wounding, but primary surgical treatment had not been adequate. In 1 case a mid-thigh amputation was required. In the other case where the leg was involved, there was gangrene of the distal half with proximal extension in the extensor muscle group; by excising this group it was possible to leave enough tissue to justify a below knee amputation. For the case in which the arm was affected, dead and damaged tissue was widely excised and the wound left open in the hope of preserving the limb; but amputation was done later since the loss of structure was so widespread that the limb could never be useful. It is known that despite the general use of antibiotics, gas gangrene developed in cases evacuated from Korea by other methods.

HÆMORRHAGE

For the most part patients were received and disposed of before the time when secondary hæmorrhage usually appears; and, indeed, secondary hæmorrhage should be uncommon if wound toilet has been adequate. Hæmorrhage following primary wound toilet presented a minor problem. In the first place it seems bad for the patient's morale if he can see a spreading patch on his dressing; and secondly, if the operation has been done elsewhere, there always seems to be some (usually quite unjustifiable) concern that damage to one of the larger vessels may have been overlooked. If there was evidence of continued bleeding for a few hours after admission, the patient was taken to the theatre. As a rule, only persistent capillary oozing was found; but in a few cases there was a definite bleeding point.

There was one patient with fairly profuse continued bleeding from a wound just below the level of the knee-joint on whom three attempts to stop the bleeding had been made before admission. The fourth attempt, done on board with a rather wider exposure than had been used before, showed that a circle of cortical bone about 1 in. in diameter, had been chipped off the anterior upper end of the tibia. In this case hæmostasis was secured with Horsley's bone wax; in other cases ligation of a bleeding point, firm pressure with hot packs, or the application of Oxycel gauze was effective. Diathermy was unfortunately not available.

It was noticed that in several cases the method used to control hæmorrhage at the time of primary operation was to plug the wound firmly with a gauze or soft-paraffin gauze pack. This was effective as far as control of bleeding was concerned, but it interfered seriously with the policy of leaving the wound open, and the plugs had to be removed at the first opportunity. Sometimes, too, the dressings over such wounds were fixed in place with encircling turns of adhesive plaster, which naturally soon became tourniquets. The relief to the patient by dividing this strapping was most noticeable.

It was surprising how often the line of the missile crossed the anatomical line of the main vessels of a limb without involving them. When the major vessels appear to be in the line of fire there is more than one method of dealing with the case. If the wound leads directly to the vessels and there is serious loss of blood, the surgeon has no alternative but to ligate them if repair is impossible. If, on the other hand, there has been no great loss of blood judging by the patient's condition, and the wound track does not expose the vessels, then it may be advisable to leave them undisturbed and hope for the eventual formation of a traumatic aneurysm or arteriovenous fistula which can be dealt with later when the collateral circulation is established. But it seems doubtful whether this second policy can wisely be applied to the femoral artery in the lower third of the thigh or to the popliteal artery; for in these areas the formation of a hæmatoma will tend to obstruct by pressure any collateral channels.

3 cases were seen in which the distal third of the femoral artery had been damaged. The wounds, produced by sharp-nosed, high-velocity missiles, were small and did not obviously involve the vessels. The patients were first seen on board with a tense swelling round the lower thigh with ascending gangrene of the leg, and all required mid-thigh amputations. In 2 cases this was done on board; the 3rd is mentioned later in more detail. It would probably have been wiser to explore for possible vascular damage at the time of primary surgical treatment, and, having found it, to ligate the damaged vessels, and to rely on a paravertebral block or reflex dilatation to encourage opening up of the collateral channels. This area of the body is notoriously bad for vascular injuries; and, because of tension, there seemed in these cases to be no possibility of the reserve channels opening up.

With regard to amputations, these were done, whenever possible, at the site of election. Skin flaps were cut, although sometimes the position of the original wound necessitated slight modifications of the usual anterior and posterior flaps. In infected cases the flaps were brought loosely together over gauze; in the others primary closure was done, leaving a rubber drain in for two or three days.

WOUNDS COMPLICATED BY COMPOUND FRACTURES

Fractures, generally, were treated in padded plasters, and if there was no real complaint they were left alone. The criteria for further intervention were the same as for soft-tissue wounds. Adequate wound surgery is, if possible, even more important than when bone is not involved, and the remarks about the treatment of soft-tissue wounds apply here with equal force.

The standard plasters were used: for femurs a pin through the upper end of the tibia incorporated in a plaster spica was the routine method of fixation, although in the early days a Tobruk splint was commonly used. Handling the patient was much easier when the splint was used, but it did not give the same degree of immobilisation and, therefore, of comfort to the leg. No attempt was made to check radiologically the position of the bone ends; if the limbs were of equal length and the contours were approximately the same, the position was accepted as adequate until the patient could be given definitive treatment. With regard to plasters in general, two points seem worth making.

The first is that it is desirable, under the circumstances described here, to split the plaster as soon as it is applied. This had not been done with the first patients carried, and it was almost always necessary to do it; it is much easier to do this at the time of application than later, on a conscious apprehensive patient with a swollen limb. Later on, plasters were being split; but the division must be in the whole length of the plaster, and it should also include any bandages which have been used to fix dressings in place before the plaster was applied.

The second point is that there is a case for the routine description on the outside of the plaster shell of the injuries underneath, preferably using a rough sketch. One patient arrived on board without any notes. He had a laparotomy wound, and a silent abdomen; and he was in a left hip spica which had been extended to include the right thigh. There was nothing to show that this extension concealed a wound of the right thigh which, as it happened, involved the right femoral artery. The patient did not complain particularly of this leg; he was toxic, but this was thought to be due to the paralytic ileus which he had; and the first indication of the true state of affairs was gangrene of the foot. It is just possible that with a little extra attention his leg might have been saved; as it was, it had to be amputated.

INTRATHORACIC WOUNDS

82 patients with thoracic or thoraco-abdominal wounds were carried. There were 2 deaths in this group. All combinations of pneumothorax and hæmothorax, both unilateral and bilateral, with and without injury to the lung, were observed. All these patients had been treated before embarkation; but the majority of them were in an unstable state and required careful and constant supervision. Most of them arrived on board with one or more intercostal catheters connected to water-sealed drainage bottles. These catheters, usually of 12 or 14 F size, were not efficient drainage tubes.

Possibly, with continuous gentle suction they might have proved satisfactory; without this they quickly became blocked with fibrinous clots. Unless continuous suction is available, a tube of much wider bore is required. As a routine the catheter was removed except in those rare cases where there was drainage, and we relied on intermittent aspiration of the chest with a syringe. On one occasion removal of the catheter was followed by the rapid escape of 17 oz. of serosanguinous fluid which had been dammed back.

Pneumothoraces were released by using an intercostal needle attached to a water-sealed drainage bottle. No attempt was made to aspirate air; it was considered adequate if the intrapleural air pressure was reduced to atmospheric pressure. Whenever possible radiological control was used; but for technical reasons it was impossible to use the X-ray apparatus while we were at sea, and it was necessary to depend largely upon clinical findings for deciding when to aspirate. This was, of course, not satisfactory; for, while almost all the patients showed some improvement judging by their increased comfort, loss of apprehension, and increased exercise tolerance, the clearance of the pleural cavities was delayed and a greater number of thoracotomies would probably be required at a later date.

The common emergency was tension pneumothorax.

Sudden development of this in a patient who had been comfortable with no cyanosis or dyspnœa on slight exertion was very alarming. It was found that a readily available water-seal drainage apparatus was an M.R.C. giving set connected to the air inlet tube of an M.R.C. bottle. In one patient who suddenly developed acute dyspnœa, a needle connected to this device was put into the lower part of the chest, and 3 pints of blood were literally pushed out in twenty minutes by the tension of the air above the hæmothorax. Oxygen was tried in many cases of thoracic injury but it was found that the only patients who really appreciated it were those chest emergencies, who clutched the B.L.B. mask as though it was a lifebelt.

Of the 2 patients who died, 1 had a left hæmopneumothorax with collapse of the lung. This had been aspirated but the lung had not yet re-expanded. He suddenly developed a tension pneumothorax on the opposite side, and despite early release of this died of asphyxia. The other case was of bilateral hæmopneumothorax with a valvular opening on the anterior chest wall. In addition, this patient had severe jaundice, probably of infective origin. His hæmothorax persisted despite drainage, aspiration, and vitamin-K therapy.

ABDOMINAL INJURIES

Of the 40 patients with abdominal injuries, 3 died. All were in the postoperative stage, apart from 1, on whom a colostomy was done for rectal damage which, reasonably enough, had been overlooked.

As in the other groups of cases, there were many about which there was little or no information. It was found, however, that this was only a theoretical disadvantage, and that clinically the cases could be divided into two principal groups: those in which bowel sounds could be heard, and those with a silent abdomen. If there was any doubt the case was put in the second category; for, early in this series, the doubtful patients were given a trial period on a limited fluid intake by mouth, and a few showed fairly serious deterioration Because of pressure of other work, it was not possible to observe closely these doubtful cases, and it seemed safer to treat them as being worse than they possibly were

It was assumed that patients with silent abdomens had a true paralytic ileus following peritoneal contamination or infection, and not a postoperative or traumatic ileus Routine treatment with gastric suction and intravenous fluids was given A Levine's tube was preferred to Ryle's because of its slightly bigger bore the Miller Abbott tube was not used, since a paralytic condition was being dealt with. At first, intermittent aspiration with a syringe was carried out Later, continuous suction using the two bottle siphon method was applied, and this proved much more satisfactory and efficient It was difficult to keep a check on blood-chemistry, but a theoretical fluid and chloride balance was worked out daily for each patient , and during the short time they were with us, this was apparently satisfactory It is unfortunate that intravenous glucose, which can be given almost ad lib , is so much more likely to irritate the wall of a vein than is normal saline, which has to be rationed

All the patients in this group were given routine penicillin and streptomycin with large doses of vitamin C In the absence of definite information about dates of operation, it is difficult to make a statement about the healing of wounds, but my impression is that this was delayed Of 14 colostomies which were opened, it was thought advisable to use a Paul's tube in 3, for it appeared that sealing off of the peritoneal cavity had hardly begun by the third or fourth postoperative day In another 3 cases large abscesses containing upwards of 4 oz of thick pus were opened through the laparotomy wound Since these discharged satisfactorily they were not explored, but they appeared to originate intraperitoneally A feature of them all was that they were almost asymptomatic, and they were obvious chiefly because of their size , it seems likely that the antibiotic therapy had something to do with this

About 12 cases in this group had damage to one kidney, and in all but 2 the injured kidney had been removed All those on which a blood urea estimation was done showed a level of over 100 mg per 100 ml., and urine output was not satisfactory, though this could have been related to an inadequate postoperative intake They were given a controlled, gradually increasing fluid intake with a glucose basis, and they all did well

Of the cases in which the damaged kidney was not removed 1 was admitted with a blood urea level of 180 mg per 100 ml and the level rose to 250 mg per 100 ml in the next two days, after which the patient died Intravenous glucose and isotonic sodium sulphate were both administered but they did not influence his condition in any way

The other case in which nephrectomy had not been done had on admission oliguria with a blood urea level of 150 mg per 100 ml Intravenous glucose produced no response, but there was a temporary increase in urine output after administration of 1 pint of sodium sulphate This improvement was not maintained and anuria gradually supervened

It seems possible that these were 2 cases of reflex anuria, and that primary nephrectomy might have saved them, but on admission they were too ill to withstand operation

A few cases of wounds of the bladder and urethra were seen.

HEAD INJURIES

Of the 19 patients with head injury, 2 died One arrived on board unconscious and died without regaining consciousness ; no notes were available, but it seems likely that he had severe damage to his basal ganglia The other had a compound fracture of the skull which had been operated on , it is thought that he had a septic encephalitis The other cases were of compound fractures of the skull, which had been operated on , and these did well on restricted fluids (2 pints daily) and fairly continuous sedation with intramuscular paraldehyde or sodium phenobarbitone Routine penicillin and one of the sulphonamides were given

BURNS

Of 19 cases of severe burns, 2 died The majority were petrol burns, and most of them had resulted from using petrol to light fires The value of protective clothing was obvious, and the inflammability of the mechanic's working dress was demonstrated only too clearly Treatment consisted in gentle cleaning with cetrimide ('Cetavlon') and saline, followed by dusting with penicillin sulphonamide powder and dressing with soft-paraffin gauze, padding, and a pressure bandage

With extensive burns, even when it appeared that a satisfactory pressure dressing had been achieved, the amount of leakage through the dressings was surprising and almost alarming , and blood, plasma, and electrolytes had to be infused fairly quickly Frequent blood checks were required. In the 2 fatal cases the necessary fluids were probably not given fast enough It would seem that there is still a place for coagulation therapy on extensive flat surfaces in an attempt to cut down fluid loss

INTRAVENOUS THERAPY

A good deal of practical experience in intravenous therapy was obtained, though control by blood chemistry observations was less exact than was desirable

The equipment used was the standard M.R C apparatus , but reserves had to be obtained from American sources, and it was found that the different parts of the two types of sets are not readily interchangeable It seemed that the M R C equipment was easier to supervise, though this may have been only because of familiarity, and all fluids of American origin were transferred to M.R C bottles This was usually done in the laboratory , but occasionally, when an emergency arose it had to be done in the ward No complication followed this potentially dangerous manœuvre

Blood —Fresh blood was taken from the ship's company as required, but supplies were also obtained from an American blood bank For some reason which was never discovered, this stored blood did not run easily through the M R C apparatus, although there was no difficulty with fresh blood Eventually, as a routine, each pint of stored blood was diluted with a similar quantity of saline, and the resulting mixture gave no trouble

Plasma —Although dried plasma is supposed to keep indefinitely, the available stocks which were of 1942 and 1944 vintage were for the most part, unfit for use This may have been due to ineffective sealing of the bottles , but it is perhaps worth mentioning that dried plasma obtained from American sources was marked with a date of expiry

Technique —A supply of small bottles containing 10 ml of sterile isotonic sodium citrate was kept in each ward, and this fluid was used to clear intravenous drips which were not running satisfactorily It is true that small clots may be set free by injecting the citrate under pressure into the giving set , but there was no evidence that this actually happened, and no complication resulted When the number of available veins is getting small, every means of maintaining the patency of a vein has to be used Finally, it is most desirable to avoid inserting an intravenous needle near a joint The patient should be free to move, within limits, the limb that is being used for an intravenous drip, more especially if for any reason he is not fully coöperative Effective splinting of the limb was found to be difficult to secure, and it rather tended to obstruct the free flow of fluid The most easily accessible veins are those on the forearm , but, if these were not available, we cut down on the internal saphenous vein near the ankle If one of the veins in the antecubital fossa had to be used, a plaster of paris splint was applied in preference to a prefabricated splint

Public Health

PERSONAL HYGIENE AND THE SPREAD OF DISEASE

I H J Bourne
M B Lond
GENERAL PRACTITIONER, HORNCHURCH, ESSEX

It has often been suggested that the virus of poliomyelitis may be transmitted by fæces, certainly they are the source of infection in some other diseases, notably gastro enteritis My aim here is to show that such infections, and possibly poliomyelitis too, can be spread as a result of faulty personal hygiene in lavatories

Poliomyelitis virus has been found in the fæces of healthy adults in five out of six households where a case occurs (Pearson and Rendtorff 1945) Burnet (1940) points out that the high incidence of infection in infants is always associated with an abundant source of virus in the environment, excreted in the fæces by adults and older children

THE MODE OF TRANSMISSION

If lavatory fitments could be incriminated as factors in transmitting the virus from person to person, light might be thrown on the mystery of epidemic spread of poliomyelitis, as well as on the transmission of gastro-intestinal infections

The crimes of serving and eating food, and washing up, with unwashed hands are so common, and so hard to combat in large communities, that they come to be tolerated even by those who have fought to eliminate them Printed injunctions, supply of washing facilities, personal supervision by a responsible officer—all these wax and wane because of human frailty The battle is still being waged by our public hygienists, and is fore most in all pamphlets advising on the prevention of disease

There is a general aversion to such unhygienic activities as sharing eating utensils, towels, and shaving mugs Moreover, the man in the street in most countries is increasingly aware that epidemic disease may spread via contaminated hands, food, water, or milk All the more surprising, therefore, is the world wide existence of a "blind spot" *in the toleration of modern lavatory* routine

SOME CURRENT PRACTICES

Ideally, a person entering any lavatory should find a wash basin, soap, and clean towel provided, in addition to equipment which is often disinfected, and a clean seat towel Hygienic toilet paper should also be provided In many conveniences in offices, restaurants, and shops neither paper nor washing facilities are supplied Even in public lavatories supplied by local health authorities a charge is made for the use of washing facilities—if they are provided at all In the home, even the best of small children do not wash carefully unless supervised It is worth considering the conditions in some primary schools Within ten minutes of school opening the closets are turned into a hygienist's nightmare The seats, chains, and handles become soiled with excreta Any infective organism could be transferred from these places to the hands of other users of the same closet The time elapsing between visits would be very short, especially in the rush hours of morning break and lunch time In summer the germ might not cool sufficiently to be destroyed it could remain viable for some time

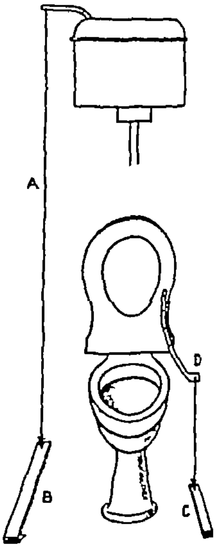
FOOT CONTROL OF CLOSET APPARATUS

Even in a perfectly equipped lavatory it is possible for a user to leave with germ contaminated hands, in spite of conscientious washing An infected person may touch not only the articles mentioned, he may deposit infected material on the door handle, door lock, door surface, the hand-taps, the soap container, the paper box Thus it is easy to feel a false sense of security

Malten (1946) has described a foot operated flushing system A simple foot lever is fastened to the floor and the chain lengthened to meet it Dr Malten points out that many people use the chain rather than the handle He therefore encloses the adaptor chain in a metal gas pipe fastened to the wall Incidentally he refers to the increase of threadworm infection during the "soapless war years"

Foot control being an advance, it is reasonable to apply it to water tap manipulation, to the raising or lowering of the lavatory seat, and to door control Many hospitals are fitted with foot operated wash basins In future such fitments should be made compulsory in lavatories The door could be closed after entry and fastened by an automatic spring catch at floor level, by means of a foot release mechanism it could also be made to swing open automatically, and remain ajar This would allow the occupant to leave without handling the door It is noteworthy that in New York doors are not considered necessary in some public lavatories

There are several practical advantages in foot control First it conforms to generally accepted principles of hygiene and æsthetics Then the cistern lever is less liable to strain and damage, because the foot pedal descent is checked by the floor Sanitary engineers might well devise new models in which the only visible parts need be foot-buttons projecting through the floor to operate the cistern and the seat Existing systems can be adapted immediately by a handy man equipped with wood, screws, hinges, and a length of chain, as shown in the illustration By this device children are spared the problem of how to reach the chain, and adults are spared the consequences of some of the solutions they commonly find for this problem.



The hand chain is replaced by a long chain (A) which connects the cistern lever to one end of a wooden pedal (B) The other end of the pedal is hinged to the floor The lavatory seat is shown in the raised position This is achieved by stepping on the wooden pedal (C), which is attached by a short chain to a lever (D) made of 5-ply wood.

Even if it be generally conceded that such a reform is desirable, the changeover to foot operated closets is likely to be gradual Meanwhile some other devices should help us to attain a measure of safety Paper can be used to cover and handle the seat, and paper towels for individual use can be obtained A bowl of chlorinated water would be an asset as a hand steriliser in closets and kitchens Sellers of soft fruit should use scoops where possible, and cooks should use ladles and servers

I wish to thank Dr Charles Wilcocks, Dr J Gorman, and Dr P X O'Dwyer for their help and advice, and Mr D Chaffey for help with the illustration

REFERENCES

Burnet F M (1940) *Med J Aust* 1 325
Malten H (1946) *Med Clin* 41 546
Pearson H E Rendtorff R C (1945) *Amer J Hyg* 41, 179

Influenza

In the great towns of England and Wales deaths from influenza increased from 458 in the week ended Jan 6 to 890 in the week ended Jan 13—the largest increment in the last twenty years Pneumonia cases and deaths, and influenza deaths, in the great towns during the seven weeks up to Jan 13 were as follows

	Week ended						
	Dec 2	*Dec 9*	*Dec 16*	*Dec 23*	*Dec 30*	*Jan 6*	*Jan 13*
Pneumonia							
Cases	282	347	374	364	503	956	1300
Deaths	198	236	289	351	383	770	982
Influenza deaths	28	34	33	54	102	458	890

Totals for the great towns during the first two weeks of this year, compared with the corresponding period in the preceding two years, are as follows

	1949	*1950*	*1951*
Pneumonia			
Cases	1237	1189	2256
Deaths	799	509	1752
Influenza deaths	87	99	1348

For the whole of England and Wales notifications of primary and influenzal pneumonia in the seven weeks up to Jan 18 were 497, 573, 684, 647, 962, 1774, and 2538

The bulk of the increase in influenza deaths has occurred in the Northern and North-Western regions, as is shown by the following summary of the incidence of deaths from influenza per million population in the great towns grouped regionally

	Week ended	
Region	*Jan 6*	*Jan 13*
Northern	83	91
North Western	63	138
London and South Eastern	11	21
Others (average)	5	13

Of the 890 deaths from influenza in the great towns during the week ended Jan 13, 85% were of patients over 55 years of age The total for each age group is as follows under *1* year, 12 , *1–15*, 4 *15–25*, 3 , *25–35*, 7 , *35–45*, 33 , *45–55*, 75 , *55–65*, 156 , *65–75*, 277 , *75* and over, 323

Pneumonia cases and deaths notified in the great towns have increased proportionately much less than influenza deaths Deaths from pneumonia and influenza have been relatively very numerous in the great towns in the more northerly regions and especially in Liverpool In the week ended Jan 13 Liverpool suffered more than any of the other great towns of 949 deaths in the city during this week 216 were attributed to influenza and 214 to pneumonia (Prof W M. Frazer, the medical officer of health, is reported[1] to have said that an average weekly figure for deaths in the city at this time of year was 200)

Though the incidence of influenza is increasing throughout the country, it seems that no situation has developed elsewhere comparable to that in the North and North-West , in London and the rest of the country the disease is comparatively mild, with some more intense localised outbreaks

Claims to Sickness Benefit —In England and Wales new claims to sickness benefit under the National Insurance Act numbered 370,500 in the week ended Jan 9, compared with 233,400 in the week ended Jan 2[2] For the guidance of people claiming sickness benefit whom the doctor cannot see without some delay, the Ministry of National Insurance has issued advice in the following terms

> To avoid loss of benefit a person who is prevented by illness from working should give the local National Insurance Office written notice of incapacity within the first three days This notice is normally given on the First Medical Certificate (MED 1) issued by the doctor when he first attends the patient , but where exceptionally the patient has not been seen by the doctor within the first three days, a note written by or on behalf of the patient is accepted as notice Where notice has been given without a medical certificate, the formal claim on the doctor s First Medical Certificate should follow as soon as the doctor has been seen, and in any case within ten days of the start of the illness Patients who have to give notice without a medical certificate should give their full name and address and their National Insurance number If they are claiming an increase of benefit for wife or other dependant details should be given If the doctor s examination has been delayed and he wishes his certificate to cover any earlier period of incapacity he can give a supplementary certificate (MED 5) or he can make a suitable note in the ' remarks space on the first medical certificate

Influenza Abroad —The situation in Europe was reviewed last week (p 168) Influenza is now prevalent also in Finland, where cases have been shown to be due to the A prime strain In Spain, as in Holland, there is evidence that the disease is due to virus A

Last week W H O issued the following comment

> ' The fact that in 1949 influenza was more prevalent in European countries other than Scandinavia and Britain leads one to think that the contrary will happen this year, and that regions so far spared this winter will remain less seriously affected Latest information indicates a decrease in the number of cases observed in Copenhagen and Oslo Research indicates that the virus causing the current outbreak belongs to type A Neither the spread nor the severity of the influenza epidemic now prevalent can be compared with the more serious epidemics which occurred in the first part of the century So far complications are rare and the mortality rate remains very low Influenza is now present not only in Europe The World Health Organization has also been notified of outbreaks in Hawaii and Japan, while the disease has made its appearance in Canada and the United States as well "

Smallpox at Brighton

Up to noon on Jan 22 there had been no notifications of smallpox outside the Brighton area The total number of cases notified (uncorrected) is 30, and there have been 9 deaths With 2 exceptions the recent cases have been in contacts under surveillance In view of the occurrence of a suspected case at Crowborough, Sussex, it would be premature to state that all the sources of infection in Brighton are known or that the end of the outbreak can be foreseen The need for special vigilance continues throughout the country

Poliomyelitis

In England and Wales notifications of poliomyelitis during the week ended Jan 13 were paralytic 27 (37), and non-paralytic 11 (10) total 38 (47) These figures represent a decrease in notifications of 9 compared with the previous week, for which the figures are given in parentheses

Notifications in the corresponding week of the previous four years were 1947, 16 , 1948, 49 1949, 37 , and 1950, 50 The notifications in the second week of 1951—38—are therefore well below those for the corresponding week in 1948 and 1950 These three years are comparable in that they followed years of very high prevalence

Births and Deaths in 1950

In England and Wales the provisional stillbirth-rate and infant-mortality rate for 1950 were the lowest ever recorded The Registrar-General reports[1] that the stillbirth-rate was 22 6 per 1000 total births and the infant-mortality rate 29 8 per 1000 live births, compared with 22 7 and 32 4 in 1949 The birth-rate was 15 8 per 1000 population, compared with 16 7 in 1949 , and the death-rate was 11 6 per 1000 population, compared with 11 7 in 1949

---

[1] *Times* Jan 17

[2] Figures supplied by the Ministry of National Insurance See Registrar General's Return for the week ended Jan 13 p 18

[1] The Registrar General s Weekly Return for the week ended Jan 13 H M Stationery Office Pp 20 6d

Public Health

PERSONAL HYGIENE AND THE SPREAD OF DISEASE

I H J Bourne
M B Lond

GENERAL PRACTITIONER, HORNCHURCH, ESSEX

It has often been suggested that the virus of poliomyelitis may be transmitted by fæces, certainly they are the source of infection in some other diseases, notably gastro enteritis My aim here is to show that such infections, and possibly poliomyelitis too, can be spread as a result of faulty personal hygiene in lavatories

Poliomyelitis virus has been found in the fæces of healthy adults in five out of six households where a case occurs (Pearson and Rendtorff 1945) Burnet (1940) points out that the high incidence of infection in infants is always associated with an abundant *source of virus in the environment*, excreted in the fæces by adults and older children

THE MODE OF TRANSMISSION

If lavatory fitments could be incriminated as factors in transmitting the virus from person to person, light might be thrown on the mystery of epidemic spread of poliomyelitis, as well as on the transmission of gastro-intestinal infections

The crimes of serving and eating food, and washing up, with unwashed hands are so common, and so hard to combat in large communities, that they come to be tolerated even by those who have fought to eliminate them Printed injunctions, supply of washing facilities, personal supervision by a responsible officer—all these wax and wane because of human frailty The battle is still being waged by our public hygienists, and is foremost in all pamphlets advising on the prevention of disease

There is a general aversion to such unhygienic activities as sharing eating utensils, towels, and shaving mugs Moreover, the man in the street in most countries is increasingly aware that epidemic disease may spread via contaminated hands, food, water, or milk All the more surprising, therefore, is the world wide existence of a "blind spot" in the toleration of modern lavatory routine

SOME CURRENT PRACTICES

Ideally, a person entering any lavatory should find a wash basin, soap, and clean towel provided, in addition to equipment which is often disinfected, and a clean seat towel Hygienic toilet paper should also be provided In many conveniences in offices, restaurants, and shops neither paper nor washing facilities are supplied Even in public lavatories supplied by local health authorities a charge is made for the use of washing facilities—if they are provided at all In the home, even the best of small children do not wash carefully unless supervised It is worth considering the conditions in some primary schools Within ten minutes of school opening the closets are turned into a hygienist's nightmare The seats, chains, and handles become soiled with excreta Any infective organism could be transferred from these places to the hands of other users of the same closet The time elapsing between visits would be very short, especially in the rush hours of morning break and lunch time In summer the germ might not cool sufficiently to be destroyed it could remain viable for some time

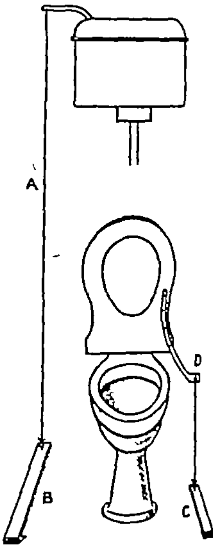
FOOT CONTROL OF CLOSET APPARATUS

Even in a perfectly equipped lavatory it is possible for a user to leave with germ contaminated hands, in spite of conscientious washing An infected person may touch not only the articles mentioned, he may deposit infected material on the door handle, door lock, door surface, the hand taps, the soap container, the paper box Thus it is easy to feel a false sense of security

Malten (1946) has described a foot operated flushing system A simple foot lever is fastened to the floor and the chain lengthened to meet it Dr Malten points out that many people use the chain rather than the handle He therefore encloses the adaptor chain in a metal gas-pipe fastened to the wall Incidentally he refers to the increase of threadworm infection during the "soapless war years"

Foot control being an advance, it is reasonable to apply it to water tap manipulation, to the raising or lowering of the lavatory seat, and to door control Many hospitals are fitted with foot operated wash basins In future such fitments should be made compulsory in lavatories The door could be closed after entry and fastened by an automatic spring catch at floor level, by means of a foot release mechanism it could also be made to swing open automatically, and remain ajar This would allow the occupant to leave without handling the door It is noteworthy that in New York doors are not considered necessary in some public lavatories

There are several practical advantages in foot control First it conforms to generally accepted principles of hygiene and æsthetics Then the cistern lever is less liable to strain and damage, because the foot pedal descent is checked by the floor Sanitary engineers might well devise new models in which the only visible parts need be foot buttons projecting through the floor to operate the cistern and the seat Existing systems can be adapted immediately by a handy man equipped with wood, screws, hinges, and a length of chain, as shown in the illustration By this device children are spared the problem of how to reach the chain, and adults are spared the consequences of some of the solutions they commonly find for this problem



The hand-chain is replaced by a long chain (A), which connects the cistern lever to one end of a wooden pedal (B) The other end of the pedal is hinged to the floor The lavatory seat is shown in the raised position This is achieved by stepping on the wooden pedal (C), which is attached by a short chain to a lever (D) made of 5-ply wood.

Even if it be generally conceded that such a reform is desirable, the changeover to foot operated closets is likely to be gradual Meanwhile some other devices should help us to attain a measure of safety Paper can be used to cover and handle the seat, and paper towels for individual use can be obtained A bowl of chlorinated water would be an asset as a hand steriliser in closets and kitchens Sellers of soft fruit should use scoops where possible, and cooks should use ladles and servers

I wish to thank Dr Charles Wilcocks, Dr J Gorman, and Dr P X O'Dwyer for their help and advice, and Mr D Chaffey for help with the illustration

REFERENCES

Burnet F M. (1940) *Med J Aust* 1 325
Malten H (1946) *Med Clin* 41, 546
Pearson H E Rendtorff R C (1945) *Amer J Hyg* 41, 179

Letters to the Editor

PROSPECT OF WAR

SIR,—There must be thousands of doctors who would like to join with Professor Penrose and his colleagues (Jan 20) to press, as doctors, for the healing of the world-wide disease of war, if they could but see their way But, like so many of our fellow citizens, we are afraid of being "misled by quasi communism" (*Manchester Guardian*, Jan 19) or playing some other enemy's game if we so much as toy with the idea of negotiation from equality instead of striving after what may well be a receding illusion of "negotiation from strength"

Our political leaders dissect recent history as if it gave us the clue to everything Even so the Power that negotiated from strength at Munich lost the subsequent war, following the historical pattern that it is usually the stronger Power that attacks—and gets beaten (Quincy Wright *Study of War*) It is ingenuous too to assume that, because appeasement at Munich failed to prevent war, the reverse must either have succeeded then or be the golden rule for all the future There are many ways of going to the devil, and among nations challenge and armament must have proved at least as reliable routes as appeasement has ever done *Facilis descensus averno*

The attitudes of peace are positive attitudes Doctors need not become politicians to proclaim to the world that it is their habit to treat foreigners as human beings Whatever their ideology the dose is the same We can go on and attempt to recall politicians and journalists from their frenzies of hatred to the solid need of all men everywhere to be treated as equals, or at least as similars, whether they are misled by Communists, led by Socialists, or guided by capitalists And, like sick men, the sick nations of the world need peace and quiet, an end of past irritations, and a period, not of feverish activity, but of absolute rest for inflamed parts

Finally, could not some international medical or medicolegal congress meet and commend to governments the need for, and the conditions of, a peaceful regulation of our lives ? It seems an infinite pity that the conditions of world wide law and order are known to international lawyers today and yet can still be so deliberately flouted by every sovereign State as such

Edinburgh RANYARD WEST

SIR,—Much as I sympathise with all appeals for reason and peace, I am bound to say that last week's appeal by seven doctors to their fellow doctors in this country to do "all in their power to halt preparation for war and to bring about a new and determined approach to the peaceful settlement of disputes and to world disarmament" seems to be wrongly addressed

These seven doctors are opposed to the policy of the Government and the Opposition in preparing for the defence of democracy against the onslaught of totalitarianism They are certainly entitled to their views, and they have (and should have) every right to express them But when they explain to British doctors that "willingness to cooperate and to understand the other man's rights and needs are hallmarks of civilisation" they are stating only a truism, as long as they are not able to produce evidence that Czechoslovak (or Hungarian or Polish) doctors are likewise free to express the same opinions and to oppose the governments of their country in the same way Willingness to cooperate and to understand the other man's rights and needs *are* the hallmarks of civilisation, but precisely because doctors in Czechoslovakia and other countries are forbidden to show any willingness to coöperate, and because they are denied any chance to understand the other man's rights and needs, the world is once more at the cross roads The danger of war is—as it was just over a decade ago—the consequence of dictatorship and not of the belated willingness of the democracies to defend themselves and the right to understand the other man's rights and needs "Cet animal est bien méchant ! Quand on l'attaque, il se défend"

BOHEMICUS

SIR—For some time I, and many of my young colleagues, have been oppressed by an overwhelming sense of shame and disgust at the apparently defeatist attitude of the medical profession towards the senseless drift to a Third World War We have waited impatiently for responsible medical men to raise their voices in protest, and until last week we had waited in vain Our wait was not altogether passive and we have attempted often to give a lead albeit unsuccessfully

The signatories to the letter "Prospect of War" have to some extent relieved this sense of oppression and shame May I say, therefore, that I wish to associate myself wholeheartedly with the sentiments they have expressed and their appeal to fellow doctors

London N W 6 JOHN Z GARSON

SIR,—It is becoming increasingly obvious that politics and medicine together are undergoing a shift to the left An already incongruous commensalism is being changed into a more virulent parasitism Presumably in the end politics only will be remaining

It was all the more alarming to see the rate of this change so exposed in your last issue, when political propaganda was allowed to invade the columns which have hitherto been spared for medicine, under the title "Prospect of War"

If such political missionaries "feel compelled to express themselves publicly" again may I, Sir, suggest it be in a special supplement, in limited edition, distributed only to those who express a wish for it ?

Woking D W S SHELDON

SIR,—As one of the many liable to early recall to the Forces should hostilities break out again, I should like to express my appreciation of the comments on this subject by Professor Penrose and his colleagues It seems to me that some recognition of the dangerous international situation is no more out of place in a medical journal than it is in any other publication, the more so as doctors would be expected to play a greater part than ever before in any future war On the contrary, such references merely reflect the growing concern of all sections of public opinion over the present catastrophic drift to war

It is not my intention, however, to try to turn your columns into a political forum Rather would I content myself with applauding the increasing preoccupation of men of science with world affairs and hoping that they may thereby recognise their own responsibility in this respect Such interest in the past might have gone a long way to averting previous disasters

As yet, however, there is no organised movement in this country to make known the views of responsible scientific workers, medical or otherwise, on this matter, so vital to us all The United States, however, is a jump ahead of us for in 1949 a group of American scientists formed a Society for Social Responsibility in Science, one of whose main objects is to resist the increasing military and political encroachment on human knowledge and scientific research This body includes many eminent men of science, doctors among them, in its membership roll, and I consider that we could with profit follow its lead, if only to show that all eminent scientists in this country are not Communists or fellow travellers It takes greater courage to form such a progressive movement in present day America than it would here in Britain, but as yet we have had no lead from our own eminent men of science As of all professions Medicine should stand

In England Now

A Running Commentary by Peripatetic Correspondents

IN our first house-jobs we owe a great deal to the tactful guidance of that fine body of women, the ward sisters I have never ceased to wonder at the apparently implicit faith with which, later on, they gracefully accept our instructions But in recent years they have fought and lost the battle for beef-tea against its commercial substitutes "Is he eating?" I used to ask, and sister would reply, "Yes, Doctor, I'm very pleased with him today, he took a little beef-tea" Years of facial grimaces and firm remonstrance have been needed to convince them that the goodness of the meat is not in the brew but in the dustbin

Now, when we doctors have almost won this battle, I am faced as a pædiatrician with a new engagement It concerns the latest method of dealing with premature infants I can feel the almost personal animosity aroused by my sadistic action Can there be a more cruel and heartless beast than I, who would starve a newborn baby—a baby weighing only 2½ lb For years the first flavour that such babies tasted has been the gentle warmth of Cognac brandy "And now," I can hear one sister saying to another over their private cup of tea, "these so called specialists, who a few years back couldn't tell a nappie from a kaolin poultice, give us orders that not even diluted milk must pass their lips for two, three, or sometimes four days" It will be a long battle this time, calling for eternal vigilance, even in the early hours of the morning, with every probationer, every student nurse, a potential enemy

* * *

Now that attention has been called to Mr S Potter's omission of doctors from his great works, *Gamesmanship* and *Lifemanship,* I shall certainly be swamped with requests for some account of my own painstaking (and -giving) investigations on Doctorship, Patientship, and Nursewomanship Though my results are not yet codified, I am therefore publishing these preliminary notes

1 *Doctorship* is defined as getting one up on the patient without actually killing him One need not say much more in a medical journal, since any doctor who has survived even a fortnight in general practice must have acquired a detailed knowledge of the more important ploys

2 *Patientship* is getting one up on the doctor without actually invoking the General Medical Council or committing suicide In its highest form this often passes unrecognised until the surgery door is closing and the doctor senses that he is not entirely master of the situation Only then will it dawn on him that he has been the subject of a Patientship Ploy—too late for any effective counter-ploy An example of this technique is the Name Ploy Many doctors, in the interests of dignity, adopt a double barrelled name An elementary patientship ploy is to ignore the first part and address the doctor by the second, and often more vulgar, name—thus Dr Fotheringay-Smith and Mr Beauchamp Jones become simply 'Dr Smith" and 'Mr Jones" This ploy is effective only against general practitioners and newly established consultants The experienced consultant will retort with the equally simple counter ploy of expressing gratification at the single name as a sign that his fame is now so great that identification by the first name is no longer needed A variation on this ploy, suitable only for the most senior Patientmen, is mispronunciation of the doctor's name This works best if the name is unusually flamboyant On one occasion my friend Hopking was greeted on his admission to hospital by the genito urinary surgeon, a Mr Leigh-Kerr, with 'Ah! Good morning, Hopkins" He replied "Hop*king*, please, Mr Leaker," and the next day was given the only single-bedded ward in the hospital

Fildes Priestley based the gambit since known by his name on the hypothesis that nothing rattles a doctor worse than a hint that he is ailing Certainly few doctors could withstand Fildes-Priestley's own hearty greeting of "Hello, Doc, you *are* looking tired these days" Another approach, favoured by J Grenfell, is to interrupt the doctor's history-taking with "And how's the doctor himself? Nobody asks after *his* health" The most advanced Patientmen sometimes embroider this ploy with technical terms, but these are apt to rebound if not absolutely fresh My distinguished friend, J Hopking, usually scored heavily by stepping up to his doctor, examining his conjunctivæ, and remarking "Hm, ha A little anæmic, I see, Doctor" But on one occasion he was met by the counter ploy of "Yes, I was badly let down by that fallacy in my student days Nowadays students learn in their first term that only hæmoglobinometer readings can be relied on On the Sahli scale my Hb is 105%" Because of this danger D Sharp prefers the simpler ploy of addressing his doctor as "Sir," in tones implying reverence for advanced years rather than respect for professional attainments.

3 *Nursewomanship* is defined as getting one up on the doctor and/or the patient (but preferably both) without actually marrying either An additional and important aspect of Nursewomanship consists, of course, in the Anti-Sister and Contra Matron Gambits

The leading exponent of Nursewomanship in the London region tells me that her basic ploy is to confess frankly, in full detail and at great length, to doctor, patient, and sister alike, every mistake she makes (except of course the fatal ones) In this way she attains a position where she can lead, so to speak, from strength

* * *

What doctor is not a good driver, and what doctor has not had a motor-car accident? After a late Sunday morning round I sipped coffee with the theatre staff, vowed I was going away till next year, and went out to my car in the snow I had intended to walk to the hospital that morning, for the snow was deep and the roads treacherous, but a farewell remark of my wife's that she supposed I'd be as late home as usual had made me quietly change my mind Now, eager to spring a surprise, I left for home

The drive, as it twists and turns through the hospital grounds, passes through a narrow one way defile, carefully protected by two blind corners I had passed the worst part and was moving on to the open road beyond when I espied our elegant medical registrar, preoccupied and even later than I, heading for the hospital as fast as his A40 would go Fascinated, I just had time to remark to myself, "If he's not careful there will be trouble," when I realised I was in the direct line of the trouble Tooting valiantly and drawing in to the side, I then sat spellbound as he applied his brakes on the ice and catapulted with a crash against the door of my car

We both alighted, both smiled sickly smiles, and both realised that our car was out of action for at least three weeks, that our no claim bonuses had gone with the wind, and that we would both be late home for lunch

Returning sheepishly from telephoning our respective wives, we found the impacted cars surrounded by a team of gleeful surgical registrars who, having critically examined and photographed the remains, advanced some colourful theories on the cause of the disaster Finally, turning their energies to good account, they disimpacted the cars, pushed them to safety, and declared the accident an excellent excuse for a further party

Trudging home later, I reflected that Sunday should indeed be a day of rest, that our medical registrar was really too conscientious for a physician, and that the time had come for me to apply to the Regional Board for *danger money*, if only to offset the projected cuts in car allowances and the 'loading" for specially risky occupations which any insurance company would hereafter add to my premiums

* * *

Could you alter my little girl's certificate, please, doctor? The club man called today and said if she'd broken her arm she'd have got 10*s* a week, but as she's fractured it she'll only get 5*s*

* * *

Aphorism of the Week

Tonight's mystery may be solved by tomorrow's otorrhœa

I think that Mr Stansfield and Mr Drabble are very weeping in their condemnation of cervical incisions, hese, when carried out carefully, can only be of benefit n the Ayrshire unit, with over 1900 confinements per annum, an average of 3 cases each year have been delivered by this method, without any maternal mortality, and the convalescence after vaginal delivery is still in the main more comfortable than after abdominal operation

It would appear from the criteria quoted by Mr Stansfield and Mr Drabble that many of the complications indicating extraperitoneal section are manufactured by ourselves in our maternity hospitals and could well be treated by transperitoneal section, with the one rare exception I have indicated

Ayrshire Central Hospital,
Irvine
RICHARD DE SOLDENHOFF

A C T H

SIR,—In his article last week Dr Morris says that adrenocorticotropic hormone (A C T H) is unlikely to be present in normal blood This opinion is based upon the observation that intravenously administered A C T H cannot be detected in whole plasma after 20 minutes and that multiple divided doses are more efficacious in therapeutic use

It is likely that Dr Morris's review was written before the publication of Bornstein and Trewhella's paper[1] on adrenocorticotropic activity of acid acetone extracts of plasma I have confirmed this work, such extracts are active in the ascorbic acid depletion test of Sayers, Sayers, and Woodbury[2]

In my opinion therefore, adrenocorticotropic hormone is normally present in plasma, and the observations referred to above could be interpreted as indicating a rapid turnover rate of the hormone

Department of Chemical Pathology
King s College Hospital Medical
School London S E 5
D M V PARROTT

SIR,—In Dr Morris's review, two very important contributions to the chemistry of the formation of the cortical steroids have not been considered Dr Morris states that it is likely that secretion of both the "glycogenic" and "mineral" cortical hormones is under the control of the pituitary In view of the fact that all the so called "glycogenic" hormones affect sodium metabolism[3] this division appears rather arbitrary and will confuse an already difficult subject

Pincus et al[4] have shown that 11 desoxy compounds are oxygenated in the 11 position by perfusion through the surviving adrenal gland Also Zaffaroni et al[5] have been able to identify 17 hydroxycorticosterone and corticosterone in the adrenal vein blood of dogs It is significant, too, that, although desoxycorticosterone has been well known for such a long time, apart from one unsubstantiated claim it has never been found in biological material This is of the utmost importance for it has been previously shown that the injection of 17 hydroxycorticosterone leads to sodium excretion[3] and the injection of corticosterone to sodium retention[3] although both have considerable "glycogenic" effects[6]

We thus agree with Dr Morris that the effect of A C T H on mineral metabolism will depend upon the relative proportions of steroids the adrenals are stimulated to secrete, but consider that the division into "glycogenic" and "mineral" corticoid hormones is undesirable

Department of Chemical Pathology
King's College Hospital Medical
School London S E 5
J BORNSTEIN
CHARLES H GRAY

---

1. Bornstein, J, Trewhella P *Lancet* 1950 ii 678
2. Sayers M A Sayers G Woodbury L A *Endocrinology* 1948 42 379
3. Thorn G W Engel L L Lewis R A *Science* 1941, 94 348
4. Hechter O, Jacobsen, R P Jeanloz R Levy H Marshall C W, Pincus G Schenker V *J Amer chem Soc* 1949 71 3261
5. Reich H Nelson D H Zaffaroni A *J biol Chem* 1950 187 411
6. Olson, R E Thayer J A, Kopp L J *Endocrinology* 1944 35 464

RESEARCH IN ANTHROPOMETRY

SIR,—The Medical Research Council have appointed a committee on growth and form, under the chairmanship of Prof P B Medawar, F R S, with the following terms of reference

> "To advise and assist the council (*a*) in promoting research on the growth and form of the human body with particular regard to the provision of basic scientific data, including the elucidation of factors affecting the rate of growth of the whole body and of its parts and the establishment of norms of stature and weight for different ages and different sections of the population, and (*b*) in facilitating the application of such data to various practical problems, including such as arise within the field of clinical medicine"

One of the committee's first tasks is to make a review of work in the field of anthropometry The committee would accordingly be glad to have information about current or completed anthropometric surveys, including unpublished records, so as to avoid any unnecessary repetition of work and to ensure, if possible, that use is made of existing material It is believed that there are in existence records of height, weight, and other body measurements which, if analysed, could form the basis for research into growth and development Serial records of the growth of the same children from year to year, as well as measurements which have been recorded over a long period of time, would be particularly valuable

Medical School, Hospitals Centre
Birmingham 15
E M B CLEMENTS
Secretary

BILE PIGMENTS IN URINE

SIR,—The test for bile pigments in urine described by Mr Ingham (Jan 20) is a test for bilirubin only Much confusion has arisen because of the failure to recognise that there are two main groups of bile pigments occurring in pathological urines—bilirubin and biliverdin on the one hand, and on the other "urobilin" and "urobilinogen," the latter group requiring tests different from those used for the former group The detection of urobilinogen and urobilin may be of great value not only in the differentiation of the various types of jaundice but also in the assessment of the stage and progress of cases of infective hepatitis

Department of Chemical Pathology
King s College Hospital Medical School
London S E 5
M J H SMITH

VITAMIN B_{12} IN PERNICIOUS ANÆMIA

SIR,—The view has been expressed from time to time that liver extracts contain factors additional to vitamin B_{12} which are necessary for the well being of patients with pernicious anæmia

We have always held that the question whether vitamin B_{12} is an adequate treatment for pernicious anæmia could only be answered after a large number of patients had been satisfactorily maintained for not less than two years In this hospital we have a number of patients who have been on controlled maintenance treatment for many years, various liver extracts having been used Since January, 1950, all patients have been treated by vitamin B_{12}, and we believe that the results of maintaining such a group for one year are of interest

The patients were divided into three groups (1) 37 received 20 µg, (2) 49 received 40 µg, and (3) 58 received 80 µg of vitamin B_{12} ('Cytamen) each month by intramuscular injection Taking a red-cell level of less than 4,000,000 per c mm as indication of relapse none of these patients relapsed Those receiving 40 µg each month showed higher average red cell levels than those receiving 20 µg each month, and those receiving 80 µg each month showed a higher red cell level than those receiving 40 µg each month On the 80 µg dose 98% of the patients showed red cell levels above 4,500 000 per c.mm, and 70% red-cell levels above 5,000,000 per c.mm for Wisdom and Peace I am hoping that Professor Penrose and his colleagues may provide this lead

London N 4 ADAIR GIRBY

SALICYLATE, GENTISATE, AND CIRCULATING EOSINOPHILS

SIR,—The letters from Dr Kelemen and his colleagues [1] and Dr Bertolani and his colleagues [2] prompt us to report some of our results These workers found that the administration of salicylate and gentisate in animals, and of salicylate in man,[1] was followed by a marked reduction in the number of circulating eosinophils This latter phenomenon has been used as an indication of adrenal cortical activity, and is of great interest because of the suggestion that the activity of salicylates may be related to stimulation of the adrenal cortex causing a liberation of corticoid substances which relieve rheumatic manifestations,[3] and also because of the report of a mild Cushing's syndrome produced by aspirin [4]

We have investigated the effect of oral administration of sodium salicylate and sodium gentisate on the number of circulating eosinophils in eight normal healthy subjects after establishing the functional integrity of the pituitary/adrenal cortex system by means of ephedrine [5] No significant depression in the number of circulating eosinophils was observed with plasma salicylate concentrations of up to 30 mg per 100 ml and plasma gentisate levels of up to 25 5 mg per 100 ml Kelemen (personal communication) states that plasma salicylate concentrations of over 30 mg per 100 ml were necessary to produce such an effect, and the work is being continued to include investigation of higher plasma salicylate and plasma gentisate concentrations

Department of Chemical Pathology,
King s College Hospital, London

B W MEADE
M J H SMITH

VACCINATION AGAINST SMALLPOX

SIR,—However mistaken Dr Killick Millard's views and however pernicious the effect on the public mind when garbled versions of his article are reported in the public press, you are to be congratulated on your wisdom in publishing the article It is a comforting sign that we have not yet reached the state of totalitarian countries which only permit the dissemination of orthodox views on scientific matters The editor's liberal attitude does, however, make it even more necessary that an authoritative statement of the case against Dr Millard's curious reasoning should be published, and I hope this will be forthcoming

Dr Millard's article (Jan 13) is so full of non-sequiturs that a considered reply would necessarily far exceed the limits of a letter, but some passing reflections may be made , his attitude reminds me of old Father William, who persisted in standing on his head Dr Millard's central argument is that while vaccination undoubtedly protects the individual it is detrimental to the community If, on the other hand, he had said that whereas one cannot guarantee that vaccination will protect every individual there is no doubt that a well vaccinated community is protected against smallpox, he would have carried informed opinion with him It is well known that a small proportion of individual men and animals do not respond to vaccination or immunisation by developing immunity and that they may succumb to subsequent infection although the immunised herd as a whole will have acquired adequate protection

Carried to its logical conclusion, Dr Millard's argument could be used to discredit inoculation against diphtheria since it is well known that immunised insusceptible children can act as healthy carriers of the infection and so infect unimmunised susceptible children Does Dr Millard therefore suggest that the strikingly successful campaign against diphtheria should be dropped or that all children should be immunised ?

Incidentally, Dr Millard himself says "I am all in favour of everyone who visits the East being efficiently protected by recent vaccination " It is surely relevant that both last year's Glasgow outbreak and the current episode at Brighton were initiated by this type of person Does Dr Millard then suggest that contacts of these people should not be vaccinated ? Or perhaps he would advocate that any such people who insist on returning to this country should be kept in quarantine for at least a fortnight because of the unvaccinated state of the population here ?

South Mimms Barnet, Herts DOUGLAS MCCLEAN

ADJUVANTS TO STREPTOMYCIN

SIR,—In his paper of Dec 16 on tuberculous meningitis, Dr Cathie cites a report by Dr Kirmse and me regarding the treatment of tuberculous meningitis with streptomycin and 'Promizole' [1] He states that we reported that "13 out of 18 cases appeared to be doing well 3–6 months after treatment had started" and expresses interest in a later report of these cases

In our report table III showed that 8 patients had already survived for 12–21 months, and the remaining 5 for 7, 7, 6, 5, and 3 months Up till now (Jan 4) there has been 1 further death during a relapse of meningitis, leaving 12 survivors of the original 18 cases with a survival range of 45 to 27 months

Department of Pediatrics,
New York University—
Bellevue Medical Center

EDITH M LINCOLN

EXTRAPERITONEAL CÆSAREAN SECTION

SIR,—I read with considerable interest the article of Jan 13 by Mr Stansfield and Mr Drabble

Since 1946 I have done an extraperitoneal cæsarean section in 15 cases , but I find that I am doing gradually fewer each year - It is an appealing operation, because of the technical artistry required , but one must not be distracted by this lure With the present array of antibiotics to combat the spread of infection to the peritoneal cavity, the success of the transperitoneal lower segment operation can be assured, and the premier advantage of the extraperitoneal operation has disappeared

In my experience, there is only one type of case where the extraperitoneal operation is required that is where cæsarean section is necessary on obstetrical grounds with the additional complication of a protracted labour with the concomitant severe distension of the gut, and the patient is in poor general condition These cases do extremely well under local anæsthesia and even the risk of spinal anæsthesia can be avoided The greatly distended gut is under the control of the peritoneum, thus avoiding any difficulty when the wound has to be closed The convalescence is also easier and there is, as Mr Stansfield and Mr Drabble state, less postoperative ileus With incipient shock the tissues can be handled gently and there is no worry about adding to the shock by either general or spinal anæsthesia

I am sorry that the article does not mention the simplest way of doing this operation, and the one which is certainly the easiest to learn—namely, the method introduced by Caccıarelli In this operation a small button hole is made in the peritoneum above the bladder, and, with the finger through this, the vesical peritoneum is dissected off Thereupon, the small opening is closed with a purse string suture, so that the peritoneum is then a closed cavity, before opening the lower segment

---

1 Kelemen E Majoros M Tanos B *Lancet* 1950 ii, 457
2 Bertolani F Lorenzini R Bonati B *Ibid* Jan 6 1951 p 54
3 Calesnick B , Beutner, R *Proc Soc exp Biol N Y* 1949 72, 632
4 Cochran, B Watson, R D , Reid J *Brit med J* 1950 ii 1411
5 Abelson D , Moyes, E N *Lancet* 1950 ii 50

1 Lincoln E M Kirmse T W *Lancet* 1949 i 767
2 Cacciarelli R *Amer J Obstet Gynec* 1947 53 100

4 4 g total proteins 6 0 g per 100 ml van den Bergh reaction direct, positive delayed 1 min , indirect, 4 units Thymol turbidity 1 Cephalin cholesterol positive

On Sept 6 the icterus had disappeared but he complained of intense itching mainly on the soles of his feet

On Sept 12 patch tests were done with 20% P A S solution, with 20% streptomycin solution and with a saline control All three gave a negative reading after 24 hours

Shortly afterwards the man left my care and returned home I understand that he has since made fairly good progress and was doing light work early in November He had had no more P A S

The sodium P A.S in this case was at first given in tablets of 0 5 g and from July 31 in 3 g cachets The tablets and cachets had been specially ordered and were fresh; there did not seem to be any possibility of deterioration

The patient denied having ever had a blood transfusion He had had a course of penicillin injections in 1947, and a second course from April 11 to 18, 1950, in which a rash had appeared, though with the help of anti histamine drugs it was possible to complete the injections Neither the patient's doctor nor his partners knew of any case of infectious jaundice in the neighbourhood during the six weeks before his visit to Whitby

The acute feverish illness, with severe headache and erythema, followed in five days by jaundice, may reasonably be ascribed to an acquired P A S sensitivity The eosinophilia of 11% indicates an allergic reaction The alternative of infective hepatitis does not seem likely in view of the clinical findings and the absence of a known source of infection Weil's disease was excluded by the urine examination, and again no source of infection was discovered Serum jaundice may be ruled out since the man had not received any injections within four months of the onset of jaundice

The patient shows a well marked tendency to allergic reactions, illustrated by the rash in his second course of penicillin injections The first reaction to P A S , which appeared nine days after the start of treatment when a total of 80 g of P A S had been given, consisted only of erythema and pruritus The reaction 58 days from the beginning of treatment, when 480 g of P A S had been given, was much more severe The 5 cases of P A S sensitivity already described also show this apparent relation between the severity of the reaction and the amount of P A.S administered

In Cuthbert s case where the complications (erythema, fever severe jaundice, and anuria) were the most severe and of longest duration the total of 720 g of P A S was the greatest amount in all that any of the cases had received

The cases of Climie [2] and of Morrison [3] developed fever and erythema only , the former had received 324 g and the latter 308 g of P A S (calculated from the data)

The case of Livingstone and Street [4] had headache and high fever followed by jaundice a macular rash, and finally anuria in severity this was second only to Cuthbert s case , the amount of P.A S (560 g) was also the second highest in the series

The case of Scott and McCann [5] developed a macular rash and high fever followed by urticaria and later a mild jaundice 380 g of P A S had been given (calculated)

A common finding in these cases is the absence of vomiting and diarrhœa during the administration of the drug Cuthbert found that cases in which these symptoms are absent usually have a high blood P A S level, and this may be a necessary condition for the development of a severe reaction , further observations are required on this point In the present case, though at times vomiting was a prominent symptom, the patient only vomited once during the 20 days before the severe reaction, when his daily intake of P A S was 15 g , in this period his blood P A S level would have been steadily rising, and it probably reached its highest peak at the time of the reaction

My thanks are due to Dr A C Brown of Ripon, who kindly verified the earlier part of the case record, which was obtained from the patient's own notes , and to Dr K Froome, pathologist to Scarborough Hospital, for his help with the investigations

Whitby   J D LITTLE

CORONARY DISEASE AND MODERN STRESS

SIR,—According to Professor Platt (Jan 6) the premises assumed in my article of Dec 23 are " very controversial " He thus includes in this category the statements that there has been " a vast increase in coronary disease during the present century," and that the " malady strikes predominantly men in middle life "

Terminology must, surely, be the cause of my failure to secure these limited concessions Indeed the phrase " coronary disease " is *far from satisfactory* I resorted to it in the same sense, and for the same reasons, as those given by Dr Morris in his article of Jan 6 My own brief definition was " coronary atheroma and its syndromes." By " coronary disease," therefore, is implied not an isolated pathological entity but two main clinical concepts —those of " angina " and of " coronary thrombosis "— occurring in association with coronary atheroma, clinical " thrombosis " further being accompanied usually by the morbid appearances of infarction, with or without an evident clot Gross coronary atheroma does not alone constitute " coronary disease " That such a finding is common in the absence of any previous indication of angina was mentioned by Osler in his textbook Dr Morris now suggests that coronary atheroma may have become less in recent years, though whether this generality applies to the incidence of premature plaques appearing selectively close to the left coronary bifurcation must be doubtful By contrast " coronary disease " has indeed become more widespread The best evidence for this would appear to be much the same as that which convinces historians that there was a sharp increase of plague during 1665—that is, recorded clinical experience

With this definition the statement that coronary disease affects predominantly middle aged men would appear not unduly controversial In support of the postulate that brain-workers are more threatened than their fellows I quoted the Registrar-General's Decennial Supplement for 1931, which shows a selectively increased incidence among professional people Professor Platt now confronts me with a further excerpt from this treatise

> ' Degenerative disease in the heart affects all classes of males to much the same extent, but whereas amongst men whose social conditions are most favourable it tends to express itself as angina pectoris or coronary disease, at the other end of the scale it tends to take forms described on death certificates as myocarditis or myocardial or cardio vascular degeneration '

This pronouncement, says Professor Platt, renders the occupational figures ' almost meaningless "

So far from discrediting them I maintain that it does much to fortify them Angina pectoris is a good honest symptom, fairly easily recognised, and known to be associated nearly always with coronary atheroma It thus virtually identifies coronary disease Without autopsy the only certified cause of death that can have any value must be founded upon some such reputable clinical grounds If, therefore the term " angina pectoris " appears most often upon the certificates of men whose " social conditions " were " most favourable," is it not reasonable to assume that this is because such people

---

1 Cuthbert, J *Lancet* 1950 ii 209
2 Climie H *Ibid* p 308
3 Morrison J B *Ibid* p 308
4 Livingstone R Street E W *Ibid* p 308
5 Scott A B A McCann J J *Ibid*, p 366

When the condition of these patients treated with vitamin B_{12} is compared with their previous record under liver therapy, it is found that 3% show slightly lower red cell levels on vitamin B_{12} than on liver extract, 32% show no significant difference, and 65% are distinctly better on vitamin B_{12} than they were on liver therapy. Thus a majority of our patients are distinctly better when treated with vitamin B_{12} than they were on liver therapy even though, as shown above, more than half the patients are receiving less than an optimal dose of vitamin B_{12}. In the group receiving 80 µg of B_{12} each month, 80% show a higher red cell level than they did on liver therapy.

From these observations, therefore, it would appear advisable to give at least 80 µg of vitamin B_{12} at monthly intervals to maintain a red cell level of 5,000,000 per c mm, and it is possible that a larger dose will give still better results. There is no doubt in our minds that these patients have been better in every respect since vitamin B_{12} replaced liver therapy.

Royal Berkshire Hospital
Reading

J MILLS
E H HEMSTED

DUAL CAUSE OF RAPID DEATH

SIR,—In his letter of July 15, 1950, Dr I B Morris, pathologist to the Kent and Canterbury Hospital, reports a case of sudden death for which necropsy revealed two possible causes—cerebral hæmorrhage and rupture of the aorta. Cases of this kind are important in medicolegal practice. In 1867 Skrzeczka called the condition "concurrent causes of sudden death", but this was not quite accurate, and it was Fischer, of Breslau, who in 1923, at the instigation of Professor Puppe, reviewed a number of cases at the Forensic Institute and chose the title "coincidental causes of death". He distinguished three categories: (1) two natural causes, (2) a natural and unnatural cause, and (3) two unnatural causes. The fewest cases, he said, occurred in the first category, and this is supported by my own experience, for I have seen but one case in 10,000 necropsies on adults. (I am not including a case of bilateral rupture of aneurysms of the common iliac arteries with a massive retroperitoneal hæmorrhage. This occurred in a man of 65.)

The case I am about to report is unusual in that there was a hæmopericardium, due to spontaneous rupture of the right ventricle, and a large left-sided lenticulostriate hæmorrhage which had burst into the left lateral ventricle of the brain. According to Huchard,[1] of 259 cases, rupture of the right ventricle occurred in 10.1%, and of the left ventricle in 79.9%. This indicates that spontaneous rupture of the right ventricle is relatively infrequent, which makes my case still more unusual. These percentages accord with those of most authors who have reviewed a number of cases.

A young woman, 32 years old, appeared to be in normal health when he husband went to work early in the morning. Visitors during the morning were unable to get any response, and when the room was forcibly entered by the police she lay dead on the floor near a bed. At necropsy the body was that of a frail woman; there were abrasions about the outer aspect of the right elbow and about the left eyebrow, and a dry brownish stain round the mouth. The scalp and skull were intact. A horizontal section of the brain at the saw line of the skull (Vienna method used at this institution) revealed a large left-sided lenticulostriate hæmorrhage which had burst into the left lateral ventricle; no atheroma of the circle of Willis; no injury to brain; some noticeable coning. The pericardial sac contained 180 ml of fluid and clotted blood. On the anterior aspect of the right ventricle there was a rupture of the wall $^{3}/_{4}$ in. long. The heart was slightly enlarged and weighed 13 oz. The left ventricle showed some hypertrophy; no macroscopic fibrosis. There was a moderate amount of atheroma of both coronaries, particularly the right, and at the commencement of the aorta; the lungs were acutely congested and œdematous and weighed 26 oz (right) and 24 oz (left); the liver, spleen, and kidneys were congested, the bladder and ureters were normal. The uterus contained a fœtus of $8^{1}/_{2}$ months. A complete toxicological examination of the organs was negative. There was no hypoplasia of the aorta. As the pericardial effusion of blood leads to death within a few minutes—usually, though by no means always, by compression of the heart and large veins—it must be supposed that the cerebral hæmorrhage occurred first.

Kehrer in his comprehensive monograph does not mention a case of coincidental causes of death during pregnancy. Wenger[3] of Sucre, Bolivia, describes a case of incomplete rupture of the aorta and a large fresh hæmorrhage in the area of the basal ganglions and internal capsule. The deceased was 70 years old. He says: "It seems that such an occurrence has not yet been reported."

South African Police
Medico Legal Laboratories
Johannesburg
South Africa

R H MACKINTOSH
Director

ACQUIRED IDIOSYNCRASY TO SODIUM *p*-AMINOSALICYLATE

SIR,—The following case is a further illustration of the reaction to sodium *p* aminosalicylate (P.A.S.) described in your columns by Dr Cuthbert[1] and others.

A married man, aged 44, suffering from tuberculous epididymitis and pulmonary tuberculosis, was confined to bed at home in Ripon on June 15, 1950. On June 27 P.A.S. was started in a daily dosage of 7.5 g, increased on July 1 to 10 g. The drug was withheld every seventh day.

On July 4 the man vomited four times; 'Benadryl,' 50 mg t.i.d., was given. Next day the vomiting had ceased, but there was a generalised erythema with severe pruritus. On the 6th he vomited three times; pruritus was still severe; P.A.S. was discontinued. On the 7th he felt generally better. On the 13th he vomited once at 3 A.M., but P.A.S. was recommenced with 5 g daily. On the 14th he vomited about six times in the night, but vomiting ceased by the 16th. On the 23rd the dose of P.A.S. was raised to 7.5 g daily. On the 29th the drug was stopped for two days, after which the daily dose was increased to 15 g. On Aug 2 he vomited twice in the night. The P.A.S. was stopped next day and vomiting then ceased. From Aug 4 he was again given 15 g of P.A.S. daily. On the 6th he vomited once. From the 9th he was allowed out for half an hour morning and afternoon.

On Aug 20 he travelled to Whitby, taking a supply of P.A.S. with him. During and after the journey he vomited several times, but walked about a mile in the evening. On returning home he felt ill, shivered, and had a headache. On getting to bed he sweated profusely.

When seen on Aug 23, he complained of frequent vomiting and severe occipital headache. His skin was flushed and moist with sweat, and he appeared acutely ill; temperature 104°F. A generalised rubelliform macular erythema was present. No enlargement of the cervical glands could be detected. P.A.S. was discontinued, a total of 480 g having been administered. Next day vomiting persisted. The vomitus at first contained blood clots and later some blood-stained mucus. On the 25th he felt better and had stopped vomiting. He was now afebrile and the rash had faded, but there was a faint icterus, best seen in the sclerotics. The liver was enlarged two fingerbreadths below the costal margin and was slightly tender. The urine was dark; Gmelin's test showed the presence of bile pigment. On Aug 27 his jaundice was slightly deeper, but his general condition had improved, and his appetite was returning. There was no desquamation. On the 31st there was further improvement; the liver edge was now only just palpable.

On Sept 1 the urine was reported on as: acid, slight trace of protein, no sugar or acetone; few hyaline and granular casts; no red cells, spirochætes, or other organisms; sterile on culture. Blood findings were: Hb 80% (Haldane), red cells 4,850,000 per c mm, colour index 0.9, white cells 5600 per c mm. (neutrophils 53%, eosinophils 11%, basophils 1%, lymphocytes 30%, monocytes 5%). Serum albumin

---

[1] Huchard H Maladies du coeur Paris 1889, vol 1 p 229

[2] Kehrer E Der unvermutet schnelle Tod in Schwangerschaft Geburt und Wochenbett Stuttgart, 1934

[3] Wenger F *Arch Path* 1943, 36 253

4 4 g total proteins 6 0 g per 100 ml van den Bergh reaction direct, positive, delayed 1 min indirect, 4 units Thymol turbidity, 1 Cephalin cholesterol positive

On Sept 6 the icterus had disappeared but he complained of intense itching, mainly on the soles of his feet

On Sept 12 patch tests were done with 20% PAS solution, with 20% streptomycin solution and with a saline control All three gave a negative reading after 24 hours

Shortly afterwards the man left my care and returned home I understand that he has since made fairly good progress and was doing light work early in November He ad had no more PAS

The sodium PAS in this case was at first given in tablets of 0 5 g and from July 31 in 3 g cachets The tablets and cachets had been specially ordered and were fresh, there did not seem to be any possibility of deterioration

The patient denied having ever had a blood transfusion He had had a course of penicillin injections in 947, and a second course from April 11 to 18, 1950, in which a rash had appeared, though with the help of anti histamine drugs it was possible to complete the injections Neither the patient's doctor nor his partners knew of any case of infectious jaundice in the neighbourhood during the six weeks before his visit to Whitby

The acute feverish illness, with severe headache and erythema, followed in five days by jaundice, may reasonably be ascribed to an acquired PAS sensitivity The eosinophilia of 11% indicates an allergic reaction The alternative of infective hepatitis does not seem likely in view of the clinical findings and the absence of a known source of infection Weil's disease was excluded by the urine examination, and again no source of infection was discovered Serum jaundice may be ruled out since the man had not received any injections within four months of the onset of jaundice

The patient shows a well marked tendency to allergic reactions, illustrated by the rash in his second course of penicillin injections The first reaction to PAS, which appeared nine days after the start of treatment when a total of 80 g of PAS had been given, consisted only of erythema and pruritus The reaction 58 days from the beginning of treatment, when 480 g of PAS had been given, was much more severe The 5 cases of PAS sensitivity already described also show this apparent relation between the severity of the reaction and the amount of PAS administered

In Cuthbert's case, where the complications (erythema, fever, severe jaundice and anuria) were the most severe and of longest duration, the total of 720 g of PAS was the greatest amount in all that any of the cases had received

The cases of Climie[2] and of Morrison[3] developed fever and erythema only, the former had received 324 g and the latter 308 g of PAS (calculated from the data)

The case of Livingstone and Street[4] had headache and high fever, followed by jaundice a macular rash, and finally anuria, in severity this was second only to Cuthbert's case, the amount of PAS (560 g) was also the second highest in the series

The case of Scott and McCann[5] developed a macular rash and high fever followed by urticaria and later a mild jaundice 380 g of PAS had been given (calculated)

A common finding in these cases is the absence of vomiting and diarrhœa during the administration of the drug Cuthbert found that cases in which these symptoms are absent usually have a high blood PAS level, and this may be a necessary condition for the development of a severe reaction, further observations are required on this point In the present case, though at times vomiting was a prominent symptom, the patient only vomited once during the 20 days before the severe reaction, when his daily intake of PAS was 15 g, in this period his blood-PAS level would have been steadily rising, and it probably reached its highest peak at the time of the reaction

My thanks are due to Dr A C Brown of Ripon, who kindly verified the earlier part of the case record, which was obtained from the patient's own notes, and to Dr K. Froome, pathologist to Scarborough Hospital, for his help with the investigations

Whitby J D LITTLE

---

[1] Cuthbert, J *Lancet* 1950, ii 209
[2] Climie H *Ibid* p 308
[3] Morrison J B *Ibid* p 308
[4] Livingstone R Street E W *Ibid*, p 308
[5] Scott, A B A McCann J J *Ibid*, p 366

CORONARY DISEASE AND MODERN STRESS

SIR,—According to Professor Platt (Jan 6) the premises assumed in my article of Dec 23 are "very controversial" He thus includes in this category the statements that there has been "a vast increase in coronary disease during the present century," and that the "malady strikes predominantly men in middle life"

Terminology must, surely, be the cause of my failure to secure these limited concessions Indeed the phrase "coronary disease" is far from satisfactory I resorted to it in the same sense, and for the same reasons, as those given by Dr Morris in his article of Jan 6 My own brief definition was "coronary atheroma and its syndromes" By "coronary disease," therefore, is implied not an isolated pathological entity but two main clinical concepts —those of "angina" and of "coronary thrombosis"— occurring in association with coronary atheroma, clinical "thrombosis" further being accompanied usually by the morbid appearances of infarction, with or without an evident clot Gross coronary atheroma does *not* alone constitute "coronary disease" That such a finding is common in the absence of any previous indication of angina was mentioned by Osler in his textbook Dr Morris now suggests that coronary atheroma may have become less in recent years, though whether this generality applies to the incidence of *premature* plaques appearing selectively close to the left coronary bifurcation must be doubtful By contrast "coronary disease" has indeed become more widespread The best evidence for this would appear to be much the same as that which convinces historians that there was a sharp increase of plague during 1665—that is, *recorded clinical experience*

With this definition the statement that coronary disease affects predominantly middle aged men would appear not unduly controversial In support of the postulate that brain workers are more threatened than their fellows I quoted the Registrar General's Decennial Supplement for 1931, which shows a selectively increased incidence among professional people Professor Platt now confronts me with a further excerpt from this treatise

> "Degenerative disease in the heart affects all classes of males to much the same extent, but whereas amongst men whose social conditions are most favourable it tends to express itself as angina pectoris or coronary disease, at the other end of the scale it tends to take forms described on death certificates as myocarditis or myocardial or cardio vascular degeneration"

This pronouncement, says Professor Platt, renders the occupational figures "almost meaningless"

So far from discrediting them I maintain that it does much to fortify them Angina pectoris is a good honest symptom, fairly easily recognised, and known to be associated nearly always with coronary atheroma It thus virtually identifies coronary disease Without autopsy the only certified cause of death that can have any value must be founded upon some such reputable clinical grounds If, therefore, the term "angina pectoris" appears most often upon the certificates of men whose "social conditions" were "most favourable," is it not reasonable to assume that this is because such people

When the condition of these patients treated with vitamin B_{12} is compared with their previous record under liver therapy, it is found that 3% show slightly lower red cell levels on vitamin B_{12} than on liver extract, 32% show no significant difference, and 65% are distinctly better on vitamin B_{12} than they were on liver therapy Thus a majority of our patients are distinctly better when treated with vitamin B_{12} than they were on liver therapy even though, as shown above, more than half the patients are receiving less than an optimal dose of vitamin B_{12} In the group receiving 80 µg of B_{12} each month, 80% show a higher red cell level than they did on liver therapy

From these observations, therefore, it would appear advisable to give at least 80 µg of vitamin B_{12} at monthly intervals to maintain a red cell level of 5,000,000 per c mm , and it is possible that a larger dose will give still better results There is no doubt in our minds that these patients have been better in every respect since vitamin B_{12} replaced liver therapy

Royal Berkshire Hospital
Reading

J MILLS
E H HEMSTED

DUAL CAUSE OF RAPID DEATH

SIR,—In his letter of July 15, 1950, Dr I B Morris, pathologist to the Kent and Canterbury Hospital, reports a case of sudden death for which necropsy revealed two possible causes—cerebral hæmorrhage and rupture of the aorta Cases of this kind are important in medicolegal practice In 1867 Skrzeczka called the condition "concurrent causes of sudden death", but this was not quite accurate, and it was Fischer, of Breslau, who in 1923, at the instigation of Professor Puppe, reviewed a number of cases at the Forensic Institute and chose the title "coincidental causes of death" He distinguished three categories (1) two natural causes, (2) a natural and unnatural cause, and (3) two unnatural causes The fewest cases, he said, occurred in the first category, and this is supported by my own experience, for I have seen but one case in 10,000 necropsies on adults (I am not including a case of bilateral rupture of aneurysms of the common iliac arteries with a massive retroperitoneal hæmorrhage This occurred in a man of 65)

The case I am about to report is unusual in that there was a hæmopericardium, due to spontaneous rupture of the right ventricle, and a large left sided lenticulostriate hæmorrhage which had burst into the left lateral ventricle of the brain According to Huchard,[1] of 259 cases, rupture of the right ventricle occurred in 10 1%, and of the left ventricle in 79 9% This indicates that spontaneous rupture of the right ventricle is relatively infrequent, which makes my case still more unusual These percentages accord with those of most authors who have reviewed a number of cases

A young woman, 32 years old appeared to be in normal health when he husband went to work early in the morning Visitors during the morning were unable to get any response, and when the room was forcibly entered by the police she lay dead on the floor near a bed At necropsy the body was that of a frail woman , there were abrasions about the outer aspect of the right elbow and about the left eyebrow, and a dry brownish stain round the mouth The scalp and skull were intact A horizontal section of the brain at the saw line of the skull (Vienna method used at this institution) revealed a large left sided lenticulostriate hæmorrhage which had burst into the left lateral ventricle no atheroma of the circle of Willis , no injury to brain , some noticeable coning The pericardial sac contained 180 ml of fluid and clotted blood On the anterior aspect of the right ventricle there was a rupture of the wall $^3/_4$ in long The heart was slightly enlarged and weighed 13 oz The left ventricle showed some hypertrophy , no macroscopic fibrosis There was a moderate amount of atheroma of both coronaries, particularly the right, and at the commencement of the aorta , the lungs were acutely congested and œdematous and weighed 26 oz (right) and 24 oz (left) , the liver, spleen, and kidneys were congested the bladder and ureters were normal The uterus contained a fœtus of $8^1/_2$ months A complete toxicological examination of the organs was negative There was no hypoplasia of the aorta As the pericardial effusion of blood leads to death within a few minutes—usually, though by no means always, by compression of the heart and large veins—it must be supposed that the cerebral hæmorrhage occurred first

Kehrer in his comprehensive monograph does not mention a case of coincidental causes of death during pregnancy Wenger[3] of Sucre, Bolivia, describes a case of incomplete rupture of the aorta and a large fresh hæmorrhage in the area of the basal ganglions and internal capsule The deceased was 70 years old. He says "It seems that such an occurrence has not yet been reported"

South African Police
Medico Legal Laboratories
Johannesburg
South Africa

R H MACKINTOSH
Director

ACQUIRED IDIOSYNCRASY TO SODIUM *p*-AMINOSALICYLATE

SIR,—The following case is a further illustration of the reaction to sodium *p* aminosalicylate (P A S) described *in your columns by Dr Cuthbert*[1] *and others*

A married man, aged 44, suffering from tuberculous epididymitis and pulmonary tuberculosis, was confined to bed at home in Ripon on June 15, 1950 On June 27 P.A.S was started in a daily dosage of 7 5 g , increased on July 1 to 10 g The drug was withheld every seventh day

On July 4 the man vomited four times , 'Benadryl,' 50 mg t i d , was given Next day the vomiting had ceased, but there was a generalised erythema with severe pruritus On the 6th he vomited three times , pruritus was still severe, P A S was discontinued On the 7th he felt generally better On the 13th he vomited once at 3 A M , but P.A.S was recommenced with 5 g daily On the 14th he vomited about six times in the night, but vomiting ceased by the 16th On the 23rd the dose of P A S was raised to 7 5 g daily On the 29th the drug was stopped for two days, after which the daily dose was increased to 15 g On Aug he vomited twice in the night The P A.S was stopped next day and vomiting then ceased From Aug 4 he was again given 15 g of P A S daily On the 6th he vomited once From the 9th he was allowed out for half an hour morning and afternoon

On Aug 20 he travelled to Whitby, taking a supply of P A S with him During and after the journey he vomited several times, but walked about a mile in the evening On returning home he felt ill, shivered, and had a headache On getting to bed he sweated profusely

When seen on Aug 23, he complained of frequent vomiting and severe occipital headache His skin was flushed and moist with sweat, and he appeared acutely ill , temperature 104°F A generalised rubelliform macular erythema was present No enlargement of the cervical glands could be detected P A S was discontinued, a total of 480 g having been administered Next day vomiting persisted. The vomitus at first contained blood clots and later some blood stained mucus On the 25th he felt better and had stopped vomiting He was now afebrile and the rash had faded, but there was a faint icterus, best seen in the sclerotics The liver was enlarged two fingerbreadths below the costal margin and was slightly tender The urine was dark , Gmelin's test showed the presence of bile pigment On Aug 27 his jaundice was slightly deeper, but his general condition had improved, and his appetite was returning There was no desquamation On the 31st there was further improvement , the liver edge was now only just palpable

On Sept 1 the urine was reported on as acid, slight trace of protein, no sugar or acetone , few hyaline and granular casts , no red cells, spirochætes, or other organisms , sterile on culture Blood findings were Hb 86% (Haldane), red cells 4,850,000 per c mm , colour index 0 9, white cells 5600 per c mm (neutrophils 53%, eosinophils 11%, basophils 1%, lymphocytes 30%, monocytes 5%) Serum albumin ion for his patients . . . was always near the surface of his mind."

---

[1] Huchard H Maladies du cœur Paris 1889 vol 1 p 229

[2] Kehrer E Der unvermutet schnelle Tod in Schwangerschaft, Geburt und Wochenbett Stuttgart 1934

[3] Wenger, F *Arch Path* 1943, 36 253

R. M. V. adds to the picture:

Gask was a quiet accurate teacher. He was also a strict disciplinarian with a well-developed sense of time. When he was on duty it was his custom to go round the boxes and remonstrate with any dressers who were habitually late. As a professor he was essentially a devolutionist. He always saw to it that all the members of his unit had plenty of work to do and plenty of responsibility. And thus he trained many generations of first-class surgeons.

Soon after Gask took charge of the unit at Barts he began to invite a distinguished surgeon to take his place for a fortnight each alternate summer. Harvey Cushing, Moynihan, Grey Turner, David Wilkie, Max Page were among these professional visitors. The comradeship which began at home did not end there, and he was the moving spirit and adroit courier who made possible the Pilgrim Surgeons' visits in the '30s to European centres of surgery. One of his fellow pilgrims recalls how:

'With Cuthbert Wallace as the born compere, a visiting team of ten or more teachers worked and played with home teams of medical schools of Western Europe, learning each other's techniques and coining a common currency. Gask's staff work was behind all this, and his success as a breaker of barriers has been ascribed to his calm unworrying temperament. He saved time and effort by not getting excited. He was probably unaware of this but he had an instinctive distrust of enthusiasm in medicine, using the word in the sense Monsignor Knox attaches to it in religion.'

His close relationship with his colleagues abroad was appropriately reflected in his honorary membership of surgical bodies in America, France, and Italy.

Outside his hospital, but within his specialty, lay his work for the *British Journal of Surgery*, which was commemorated in a special issue of the journal last July. He was elected to the editorial committee in 1919, and from 1936 to 1947 he was chairman. The birthday tribute to him contains the following passage:

> In directing the affairs of the *Journal* Gask showed again his capacity for the quiet and effective management of his fellow men and for the broadminded enrolment of all who could help in forwarding the interests of British surgery."

To this end he arranged for Elliot Cutler, consulting surgeon to the American Forces in Europe, to be appointed to the editorial committee, and later he enlarged it to contain representatives of anæsthetics, pathology, ophthalmology, and industrial medicine, and of the provincial and municipal non-teaching hospitals.

He had a great enthusiasm for good clinical records and the follow-up clinic. In Changing Surgery, his presidential address to the Medical Society of London in 1935, he said:

> "It is abundantly clear that what the medical profession needs are reliable records. It should be furnished with the results of various types of operation performed, and it needs these in large numbers. What is required are statistics of a comprehensive and national character and not merely the figures of a few gifted and energetic individuals."

He realised that a satisfactory disease classification was the first requisite, and again he became the catalyst. He encouraged Dr. Percy Stocks of the General Register Office to see whether a morbidity classification could not be drawn up; out of this developed the Medical Research Council's Provisional Classification of Diseases and Injuries, which was one of the main foundations for the World Health Organisation's International Statistical Classification of Diseases, Injuries, and Causes of Death which was adopted in 1948. Beside his membership of the Medical Research Council, he also served on the Radium Commission and on the council and as a vice-president of the Royal College of Surgeons. He delivered before the college Hunterian, Bradshaw, and Vicary lectures, and before the Medical Society of London the Lettsomian lectures on Surgery of the Lung and Pleura. As collaborator for the succeeding editions of his textbook on *Surgery* he had first W. G. Spencer and later H. W. Wilson. His co-author in *Surgery of the Sympathetic Nervous System* (1934) was Paterson Ross who succeeded him in his chair.

When war came again in 1939 it was unthinkable that Gask would continue in retirement at Hambledon, growing lilies and sitting on the magistrates' bench; he gladly accepted Sir Farquhar Buzzard's invitation to help with the teaching in the Oxford clinical school which had been established at the Radcliffe Infirmary almost overnight; and so it was that a new generation of medical students came to know "Uncle George," his clear exposition of the basic principles of surgery, and his leisured operative skill. On going to live in Oxford he was made a member of Christ Church senior common-room and he received the degree of M.A. by decree in 1940. He found as great a pleasure in the conversation of the canons and students as they found in him; the atmosphere stimulated his studies into the history of science, and it was at this time that he wrote his essays on the *Early Medical Schools of Greece and Rome* and began work on his unfinished biographical dictionary of ancient Greek physicians.

Buzzard soon realised that he had brought to Oxford not only an excellent teacher of surgery but also a man of vision and ideas about hospital coördination. Gask became a member of the medical advisory council of the Nuffield Provincial Hospitals Trust and chairman of the medical advisory committee of the Berks, Bucks, and Oxon Regional Hospitals Council. He spurred his committee to action, to collect information, and, in the light of the facts, to plan for the future. Soon memoranda appeared—which were not only of value for the local services but served as models for other centres—on a cancer service, which estimated for the first time the incidence of cancer in terms of the living population and so showed the needs for beds and special equipment; on a comprehensive maternity service; and on child health services. Again it was natural that Gask should take part in the hospital surveys initiated by the trust and the Ministry, for as a regional adviser in surgery to the Ministry he had gained an intimate knowledge of the hospitals of his area. When the wounded, evacuated from Dunkirk, came to the Oxford hospitals, he was ready with help and advice, and he played a big part in the later plans when air transport was used for bringing casualties from Northern France to Wiltshire.

Gask renewed one of his earlier interests by his share in the establishment of the Trust's bureau of health and sickness records at Oxford, and, when the National Health Service came into being, he, as chairman of the medical advisory committee of the Oxford regional board, persuaded the officers of the board of their need for accurate statistical information which the bureau could provide.

'It was impossible' writes A. H. T. R. S., 'to expect a man even of Gask's stamina, to continue all his activities untrammelled, and as his health began to interfere with his enthusiasm, he had, unwillingly but with a good grace, to give up things; first it was his teaching, then the chairmanship of some of his committees, then the chairmanship of the medical advisory committee, and lastly the chairmanship of the bureau committee. But enforced retirement from active membership of a committee did not mean loss of interest, and letters would arrive starting "What are you going to do about this?" or "Isn't it time so and so was finished?" and there were delightful afternoons at Hambledon in the garden or looking over the Chilterns when plans would be hatched with the aid of Mrs. Gask's scones and quince jelly. Some little time before his 75th birthday, Gask's friends felt a fitting present would be the publication of some of his historical essays and friends from all over the world subscribed; the secret was well kept, but the presentation of a bound copy of the book was wisely a simple and homely birthday party in his bedroom. His pleasure was great, at the thought and for the book, but most of all there was surprise that so many people should wish to join in expressing their admiration and affection for him. His modesty was as fundamental a facet of his character as was his enthusiasm and honesty, and as he said in Changing Surgery, which in a way expresses his professional credo: "Let us remember the story of the race of the torch. They were not always the fastest runners who kept their torch alight."'

In 1913 Professor Gask married Ada Alexandra, daughter of Lieut.-Colonel Alexander Crombie, C.B., I.M.S. She survives him with one son, Dr. John Gask.

suffer relatively more from coronary disease ? "Myocarditis," "myocardial degeneration," and the rest, provide the small change of certification They do very well in default of anything much to go on Now these expressions, it seems, are found particularly at the "other end of the scale" Is it not possible that their very presence implies the absence of any striking past manifestations such as those of the coronary ischæmic syndromes, that in fact the people whose deaths they purport to explain, though they may have had coronary atheroma if anyone cared to look for it, did not suffer from coronary disease ? It can scarcely be suggested that the Registrar General, or any of his henchmen, would so far desert his proper sphere as to hint that doctors weigh the social standing of their late patients before awarding them appropriate causes of death Neither can it be valid to maintain that, in 1931, only a consultant could be expected to make an accurate diagnosis of this form of heart disease In that year a consultant, who probably even then would see in public wards many more patients than he saw in private, would have been likely enough to miss a coronary thrombosis, or to call it angina The deaths of those relatively few victims who succumbed to it without previous chest pain he might well have found almost as inexplicable as did his general practitioner colleagues He, too, might have resorted to the myocardial degeneration formula On the other hand, though for long it remained rare, angina had been described in England by Heberden at the end of the 18th century, and its coronary association recognised by Jenner Most practitioners would certainly be familiar with it What, in working-class life, apart perhaps from birth and death, could be more calculated to result in a call to the doctor than an unheralded, frightening, and crippling affliction of the bread winner ? If such a call was seldom made the implication is that its occasion seldom arose

Within their limitations, then—and it can scarcely be maintained that this form of statistics is completely worthless—the Registrar General's figures, together with his enlightened observations, would seem to support my contention that the better educated, and the personally ambitious, suffer coronary disease more than do manual labourers

From Dr Geiringer (Jan 13) I gather that I am a victim of sublimated Da Costa's syndrome But he misunderstands me The division which exists in England today between two attitudes of mind has nothing to do with moral values For all I know, or care, industry may be a vice and idleness a virtue And I offer no theories upon ætiological mechanisms I merely point a parallel

University of Bristol I McD G STEWART

RECENT HISTORY OF CORONARY DISEASE

SIR,—In his article (Jan 6 and 13) Dr Morris has brought forward a very interesting fact—that, despite the sevenfold increase in the number of cases of occlusive coronary heart disease, there has been during the same period a substantial decrease in advanced coronary atheroma, as defined by the report of calcified lesions in the arteries

However, from this we cannot deduce that occlusive heart disease may not be due to atheroma without extensive calcification By way of illustration may I point out that the coronary vessels tend to be constricted during cardiac systole, thus reducing the flow in them and predisposing to thrombosis It will be apparent that if the vessels are calcified this advanced condition will tend to keep them patent, thus reducing the possibility of thrombosis Coronary occlusion can thus still be due to non calcified atheroma

Ilford I GORDON

Obituary

GEORGE ERNEST GASK

C M G, D S O, M A Oxfd, F R C S, Hon F A C S

Professor George Gask, who held the chair of surgery at St Bartholomew s Hospital from 1919 to 1935 and was director of the first professorial surgical unit of the University of London, died on Jan 16 at his home at Hambledon at the age of 75

He was educated at Dulwich College, and after spending some time abroad at Lausanne and Freiburg, he entered Barts in 1893, qualifying five years later From his first appointment as house-surgeon to John Langton he held a succession of junior posts before his election to the staff in 1907, and for several years he lived at the hospital as warden of the medical college

When war broke out in 1914 he was established as a consultant in surgery, and his bent for chest surgery was already clear Whether at a casualty-clearing station in France in the early years, or later as consulting surgeon to the Fourth Army, with the rank of colonel A M S, he did much to develop the treatment of thoracic injuries For his services he was four times mentioned in despatches, was awarded the D S O in 1917, and was appointed C M G in 1919 His work on the chest won him the gold medal of the West London Medico Chirurgical Society

Gask had early gained a reputation as an accomplished operator, and his gentle methods were in striking contrast to those of many surgeons of his generation who thought speed more important than delicate handling of the tissues But his interests were never limited to his specialty As he was later to say, he believed a good hospital should be a "seedplot of wisdom," and his interest in medical education was keen and creative After the war his personality was one of the factors that led to the establishment of the first professorial surgical unit at Barts, and the success of this experimental unit was his justification How much it owed to him is explained by J H

> "Gask had a remarkable quiet, easy, and friendly manner with everyone, whether it was a colleague, a visiting surgeon, or a junior dresser, but behind this exterior there was at times great force and persistence in carrying out some project or new piece of work which continued until it was completed He had the knack of choosing good men and gathering them round him on the professorial unit and then giving them a free rein to develop their special interest and work And thus the unit became a live concern "

As in all live concerns, the flavour of the unit was spiced by the endearing foibles of its chief Gask had been a keen mountaineer—he was a former secretary of the Alpine Club—and he remained an enthusiastic walker even in London

> ' It was a familiar sight " J H continues, "to see him arriving on foot at Barts at nine o'clock, or before, having walked the whole way from his home in Regent's Park, and ready to start a morning s operating All who worked at his unit will remember him in his characteristic garb of a bath towel thrown over his shoulders as he walked about the operating theatre between cases A careful conservative operator, he was always outwardly calm, and if difficulties arose he only became calmer "

Indeed, as someone else once said

> ' A really desperate situation would be the signal for packing off the wound and smoking a mental cigarette His younger assistants he would instruct never to run or even hurry across the Hospital square No emergency, he would imply, could justify so hasty an approach If the surgeon was not calm the patient would suffer, and Gask s considera

Notes and News

MEDICAL EXPENDITURE

HE cost of medical care is somewhat higher in the U.S.A. n in Great Britain, relative to consumption expenditures, national income, and to income per head of population is conclusion was reached by Mr Seymour E Harris PH.D., fessor of economics in Harvard University, when he dressed the American Economic Association in Chicago t month. He found that in Great Britain (1950) and , U.S.A. (1949) the cost of health services was as lows percentage of total consumption expenditure, itain 4.5 and U.S.A. 5.0, percentage of personal income itain 3.7 and U.S.A. 4.4 (the figures for medical expenditure - head as percentage of income per head were also 3.7 d 4.4) Professor Harris remarked that under the National alth Service more money had been canalised into medicine By virtue of its taxing power the Government forces the tion to spend more on medicine and less on other con mption goods or possibly on investment.' Taking the ures for 1938 as 100, expenditure on various goods and vices in Britain during 1948 is shown in the following figures gether with the prices of these goods and services

	Expenditure	*Prices*
Tobacco	112	388
Alcoholic drinks	93	288
Durable household goods	79	236
Private motoring	35	180
Domestic services	37	218
Other services	120	154
All	104	182

It is clear, said Professor Harris 'that large rises of prices relatively non-essential areas of consumption have tended reduce consumption of these non-essentials. When prices ve risen greatly and consumption has increased or has en maintained remarkably well, the explanation is inelastic nsistent) demand. The rise of prices in these sectors of the onomy stems largely from tax policy. For example the crease of consumption for tobacco was 12% of prices 288% ut the rise of prices after allowing for the increase of xes was but 50%. From 1938 to 1948 tobacco taxes se from £84 million to £610 million. All of this ggests that the British Government by a conscious tax nd to some extent price policy has tended to discourage e consumption of tobacco alcohol, durable consumers oods &c., and use part of the receipts to stimulate the outlay n medicine. Few will dispute the fact that the diversion f spending from alcohol tobacco, radio &c to medicine rings an improved pattern of spending. But many in this ountry will not approve governmental intervention in the eld of consumption."

NTERNATIONAL CONGRESS ON CHEST DISEASES

THE First International Congress on Diseases of the Chest, ponsored by the council on international affairs, American ollege of Chest Physicians, was held in Rome between ept 17 and 22, and was attended by about a thousand elegates and their wives. At the inaugural session the ollege medal was presented to Sir Alexander Fleming, R.S for his discovery of penicillin. Altogether more than hundred scientific papers were presented by physicians rom forty countries including the U.S.S.R. Delegates from reat Britain included Sir Harold Boldero Dr A. J Benatt, Dr C K. Cullen, Dr W Griffel Dr W Paton Philip Dr P R Trail and Dr M. Weinberger. A European chapter of he college was organised with Dr André Meyer (Paris) as he general secretary. The regents of the college in Europe who will serve as the executive council for the chapter are Prof Gustav Maurer (Davos Switzerland), Prof Etienne Bernard (Paris) Prof Lopo de Carvalho (Lisbon) Prof Nicholas Oekonomopoulos (Athens), Prof. Eugenio Morelli (Rome) and Sir Alexander Fleming

EMPIRE RHEUMATISM COUNCIL

THE report by Lord Horder the chairman, presented at the annual meeting of the Empire Rheumatism Council in London last Wednesday declares that this body was active in the new and revolutionary field of research opened up by the discoveries of Dr Philip Hench and his colleagues in the U.S.A. At the Westminster Medical School in work aided by a grant from the council, good progress was being made towards the preparation of '*Cortisone*' *analogues*, and the council was publishing a critical quarterly bibliography of cortisone, A.C.T.H., and related hormonal substances. As to the council's education programme, the postgraduate courses held at the Apothecaries' Hall had again been fully attended. Inquiry had been made as to the number of physicians of registrar or senior registrar status who were members of the Royal College of Physicians and had at least two years training in some *recognised rheumatic treatment centre*, and for whom no consultant posts in this specialty were at present available, in October 1950 there were some 15 such senior registrars.

The finance committee reported that in 1949-50 *ordinary* income amounted to £12,222 and legacies brought in £6240 the total expenditure rose to £10,243

Royal College of Physicians of London

Dr J C Broom will deliver the Milroy lectures on Tuesday and Thursday, Feb 13 and 15 at 5 P.M. at the college, Pall Mall East, S.W.1. He is to speak on Leptospirosis

Hunterian Society

The annual dinner will be held at Claridge's, Brook Street London, W.1 on Thursday, Feb 15. Tickets (30s.) may be had from Mr A. W Badenoch 110, Harley Street, W.1

The subject for the 1951 gold medal essay is the Treatment of Asthma in General Practice. The competition is open to all general practitioners. Further details may be had from the honorary secretary, Mr Clement Francis, 75, Wimpole Street, London, W.1

Heberden Society

Sir Henry Cohen has been elected *president of this society* for 1951

Scottish Health Services Council

Prof. J M. Graham F.R.C.S.E., Dr W Nicol Gray, Dr G W Ireland *Prof* G L Montgomery F.R.F.P.S., and Dr E Neil Reid have been appointed members of the council, Dr A. D Briggs and Dr R C Scott Dow, L.D.S have been reappointed. All will hold office until *Dec. 31, 1953*

British Association of Physical Medicine

The association is to hold a meeting in London on Friday and Saturday April 20 and 21. The programme will include a lecture-demonstration by Dr A. C Boyle *on* Micro waves and a demonstration on Ultrasonics. A visit will be made to the R.A.F *rehabilitation* centre at Headley Court Epsom. Further particulars may be had from Dr W S Tegner, the hon secretary 45 Lincoln's Inn Fields W.C.2

Ophthalmic Services

Meeting in London on Jan 17 the general council of the Association of Optical Practitioners called on the Minister of Health to establish the existing supplementary ophthalmic service on a permanent basis like the medical and dental services. A further resolution urged members of the association not to take a post in the hospital eye service unless the hospital authority concerned declared its intention 'that the refraction of non pathological cases shall be actively discouraged.' Mr L. Evershed Martin *chairman* of the council, told a press conference that it had been estimated that only 50% of opticians would be used in the hospital scheme. The remainder 'would be out of practice with no compensation whatever. The optical profession is walking the plank."

The Minister of Health

The Rt Hon. Hilary Adair Marquand D.SC M.P has been appointed Minister of Health in succession to Mr Aneurin Bevan, who becomes Minister of Labour and National Service

Fifty years of age Mr Marquand was educated at Cardiff High School and University College Cardiff, where he graduated in history and economics. His appointments in this country have included those of professor of industrial relations at University College Cardiff, lecturer in economics at the University of Birmingham and director of industrial surveys of South Wales. He visited the United States as Laura Spelman Rockefeller fellow in social sciences in 1925 and as visiting professor of economics at Wisconsin University in 1938. During the war he became successively an acting principal at the Board of Trade, a deputy controller at the Ministry of Labour and finally labour adviser at the Ministry of Production. Since then he has been secretary for Overseas Trade (1945-47) Paymaster General (1947-48) and Minister of Pensions (1948-51). His writings include *The Dynamics of Industrial Combination* (1931) *Industrial Relations in the U.S.A* (1934) *South Wales Needs a Plan* (1936) and *Organised Labour in Four Continents* (jointly 1939)

SIDNEY PHILIP PHILLIPS

M D Lond , F R C P

To write of Sidney Phillips is almost to write of another age for he qualified in 1877, and when he died on Jan 19 in his 100th year he was the second senior fellow of the Royal College of Physicians For many years he was treasurer of the college, and, sitting in the censors' room overlooking Trafalgar Square, he used to recall that he was one of the volunteers who lined the square in the demonstration of 1887 when John Burns was arrested

Phillips studied medicine at University College Hospital, and after holding the usual house appointments there he became a demonstrator of anatomy in the medical school His early intention was to be a surgeon, but at the examination for the London B S , then distinct from the qualifying M B , he was set to amputate a much shrivelled toe To some words of criticism from the examiner, Phillips retorted that the examiner had better do it himself and walked out So ended his career as a surgeon It was a characteristic attitude and a story which he always enjoyed telling

His attention having been thus directed to medicine, he quickly made a name for himself, particularly as an expert on fevers Another of his stories was how he became a diagnostic expert in smallpox after his fellow house-physician fell a victim "I had at least seen one case" In due course he was elected to the staff of the Lock Hospital for venereal diseases, Paddington-Green Children's Hospital, the London Fever Hospital, and St Mary's Hospital, where together with the post of assistant physician he had charge of the children's department for several years He was elected F R C P in 1891

Later, when he was full physician at St Mary's, all students went to Edmund Owen for instruction in surgery, and as inevitably to Sidney Phillips before taking their final in medicine His teaching was direct, clear, and emphatic, and he used the gruelling method of question and answer His students went to him knowing well that their ignorance would be plainly exposed, but also that they would learn much that would be useful not only for the looming examination but also for their future practice of medicine He held examinerships for the Conjoint Board and the University of London

He was a brevet colonel in the 1914–18 war, when he had already resigned from St Mary's at the age of 65 During that war his keen observation and ready deduction led to the arrest of a notorious German spy In later years he was always pleased to declare he identified the spy by his Blücher boots

When he became treasurer of the college in 1924 he proved himself an efficient and astute financier He kept all accounts himself, writing them out by hand, until failing sight made resignation inevitable in 1938 In his last years he was totally blind, but his mind remained alert

Although he never published a book, he wrote many papers on fevers, gastro intestinal diseases, and disorders of the heart and circulation When acute ulcerative colitis was beginning to be recognised as a clinical entity," F L recalls, "Phillips described a series of patients whom he had attended—including the late F J Poynton then recently qualified Phillips's teaching and writings on syphilis of the heart formed much of the background of Carey Coombs's lecture to the College of Physicians, and when William Pasteur in 1908 gave a Bradshaw lecture before the same college on massive collapse of the lung, Phillips supplied him with notes of several illustrative cases

"An accurate observer and clear thinker, his diagnosis, based on the old methods, seldom went astray Though he never failed to attend a post-mortem of one of his own patients, he had little respect for those he dubbed 'test-tube' physicians, and he did not hesitate to say so Despite his several appointments he found time to visit his wards once a week—in addition to his two teaching rounds—when he would write notes on some of his cases , when the patients were discharged all the notes had to be sent to his house, where they remained, registrars' protests notwithstanding He had his foibles He did not believe in diphtheria antitoxin, holding that it increased the incidence of polyneuritis, and he always operated upon his own empyemas, without resection of ribs, on the coal chest in the children's ward—with great success

"He had a fund of anecdote The stories about him were legion and enjoyed by none more than he himself, whilst his caustic humour did not always escape repercussions to which he was completely immune There must be many of the older generation who remember him as a character not likely to be met with again, not lightly to be crossed but with a wealth of friendliness and good counsel , and many who owe much to his teaching and help"

MR C E WEST

E B B writes "Your obituary of Charles Ernest West mentions his fearless speech In fact he was a man of outstanding courage in every way His surgical courage matched his extreme skill If operation was a patient's only hope, West would operate, no matter how slender the hope might be His skill gave great speed when that was the patient's need I have seen him perform a really good radical mastoid on a patient whose breathing had ceased, and open a cerebellar abscess in 13 minutes from start to finish For those who worked for him perhaps his outstanding characteristic was his loyalty to his team West would take the blame for anything that went wrong and he would side with his junior against anyone on earth His outspokenness and a certain mischievous love of debunking the pompous militated against a universal popularity, but those who were responsible to him in their work, and also his patients, loved him After his early retirement his strength and skill were such that he used to work a six-ton cutter round the Cornish coast single handed, rejoicing openly in the risk so that it was only to himself About two years later he tore every muscle off a tend Achillis while playing badminton This reduced hi from sail to what he called water-motoring, but I nev heard him grumble After his second marriage he too up the clarinet and he and his wife used to play duet An invigorating and amusing companion, intensely ale and alive to the end, he was also a most amusi correspondent"

Appointments

Adams, Mary M B Belf D P H M O H Fulham
Anderson W L M B Glasg tuberculosis physician Manches Chest Clinic
Davidson C H M B Edin , M R C P E asst. physician Le Hospital
Dickson, Walter M B Manc , M R C P D C H consulta pædiatrician Bolton and Wigan hospital groups
Greenberg, M J , M A M B Camb M R C P consultant ch physician Manchester Chest Clinic and Baguley Hospital
Mackay R I , M B Manc , M R C P D C H consultant pædiatrici Salford
Mitchell E J M B Manc D O consultant ophthalmic surge Blackburn hospital group
Moore John, M B Dubl D A asst anæsthetist, Wigan a Leigh hospital group and Wrightington Hospital
Moss P D , M B Lpool M R C P D C H consultant pædiatrici Blackburn and Burnley hospital groups
Robertson J D M B Edin D.A anæsthetist in regional p of anæsthetists based on Royal Infirmary of Edinburgh
Smith A E M B Edin D A asst anæsthetist Barrow a Furness hospital group
Williamson James M B Glasg M R C P E tuberculosis physicia area of counties of East Lothian Berwickshire, Selkirkshi and Roxburghshire
Wilson J M G M B Camb M R C P asst physician, Deacon Hospital Edinburgh
Woods R R M B Dubl F R C.S I consultant ear, nose, a throat surgeon Oldham and Ashton hospital groups

Colonial Service

Apted F I C M B Lond D T M & H sleeping-sickn specialist Tanganyika
Barrett, R E M B Lond D P H D T M & H deputy direct of medical services Tanganyika
Caldwell J M M B Dubl D P H D T M & H senior M Uganda
Dean N M B M B Edin F R C.S E surgeon special Nigeria
Goodall J W D M D Edin F R C.P E medical special Nyasaland
Healy S J , L R C P I M O Nigeria
Hutchison A F M B Durh M O Tanganyika
Magill C W M B Edin M O Tanganyika
O Brien Norah L.R C P I M O Tanganyika
*Pilsztak Bruno*N MED DIP LWOW M O Windward Isles
Saba Charlotte M B Lond D OBST obstetrical gynæcologi M O Nigeria
Schuppler V J M D M O Tanganyika
Tereshchenko I N N F R C.S asst surgeon Public Hospi British Guiana

EXTRAPLEURAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS*

E Murstad
M.D Oslo
OPLAND FYLKESSYKEHUS, LILLEHAMMER, NORWAY

The aim of collapse treatment in pulmonary tuberculosis is to close a cavity We must therefore try in each case to select the procedure which offers the best chance of closing the cavity completely, without leaving a residual cavity, with the least operative risk and the least mutilation of the patient, and preserving as much as possible of the respiratory function of the lungs

It has been and is the prevailing opinion that an intrapleural pneumothorax is the method of choice, and that an extrapleural pneumothorax or a thoracoplasty should only be considered after an intrapleural pneumothorax has proved unsuccessful Perhaps the risk of getting a rigid lung after an intrapleural pneumothorax will change this view and lead us to prefer an extrapleural pneumothorax or a thoracoplasty even in cases where adhesions do not preclude an intrapleural pneumothorax

Operations on the phrenic nerve are of restricted value, they are indicated only in special cases, and are not discussed here

There remain two methods, extrapleural pneumothorax and thoracoplasty, to be used in cases where intrapleural pneumothorax has failed or has been deemed objectionable

The common opinion has been that the induction of an extrapleural pneumothorax is a rather poor and unreliable operation, only to be performed where a thoracoplasty is to be avoided In our hospital ten years ago, when we began to use extrapleural pneumothorax, we followed this rule But gradually it became evident that extrapleural pneumothorax has merits of its own, and for the past few years it has been preferred unless there is some special contra-indication

We have performed this operation in over 700 cases, but the statistical data given here are based only on the 600 operated on up to 1947, which were reinvestigated in 1948 by Dr Leif Martin He will publish his findings elsewhere

TECHNIQUE

General anæsthesia has been used in nearly all the cases A longitudinal incision, 10 in. long, is made between the midline of the back and the margin of the scapula The scapula is retracted, and 4 in of the 5th rib is resected After incision of the periosteum in the bed of the rib a thin layer of loose connective tissue, the endothoracic fascia, appears in the wound This is used as a plane of cleavage, and the lung is peeled off from the chest wall, first with a finger and then with a small swab on long forceps Adhesions are cut with a pair of long scissors Bleeding points are caught with forceps and coagulated. It is important not to enter the pleura or an adherent superficial cavity Small cavities in the top of the lung, with dense fibrous adhesions in the extrapleural layer, are dangerous Cavities a little further down are not so dangerous in this respect even if they are large and superficial (but they may perforate later) The lung is freed to the hilum on the mediastinal side, on the chest-wall side the extension of the stripping depends on the size and location of the cavity, an average extrapleural space has its lower limit at the eighth rib laterally

In some cases it is possible, by pushing with the gauze swab, to separate the diseased segment from the healthy part of the lung, thereby getting a very selective collapse This separation is started posteriorly in the interlobar line, and continued in a horizontal direction anteriorly The diseased segment seems to contract during this manipulation, and at the end of the operation it looks like a firm globe, the size of a small orange, on top of the remaining non collapsed lung

The extrapleural space is partially filled with an anti coagulant fluid, 300 ml of a 1% solution of sodium citrate This fluid will have to be renewed frequently during the first few days To spare the patient frequent needling, and to obtain better aspiration, a soft rubber catheter is passed through the 6th intercostal space posteriorly, and laid along the chest wall as far as the lower end of the incision, beneath the muscles (forming a kind of Witzel fistula), to prevent leakage when it is removed

The entrance to the extrapleural space is closed with two pericostal catgut sutures and a continuous silk suture in the intercostal muscles A continuous silk suture is also used in two layers in the rhomboid and trapezius muscles After the skin has been sutured, penicillin 50,000 units is injected through the catheter, which is then closed and put beneath the bandage

A few hours later the fluid is aspirated and a fresh solution of sodium citrate and penicillin is injected The frequency of further aspirations depends on the amount of bleeding, as suggested by the patient's sensation of pressure in the chest and by the radiographs The catheter is removed on the fourth day, and the later aspirations are done by acu puncture The patients are allowed out of bed the day after the operation

During the first week there is no danger of the pressure in the extrapleural space getting too low, permitting the lung to re expand, the hæmorrhage and the secretion of wound fluid will prevent this But after a week or two great care must be taken with the pressure, and refills must be given every other day for two to four weeks, then twice a week for two to four months, after which the intervals are gradually lengthened until, after a year, refills are made every two to four weeks

ADVANTAGES

The advantages of an extrapleural pneumothorax are obvious

(1) The operation does not carry with it any deformity This is very important Patients are often more worried about the disfiguration after a thoracoplasty than is commonly supposed In our hospital we have had as house-surgeons several young men who had recently had pulmonary tuberculosis and had lived as patients in sanatoria, and they have all told me that most patients, men as well as women, worry a great deal about their deformity after a thoracoplasty

(2) Extrapleural pneumothorax is a one stage operation.

(3) Above all, it gives a more complete and more selective collapse than any other procedure

The ideal procedure would free the diseased segment of the lung only, permitting it to retract completely, while the rest of the lung remained undisturbed in contact with the chest wall. An extrapleural pneumothorax gives a nearly ideal collapse, more selective than an intrapleural, especially when it is possible to do an intersegmental stripping (In two cases we have established an extrapleural pneumothorax over the lower lobe, separating it from the upper lobe, which has remained in contact with the thoracic wall.)

Modern thoracoplasty, in which long lengths of the ribs over the diseased part of the lung only are resected, gives a rather selective collapse, but the collapse after an extrapleural pneumothorax is still better When a pneumolysis is added to a thoracoplasty, the collapse is, to begin with, nearly ideal, just as in an extrapleural pneumothorax But later the collapsed lung will partially re-expand, to fill the empty space which is created when the air and the wound fluid are gradually absorbed One can observe this when doing the second stage of a thoracoplasty, and one can follow the re expansion by radiography

This re expansion may perhaps be prevented by filling the space with air or oil for a few weeks until the

---

* A lecture read to the Department of Thoracic Surgery, Royal Victoria Infirmary, Newcastle upon Tyne, on Oct 5, 1949

Mycological Reference Laboratory

Dr Jacqueline Walker has been appointed acting director of the laboratory on the resignation of Dr R W Riddell Specimens for examination for pathogenic fungi should be addressed to her at the laboratory, London School of Hygiene and Tropical Medicine, London, W C 1

Tuberculosis-free Dairy Cattle

Addressing a conference reported in the *Farmer and Stockbreeder* for Jan 16, Mr Ben Hinds, chairman of the Milk Marketing Board, said that 36% of the milk sold last month in England and Wales was from tuberculin tested cows In the three counties of West Wales (Carmarthen, Cardigan, and Pembroke) the proportion was 77% This area has been selected as the first area in Britain for free tuberculin testing under the attested herds scheme

Medical Artists' Association of Great Britain

Applications for membership of this association will be considered at a meeting of the examining subcommittee on April 6 Forms of application and full details may be obtained from the hon assistant secretary, Miss Audrey J Arnott, A R C A, The Rotunda, Radcliffe Infirmary, Oxford Work for the examination must reach Miss Arnott, c/o Dr Tompsett, at the Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2, by April 4

Statistical Research

The World Health Organisation has set up, from Jan 1, a centre for statistical research on problems arising in the use of the International Statistical Classification of Diseases, Injuries, and Causes of Death, and has appointed Dr Percy Stocks, until recently chief medical statistician at the General Register Office, to direct its work. The centre is at present situated at the General Register Office, which is providing appropriate material from its records Dr Stocks will continue for the present to be available to the department in a consultant capacity

Use of Preservatives in Food

The Food Standards Committee of the Ministry of Food has set up a subcommittee to consider the use in foods of preservatives, colouring matters, dyestuffs, and allied substances such as anti oxidants, anti staling agents, anti mould agents, stabilising agents, and emulsifying agents The ten members include the following doctors Prof E C Dodds, F R S (chairman), Dr N R Beattie, Prof S J Cowell, and Dr J M Johnston. The subcommittee may be addressed at the Ministry of Food, Food Standards and Labelling Division, 47, Portman Square, London, W 1

Hospital Administrative Staff College

Mr R A Mickelwright, F H A, and Mr A C Stuart Clark, M A, have been appointed by King Edward's Hospital Fund for London as whole time members of the tutorial staff of the college, at nos 2 and 14, Palace Court, W 2 Mr Mickelwright, who will act as senior tutor and director of studies, is resigning his appointment as secretary to the South West Middlesex Hospital Management Committee Mr Stuart Clark, who will act as senior tutor and registrar, was formerly headmaster of Brighton College The principal of the college is Mr P H Constable, M.A, F H A, house governor of St George's Hospital, who will act in a part-time capacity The first courses will begin at the college in April

Lady Tata Memorial Trust

The trustees of this fund invite applications for grants and scholarships for research on diseases of the blood, with special reference to leukæmia, in the academic year beginning on Oct 1, 1951 Grants are made for research expenses or to provide scientific or technical assistants for senior workers Scholarships are awarded as personal remuneration, and are intended chiefly for junior investigators working under suitable direction, their normal value has been £400 per annum for whole time research, with proportionate adjustment for work on a part time basis The grants and scholarships are open to workers of any nationality, and in any country in which it will be possible to make payments in the coming academic year Applications must be submitted before March 31, and the awards will be announced by the trustees in June Forms of application may be obtained from the secretary of the scientific advisory committee c/o Medical Research Council, 38, Old Queen Street, London, S W 1

Renal Association

At a meeting of the association on Wednesday, Jan 31, at 4 30 P M, at the Ciba Foundation, 41, Portland Place, London W 1, Prof E C Amoroso will speak on the Fœtal Kidney Prof E B Verney, F R.S, on the Neurohypophysis and the Kidney, and Dr Dent on Tubular Function

Memorial to C J Bond

On Jan 10 Prof G Grey Turner unveiled a memorial tablet to C J Bond in the Leicester Royal Infirmary where he had served as an active surgeon for 27 years and as a consulting surgeon until his death in 1939 at 83 The same evening Professor Grey Turner delivered the first Bond memorial lecture, before the Leicester Medical Society

Society for Endocrinology

This society will hold a symposium on Endocrinological Aspects of Fertility at the house of the Zoological Society, Regent's Park, London, N W 8, on Friday, Feb 16, at 11 A.M. Those who wish to attend should write to Prof C H Gray, department of chemical pathology, King's College Hospital, London, S E 5, not later than Feb 10

Diary of the Week

JAN 28 TO FEB 3

Monday, 29th

INSTITUTE OF NEUROLOGY, National Hospital Queen Square, W.C.1
5 P M Prof Hamilton Hartridge, F R.S Some Recent Advances in the Neurophysiology of Vision

Tuesday, 30th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene Keppel Street W.C.1) Dr F M R Walshe F R.S Organisation of Muscular Movements by the Cerebral Cortex

Thursday, 1st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Mr H J Eysenck PH D Psychology of Personality

LIVERPOOL MEDICAL INSTITUTION
3 30 P M (Broadgreen Hospital, Edge Lane Drive Liverpool, 14) Clinical demonstration

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Prof W Melville Arnott Pulmonary Circulation in Man

Friday, 2nd

UNIVERSITY COLLEGE Gower Street W C 1
5 15 P M Mr T S Work PH D Cell Metabolism and Chemotherapeutic Activity (First of two lectures)

Births, Marriages, and Deaths

BIRTHS

ATTWOOD —On Jan 20, in Manchester the wife of Dr R. W Attwood—a daughter

BANKS —On Jan 19 in London the wife of Dr P J Banks—a daughter

BARROWCLIFF —On Jan 15 at Stratford-on Avon the wife of Dr D F Barrowcliff—a son

CARTON —On Jan 19 the wife of Dr Paul Carton—a daughter

CHILDS —On Jan 11 at Southsea, Hants the wife of Dr Michael Childs—twin sons

CRAWSHAW —On Jan 16 at Winchester the wife of Dr George Crawshaw—a daughter

EDWARDS —On Jan 16, at Stanmore Middlesex, the wife of Dr D N Edwards—a daughter

FLOYER —On Jan 16 in London, the wife of Dr M A. Floyer—a son

HAY —On Jan 16 at Stoke-on Trent, Staffs the wife of Dr R K Hay—a daughter

HUTT —On Jan 18 the wife of Dr C W Hutt—a son

MINTO —On Jan 21 at Northampton the wife of Dr W H P Minto—a son

SMITH —On Jan 18, the wife of Dr Sydney Smith—a son

MARRIAGES

BENN—SIMPSON —On Jan 8 in Leicester Joseph Benn M D, to Patricia Mary Simpson, M B

MACALISTER HALL—BROOKS —On Jan 9 in Edinburgh, Malcolm Macalister Hall M C to Margaret Sheila Brooks M B

WHITAKER—THOSEBY —On Jan 13 in Manchester Tom Whitaker M B to Margaret Rosevear Thoseby, M B

DEATHS

BROWN —On Jan 18 at Minchinhampton Alfred Brown M D Edin, aged 72

GASK —On Jan 16 at Henley-on Thames George Ernest Gask C.M G D S O M A Oxfd F R C.S, aged 75

HAYES —On Jan 11, at Hove Reginald Hewlett Hayes M.R.C.S.

PHILLIPS —On Jan 19 in London Sidney Philip Phillips M.D Lond F R C.P aged 99

RAWLINSON —On Jan 14 at West Kirby, Cheshire James Herbert Rawlinson M D Lpool F R C.S and the occupation Today postoperative infection of the extrapleural space is very rare

The evils and complications commonly adduced as objections to an extrapleural pneumothorax—the difficulty of maintaining the extrapleural space, the risk of hæmorrhage, and the risk of pyogenic infection—should not be overemphasised In our view the main disadvantages are the late complications—the tuberculous empyemas and, above all, the bronchial fistulæ

It is a matter of judgment which cases should be counted as empyemas Many patients have a scanty cloudy fluid in the extrapleural space, often growing tubercle bacilli on culture The fluid may be present for a long time, it disappears either spontaneously or after a few aspirations The general health of the patient is not impaired These cases I have not counted as empyemas, nor the cases in which the fluid has been more purulent but has not tended to increase Such cases excluded, there have been 73 cases (12%) of tuberculous empyema Of these 73 patients 12 died, 10 of them of bronchial or œsophageal fistula

The most serious complication, and the strongest objection to the extensive use of extrapleural pneumothorax, is the bronchial fistula In our series there were 28 cases (4 7%) of bronchial fistula and 3 cases of œsophageal fistula

What is the ætiology of the bronchial fistula ? We have done a necropsy in 6 cases, and 4 showed an identical picture the lateral wall of the tuberculous cavity was almost entirely destroyed, the rest of the cavity forming a shallow crater, into the floor of which opened a bronchial branch Of these 4 patients, 3 had got their fistulæ within two months after the operation In 13 of our 28 cases the bronchial fistula had developed within four months after the operation, so probably the pathogenesis of the fistula in most of these early cases is the same—necrosis of the wall of a superficial cavity

In 15 cases the bronchial fistula developed several months after the operation, and in 11 of them the patients had had tuberculous empyema for weeks and months before showing signs of a bronchial fistula—expectoration of purulent fluid and impossibility of raising the pressure in the extrapleural space by refills (It may be impossible in any given case to tell which is primary, the empyema or the fistula)

If large superficial cavities and long standing empyemas are important ætiological factors in the development of bronchial fistulæ, extrapleural pneumothorax should be avoided in cases with large superficial cavities, though it may be right to deliberately run the risk of a bronchial fistula if there are weighty indications for preferring an extrapleural pneumothorax to a thoracoplasty—e g, bilateral tuberculosis with low vital capacity and poor general condition And care must be taken to evacuate an empyema often enough to prevent it from perforating into the lung and yet not too often

RESULTS

To assess the results it is absolutely necessary to group the cases, though strong objections may be raised to any system of grouping

The operative mortality and the chances of closing the cavity depend to a large extent on the following factors

1 The size and the position of the cavity The larger the cavity the greater is the risk of postoperative spread

2 *Respiratory function* The best way of assessing the respiratory function is to observe the patient in everyday life But to provide an objective scale we have used the vital capacity (we have not computed the percentage of normal taking the patient s weight and height into consideration)

3 The resistance of the patient the phase of the disease

We have adopted the following classification for unilateral operations

Group	Maximum diameter of cavity (cm)	Cavity not below	Minimum vital capacity (c cm)	Phase
I	4	5th rib	2500	Good
II	5	5th rib if there is an intrapleural pneumothorax on the other side	1300	Average
III				

Patients who fail to meet one or more of the criteria for a group are placed in the next lower group

Cases in which operation on both sides was either performed or planned are placed in group IV

As operative deaths we have counted those which seemed to be a consequence of a complication (usually pulmonary) with a plausible causal connection with the operation, regardless of the time elapsed between the operation and the death, and regardless of the patient's having left the hospital or not

Group I

In group I (fig 2) there were 107 patients, of whom 2 died (both from pulmonary embolism), 2 had pulmonary complications, and 2 infection of the extrapleural space Of the 105 surviving patients, 101 (96%) had a negative sputum and 4% a positive sputum

Fig 3 shows that of the 101 patients with negative sputum 89 (88%) had remained negative and 12 had become positive in one to eight years Only 1 of the recurrences was on the operated side

Group II

In group II (fig 2) there were 166 patients, of whom 11 (6 6%) died In 6 cases death was due to pulmonary embolism (Most of the embolisms occurred in infected cases During the period when there were many infections of the extrapleural space, we often saw thrombosis in the arm and always on the operated side During the later years, when there were no infections, there was no thrombosis and no embolism Is this a coincidence, or has there been a causal connection between infections of the extrapleural space and thrombo embolism ?) 4 8% had pulmonary complications and 4 2% infection Of the 155 surviving patients 127 (82%) had a negative sputum

Fig 3 shows that after one to eight years 112 (88%) of the 127 patients remained negative, and 12% had become positive Most of the recurrences were in the non operated lung

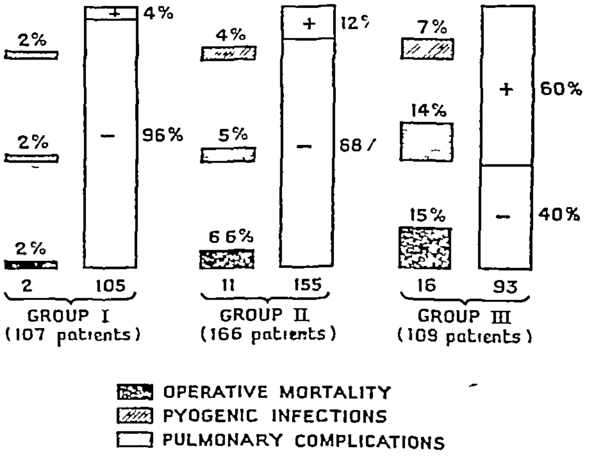


Fig 2—Immediate results of extrapleural pneumothorax White columns show sputum findings in each group

ribs covering the collapsed lung have regenerated This procedure to some extent relinquishes one of the essential advantages of thoracoplasty—i e, absence of a dead space with its inherent risk of infection and bronchial fistula But perhaps the additional layer covering the collapsed lung may give some protection against the development of a bronchial fistula

DISADVANTAGES

An extrapleural pneumothorax gives a reversible collapse This is an advantage in cases requiring only a temporary collapse, but a drawback when a permanent collapse is desired But I cannot see why an extrapleural pneumothorax should not be maintained permanently After a year the intervals between refills can be lengthened up to four weeks, and a visit to the doctor every four weeks is not a very great burden for the patient, provided he does not live too far from a hospital or a physician who can do the refills properly An extrapleural space always carries the risk of infection leading to tuberculous empyema or bronchial fistula, but experience has shown that these complications decrease in incidence when some months have elapsed after the operation Moreover, it is not easy to tell beforehand in any given case whether a permanent collapse will be required or not

It is commonly said that a cavity which has been treated by intrapleural pneumothorax and has reopened has proved that it demands a permanent collapse, and therefore should not be treated by extrapleural pneumothorax But in many cases it is doubtful whether the intrapleural pneumothorax really has offered the diseased segment of the lung the opportunity of a complete collapse In doing an open intrapleural pneumolysis I have often seen that the adhesions are much stronger than would be expected from the findings on thoracoscopy and radiography

A bronchial stenosis is considered a contra indication to all forms of temporary collapse, and therefore to an extrapleural pneumothorax The stenosis is supposed to prevent the lung from re expanding when the refills are discontinued, and, if the lung does re expand, there will be a risk of bronchiectasis This question needs further investigation It is hard to know how much of this belief is based on facts Moreover, streptomycin may possibly change the outlook

It may be impossible to establish an extrapleural pneumothorax, because of adhesions This happened in 21 (3%) of our cases One cannot tell beforehand in any given case whether the operation will be possible or not, the only warning sign of any value is the appearance of very narrow intercostal spaces on the radiographs

It is important not to force the operation, but to abandon the pneumolysis and do a thoracoplasty if the separation of adhesions is too hazardous, perforating a cavity is a very tragic event We have perforated a cavity in 6 cases (1%) I think some of these accidents ought to have been avoided, but I do not think one can completely avoid this calamity without being too cautious, abandoning too many pneumolyses

A further contention is that the maintenance of extrapleural pneumothorax is often difficult, and that it is often impossible to prevent the extrapleural space from shrinking and allowing the lung to re expand before the cavity is healed

The extrapleural and the intrapleural spaces are very different The extrapleural space is a wound space, lined with vascular connective tissue If the lung is allowed to expand, even to a small extent, adhesions are rapidly formed in the sinus (x, in fig 1) between the lung and the chest wall, and what is lost in this way is lost for ever, it cannot be regained later by refills Therefore one must be very careful to keep a sufficient pressure in the extrapleural space, preventing the lung from coming into contact with the chest wall in the sinus, even for a short time It is not necessary to have a very high pressure, but to avoid very frequent refills it is practical, and harmless, to raise the pressure to 30–40 cm of water

After two or three months the wall of the extrapleural space is no longer a wound surface In re operations and at necropsies at such a time the extrapleural space is found to be lined by a smooth, shining white membrane *not unlike pleura The danger of rapid formation of* adhesions is then much less, and the intervals between the refills can be lengthened

If there are blood clots in the recess of the extrapleural space these may become organised and cause shrinkage even if the air pressure is kept at the proper height To prevent this we have filled the extrapleural space partially with an anticoagulant fluid We have not succeeded in completely preventing *the clotting in all cases, but I* believe this device has been of considerable help The prevention of clotting and the more complete evacuation of blood may also be of importance in the prevention and treatment *of infections* of the extrapleural space

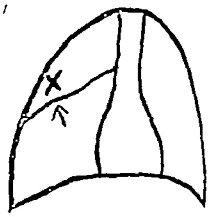


Fig 1

With due care it is nearly always possible to maintain an extrapleural space as long as one wishes In 8 (1%) of our cases the lung re expanded soon after the operation, these cases were all among our early ones

Tearing of the pleura, causing an intrapleural pneumo*thorax, occurred in 24 cases (4%) This accident* may to some extent, but not completely, be avoided by careful technique We have succeeded in closing the ruptured pleura airtight in only 1 case In most cases we have removed the diaphragm between the extrapleural and the accidental *intrapleural* spaces, but these combined spaces do not do very well, there being often much reaction and much trouble in the after treatment Perhaps the best thing to do is to inflate the lung, close the wound, and operate again after some weeks, when adhesions *have formed*

Hæmorrhage is often alleged to be a grave objection to the extrapleural pneumothorax The blood loss during the operation is in most cases 200–300 ml Bleeding uncontrollable by the usual means has occurred in 7 cases (1%) In 2 of these we did a *thoracoplasty* to get at the bleeding vessel, and in the remaining 5 we put in a pack, closed the wound without drainage, and re operated two days later

A far more serious problem is postoperative bleeding—oozing from the large wound surface of the extrapleural space We have tried to calculate the postoperative blood loss by estimating the amount of hæmoglobin in the aspirated fluid A third of the patients lost more than 2 pints, and a tenth lost 4 pints or more The hæmorrhage has in many cases been rather alarming, in 1 case 22 transfusions were *given* 1 patient died despite numerous transfusions (It is impossible to tell what part hæmorrhage has played in the mortalities counted as due to infection or spread of tuberculosis in the lungs)

Early postoperative pyogenic non tuberculous infection of the extrapleural space developed in 29 cases (5%), and 7 of these patients died This is a regrettably high incidence of postoperative infection During the last two years there has been no *infection* in 162 cases This improvement may be due to penicillin, but it must be borne in mind that there was a remarkably high incidence of pyogenic infections in our population during the war anus to the splenic flexure, and absence of ganglion cells was noted in both cases In two girls who died at 3 weeks and 4 years no necropsy was done but a narrow segment was demonstrated at laparotomy in the infant and by barium enema in the older child extending to the splenic flexure in the infant and to the pelvirectal junction in her sister In one other child (sex not given), who died at 3 days with symptoms of intestinal obstruction, barium enema suggested an abnormal segment probably involving the entire colon, organic obstruction was excluded at necropsy We consider these last 3 children clinically proved cases of Hirschsprung's disease The other 6 siblings (1 boy and 5 whose sex was not mentioned) were unaffected The father aged 37 was reported to be well but constipated since birth

Buttersack (1927) described a family in which a man, his son, a niece and a nephew were probably affected with Hirschsprung's disease The father aged 38 had symptoms of chronic intestinal obstruction from early childhood at 35 his descending and sigmoid colons were resected and were found to be enormously dilated and hypertrophied though there was no obstruction on the distal side His son died at 5 weeks with intestinal obstruction and necropsy showed hypertrophied and dilated colon and sigmoid but no stenosis distally A niece, aged 4 years at the time of the report had symptoms of intestinal obstruction since birth. A nephew died of intestinal obstruction at 11 days, there was no necropsy

Popper (1920) reported on a pair of female twins One had passed no meconium and died at 4 days from intestinal obstruction there was no necropsy The other twin was treated with repeated enemas for retention of meconium and was reported alive at 28 weeks though with a distended abdomen and visible peristalsis the barium enema X ray film published shows a typical narrow segment of average length No evidence is given whether these twins were monozygous or dizygous We consider that the first twin was probably a case of Hirschsprung's disease and we accept the radiological evidence in the other as proof of the diagnosis

1—Index case 31 and his affected twin brothers.

PRESENT INVESTIGATION

Since there are now definite pathological criteria for the diagnosis of Hirschsprung's disease, it seemed worth while to investigate the incidence of the disease in the families of a consecutive series of histologically established cases At the Hospital for Sick Children 40 cases were available for this study and by chance the children were all unrelated, 37 of the 40 were boys One was an adopted child The parents of 3 others had emigrated, but in one of these cases the grandparents provided a family history The series, therefore, includes 37 index cases of Hirschsprung's disease in which the diagnosis was established by histological examination of surgical or necropsy specimens of bowel.

The parents were interviewed and asked about their own health and that of their other children, their brothers and sisters, and their nephews and nieces With the exception of 2 adult sisters of one index case and 5 adult sisters of another, all brothers and sisters of the index cases were examined clinically for abdominal distension and by straight radiography of the abdomen for colonic dilatation Barium enemas were given in doubtful cases

Findings in Siblings

In the following 4 siblings there was radiological proof of Hirschsprung's disease None of these was found as a result of our investigation—2 were known to us before we began this work, and 2 twin brothers of one index case were brought to the hospital by their mother during our investigation but before we had written to her

Sibling Case I—Elder brother of index case 29 (fig 2), admitted under Mr Denis Browne Two sisters alive and well Passed meconium on the third day Constipated since birth, abdominal distension noted from age of 3 weeks Vomited occasionally Motions small and thin. Required regular aperients and weekly or fortnightly bowel washouts. Barium enema at 21 months showed greatly distended sigmoid and descending colon and narrow rectum, typical of Hirschsprung's disease Examination at this hospital three weeks before death showed very tense large and hard abdomen with palpable fæcal masses Died at home at age of 2 years 4 months No necropsy

Sibling Case II—Younger brother age 14½ yr., of index case 26 (fig 2) admitted under Mr T Twistington Higgins The firstborn of this family, a boy had died at the age of 9 days from "stomach trouble" and is discussed below The patient had been examined at the age of 13 by a mass radiography unit when an enormously distended colon was found. The family doctor, knowing the condition of the older brother, referred the patient to this hospital at the age of 14. His complaints were minimal. He needed liquid paraffin since starting school There was occasional abdominal distension with flatus at night He had a moderately enlarged abdomen, displaying enormous peristaltic waves and an empty rectum, and a barium enema revealed a typical narrow distal segment of intermediate length. He is being treated conservatively

Sibling Cases III and IV—Younger twin brothers of index case 31 (figs 1 and 2), admitted under Mr Charles Donald age 3½ yr An older sister is normal. Their mother brought the twins to the hospital because she thought they were also affected

One twin weighed 7 lb 3 oz. at birth. He was well until the end of the first year of life but then he gradually became increasingly constipated requiring daily laxatives His weight gain was normal His abdomen was less enlarged than his twin brother's and he was slightly the taller of the two Barium enema revealed a typical short narrow segment affecting the rectum.

The other twin weighed 6 lb at birth He began to vomit every feed at 7 weeks and was then an inpatient at a local hospital for six weeks Constipation began at 1 year and became gradually more obstinate necessitating laxatives every day His abdomen had been protuberant since the age of 1 year His weight gain was normal. He was pot-bellied with a tympanitic abdomen in which fæcal masses

Group III

In group III (fig 2) there were 109 cases, many of them very poor cases, and the mortality was high (15%) Most of the deaths were due to spread of tuberculosis The frequency of spreads and of infection was high, being 14% and 7% respectively Of the surviving 93 patients 38 (40%) had a negative sputum

Fig 3 shows that after one to eight years 29 (78%) of the 38 patients had remained negative There were 7 recurrences, 2 in the operated and 5 in the non operated lung In 2 cases there was only a single positive culture during a cold, between several negative cultures

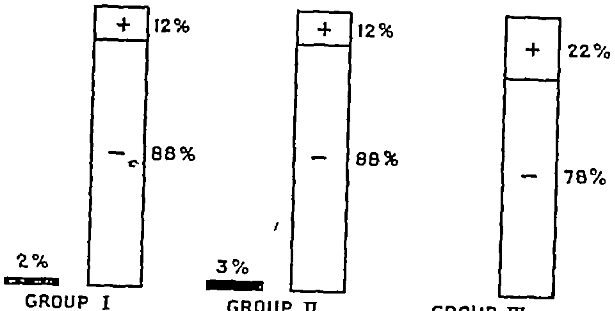


Fig 3—Follow up 1–8 years later of patients who had negative sputum immediately after operation

Group IV

Group IV was very heterogeneous, comprising good and poor cases, and cases treated by combinations of thoracoplasty and extrapleural pneumothorax In 139 cases extrapleural pneumothorax was planned on both sides In 82 of them the operation on the second side was abandoned, leaving 57 cases of bilateral extrapleural pneumothorax The operative mortality was 10% (13 patients died after the first stage, and only 1 after the second stage) Of the 57 patients who underwent the bilateral operation, in 41 (72%) the sputum became negative After one to eight years 1 of these 41 patients had died of pulmonary tuberculosis, 1 of renal tuberculosis, and 1 of rheumatic carditis The surviving 38 patients were free from clinical symptoms, and their radiograms showed no recurrence, but 5 of them had one positive culture during a cold, among numerous negative cultures 35 were able to work It is often astonishing to see how well patients with rather large extrapleural spaces on both sides are doing If their diaphragm is not rigid, and if they have learnt to breathe with their abdomen, they are not much troubled by shortness of breath

CONCLUSIONS

In summing up, I shall not try to draw strict and clear-cut conclusions about the value of, and the indications for, extrapleural pneumothorax I believe, however, that the advantages of this procedure have been underestimated, and the disadvantages exaggerated.

The most serious disadvantage is the risk of bronchial fistula

We must learn to know more about what happens when the refills are discontinued and the lung is allowed to expand The cases we have followed for periods of one to eight years have done well, but what will happen to them in another three or four years remains to be seen

Regardless of what will then be found, we can now say that in bilateral cases, and in poor cases, extrapleural pneumothorax is very valuable and in some desperate cases enables us to do something for patients who otherwise would be left untreated.

HIRSCHSPRUNG'S DISEASE

Martin Bodian
M D Vienna, D C P
DIRECTOR

C O Carter
B.M Oxfd, M.R C.P
RESEARCH GRANTEE,
NATIONAL BIRTHDAY TRUST

DEPARTMENT OF MORBID ANATOMY

With radiological observations by

B C H Ward
M R C S, D.M R
ASSISTANT, RADIOLOGICAL DEPARTMENT

THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON

THIS paper is based on 40 consecutive cases of histologically confirmed Hirschsprung's disease, and our purpose is to record (1) a genetic study of the disease in the families of 37 of these children, (2) a follow up account of the 37 cases treated by rectosigmoidectomy, and (3) our views on the pathology, especially in relation to the length of the abnormal bowel segment Lastly (4), we shall describe an example of a hitherto unreported condition which may be a variant of Hirschsprung's disease

Bodian et al (1949, 1950) have classified megacolon without organic obstruction into two principal groups Hirschsprung's disease proper and idiopathic megacolon.

The second group is much the commoner and the megacolon results from chronic constipation, which is probably acquired some time after birth Retention of fæcal material leads to passive dilatation of the colon and rectum and to shortening and flattening of the anal canal The radiological diagnosis from Hirschsprung's disease is made by demonstrating dilatation to the anus. The condition is benign and susceptible to persistent treatment with bowel washouts

Hirschsprung's disease proper is a congenital malformation, only microscopically demonstrable, affecting a variable length of terminal bowel The pathology is an agenesis of intramural ganglion cells and a dysplasia of autonomic nerve bundles Its functional manifestation is lack of coordinated peristalsis in the affected segment, leading secondarily to an active type of megacolon in the bowel proximal to this The demonstration by barium enema of undilated or narrow bowel distal to the megacolon is diagnostic Resection of the inert distal bowel by rectosigmoidectomy is now considered the rational treatment of Hirschsprung's disease

A Genetic Study of Hirschsprung's Disease

The few published reports on the familial incidence of Hirschsprung's disease refer only to isolated families, and most of them are not based on adequate diagnostic (radiological or pathological) criteria We shall discuss only four of these reports—two in which the diagnosis was confirmed histologically (Dalla Valle 1920, 1924, Zuelzer and Wilson 1948), one in which a condition that was probably Hirschsprung's disease affected more than one generation (Buttersack 1927), and one in which Hirschsprung's disease was probably present in a pair of twins (Popper 1920)

PREVIOUS PUBLICATIONS

Dalla Valle (1920, 1924) reported on 2 brothers who died at 10 months and 16 months with megacolon Histological examination in both cases revealed absence of ganglion cells from Auerbach's plexus in the sigmoid colon, which was of normal calibre Normal ganglia were found in the dilated colon These children had two normal brothers and two brothers who died at 6 and 14 days with symptoms of intestinal obstruction and probably had Hirschsprung's disease

Zuelzer and Wilson (1948) gave details of 11 of the 12 children in a remarkable family One boy and one girl died at 14 and 15 days with intestinal obstruction, at necropsy long narrow segments of bowel were found extending from the fig 6) Proximal to this again, normal intramural plexuses were found (fig 7) It is not possible, from the macroscopic appearances, to predict exactly the sites of transition from normal to transitional and to aganglionic segments As a rule the surgeons at this hospital have resected, in addition to the terminal undilated segment, rather more than the distal half of the funnel shaped zone proximal to it Our follow up shows that this is adequate

We have not yet observed the rare variant of zonal absence of ganglion cells with normal ganglia both proximal and distal to the zone, but 3 examples of this have been reported by Perrot and Danon (1935), Tiffin et al (1940), and Swenson et al (1949)

One of our infants, who died at the age of 17 days, had a pathological segment of bowel extending from the anal margin to the splenic flexure The proximal limit of the aganglionic zone in the other 39 cases was never above the junction of sigmoid and descending colon, and was usually well below this, though it varied from case to case

We have surveyed all the published cases (including our own) in which observations were made on the abnormal segment and some indication was given of its length The total number was 160 In 14 of these there were very long segments to the splenic flexure in 9, hepatic flexure in 1, ileocæcal valve in 1, and distal ileum in 2 Twelve of these children died at the age of 1 month or less and one at the age of 5 months One newborn baby with an affected segment reaching to the splenic flexure was twice operated on by Swenson (1950), who removed the abnormal bowel, the infant has survived The remaining 146 children had segments not extending beyond the rectum and sigmoid, and 6 of these died in the neonatal period

If only histologically confirmed cases are considered, the total is 90, of which 8 had very long segments (splenic flexure 5, hepatic flexure 1, distal ileum 2), 82 had "rectosigmoid" segments, and only 1 died in the neonatal period

The number of reported neonatal deaths from Hirschsprung's disease is only about 10–12% of the total children affected, most of these fatal cases were of the long segment variety

Several interesting points arise from this survey

(1) The "long segment" variety of Hirschsprung's disease comprises somewhat less than 10% of all cases It is probably incompatible with life unless treated, and the affected children usually die in the neonatal period

(2) The "short-segment" and "intermediate segment" varieties form the vast bulk of all cases (at least 90%) Relatively few of these die in the neonatal period The pathological segment is in the rectum and often also involves part or all of the sigmoid The term rectosigmoidectomy is a highly appropriate description of the operation needed in this group

(3) The histological appearances in all these cases are identical

(4) The occurrence of long and short pathological segments in different siblings of one family (Zuelzer and Wilson 1948) suggests that they are genetically the same

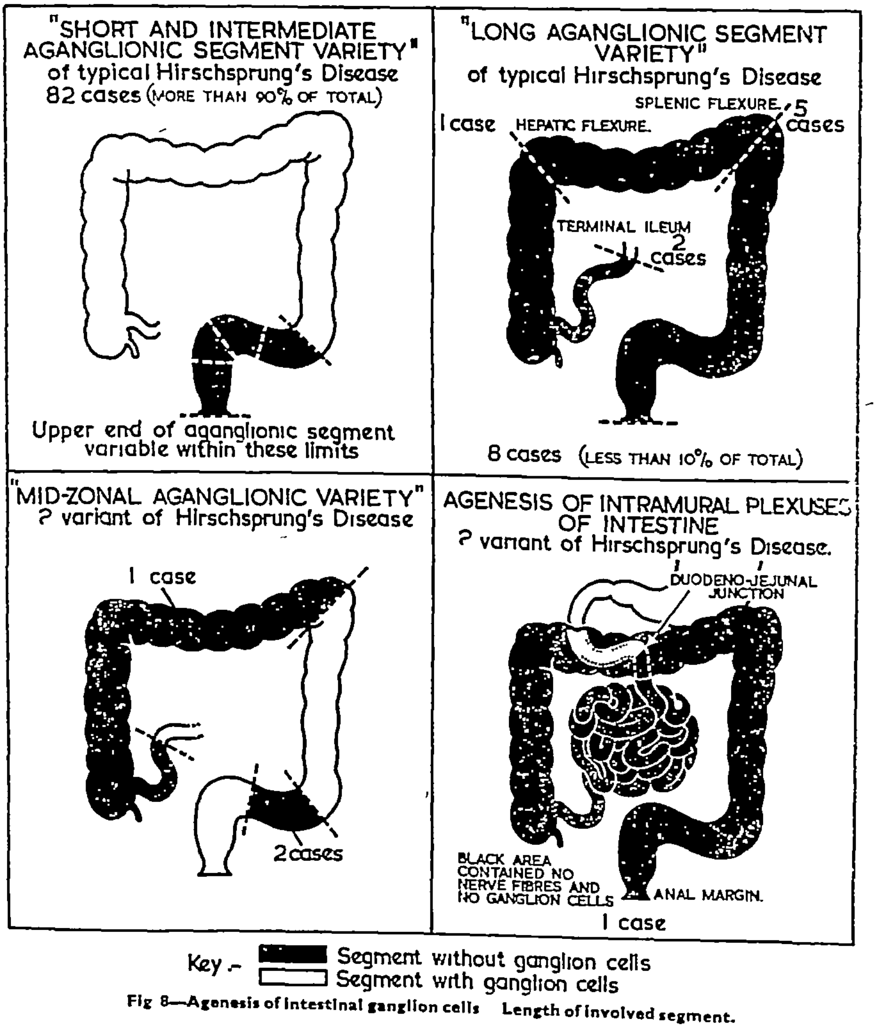

"SHORT AND INTERMEDIATE AGANGLIONIC SEGMENT VARIETY"
of typical Hirschsprung's Disease
82 cases (MORE THAN 90% OF TOTAL)
Upper end of aganglionic segment variable within these limits
"LONG AGANGLIONIC SEGMENT VARIETY"
of typical Hirschsprung's Disease
SPLENIC FLEXURE 5 cases
1 case HEPATIC FLEXURE
TERMINAL ILEUM 2 cases
8 cases (LESS THAN 10% OF TOTAL)
"MID-ZONAL AGANGLIONIC VARIETY"
? variant of Hirschsprung's Disease
1 case
2 cases
AGENESIS OF INTRAMURAL PLEXUSES OF INTESTINE
? variant of Hirschsprung's Disease.
DUODENO-JEJUNAL JUNCTION
BLACK AREA CONTAINED NO NERVE FIBRES AND NO GANGLION CELLS
ANAL MARGIN.
1 case
Key.–
Segment without ganglion cells
Segment with ganglion cells

Fig 8—Agenesis of intestinal ganglion cells Length of involved segment.

INTERPRETATION OF PATHOLOGICAL FINDINGS

It has been suggested that the proximal colon receives its parasympathetic nerve supply from the vagus, while the distal end of the colon is supplied by the parasympathetic pelvic nerves, and that Auerbach's plexuses contain ganglion cells of the parasympathetic supply to the bowel

Swenson (1950), considering Hirschsprung's disease to be a failure of development of Auerbach's plexuses in rectum and rectosigmoid, suggests that failure of the pelvic parasympathetic nerve supply to develop may be the explanation of the location of the aganglionic lesion This theory is hardly compatible with the great variability in length of the aganglionic segment

We suggest that the primary pathology of Hirschsprung's disease is an agenesis, in a distal part of the gut of variable length, of the ganglion cells which form Auerbach's and Meissner's plexuses, and that this change is not conditioned by any failure of development of the extrinsic nerve supply of the intestine Embryological development generally begins at the cranial extremity and progresses caudally If this applies to the intramural ganglion cells, a genetically determined disturbance of development with variable time of onset would explain long, intermediate, and short aganglionic desirable (1) for other workers to make similar investigations and supply additional data on familial incidence and on twins, and (2) to follow our successfully treated patients through their marital life and study their offspring

As this paper was going to press, a histologically established case of Hirschsprung's disease in a man of 54 was reported by Rosin et al (1950) from the Mayo Clinic The man has three normal children but their sex is not stated

Genetic Prognosis

Provisionally, we suggest that parents who have one child with Hirschsprung's disease should be told that the chances of the disorder occurring in subsequent female children are small, and in subsequent male children about 1 in 5 From a series of this size one cannot determine whether a calculated average chance will apply equally to any particular family It is possible that in families where two children have been affected the chances of the disease occurring in subsequent male children are considerably higher, and in those with one affected child they are correspondingly lower, resulting in the same average figure as if the series was homogeneous

Follow-up of Cases after Rectosigmoidectomy

The first 12 and the next 14 cases treated by rectosigmoidectomy at this hospital have already been reported (Bodian et al 1949, 1950) During 1950 a further 11 children have been operated on, and we can now summarise the follow up results in all 37 cases

There have been 3 deaths in the series 2 under anæsthesia and 1 from peritonitis, The follow up period is calculated from the final closure of the colostomy after rectosigmoidectomy, and 2 of the cases are too recent to be included The remaining 32 children were divided into three groups 12 followed for two years or longer, 11 followed for a year to a year and eleven months, and 9 followed for six to eleven months All these children have recently been examined, and their data are summarised in fig 4

The 32 children are all in excellent general condition All but one pass regular and spontaneous motions, roughly half without laxatives, the remainder are given aperients by their mothers Only 3 complain of occasional abdominal distension Some pass flatus at night but experience no difficulty Some soil their pants occasionally, but there is a tendency to grow out of this habit and to acquire complete sensory and motor control with age

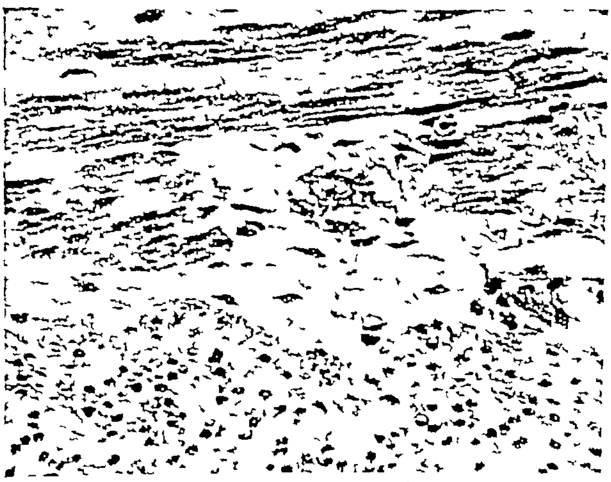


Fig 6—Intramural plexus in transitional zone (× 300)

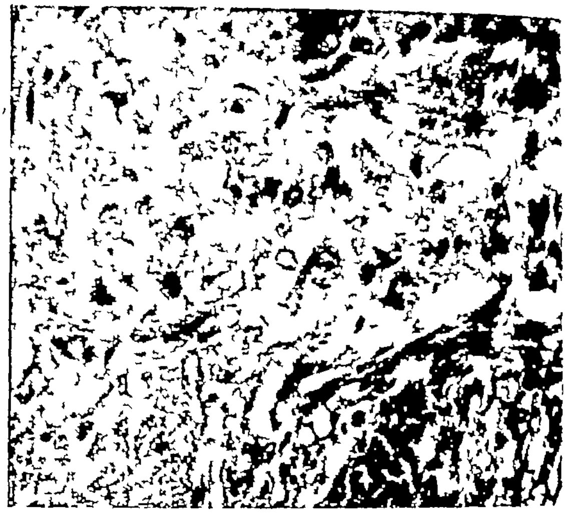


Fig 7—Intramural plexus in dilated segment with normal ganglion cells (× 280)

The weights of the children have been rather informative We have not considered their weights before surgical treatment because fæcal accumulations tend to vitiate the figures We have merely compared the weights at the time of closure of the colostomy with present weights and related these figures to norms for the age

Of the first 12 children only 1 is still below average The remainder are now of average weight or well above it, 6 of these had previously been underweight but have caught up

Of the second group of 11 cases, 3 underweight children are now of average weight, 1 is catching up, and 1 is still well below average

The last group, of 9 children, were all of average weight at the time of closure of the colostomy and have maintained or exceeded the normal rate of weight gain

Three children had anastomotic anal strictures which were treated by dilatation with improvement, their general progress has not been affected adversely One child had a bladder palsy which recovered completely after six months' treatment One has relapsed owing to a residual short narrow segment, he requires daily enemas but has otherwise made good progress

None of the children were recently given barium enemas In our last report, however, we demonstrated a considerable regression in the size of the dilated colon which had been anastomosed to the anal canal

Pathology

THE LENGTH OF SEGMENT INVOLVED

Histological examination in all our 40 cases of Hirschsprung's disease uniformly revealed the characteristic pathological findings previously reported (Bodian et al 1949) Two of the children died in the neonatal period, one died after subtotal colectomy, and of the 37 cases treated by rectosigmoidectomy, in which the resected bowel segments were submitted for investigation, 3 died and necropsies were performed on them

No ganglion cells were found in the undilated or narrow distal segment of bowel and in a few centimetres of adjoining hypertrophied dilated intestine Abnormal non medullated nerve trunks were present at the customary sites of the intramural ganglia, they were largest in the rectum and anal canal (fig 5) Proximal to the aganglionic segment there was a short transitional zone of scanty small abnormal ganglia to point of maximum distension 65 cm from duodenojejunal flexure, where circumference was 6 2 cm Dilatation then progressively less to point 118 cm from duodenojejunal flexure, where circumference of ileum was only 1 2 cm Terminal 46 cm of ileum unexpanded but contained little meconium of normal consistence Ileum proximal to this contained brownish green meconium of normal consistence Colon and rectum about 38 cm long Cæcum and most proximal part of ascending colon moderately distended with meconium of firmer consistence than in any other part of bowel Colostomy situated just beyond hepatic flexure Colon distal to colostomy contained little meconium of normal consistence Except for most proximal part of ascending colon, average diameter of large bowel was about 1 8 cm All the intestinal tract was freely patent

Blocks taken from consecutive levels of the entire intestinal tract from hypopharynx to anus were examined histologically Inflammatory changes, mainly of the peritoneum, were fairly widespread and led to œdematous thickening of the bowel wall Intramural ganglia were normal in the œsophagus, the stomach, and the proximal part of the duodenum, but scanty and small in the distal part of the duodenum

The plexuses including both ganglion cells and nerve fibres were completely absent from all sections from the level of duodenojejunal flexure to the anal margin A representative photomicrograph is shown in fig 10 It is noteworthy that dilatation of the bowel wall extended well into the parts without intramural plexuses Paravertebral sympathetic ganglia and ganglia in the bladder wall were normal. Normal nerve bundles were found in random sections taken through the mesentery of the small and the large gut The pancreas was histologically normal

We can only speculate on the relationship of this condition of agenesis of intramural plexuses to Hirschsprung's disease It may well be a severe variant of the disease, and this view is supported by the observation of normal ganglia in both conditions in a proximal part of the intestinal tract, gradually disappearing towards the pathological segment

The aganglionic segment was, however, considerably longer than in any of the reported cases of Hirschsprung's disease, and, in contradistinction to the typical case, there were no nerve bundles in the affected part of the intestine

This case might illustrate a very early disturbance of the craniocaudal differentiation of intestinal neurones before the growth of nerve fibres into the bowel wall

Summary

We have presented the first study of the familial incidence of Hirschsprung's disease The evidence supports a genetic determination of the disease The over all chances of a male sibling of a known case being affected are about 1 in 5, those of a female sibling being effected are small

We have produced a follow up report of 37 cases treated by rectosigmoidectomy

A pathological study of our 40 cases has uniformly confirmed the previously reported absence of intramural ganglion cells, and the presence of abnormal nerve bundles in the terminal undilated segment of bowel A review of published reports shows that the length of the involved segment varies considerably The bulk of the reported cases (over 90%) show pathological changes in the rectum and part or all of the sigmoid colon Less than 10% have extremely long abnormal segments which appear to be incompatible with life if untreated

A case is reported showing a hitherto unrecorded condition of agenesis of both nerve fibres and ganglion cells of the intramural plexuses distal to the duodenojejunal junction Its possible relationship to Hirschsprung s disease is discussed

A theory is suggested to explain the histopathological findings in Hirschsprung's disease and its variants

We wish to thank the medical and surgical staff of the Hospital for Sick Children Great Ormond Street, for access to their patients, Dr S Lawler and Dr I A B Cathie for determining the blood groups of the twins, and Dr Eliot Slater for the opinion on the fingerprints of the twins in family 36 Our thanks are due to Mr Derek Martin, of the Department of Medical Illustration, for the photographs and the diagrams which were drawn by Mr P G Cull

BIBLIOGRAPHY

Bodian M Stephens F D Ward B C H (1949) *Lancet*, i, 6
— — — (1950) *Ibid*, i 19
Buttersack P (1927) *Münch med Wschr* 74, 1626
Burnard E D (1950) *Brit med J* i 151
Dalla Valle A (1920) *Pediatria* 28 740
— (1924) *Ibid* 32 569
Ehrenpreis Th (1946) *Acta chir scand* 94 suppl 112
Haldane J. B S (1938) *Ann Eugen Camb* 8 255
Hirschsprung H (1888) *J Kinderheilk* 27 1
Lee C. M jun Bebb K C Brown J R (1950) *Surg Gynec Obstet* 91 281
Perrot A Danon L (1935) *Ann Anat path méd Chir* 12 157
Popper J (1920) *New York med J* 112 1030
Rosin, J D Bargen J A Waugh J M (1950) *Proc. Mayo Clin* 25 710
Swenson O (1950) *Surgery* 28, 371
— Rheinlander H F Diamond I (1949) *New Engl J Med* 241 551
Tiffin M E Chandler L R., Faber H K (1940) *Amer J Dis Child* 59 1071
van Campenhout E (1931) *Arch Biol* 42 479
Whitehouse F R Kernohan J W (1948) *Arch intern Med* 82 75
Wood Jones, F (1946) in Buchanan s Manual of Anatomy Baltimore, p 864
Zuelzer W W, Wilson, J L (1948) *Amer J Dis Child* 75, 40

RELATION OF PENICILLIN SENSITIVITY IN STAPHYLOCOCCI TO CLINICAL MANIFESTATIONS OF INFECTION

J C SHERRIS
M.D Lond
LATE ASSISTANT PATHOLOGIST, AYLESBURY PATHOLOGY LABORATORY

M. E FLOREY
M.D Adelaide
OF THE CHRONIC INFECTIONS UNIT, STOKE MANDEVILLE MINISTRY OF PENSIONS HOSPITAL

AYLESBURY, BUCKS

IN the past three years several bacteriological laboratories have reported an increasing incidence of penicillin resistant strains of *Staphylococcus pyogenes* in their routine work, and some writers have concluded that the clinical value of penicillin is steadily diminishing It seemed worth while, therefore, in a laboratory serving both an urban and a rural area, to see whether a clear cut distinction could be established between penicillin-sensitive and penicillin resistant strains of staphylococci, and, if so, whether this distinction was reflected in the clinical manifestations of infection in the lesions where they were found

The material for the inquiry was collected between November, 1948, and May, 1950, some from practitioners and two general hospitals, but mostly from a Ministry of Pensions hospital containing special units for plastic surgery, paraplegia and chronic-wound infections The great majority of the patients from whom the material was obtained had previously received penicillin treatment in one form or another, and the paraplegic patients had had many courses Special study of the signs of inflammation associated with these organisms was confined to the Ministry of Pensions Hospital Once it was found that the results of the bacteriological studies were consistent irrespective of the source of the staphylococci only lesions containing these organisms in the chronic infections unit were studied

BACTERIOLOGICAL INVESTIGATION

Methods

Detailed investigations were made on the first 156 strains isolated These were consecutive strains isolated in the laboratory during the period of the investigation excluding only those obtained from healthy carriers or on more than one occasion from the same lesion When an apparently representative collection from all sources had been obtained and the results were found to be consistent, segments extending to the anal margin, which is the typical finding in Hirschsprung's disease Ganglion cells which were in the process of formation at the time of onset of the disturbance would be imperfect (ganglia in transitional zone)

We have found no evidence in our histological material that the pathology is one of degeneration of previously formed ganglion cells, since reactionary changes, cellular infiltration, and fibrosis were not observed

It is the accepted anatomical teaching that the ganglion cells of the intramural plexuses relay parasympathetic fibres, and that the sympathetic fibres pass through the plexuses uninterruptedly, having been relayed in the abdominal sympathetic ganglia We postulate that the preganglionic parasympathetic nerve fibres, failing to terminate at a ganglion cell, grow caudally between the muscle layers and in the submucosa for a considerable distance Thus nerve trunks would be formed in the aganglionic segment consisting mostly of these fibres with a normal component of sympathetic fibres One would expect the nerve trunks, as they include increasing numbers of nerve fibres in the more distal parts of the aganglionic segment, to increase in density and ultimately in size, and this is in fact what has been found

Agenesis of the intramural ganglion cells would thus be the primary pathology, and development of abnormally dense and large nerve trunks, consisting of normal autonomic nerve fibres, a secondary phenomenon

The 3 reported cases of zonal absence of ganglion cells with normal ganglia both above and below cannot be simply explained on the basis of this hypothesis alone The occurrence of this rare variant suggests that sometimes, in addition to the craniocaudal differentiation of intramural intestinal neurones, there is a caudocranial differentiation with a final link up between the two A disturbance sometime before the completion of differentiation would explain the finding of zonal agenesis with normal ganglia both above and below

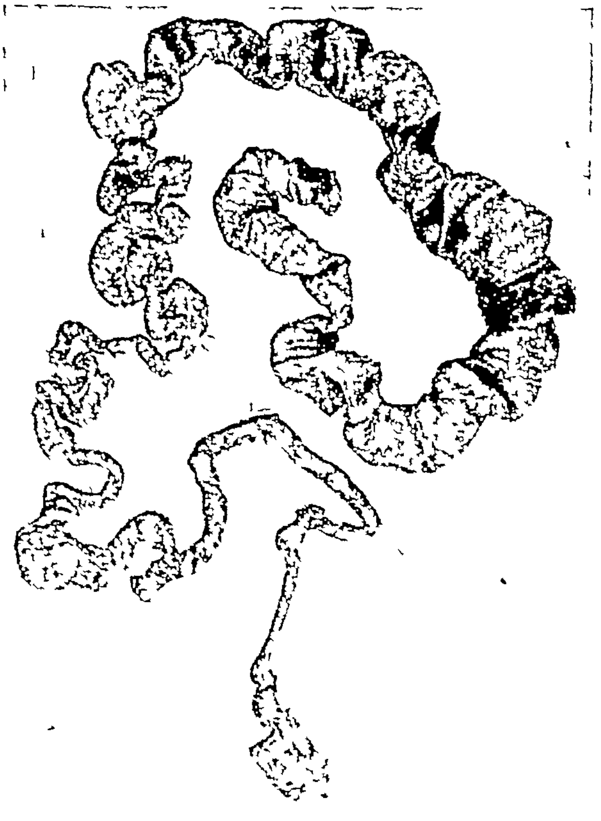


Fig 9—Intestinal tract from duodenojejunal junction to anal margin in a case of agenesis of intramural plexuses

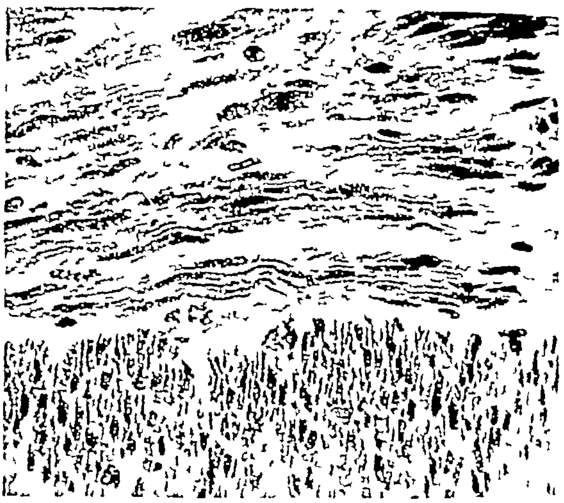


Fig 10—Representative section of bowel wall in agenesis of intramural plexuses (same case as fig 9) (× 300)

Our hypothetical view of the development of Hirschsprung's disease is purely theoretical and was produced in an attempt to explain the histopathological observations Recently, however, Prof J D Boyd kindly drew our attention to the work of van Campenhout (1931), who demonstrated in chick embryos that differentiation of intestinal neurones in the foregut preceded that in the hindgut, he also claimed that the intramural ganglion cells probably developed as an outgrowth of the thoracolumbar neural crest, and that the vagus played no part in their formation

A Case of Agenesis of Intramural Plexuses

The case reported below may possibly be a particularly severe variant of Hirschsprung's disease (see fig 9). We have not been able to find any published report of this condition

A boy, aged 4 days, an only child, was admitted to the Hospital for Sick Children under Mr G H Macnab, with complete intestinal obstruction from birth He vomited every feed, and throughout his life his bowels did not open. Abdominal distension was at first slight

Laparotomy at the age of 4 days revealed dilated loops of small intestine The distended parts tapered gradually away into an undistended terminal ileum without any sign of localised obstruction The whole length of the large intestine was completely undistended but contained a small quantity of meconium as far as the mid point of the descending colon. The meconium in the small intestine was apparently semi fluid A rubber catheter was passed per rectum and could be guided under vision into the descending colon No further interference seemed indicated, and the abdomen was closed

In view of the fact that no meconium had passed and the abdomen was increasingly distended, the abdomen was reopened on the seventh day of life Distension of the collapsed gut had proceeded a little further Ileo transverse colostomy was considered, but in view of the child s poor condition only a transverse spur colostomy was established.

The child s condition deteriorated, and he died at the age of 10 days without having passed meconium

Necropsy revealed moderate dilatation of the right atrium and ventricle in the heart, confluent lobular collapse, hypostatic congestion and œdema of the lungs localised fibrinopurulent peritonitis a very fatty liver, a normal pancreas, and the following changes in the gastro intestinal tract (fig 9) Œsophageal mucosa much congested Stomach moderately dilated, containing recent and altered blood mixed with mucus Duodenal contents deeply bloodstained Approximate total length of the jejunum and ileum, 164 cm First 27 cm of jejunum mildly dilated but not hypertrophied. Progressive dilatation of slightly thickened small bowel up coliform bacilli, or non hæmolytic streptococci, because their presence did not significantly affect the incidence of the specified signs of inflammation The presence of diphtheroid bacilli and micrococci was ignored In 2 of the patients studied pyrexia was discounted because both had severe urinary infections as well as the lesions from which the staphylococci were isolated, which were trophic sores free from pus or surrounding inflammation

Clinical Findings

The types of lesions from which the strains were isolated are shown in table II the numbers of each type in the whole series are shown in column A, and those in which the clinical manifestations of infection were studied and analysed statistically in column B It will be seen that those in column B form a fairly representative sample In each column the lesions are divided into those infected with sensitive and with resistant staphylococci The lesions have then been arranged in three groups, according to the penicillin sensitivity of their staphylococci, group I being those in which sensitive organisms predominate, group II those with predominantly resistant organisms, and group III those where the proportions were about equal.

It will be seen that the lesions in the first two groups are in the main distinct Group I, with 56 lesions, from 50 of which sensitive staphylococci were isolated, includes all the acute and originally closed lesions and all the chronic bone infections The resistant staphylococci in this group were obtained from (*a*) a perinephric abscess in a paraplegic patient admitted for a chronic urinary infection from which a penicillin resistant staphylococcus had been isolated , (*b*) a case of chronic suppurative arthritis, also in a paraplegic , and (*c*) 4 cases originally admitted for chronic osteitis which acquired a resistant infection after admission to hospital Group II contains 84 lesions, 78 of which yielded resistant staphylococci , it is mainly composed of infected operation wounds, superficial trophic lesions in paraplegic patients, burns, and other open traumatic lesions, and low grade puerperal infections where the staphylococci were isolated from the patient's cervix In the 4 cases of long-standing sinuses the organisms were isolated from the mouths of the sinuses, which were too narrow for the swab to be inserted without touching the skin , staphylococci were not isolated on subsequent occasions

TABLE II—TYPES OF LESIONS ASSOCIATED WITH SENSITIVE OR RESISTANT STAPHYLOCOCCI (EXCLUDING 31 STRAINS YIELDING β HÆMOLYTIC STREPTOCOCCI)

Nature of lesions	No from which staphylococci were isolated			
	A Whole series		B Those studied and analysed	
	Sens	Resis	Sens	Resis
Group I (predominantly sensitive)				
Abscesses boils and carbuncles	22	1	10	1
Chronic osteitis and subacute osteomyelitis	15	4*	14	3*
Tonsillitis	3	0		
Cellulitis	3	0	3	0
Suppurative arthritis	2	1	2	1
Septic finger or toe	2	0	1	0
Empyema of gall bladder	1	0		
Endocarditis	1	0		
Acute mastoiditis	1	0		
	50	6	30	5
Group II (predominantly resistant)				
Postoperative infections	0	28	0	18
Pressure sores in paraplegics	2	27	1	22
Puerperal infections	0	5		
Burns and open traumatic wounds	4	11	2	6
Mouths of sinuses	0	4	0	4
Otitis media†	0	2		
Chronic balanitis	0	1		
	6	78	3	50
Group III (sensitive or resistant)				
Chronic ulcers (traumatic or due to stasis)	16	12	15	12
Soft tissue sinuses	5	5	4	5
Dermatitis	4	6	4	6
Otitis externa	1	1		
Para nasal sinusitis	1	1	1	0
Urinary infections	1	1‡		
	28	26	24	23
Totals	84	110	57	78

* All known to have acquired resistant *Staphylococcus pyogenes* in residual sinuses after operation in hospital

† The middle ears were already draining and the organisms were isolated from ear swabs

‡ From cystitis developing after repeated catheterisation for enlarged prostate

TABLE III—INCIDENCE OF CLINICAL SIGNS OF INFLAMMATION IN LESIONS INFECTED WITH PENICILLIN SENSITIVE AND PENICILLIN RESISTANT STRAINS

Penicillin sensitivity of staphylococci	Total lesions*	Inflammatory signs absent	Inflammatory signs present		
			With pus	Without pus	Total
Sensitive	57	9	34	14	48
Resistant	78	43	21	14	35

$\chi^2 = 22\ 60 \quad P < 0\ 001$

* Exclusions explained in text.

In group III, where little distinction could be drawn between those with sensitive and with resistant staphylococci, the lesions were largely superficial ones, such as ulcers, dermatitis, and soft tissue sinuses

A statistical analysis of the clinical findings (table III) shows that manifestations of inflammation were noted in 48 of the 57 lesions from which penicillin sensitive staphylococci were isolated (i e , 84%) but in only 35 of the 78 lesions yielding penicillin-resistant strains (i e , 45%) Suppuration was noted in 60% of the penicillin sensitive group but in only 27% of the penicillin-resistant group In each case the difference is statistically significant The signs of inflammation were absent in 9 of the 57 lesions yielding sensitive staphylococci compared with 43 of the 78 yielding resistant strains—i e , 16% as against 55%

DISCUSSION

The published work on the penicillin sensitivity of staphylococci was reviewed by Florey et al (1949), and our findings confirm several previous contentions They showed that resistant staphylococci might be divided into (1) naturally resistant or penicillinase producing organisms , (2) those with resistance acquired in vitro, associated with diminution of virulence, slower growth than the original strain, and inability to produce penicillinase , (3) those with resistance acquired in vivo They considered that those reported as falling into the third group resemble naturally resistant staphylococci which have never been in contact with penicillin rather than those which have become resistant in vitro They concluded that there was no conclusive evidence that staphylococci can become resistant by more than one mechanism Despite the fact that many patients in the Ministry of Pensions Hospital had chronically infected open wounds which had been treated liberally with penicillin, no resistant non penicillinase producing strains, such as might result from resistance acquired in vivo, were found in the swabs from this hospital

Bondi and Dietz (1945) and Forbes (1949) found that the penicillin sensitivities of the non penicillinase producing strains they isolated all fell within a limited range A similar sharp distinction between resistant and sensitive strains was noted in the present investigation the bacteriological observations were restricted to the primary isolation and plate tests for penicillin sensitivity

The swabs received were inoculated on blood agar plates, aerobically and anaerobically, and also on segments of 'Cetavlon' and 7% salt agar plates In some cases the swab was then cut off into Robertson's cooked meat medium

Strains of *Staph pyogenes* were tested for coagulase production on primary isolation by the slide method of Cadness Graves et al (1943), or, when the results of this test were equivocal, by the tube method of Fisk (1940)

Tests for penicillin sensitivity were then made by streaking an inoculum of four or five colonies across half a ditch plate A single control streak of the Oxford staphylococcus was made across the centre and a second organism streaked across the other half The ditch contained 10 units per ml of penicillin incorporated in the agar The plates were incubated for 16–24 hours and read in the morning All strains reported sensitive showed an even band of inhibition on either side of the ditch approximating to that of the Oxford staphylococcus, those reported resistant grew up to or over the ditch at the site of heaviest inoculum, with an increasing zone of inhibition as the inoculum became dilute, but in no case was the zone as great as that of the Oxford staphylococcus This latter appearance was described by Barber (1947) as characteristic of penicillinase producing strains, and is in contrast to that of organisms resistant to penicillin but not destroying it, where growth proceeds evenly up to, or over, the ditch

The strains were kept for detailed bacteriological study of penicillinase production or quantitative assessment of sensitivity by subculturing from the original plate on to broth agar slopes, and were maintained in stock culture under liquid paraffin by the method of Morton and Pulaski (1938) After the period of collection all but 3 of the sensitive strains were recovered from stock culture and were tested quantitatively for penicillin sensitivity by the following method

To ensure uniform conditions for all strains, 60 ml quantities of broth containing commercial crystalline penicillin G in concentrations of 0 0025, 0 005, 0 01, 0 02, 0 04, 0 08, and 0 16 unit per ml were distributed in 3 × ½ in tubes in 1 ml amounts A set of these tubes for each sensitive organism was inoculated with 0 025 ml of a 1/100 dilution of an overnight culture of its respective staphylococcus One set received a similar inoculum of the Oxford staphylococcus In two instances the turbidity of the overnight culture, as judged by the naked eye, was less than that of the Oxford staphylococcus, and the dilution of these cultures was modified appropriately

All the tests were incubated simultaneously at 37°C for 18 hours, and the first tube showing no turbidity to the naked eye was taken as the end point In all cases this was clear cut

All but 8 of the resistant strains were recovered from stock culture, and these, together with the sensitive strains, were tested directly for penicillinase production by a method similar to that described by Bondi and Dietz (1944)

Plates inoculated with the Oxford staphylococcus were prepared according to the cylinder plate method of Heatley (1944) Into the cups were pipetted equal quantities of penicillin solution containing 5 units per ml and of overnight cultures of the staphylococci A control cup on each plate contained equal quantities of the penicillin solution and of an overnight culture of the Oxford staphylococcus The plates were incubated overnight at 37°C and the diameter of the zones of inhibition round the cups measured next morning

No attempt was made to assess quantitatively the resistance of penicillinase producing strains, because Kirby (1945) and later workers (see Florey et al 1949) have shown that the end point obtained depends on the size of the inoculum

Results

Of the 225 strains of *Staph pyogenes* isolated from 224 lesions, 97 were reported "sensitive" and 128 "resistant" by the plate method From one bedsore both sensitive and resistant staphylococci were isolated from the primary plate

On direct testing for penicillinase production the difference between the two varieties was distinct, for no zone of inhibition was produced round the cups containing the "resistant" staphylococci, whereas the cups containing the "sensitive" staphylococci were surrounded by a zone of inhibition whose diameter was in every case within 0 3 cm of that surrounding the control cup containing the Oxford staphylococcus The diameter of the zone of inhibition around this control cup varied between 2 2 and 2 5 cm, with an average value of 2 4 cm Quantitative testing of the "sensitive" strains demonstrated that all produced an end point of inhibition within the range examined These results are set out in table I

TABLE I—PENICILLIN SENSITIVITY OF 145 OUT OF 156 CONSECUTIVE STRAINS OF STAPHYLOCOCCI RECEIVED AT THE LABORATORY

Penicillin sensitive strains						Penicillin resistant penicillinase-producing strains
Total	Inhibition in units per ml					
	0 005	0 01	0 02	0 04	0 08	
55	4	7	33	10	1	90

3 sensitive and 8 resistant strains were lost in stock culture

All the strains examined could thus be divided sharply into two classes—(1) resistant or penicillinase producing, and (2) sensitive or non penicillinase producing—all the sensitive class falling within a limited range of sensitivity between 0 005 and 0 08 unit per ml under the conditions of the test (The Oxford staphylococcus was sensitive to 0 02 unit per ml)

CLINICAL INVESTIGATION

Methods

In the chronic infections ward routine swabs were always taken on the patient's admission and thereafter once or twice a week Notes were made on the presence or absence of signs of inflammation before the bacteriological findings were known In the rest of the hospital swabs were taken as the doctor in charge of the case thought necessary

On receipt of the laboratory report each patient in the group investigated clinically was visited by one of us and information was also obtained from the ward staff Further visits were made to assess the progress of the lesion and its relation to the presence of staphylococci In some cases the information was not complete and this is reflected in the different totals in the tables

Records were kept of the type of each lesion, and at each visit the presence or absence of the following signs of inflammation was noted (1) erythema, œdema, and tenderness around the lesion, (2) pus formation, and (3) pyrexia In some cases—notably deep seated infections in paraplegics—it was not possible to demonstrate the first of these signs No attempt was made to assess the manifestations of infection *quantitatively* because of the wide differences in the severity of the lesions, depending on their site, extent, and duration and their reaction after penicillin was administered The investigation was solely concerned with the presence or absence of the specified signs of infection during the time the staphylococci were known to be present

Exclusions

The 31 lesions infected with β hæmolytic streptococci in addition to the staphylococci were excluded from the clinical assessment, as were 50 cases in various hospitals and general practices beyond the reach of the clinical investigator and 9 others in which complete information on all the criteria could not be obtained The remaining lesions, which were *included in the statistical analysis*, totalled 135

We have not excluded lesions in which there was additional infection with *Ps pyocyanea*, *Proteus vulgaris*, fossa and groin. The loss was large for three days and attacks came every few minutes she had the feeling that her insides were being pressed down into the vagina, and she was doubled up with pain No medicines had been effective She had no frequency of micturition Her appendix was removed 4 or 5 years ago, but this made no difference to the severity of her attacks She had been advised to have her uterus removed

Examination —Her physique was excellent, and no abnormality was found on general examination Pelvic examination, without an anæsthetic, showed that her uterus was anteverted, small but not infantile of the type often found in nulliparous women of her age The ovaries were both palpable, but not tender A point to the right of the fundus uteri, but distinct from both ovaries and uterus, was acutely tender to gentle bimanual palpation No other evidence of disease was found Pelvic examination under anæsthesia revealed no abnormality

Cystoscopy and Pyelography —Cystoscopy showed marked pseudomembranous trigonitis and basal cystitis Catheters passed easily into the ureters The Braasch bulb size 16 was tight size 22 met with firm resistance to extraction, particularly on the right Gradual dilatation to Braasch 24 was successful On extraction of the bulb, white stringy flecks of mucosa came out of the ureter, probably from an extension of the pseudomembranous patches in the bladder The ureters were tortuous and irregularly dilated, indicating chronic ureteritis The right renal pelvis was dilated and the emptying film showed a large residue of dye There was no renal ptosis Urine taken during the examination was normal and sterile Recovery was complete in 24 hours the patient left hospital 36 hours after her admission

Result —Since the dilatation of the ureters, there has been no pain or discomfort with menstruation. The mental and physical effect upon the woman has been dramatic

Case 3 —Mrs C, aged 25, married 4 years, no children

Symptoms —Her menses started at the age of 15, but then stopped for 6 months At 16 they became regular, with no discomfort After her matriculation she experienced some pain at her periods It gradually increased until at 19 she had to go to bed immediately she started menstruating Standing or walking aggravated her discomfort and she felt that her "insides were dropping out" A variety of medicines and hormone treatments did not relieve her, nor did physiotherapy Dilatation and curettage had no effect Because of the fixed idea that she was imperfectly made, she refused to become pregnant, and she became terrified of childbirth

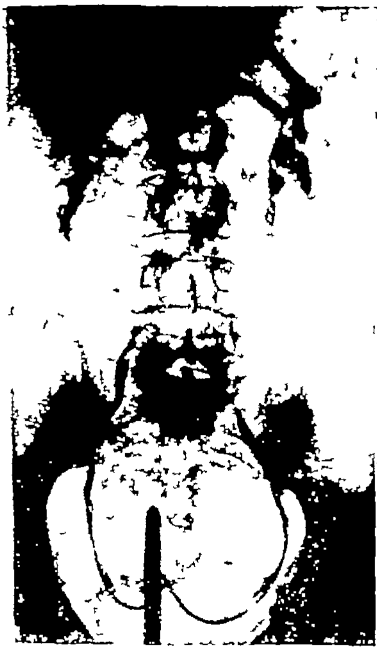


Fig 1

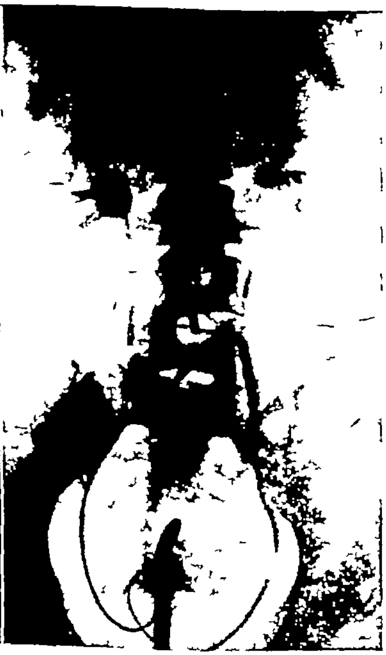


Fig 2

Fig 1 (case 1)—Right ureter is kinked opposite the 2nd lumbar vertebra Irregularly dilated and tortuous. The pain was more severe on the right side

Fig 2 (case 3)—Dilatation and tortuosity more marked on left—the side on which the pain was severe.

The pain was spasmodic and severe, chiefly in the left side and in the left iliac fossa but sometimes in the back There was no frequency of micturition but she had found that if she retained her urine for any length of time the pain worsened She complained of deep dyspareunia and 2–3 hours pain, simulating her menstrual pain, after orgasm at any phase of the intermenstrual cycle

Examination —The only abnormality found on general examination was slight ptosis of the right kidney Vaginal examination showed a small and antiflexed uterus, the right ovary was prolapsed but not tender, the left ovary was palpable high up, without discomfort There was a localised area of tenderness to the left of the body of the uterus where bimanual palpation caused pain "similar to menstruation"

Cystoscopy and Pyelography —Cystoscopy showed trigonitis, spreading up to and involving both ureteric orifices Catheters passed freely into and up both ureters Retrograde pyelography revealed bilateral ureteritis, the left ureter being more affected than the right (fig 2) In the erect posture there was considerable ptosis of the right kidney but no ureteric kink The emptying picture showed that neither kidney retained any dye Braasch bulbs met with some resistance, but the pelvic ureter was gently dilated to receive size 24 Recovery was complete in 24 hours

Result —Since the ureters were dilated, menstruation has been entirely free from the left sided spasmodic pain There is no longer dyspareunia or pain after orgasm After "that awful pain" went she developed an entirely different outlook on life and wanted to be told all about childbirth. I have recently heard from her that she is pregnant and very happy

DETAILS OF PROCEDURE

Before discussing these cases it may be well to state precisely how the investigation was made

The patient was anæsthetised with sodium thiopentone on a urological operating table so that the X ray pictures could be taken as soon as the investigator said the word Dr Ernst Widrich performed the urological investigations for me, and Dr I A. Brotman the radiological examinations The order of procedure was as follows

1 Vaginal examination
2 Cystoscopy A specimen of urine was collected in a sterile container
3 Ureteric catheters passed
4 Control film taken
5 Injection of 5–6 ml 12 5% sodium iodide into each ureter
6 Filling picture taken
7 Catheters withdrawn Dilatation of the ureters with Braasch bulbs up to size 22–24 (according to resistance)
8 Table rotated into vertical position for erect picture
9 Emptying picture taken in horizontal position

The films are developed immediately and unless there is any indication for further investigation the whole procedure occupies a maximum of 20 minutes If there is any evidence of infection 4–5 ml of 2% Argyrol is instilled into each ureter, and intramuscular penicillin (500,000 units) is given in a single intramuscular dose If it is believed that infection is due to a penicillin resistant organism, streptomycin 0 5 g may be given 6 hourly for 24 hours Most patients have little or no postoperative discomfort and return home 36–48 hours after admission. Occasionally there is pain for 12–16 hours, which is treated with antispasmodics

DISCUSSION

About 3% of women suffer from intractable or disabling pain at the menses All pain in the human body is unnatural and has a cause "Physiological pain" is a contradiction in terms Wharton (1943a) follows accepted principles and divides dysmenorrhœa into primary and secondary types 'the term 'primary dysmenorrhœa,'" he writes, "is synonymous with essential, Evidence has been produced to show that resistant staphylococci are isolated more frequently from hospital inpatients than from the population at large Forbes (1949) found that the proportion of resistant strains in staphylococci isolated from lesions contracted outside hospital was 12 5% compared with 68 4% from those contracted inside Rountree and Thomson (1949) showed that, in their series of lesions associated with resistant staphylococci, 54 had been cross infected in hospital compared with 8 infected before admission Cairns and Summers (1950) reported that 78% of the staphylococci isolated from hospital infections were resistant to penicillin compared with 19% of those isolated from closed abscesses present on admission, moreover, the proportion of resistant strains isolated from patients admitted to hospital with open infections rose with increasing stay in hospital Barber et al (1949), investigating the carrier rate of staphylococci in a maternity hospital, found 70–80% of resistant strains among the staphylococci isolated from carriers but found none among staphylococcal carriers in a control group outside hospital

Less attention has hitherto been paid to the lesions associated with resistant and sensitive organisms and the clinical manifestations of infection with the two types In the present series penicillin sensitive staphylococci were mostly isolated from acute lesions closed till operation or from chronic bone infections, some of which were of long standing and due to gunshot wounds in the 1914–18 and 1939–45 wars Resistant staphylococci, on the other hand, were mainly isolated from postoperative wounds, half of which followed plastic repair, and from other superficial lesions such as trophic sores in paraplegic patients These results appear to support the view that the high proportion of penicillin resistant strains now being isolated in bacteriological laboratories is a result of either the high carrier rate of these organisms in hospital staffs or their greater chances of survival in an environment where penicillin abounds Our clinical analysis shows, however, that the high carrier rate is not a reflection of the relative incidence of resistant and sensitive strains present in serious inflammatory infections The specified signs of infection were found significantly less often in lesions yielding resistant than in those yielding sensitive staphylococci

In view of the different types of lesion with which they were associated, this result cannot be interpreted as indicating that the resistant strains were less virulent than the sensitive, but the difference in the inflammatory signs associated with the two types of infection may help to bring into perspective the clinical importance of the reports of an increasing incidence of penicillin resistant staphylococci

CONCLUSIONS

In this study there was a clear bacteriological distinction between penicillin sensitive and penicillin resistant staphylococci All sensitive strains were of the same order of sensitivity as the Oxford staphylococcus and all the resistant strains produced penicillinase

The two types of staphylococci were in the main associated with different types of lesions—the penicillin sensitive strains with acute and closed or deep seated infections, whether acute or chronic, the resistant strains with superficial lesions

The penicillin resistant staphylococci were significantly less often associated with signs of inflammation or suppuration than the sensitive strains

We wish to thank the many doctors who gave us their permission to carry out this investigation on their patients Dr A Wilson for continuing the routine bacteriological examination after one of us (J C S) had left the laboratory, the ward sisters of Stoke Mandeville Ministry of Pensions Hospital for their willing coöperation in obtaining data, Miss Randall and Miss Ridley Thompson for the typing We are also indebted to Mr P H Leslie for the statistical analysis of the figures obtained, and Dr R L Vollum for his criticisms of the bacteriological section

REFERENCES

Barber, M (1947) *Brit med J* ii, 863
— Hayhoe, F G J, Whitehead, J E M (1949) *Lancet* ii 1190
Bondi, A, Dietz C C (1944) *Proc Soc exp Biol, N Y* 56 139
— — (1945) *Ibid* 60 55
Cadness Graves B, Williams, R, Harper G J Miles, A A (1943) *Lancet*, i, 736
Cairns H J F, Summers, G A C (1950) *Ibid*, i, 446
Fisk A (1940) *Brit J exp Path* 21 311
Florey, H W, Chain E Heatley, N G Jennings M A Sanders A G Abraham E P, Florey, M E (1949) Antibiotics London vol ii
Forbes, G B (1949) *Brit med J* ii 569
Heatley, N G (1944) *Biochem J* 38, 61
Kirby W M M (1945) *J clin Invest* 24 165
Morton H E, Pulaski E J (1938) *J Bact* 35 163
Rountree P, Thomson, E F (1949) *Lancet* ii, 501

URETERIC DYSMENORRHŒA

Grantly Dick Read
M.A., M D Camb

Three cases of intractable pain at the time of the menses are recorded here as examples of one type of dysmenorrhœa The origin and nature of the pain are discussed, and a method of investigation and treatment is suggested

CASE RECORDS

Case 1 —Mrs A, aged 36, no children, 8 week abortion 10 years ago, no other pregnancy

Symptoms —Menstruation was preceded by backache for several days and she suffered from lassitude and depression. At first the pain was suprapubic and extended across the lower abdomen It was most severe on the right, and extended upwards around the right loin there were exacerbations every few minutes, which doubled her up This phase of the menses was accompanied by distension of the abdomen, a sensation of pressure and fullness in the vagina, and sometimes frequency of micturition There was a bright red loss for one day, followed by drainage for anything up to ten days.

Examination —She was a thin, alert, healthy, and active woman. A slight, low dorsal scoliosis, and ptosis of the right kidney were the only abnormalities found on general examination Pelvic examination both with and without an anæsthetic revealed nothing that could account for her symptoms. Her urine was normal

Intravenous pyelography showed ptosis of the right kidney associated with kinking of the ureter immediately below its junction with the renal pelvis Both ureters were tortuous and irregular in outline

Cystoscopy and retrograde pyelography showed mild trigonitis. The ureteric catheters passed easily The right ureter was dilated with Braasch bulbs up to size 22 The left kidney was normal in position, and the left ureter less affected than the right (fig 1) Radiography in the erect position demonstrated that the right kidney dropped into the right iliac fossa Urine collected during the investigation was normal, and sterile

Treatment —Nephropexy was undertaken, using Demmings's method of slinging by closing the lower opening of the perinephric capsule The sympathetic nerve supply was interrupted by stripping the renal artery back to the aorta, and also stripping the upper end of the ureter Recovery from the operation was uneventful

Result —Since the operation, all menstrual periods have been free from pain There has been no premenstrual backache, lassitude, or depression The menstrual flow lasts for 3–4 days only, and ceases abruptly She has put on 5 lb in weight and can walk 2–3 miles without backache or fatigue She no longer dreads her menses and reports that her outlook on life is entirely different

Case 2 —Mrs B, aged 43, no children, one miscarriage about 15 years ago

Symptoms —From the menarche at 13 she had always had some discomfort at menstruation For the last 20 years it had been worse, and for the last 10 years she had had very severe pain which came on with the menstrual flow She dreaded the beginning of menstruation

The pain was suprapubic at its onset extending across the lower abdomen to the right iliac fossa but not to the posterior renal area There was some stabbing pain in the left iliac issues of that ureter will record the greater sensory eaction and take precedence over the afferent response of the uterus and the other ureter, in keeping with Sherrington's (1906) theory of the common path The converse occurs when the ureters are healthy and the uterus is disorganised by disease

The fear tension pain syndrome can be arrested by eliminating either the psychic or the somatic causes The pain can be relieved by drugs and analgesics The psychiatrist can break down the syndrome by psychic rectification and the therapeutic implantation of rational fear destroying mental processes Destructive operations, such as presacral sympathectomy or hysterectomy, can be performed This is applicable both to ureteric tension and to certain forms of dysmenorrhœa which are associated with spasm of the uterine musculature If presacral sympathectomy is performed, the nerves which convey psychic stimulus are removed and therefore the tension is not increased by efferent discharges The same syndrome can also be broken down by stretching the spastic muscles But the mechanism of relief by dilatation requires further explanation

Relief by Dilatation

Dilatation of constricted orifices in the body often relieves spasmodic pain temporarily, though it does not remove the cause The extent of tissue destruction from careful dilatation is negligible no structural change takes place that could prevent a recurrence of spasm after a short time, and indeed if these cases are treated purely by surgical procedures without attention to the patients' mental attitude many have a recurrence of pain after 2–3 months Wilfred Shaw (1948) writes "It is difficult to understand why dilatation of the cervix cures the pain in spasmodic dysmenorrhœas" Dilatation does not cure it is an important accessory to relief The stretching of the circular muscle fibres and connective tissues prevents painful spasm for a short time and establishes confidence that the dysmenorrhœa is relieved. The menses are no longer feared and the efferent sympathetic nerves do not, through emotional excitation disturb the normal harmony of action of the longitudinal and circular muscle fibres that produce painless peristalsis This offers an explanation for Wharton's (1943b) statement "If one can give the young woman a few months of relief from dysmenorrhœa she may have no more trouble from it and require no more attention" Excessive tension and spasm does not recur in women when the primary cause has been psychogenic, therefore pain is absent when the fear of pain has been obviated by painless menses If through psychic stress anxiety again becomes established pain will return Dilatation of the ureters will have to be repeated and psychological rectification again undertaken, until the bases of her fears have been eliminated.

SUMMARY AND CONCLUSIONS

Three cases of intractable incapacitating dysmenorrhœa are recorded, in which there was no evidence of uterine or ovarian disease. Stricture or spasm of one ureter was diagnosed in each case, and treatment of this condition resulted in complete relief from menstrual pain

Cystoscopy and retrograde pyelography should be a routine procedure in the investigation of intractable dysmenorrhœa Hysterectomy or presacral sympathectomy should not be advised until the urinary tract has been examined.

Dysmenorrhœa is often the somatic manifestation of a psychological state, resulting in the fear tension pain syndrome

I wish to express my thanks to Dr Widrich and Dr I A Brotman both of Johannesburg, for collaborating with me in these investigations

References at foot of next column

DR READ REFERENCES

Dick Read G (1946) *J Obstet Gynæc. Brit Emp* 53 55
Dunbar H Flanders (1935) Emotions and Bodily Changes New York p 318
Fluhmann C F (1939) Menstrual Disorders Philadelphia and London, p 266
Hunner G L (1925) *Amer J Obstet Gynec* 9 47
— (1928) *Ibid* 15 453
Langley J N Anderson H K. (1895 96) *J Physiol* 91, 71 131 327
Lewis T (1932) *Arch intern Med* 49, 713
Lowsley O S Kirwin T J (1944) Clinical Urology Baltimore vol ii p 1275
Mackenzie D W Wallace A B (1935) *J Urol* 34 516
Morison D R (1942) *Edinb med J* 50 661
Naber J (1931) *Ther d Gegenw* 72 108
Pelouze P S (1941) Office Urology Philadelphia and London p 667
Shaw W (1948) Text Book of Gynæcology London p 353
Sherrington C (1906) Integrative Action of the Nervous System London
Speransky A D (1935) A Basis for the Theory of Medicine. Moscow p 401
Wharton L R (1943a) Gynecology including Female Urology Philadelphia and London p 178
— (1943b) *Ibid* p 186

CHANGES IN BLOOD CHEMISTRY AFTER SURGICAL OPERATIONS

A W WILKINSON
Ch.M Edin, F R C S E

BARBARA H BILLING
B.A. Camb, Ph.D Edin

GABRIELLA NAGY
B Sc Lond

C P STEWART
M Sc Durh, Ph.D Edin

From the Department of Surgery, in the University of Edinburgh, and the Clinical Laboratory, Royal Infirmary, Edinburgh

In a study of the effects of surgical operations on nitrogen and electrolyte metabolism (Wilkinson et al 1949, 1950) it was shown that immediately after operation the urinary excretion of nitrogen and potassium was increased, whereas that of sodium and chloride was decreased This appeared to be a fundamental part of the body's response to injury and to be independent of the type of surgical operation, it was not abolished by dietary measures Whether or not corresponding changes took place in the composition of the blood seemed to be worth investigating, and the results obtained from 30 patients, studied in two groups, are reported here

METHODS

Group I comprised 4 healthy volunteers who acted as controls by submitting to dietary restriction but not to surgical operation, and 20 male patients who underwent surgical operation Of the latter, 17 were submitted to partial gastrectomy, and 1 each to gastro enterostomy, splanchnicectomy, and vagotomy plus gastrectomy

Blood was withdrawn at least once before and again two days, four days, and fourteen days after operation In some cases more frequent sampling was possible during the postoperative period In all cases blood was withdrawn without stasis into a glass syringe sterilised by autoclaving, transferred to tubes containing any necessary anticoagulant, and analysed without delay In most samples determinations were made of plasma-proteins (micro-Kjeldahl, with magnesium sulphate as the fractionating agent), non protein nitrogen (micro-Kjeldahl), chloride (Van Slyke 1923), and carbon dioxide combining power (Van Slyke and Cullen 1917) In some cases, limited unfortunately by the undesirability of repeatedly withdrawing large samples of blood, some or all of the following were also determined serum sodium (Peters and Van Slyke 1931), urea (Van Slyke 1929), amino acid nitrogen (Frame et al. 1943), creatinine (Folin and Wu 1919), and uric acid (Folin 1930) Determinations of hæmoglobin were made by the carboxyhæmoglobin method with a Haldane hæmoglobinometer calibrated so that 100% represented 14 8 g of hæmoglobin per 100 ml. of blood idiopathic, intrinsic or functional dysmenorrhœa" Fluhmann (1939) prefers the terms intrinsic and extrinsic In point of fact, however, there is no such entity as primary or intrinsic dysmenorrhœa menstrual pain is secondary to definite pathological disorders But these are not necessarily uterine, the disorder may be located elsewhere—even at the psychological level

These three cases, which are examples of a large category, call attention to a postulate which cannot be too frequently stated—that gynæcology is the science of the whole woman Manifestations of disease in the female organs or reproductive function may be primary and local, but they may also be *secondary to the disorganisation of almost any physiological function in the body* Psychological factors are, of course, of supreme importance

The three patients had received all the usual medical and surgical treatments Pain relieving drugs, hormones, sedatives, and tonics had been exhibited without appreciable benefit Each patient had undergone dilatation and curettage before consulting me Two of them had had their appendices removed, but no evidence of inflammation was reported Presacral sympathectomy had been advised in all three cases, and the two elder women had been urged to undergo hysterectomy But none of them had been cystoscoped or had the urinary tract examined

Pain of Ureteric Origin

No tumour, neoplastic change, or inflammation could be found to account for their intense pain, which was spasmodic, severe, and incapacitating, and occurred only at the onset of menstruation The site and nature of the pain were the same in all three cases

Hunner (1928), in his outstanding paper, "What the gynecologist should know about urology," recorded this form of dysmenorrhœa He attributed it, however, to inflammatory stricture of the ureter, which does not explain many of the associated phenomena Morison (1942) refers to these manifestations of ureteric spasm but puts the pain not at Morris's point but in the broad ligament zone, and appears to regard infection as the main ætiological factor This is a mistake Speransky (1935) is right when he says that "in our diagnosis we actually fasten on the result and do not take into account the mechanism of the pathological process"

It is not sufficient to ascribe spasm and stricture in one part of the ureter to inflammation without offering some explanation of the manner of infection Although direct or primary infection of the lumen of the ureter has been recorded by various authors, the inflammation which gives rise to stricture and spasm is intramural, and the infection is conveyed by lymphatics The lymphatics of the pelvic ureter empty into the hypogastric lymph-nodes, which also receive lymph from the cervix and the body of the uterus Segmental lymphatic drainage of the ureter is generally recognised, but Mackenzie and Wallace (1935) pointed out that free anastomosis may occur under certain conditions, allowing both ascending and descending *intramural infection* In this way the ureter may become infected from the cervix or body of the uterus, and Hunner's (1925) contention that ureteric stricture can arise from distant foci of infection, such as the teeth, tonsils, and sinuses, may be justified

Infection leads to inflammation, and the latter causes spasm The constriction may be acute, subacute, or chronic, according to the patient's ability to overcome the infection The local spasm may not be sufficiently severe to cause pain, for constrictions in the lower third of the ureter may be demonstrated by pyelography in women who have pain only at the menses that is to say, the constriction remains between the periods but only becomes painful with the onset of the menses This may explain the observations of Pelouze (1941) that Hunner claimed to have encountered clinically 2000 strictures in 8 years, whereas 479 necropsy specimens examined by five investigators failed to reveal a single primary stricture Is it not possible that in the relaxation of death macroscopic evidence of antemortem spasm may be obliterated? "Spasm simulating stricture may inject an element of confusion," say Lowsley and Kirwin (1944), and fibrous tissue appears in and about muscles in a state of persistent spasm

Spasm of smooth muscle is accompanied by vasoconstriction it is probably this that is responsible for *the acute intermittent pain of ureteric dysmenorrhœa*. Uterine spasm causes a dull suprapubic ache which extends across the lower abdomen and is not colic, but the relative ischæmia of the ureter is accompanied by pain which increases in intensity with each peristaltic wave Langley and Anderson (1895–96) demonstrated ischæmia of pelvic viscera on stimulation of the hypogastric nerves, and Lewis (1932) showed that severe and paralysing pain develops in muscles with restricted blood supply Peristalsis in the ureter is not arrested by focal areas of intramural infection, although local spasm confines the infective agent

Psychosomatic Aspects of Dysmenorrhœa

The psychological effect of menstruation has been discussed by a very large number of workers, most of whom agree with Naber (1931) that "dysmenorrhœa is generally of psychogenic origin" Dunbar (1938) gives an extensive bibliography of this subject Yet from all these published observations there is one omission—the ureter is not referred to The effect of psychic influences upon the uterus and its functions occupies the attention of all these authors, though there seems to be no explanation of the mechanism by which psychical influence can produce the results ascribed to it

The three cases I record here as examples of ureteric dysmenorrhœa exhibit many symptoms which previously have been considered uterine in origin, but which were *eliminated by treatment of the ureter* *Ureteric* peristalsis recurs at intervals corresponding to the attacks of colic complained of by the three women is any rhythmical uterine spasm recognised that could account for this phenomenon? All three spoke of a sense of fullness and dropping in the vagina, and this symptom, too, disappeared after dilatation of the lower third of the ureter

The fear tension pain syndrome (Dick Read 1946) is applicable to the inflamed pelvic ureter, which is supplied through the hypogastric plexus by the same nerves as, under emotional stress, give rise to the abnormal tensions, and therefore the pain, of labour The onset of menstruation, which is a continual reminder of the reproductive process, is not only accompanied by the fear of discomfort, but wakes up the underlying causes of anxiety associated with the whole reproductive function, which originated in what we will term "psychic trauma" at an earlier age the result is an overactivity of the *sympathetic nervous system out of all proportion* to the intensity of the afferent stimulus The already spastic ureter, which has been subjected, with the other pelvic viscera, to premenstrual congestion, receives a violent added stimulus, which causes such tension that the *threshold of pain is crossed* The vicious circle is thus established, for the presence of pain justifies the fear which, through the sympathetic nervous system, stimulates the circular smooth muscle fibres of the ureter, thereby increasing the tension and the pain, until a severe and incapacitating condition arises It may be asked why the ureter should give rise to pain if, through the hypogastric nerves, the uterus is subjected to the same efferent nervous discharges But if the uterus is healthy and one ureter is inflamed, the supersensitive

Chloride

The concentration of chloride in the blood usually fell slightly for the first day or two after operation, and thereafter rose until it was significantly higher than before operation In some cases the plasma chloride concentration showed a slight transient fall, but usually it was unaltered throughout the period of observation Calculation showed that the chloride concentration not only of the plasma but also of the erythrocytes was substantially constant, and that the changes in whole blood were due to changes in the relative proportions of plasma and cells

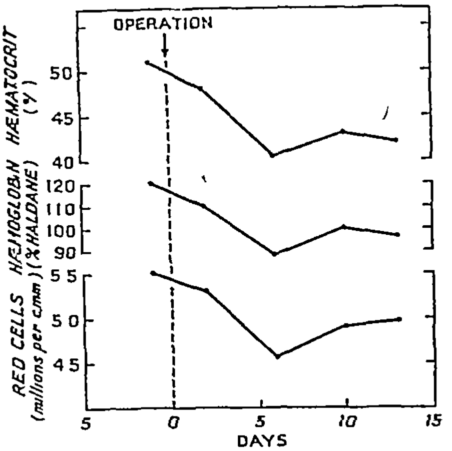


Fig 2—Changes in hæmatocrit and amounts of hæmoglobin and red cells after partial gastrectomy

Sodium and Potassium

In 3 or 4 patients the plasma sodium fell slightly, the average decrease being 17 mg per 100 ml. These changes were similar to those in chloride, but, as in the case of chloride, did not seem to be of sufficient magnitude to account for the marked decrease in urinary output of sodium in the days immediately following surgical operation

Potassium was determined in the serum in only a few cases There was no marked alteration in the post operative period, although there was at that time a very significant increase in the urinary output of potassium

The discordance between the plasma and urinary findings suggests that, whatever may be the initial cause of the metabolic disturbances, there is some interference with the normal renal control of the electrolyte balance Such an interference may be attributed to an increased production of adrenocortical hormones, indeed, several investigators claim to have demonstrated this

RESULTS IN GROUP II

Even more than at a later stage, on the day following operation the composition of the blood was liable to be disturbed by the intravenous administration of fluids Nevertheless certain general trends could be distinguished The data are summarised in the accompanying table

In all 10 cases the plasma volume was lower on the day following than on the day preceding operation, and although the amount of change was not always great it seemed to be real In 9 of the cases there was also some hæmoconcentration Evidently in addition to the loss of blood at operation (much of which was, in any case, replaced by blood transfusion), there had also been a loss, by some other route, of plasma This meant that, although the changes in plasma protein concentration observed at a later stage were not observed on the first day after operation, there was at that time an actual decrease in the total amount of circulating plasma protein This decrease was considerable, and averaged about 16% of the calculated preoperation quantity (range 8 2–29 7%), it was in many cases far too large to be explained entirely by loss of whole blood at operation Moreover the decrease in circulating protein was disproportionately a decrease in albumin Infusion experiments have shown that plasma proteins are metabolised slowly, and on this basis the observed decreases are too large to be explained by oxidation. The protein, accompanied by plasma water, must have left the circulation for some other fluid compartment The same conclusion may be drawn from the similar decreases in the total amount of chloride and sodium ions in the circulating plasma—decreases which were not paralleled by changes in concentration and which occurred at a time when urinary output of these ions had also decreased

The measurements of the "thiocyanate space," an attempt to determine the volume of extracellular fluid, were not entirely satisfactory The changes observed were never large, were inconstant in direction, and, in view of the inaccuracy of the procedure, were probably justly interpreted as insignificant The average for the 10 cases was a loss of 38 ml, compared with an average plasma loss of 478 ml This would mean (since the thiocyanate space is a measure of the total extra cellular space, including the plasma) a transference of plasma water and (though not necessarily wholly) certain plasma solutes, from the vascular space to the extracellular extravascular space

It is not to be supposed that there is a physical escape of plasma from the circulation, the changes in chemical

CHANGES IN BLOOD AND EXTRACELLULAR FLUID THE DAY AFTER OPERATION

Case no	Operation	Hæmatocrit (%)		Plasma volume (ml)		Thiocyanate space (ml)		Plasma albumin (g per 100 ml)		Plasma globulin (g per 100 ml)		Circulating albumin (g)		Circulating globulin (g)		Serum sodium (mg per 100 ml)		Circulating sodium (g)		
		Initial	Change	Initial	Change	Initial	Change	Initial	Change	Initial	Change	Initial	Change	Initial	Change	Initial	Change	Initial	Change	% loss
1	Gastroenterostomy	41 0	+2 0	2680	−220	11 400	+800	4 01	−0 09	2 60	+0 10	107	−10	70	−4	296	+3	7 49	−0 58	7 4
2	Gastroenterostomy	31 0	+7 0	2500	−400	15 500	+2000	2 56	−0 14	3 63	+0 30	64	−13	91	−8	300	Nil	7 50	−1 20	16 0
3	Partial gastrectomy	48 0	+1 0	3180	−250	16 600	−900	3 08	Nil	1 93	−0 03	98	−8	61	−5	312	−14	9 93	−1 19	12 0
4	Partial gastrectomy	44 5	+0 5	3420	−480	13 600	Nil	4 02	−0 04	2 78	−0 05	137	−20	95	−14	336	−26	11 48	−2 36	20·6
5	Partial gastrectomy	40 0	Nil	2880	−370	12 700	−700	3 72	−0 43	2 95	−0 13	107	−24 5	85	−14	324	−4	9 35	−1 30	13·0
6	Partial gastrectomy	48 5	+1 5	3410	−720	15 100	+100	3 99	−0 03	1 98	+0 57	136	−30	68	+1	308	−13	10 50	−2 64	25 1
7	Cholecystitis	42 0	+4 5	3130	−780	14 500	−1200	3 21	−0 60	2 73	+0 12	100	−10	86	−10	311	−6	9 74	−2 58	25 2
8	Nephrectomy	43 5	+3 5	3720	−880	16 300	Nil	3 67	−0 18	3 08	+0 07	137	−38	115	−26	328	−15	12 21	−3 33	27 2
9	Splenectomy	37 0	+1 0	3220	−450	19 800	−100	1 92	+0 14	3 95	+0 05	62	−5	127	−16	321	−23	10 32	−2 06	20 0
10	Splenectomy	36 5	+7 5	3300	−1030	12 350	−650	4 78	−0 20	2 10	+0 33	157	−53	69	−14	325	−5	10 71	−3 43	32 0
Mean			+2 85		−478		−38		−0 16		+0 13		−21 2		−11 0		−10 0		−2 07	19 9

Group II included 10 patients, of whom 4 were submitted to partial gastrectomy, 2 to gastro enterostomy, 2 to splenectomy, 1 to cholecystectomy, and 1 to nephrectomy In these, plasma proteins, serum sodium, and serum chloride levels were determined the day before and the day after operation Further, in an attempt to gain information as to quantities as well as concentrations, the plasma volume (Gibson and Evans 1937), and the thiocyanate space (Bowler 1944) were measured For these determinations 20 ml of blood was withdrawn by venepuncture, and then through the same needle 5 ml of 0 24% blue dye T 1824 was injected, followed by 10 ml of 5% sodium thiocyanate The exact amounts injected were determined by calibrating the syringes used for the amount they delivered from the 5 or 10 ml mark, in the case of sodium thiocyanate the fluid remaining in the needle after the injection was not included From a vein in the other arm 15 ml of blood was withdrawn ten and thirty minutes after the dye had been injected The blood was allowed to clot, and after an initial spinning the supernatant serum was spun again and used for the estimations The plasma volume was calculated from the concentration of T 1824 in the ten minute sample found by direct determination, and the thirty-minute sample, after suitable treatment, was used for determining the thiocyanate space The estimations were made with a Spekker photo electric absorptiometer, by comparison with standard solutions, water being the reference fluid in all cases The blood volume was calculated in the usual way from the plasma and hæmatocrit reading Corrections were not made in the hæmatocrit figures for plasma trapped in the red cells The assumption that the blue dye concentration ten minutes after the injection gives an accurate measure of the plasma volume has been criticised by Gregersen (1944), Davis (1942), and Rossiter (1949), since we were concerned with changes in the plasma volume rather than with the absolute amount, it seemed justifiable to use this convenient method

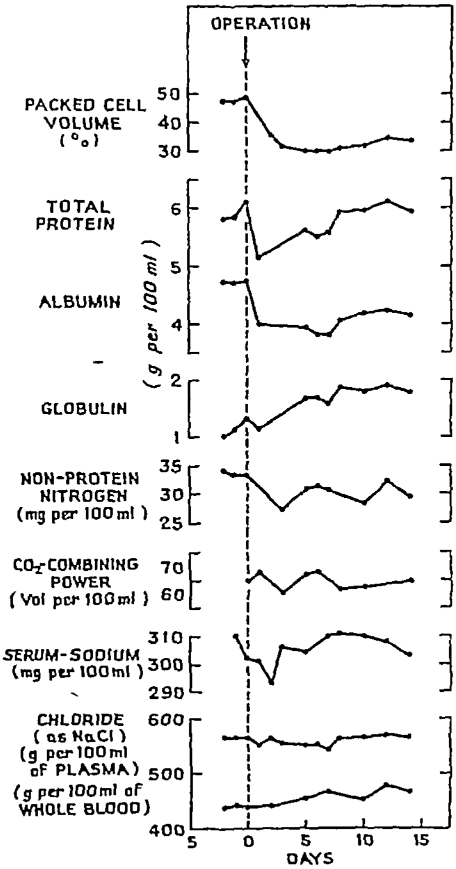


Fig 1—Typical changes in blood chemistry after partial gastrectomy.

RESULTS IN GROUP I

In the controls submitted to dietary restriction but not to operation significant changes were not observed in any of the blood constituents determined The following notes refer to the patients who underwent surgical operation The data from a typical case are given in fig 1

Plasma-proteins

About the second day after operation the total plasma protein fell sharply and remained low for two to twelve days The extent of the fall ranged in 16 patients from 0 29 to 2 0 g, with a mean of 0 73 g, per 100 ml of plasma It was the resultant of a rather greater fall in the plasma albumin *concentration* (which fell by 0 25–1 6 g, average 0 94 g, per 100 ml and remained below the preoperation level for the whole fourteen days' observation) and a gradual rise in the globulin level (which began immediately in all but 2 cases in which it followed an initial fall) It was this increase in the plasma globulin concentration which explained the early return of the total plasma protein level to, and often above, the preoperation level, while the plasma albumin concentration remained low

The different behaviour of the albumin and globulin fractions showed that the fall in total plasma protein concentration was not, as suggested by Coller et al. (1945) a mere dilution effect from infusions of saline solution and glucose Nor was it due to deprivation of food, for it did not occur in the four unoperated controls, and in any case it appeared far more rapidly than the fall which does occur slowly in semi starvation (Keys et al 1946).

The picture somewhat resembles that seen in many cases of liver functional deficiency, but unfortunately no other tests of liver function were made

Non protein Nitrogen

In most of the patients the amount of non protein nitrogen was appreciably increased as early as the day after operation The magnitude of the increase and its duration varied Thus in one patient the biggest increase, on the fourth day after operation, was 6 4 mg per 100 ml, and on the seventh day the non protein nitrogen was still 3 mg per 100 ml above the pre operation level of 36 8 mg per 100 ml However, in a few patients there was no appreciable change in the non protein nitrogen. When there was, the increase in non protein nitrogen was due mainly to an increase in urea, but part was in the " rest fraction," there being no significant alteration in uric acid, creatinine, or amino acids There is an obvious relation in time between this rather variable increase in blood urea nitrogen and the increased protein katabolism after injury, usually reflected in the urinary excretion of nitrogen, and possibly the differences in magnitude of the blood urea increases may be associated with differences in renal function

Carbon Dioxide Combining Power

Although there were minor fluctuations in both directions, the carbon dioxide combining power of the plasma always remained within the accepted normal range of 55–75 volumes %

Red cell Volume

Measurement of the red cell volume by hæmatocrit showed that there was some hæmoconcentration immediately after operation and lasting from a few hours to forty eight hours Thereafter hæmodilution took place, its maximum—i e, the lowest hæmatocrit reading—being usually found between the fifth and the eighth day after operation The mean decrease in the hæmatocrit reading was 8 7% (range 3 0–16 0%), and there were corresponding decreases in the red cell count (mean decrease 840,000, range 280,000–1,120,000, per c mm) and amount of hæmoglobin (mean decrease 17 1%, range 8 0–24 0%, Haldane) These figures suggest that during the later period of hæmodilution there is either a decrease in the number of circulating cells or an increase in the plasma volume without either hydration or dehydration of the erythrocytes Data from a typical case are shown in fig 2 Preoperative levels were *not regained* during the period of observation shorter, until in September, 1949, he was vomiting every day and suffering from severe pain in the right hypochondrium passing through to the right shoulder blade At this time a barium meal showed pyloric stenosis, about 60% remaining in the stomach after twenty four hours Reluctant to take medical advice the patient continued living on an insufficient diet of bread and butter with fish and milk occasionally, until in an exhausted dehydrated condition he was admitted to the hospital under one of us (H H S) on Jan. 23 1950.

On admission he was poorly nourished and asthenic, weighing 6 st 9 lb height 5 ft 2 in He was collapsed, pale, and dehydrated, with a dry furred tongue, pulse rate of 60–70 per min , normal temperature, and blood pressure of 95/60 mm Hg He had a large stomach with visible peristalsis and succussion splash. His bowels had not opened for several days, and very little urine was being passed

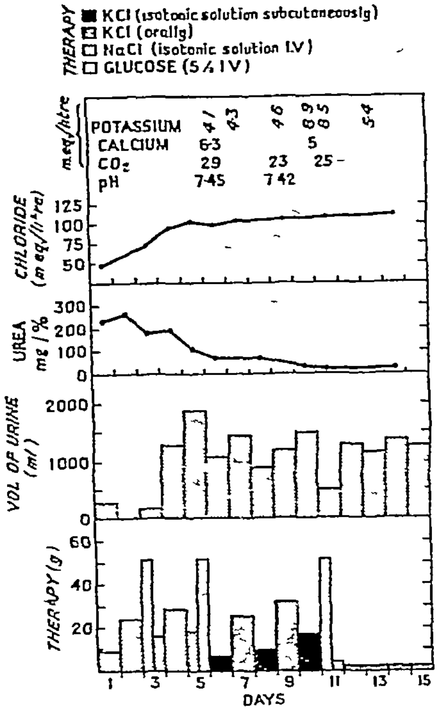


Fig. 1—Biochemical data.

Investigations showed salt-depletion and extrarenal uræmia Serum chloride 48 6 m.eq per litre (170 mg per 100 ml), blood urea 256 mg per 100 ml. Urine normal urinary chlorides 256 m eq per litre (Fantus test) Blood proteins albumin 3 9 g and globulin 2 8 g per 100 ml Fractional test-meal showed achlorhydria No occult blood in stools Red-cell count 4,150 000 per c.mm , Hb 11 6 g per 100 ml mean cell volume 80·9 c μ. , mean corpuscular Hb concentration 32 7%

Treatment and Progress—On the second day the patient had two convulsions and rapidly became comatose Almost complete anuria was present and the blood urea reached 290 mg per 100 ml Treatment consisted of intravenous infusions of physiological saline and glucose solution (total sodium chloride 90 g and glucose 100 g) until, after five days the serum-chloride reached normal figures and the blood urea fell with the return of renal function (fig 1) The patient was now conscious but in spite of the apparent success of treatment from the biochemical aspect, he still remained drowsy, rousable but very irritable and incontinent He complained of great weakness, but there was no obvious dehydration His pulse-rate was slow (46 per min.), blood pressure 90/60 mm Hg and respirations so shallow as to be almost imperceptible, regular, but more rapid than normal There was a moderate degree of cyanosis Radiography of the chest was normal The peripheral reflexes were much diminished but plantar responses normal

It seemed that some other adverse factor must be present and the serum potassium level of 4 1 m eq per litre (16 mg per 100 ml) and the electrocardiogram (fig 2) were compatible with potassium deficiency By the sixth day the patient appeared to be in extremis An isotonic solution of potassium chloride (total 5 5 g) was injected subcutaneously in a drip over four hours with hyaluronidase Recovery began six hours after the start of this treatment, and by next morning the change was remarkable, the patient being alert, feeling very well, and boasting of his vitality His pulse and respirations were normal, blood pressure 120/80 mm Hg, and peripheral reflexes and electrocardiogram (fig 3) normal Potassium chloride was continued by mouth, 2 g being added to each two hourly feed

On the 8th day the patient began to deteriorate once more, becoming weak, rather drowsy and irritable, and he then suddenly collapsed into the same apparently moribund state as before, the electrocardiogram reverting to the hypokalæmic type Potassium chloride (total 5 5 g) in isotonic solution was again given subcutaneously at the same rate, and it produced a quicker recovery than before Some weakness, with diminished reflexes, slight drowsiness, and irritability persisted but gradually disappeared over the next twenty four hours and potassium chloride 3 g was given in each two hourly feed

In spite of receiving this potassium by mouth he had a further relapse on the tenth day, which was again relieved by subcutaneous potassium chloride (total 16 6 g over eight hours) This dosage, however, led to potassium intoxication, with characteristic changes in the electrocardiogram (fig 4) when the serum level reached 8 8 m.eq per litre (35 mg per 100 ml) The condition now was one of dehydration with malaise and brisk reflexes It responded readily to intravenous glucose (50 g) and sodium chloride (4 5 g), given to reduce the serum potassium level, and twenty four hours later the electrocardiogram was reversed and again suggestive of potassium deficiency

The man's subsequent progress was uneventful He was given potassium chloride 1 g twice daily and was fit for operation after a month Later investigations confirmed the absence of organic renal disease The urine was normal in all respects Van Slyke urea-clearance test was 91% Urea-concentration test (Maclean) gave a maximum figure of 3 6% urea, and Volhard's concentration and dilution tests were normal An intravenous pyelogram was also normal

Laparotomy confirmed the diagnosis of almost complete pyloric stenosis The pylorus and gall bladder were embedded in a mass of inflammatory tissue, probably from a previously leaking duodenal ulcer Partial gastrectomy being impossible, a gastrojejunostomy was done His recovery was uneventful,

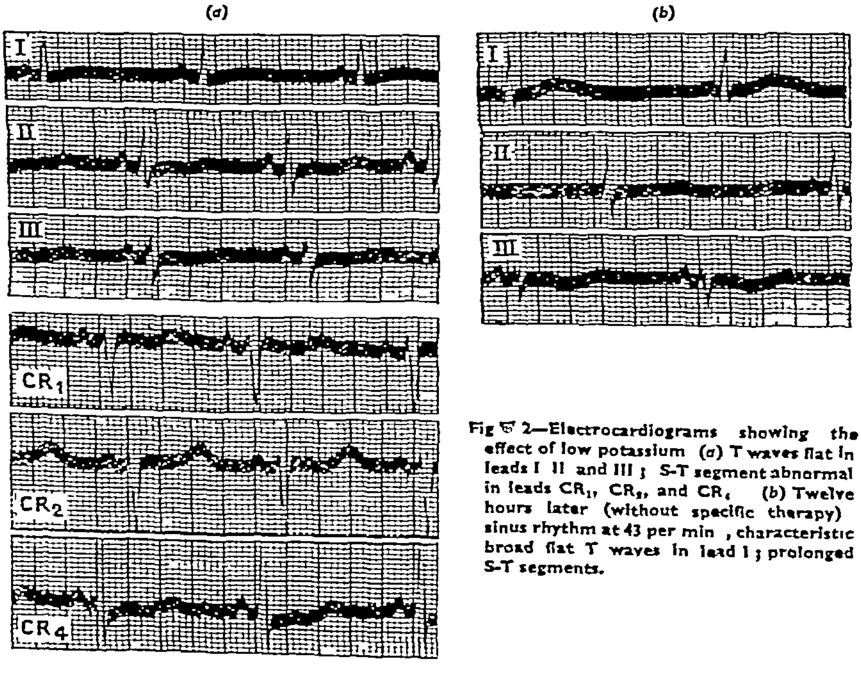


Fig 2—Electrocardiograms showing the effect of low potassium (a) T waves flat in leads I II and III ; S-T segment abnormal in leads CR1, CR2, and CR4 (b) Twelve hours later (without specific therapy) sinus rhythm at 43 per min , characteristic broad flat T waves in lead I ; prolonged S-T segments.

composition, though not pronounced, are against this view Thus, as early as the first day after operation there is a tendency for the plasma-albumin concentration to decrease and for the globulin concentration to increase, and the probable reality of these tendencies is emphasised by their more definite character on the second day Again, the plasma chloride and plasma sodium concentrations, though they have not much altered (see table), tend to decrease These findings suggest an alteration in capillary permeability such as has been proposed by Howland and Mahoney (1943) and support previous evidence—e g , Fox and Baer (1947)—for the accumulation of sodium and chloride in damaged tissue In so far as they suggest transference of albumin to the extracellular extravascular fluid, they indicate a reinforcement of conditions, initiated perhaps by the leakage of protein and inorganic ions from damaged tissue cells, which must lead to a widespread redistribution of body-water and electrolytes.

Considered in conjunction with previous observations on chloride, sodium, potassium, and water metabolism after surgical operations (Wilkinson et al. 1949, 1950), the small changes in the concentrations of the blood constituents indicate the efficiency of differential renal function in assisting the production of the inflammatory exudate They emphasise the true biological function of the blood as a vehicle The readiness with which albumin apparently passes out from the unusually permeable capillaries in the injured area suggests that this protein fraction has important functions apart from the maintenance of intravascular osmotic tension Whether the action of albumin is particularly to draw water from the capillaries to the seat of injury or to provide a local source of protein components for repair, or both, is unknown. It seems that apart from the reductions in the total quantity of albumin and in the volume of plasma in circulation, the bulk of the constituents of the inflammatory exudate is derived from the cells and the extravascular fluid in the uninjured areas. The initial disturbance at the time and site of injury may lead to the local production of some substance which affects not only the local capillaries but also, perhaps indirectly, renal function

SUMMARY

Changes in the composition and volume of the blood after severe surgical operations followed a general pattern which was independent of the type of operation or the method of postoperative feeding

In all the patients there was a sudden fall in the plasma protein, in particular the albumin concentration In most cases the globulin concentration gradually rose to values well above the preoperative levels

Increases in amount of non-protein (urea) nitrogen were observed in some patients

Hæmoconcentration on the day after operation, followed by hæmodilution, was observed in all patients. Changes in hæmatocrit values were accompanied by corresponding changes in red-cell count

An immediate reduction in total blood-chloride with an inconstant reduction in plasma chloride was followed in most patients by a rise in total blood-chloride There were corresponding changes in the serum-sodium There was some evidence that electrolyte ions were transferred from the plasma to the red cells

On the day after operation there was a significant reduction in plasma and blood volume, and in the total amounts of proteins and sodium circulating in the plasma, but no significant change in the "thiocyanate space"

The relation of the blood changes observed to the periods of salt retention and protein katabolism after operation is discussed.

We wish to thank Sir James Learmonth for providing clinical facilities and for his continued interest in our work. A grant was made to one of us (C P S) by the Medical Research Council for technical assistance and materials , and one of us (A W W) has held the Syme Surgical Fellowship at Edinburgh University during the course of these studies

REFERENCES

Bowler R. G (1944) *Biochem J* 38 385
Coller F A Iob V Vaughan H H. Kalder N B Moyer C A (1945) *Ann Surg* 122 663
Davis L J (1942) *Edinb med J.* 49 465
Folin O (1930) *J biol Chem* 86 179
— Wu H (1919) *Ibid* 38 81
Fox C L jun Baer H (1947) *Amer J Physiol* 151 155
Frame E G Russell J A. Wilhelmi A. E. (1943) *J biol Chem* 149 255
Gibson J G jun Evans W A (1937) *J clin Invest* 16 [illegible]
Gregersen M I (1944) *J Lab clin. Med* 29 1266.
Howland J W Mahoney E B (1943) *Surgery* 13 889
Keys A Taylor H L Mickelsen O Henschel A. (1946) *Science* 103 669
Peters J P Van Slyke D D (1931) Quantitative Clinical Chemistry London
Poulter L J (1949) *Lancet* i 222
Van Slyke D D (1922) *J biol Chem* 58, 523.
— (1925) *Ibid* 63 449
— Cullen G E (1917) *Ibid*, 30 289
Wilkinson A. W Billing B H Nagy G Stewart, C P (1949) *Lancet* i 640
— — — — (1950) *Ibid* i 533

POTASSIUM DEFICIENCY IN PYLORIC STENOSIS

C F HAWKINS
M.D Lond M P C.P
ASSISTANT PHYSICIAN

T L HARDY
M D Camb , F.R C.P
HONORARY PHYSICIAN

H. H. SAMPSON
O B E M.C., M.B Birm
F.R C S
HONORARY SURGEON

QUEEN ELIZABETH HOSPITAL, BIRMINGHAM

THE importance of potassium as the chief ion of the cell and an essential factor in neuromuscular transmission has been known to physiologists since the end of last century but it is only in recent years that disturbances of potassium metabolism have been clinically recognised Thus in familial periodic paralysis a fall in serum-potassium (hypokalæmia) has been shown to be the cause of the paralysis, which disappears when potassium salts are given (Aitken et al. 1937) Darrow (1946) made an exhaustive study of hypokalæmia in infantile diarrhœa and reduced their mortality from 25% to about 5% with replacement therapy The necessity for anticipating changes in potassium metabolism has also been demonstrated in renal conditions (Brown et al 1944) and in the recovery phase of diabetic acidosis, where the outcome may be fatal (Holler 1946) Hypokalæmia may also occur in Cushing's syndrome (Willson et al. 1940), in congenital alkalosis (Gamble et al. 1945), and after therapy with deoxycortone (Talbott and Schwab 1940, Ferrebee et al 1941), testosterone (Butler et al. 1942) or *p* aminosalicylic acid (Cayley 1950) The importance of potassium in surgical practice has been emphasised by Blixenkrone-Møller (1949)

Probably too little attention has been paid to the potassium ion when treating the profound electrolytic disturbances that accompany many gastro-enterological conditions in the adult, particularly those associated with vomiting and diarrhœa. The present case is reported as a typical example of hypokalæmia and its dramatic response to specific therapy

CASE RECORD

A man, aged 47, gave a history of dyspepsia starting in 1930 the chief symptoms being epigastric pain one or two hours after food, eased by milk or alkalis and relieved by vomiting Bouts of vomiting and pain, interspersed with freedom from symptoms continued until 1946 when the pain became worse and changed to a griping which reached a climax about 3 P.M each day when the patient would vomit a large quantity of material in which undigested particles of his breakfast were visible The intervals of freedom became shorter, until in September, 1949, he was vomiting every day and suffering from severe pain in the right hypochondrium passing through to the right shoulder blade At this time a barium meal showed pyloric stenosis, about 60% remaining in the stomach after twenty-four hours Reluctant to take medical advice the patient continued living on an insufficient diet of bread and butter, with fish and milk occasionally, until in an exhausted dehydrated condition he was admitted to the hospital under one of us (H H. S) on Jan 23 1950.

On admission he was poorly nourished and asthenic, weighing 6 st 9 lb height 5 ft 2 in. He was collapsed, pale and dehydrated with a dry furred tongue, pulse-rate of 60–70 per min , normal temperature, and blood pressure of 95/60 mm Hg He had a large stomach with visible peristalsis and succussion splash His bowels had not opened for several days, and very little urine was being passed.

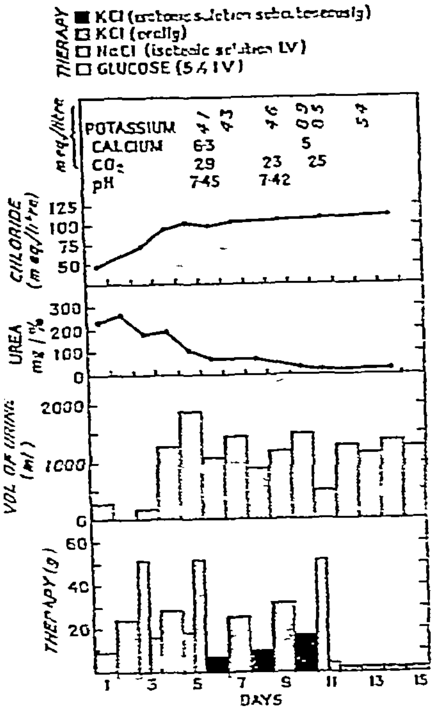


Fig. 1—Biochemical data.

Investigations showed salt-depletion and extrarenal uræmia Serum-chloride 48·6 m.eq per litre (170 mg per 100 ml), blood urea 256 mg. per 100 ml. Urine normal urinary chlorides 256 m.eq per litre (Fantus test) Blood proteins albumin 3 9 g and globulin 2 8 g per 100 ml. Fractional test-meal showed achlorhydria No occult blood in stools Red-cell count 4,150,000 per c.mm. Hb 11 6 g per 100 ml , mean cell volume 80·9 c.μ. , mean corpuscular Hb concentration 32 7%

Treatment and Progress—On the second day the patient had two convulsions and rapidly became comatose Almost complete anuria was present, and the blood urea reached 290 mg per 100 ml Treatment consisted of intravenous infusions of physiological saline and glucose solution (total sodium chloride 90 g and glucose 100 g) until after five days, the serum-chloride reached normal figures and the blood urea fell with the return of renal function (fig 1) The patient was now conscious but in spite of the apparent success of treatment from the biochemical aspect, he still remained drowsy, rousable but very irritable and incontinent He complained of great weakness but there was no obvious dehydration. His pulse-rate was slow (46 per min.) blood-pressure 90 60 mm. Hg and respirations so shallow as to be almost imperceptible regular but more rapid than normal There was a moderate degree of cyanosis Radiography of the chest was normal. The peripheral reflexes were much diminished but plantar responses normal

It seemed that some other adverse factor must be present and the serum potassium level of 4 1 m eq per litre (16 mg per 100 ml.) and the electrocardiogram (fig 2) were compatible with potassium deficiency By the sixth day the patient appeared to be in extremis An isotonic solution of potassium chloride (total 5 5 g) was injected subcutaneously in a drip over four hours with hyaluronidase Recovery began six hours after the start of this treatment and by next morning the change was remarkable, the patient being alert feeling very well, and boasting of his vitality His pulse and respirations were normal, blood pressure 120 80 mm Hg and peripheral reflexes and electrocardiogram (fig 3) normal Potassium chloride was continued by mouth, 2 g being added to each two hourly feed.

On the 8th day the patient began to deteriorate once more becoming weak, rather drowsy and irritable and he then suddenly collapsed into the same apparently moribund state as before, the electrocardiogram reverting to the hypokalæmic type Potassium chloride (total 5 5 g) in isotonic solution was again given subcutaneously at the same rate, and it produced a quicker recovery than before Some weakness with diminished reflexes slight drowsiness and irritability persisted but gradually disappeared over the next twenty four hours and potassium chloride 3 g was given in each two hourly feed

In spite of receiving this potassium by mouth he had a further relapse on the tenth day, which was again relieved by subcutaneous potassium chloride (total 16 6 g over eight hours) This dosage, however led to potassium intoxication, with characteristic changes in the electrocardiogram (fig 4) when the serum level reached 8 8 m.eq per litre (35 mg per 100 ml.) The condition now was one of dehydration with malaise and brisk reflexes It responded readily to intravenous glucose (50 g) and sodium chloride (4 5 g), given to reduce the serum potassium level and twenty four hours later the electrocardiogram was reversed and again suggestive of potassium deficiency

The man s subsequent progress was uneventful He was given potassium chloride 1 g twice daily and was fit for operation after a month. Later investigations confirmed the absence of organic renal disease The urine was normal in all respects. Van Slyke urea-clearance test was 91% Urea-concentration test (Maclean) gave a maximum figure of 3 6% urea, and Volhard's concentration and dilution tests were normal An intravenous pyelogram was also normal.

Laparotomy confirmed the diagnosis of almost complete pyloric stenosis. The pylorus and gall bladder were embedded in a mass of inflammatory tissue probably from a previously leaking duodenal ulcer Partial gastrectomy being impossible, a gastrojejunostomy was done His recovery was uneventful,

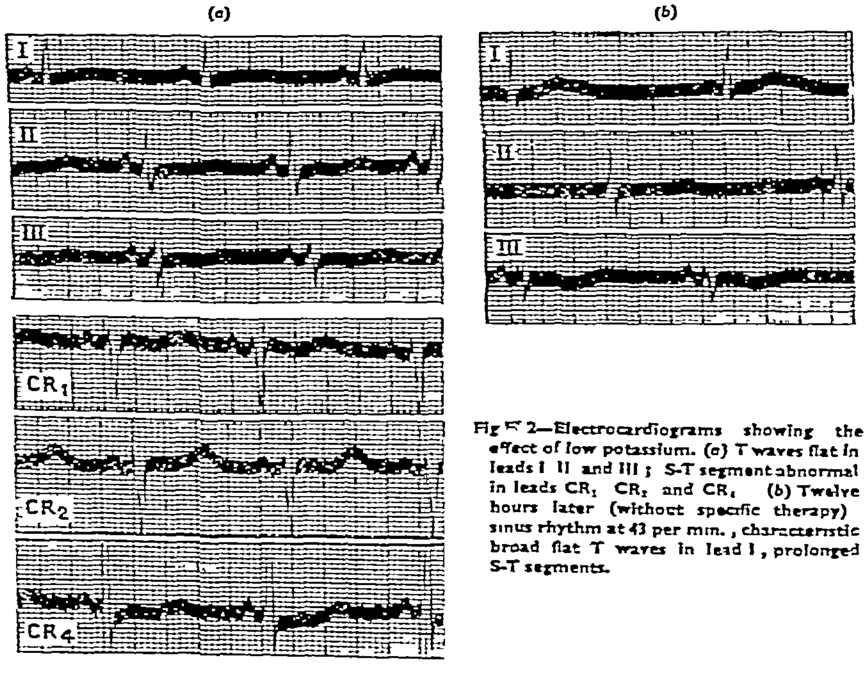


Fig. 2—Electrocardiograms showing the effect of low potassium. (a) T waves flat in leads I II and III ; S-T segment abnormal in leads CR_1 CR_2 and CR_4 (b) Twelve hours later (without specific therapy) sinus rhythm at 43 per min. , characteristic broad flat T waves in lead I , prolonged S-T segments.

with little disturbance in the serum electrolyte levels. Six months later he felt perfectly well and had gained 33 lb. in weight.

DISCUSSION

The biochemical pattern of this patient at first followed the course that is usual in pyloric stenosis with continuous vomiting. Thus the loss of hydrochloric acid and water gave rise to hypochloræmia with alkalosis. Finally, dehydration with an insufficient glomerular filtration pressure led to acute renal failure. The delay in the man's recovery after correction of salt loss and return of renal function pointed to some complicating factor, and there were clinical indications of potassium deficiency. These were the great muscular weakness with poor tone and almost absent reflexes, the bradycardia, and respirations so shallow as to be almost imperceptible, resulting in cyanosis—a state of affairs reminiscent of Holler's (1946) case where a Drinker respirator was necessary until the administration of potassium produced a prompt recovery of respiratory function. The earliest warning of the relapse when parenteral potassium therapy was discontinued was a change of personality, consisting of irritability and apathy, together with asthenia and diminution of reflexes. The reversal of these attacks by a single line of therapy on three separate occasions confirmed the diagnosis.

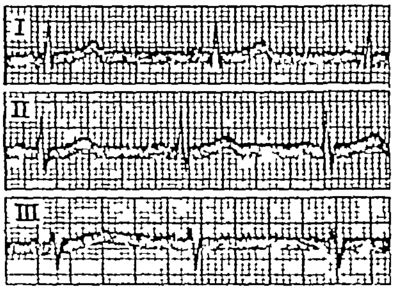


Fig. 3—Twelve hours after fig. 2(b), showing return to normal following parenteral potassium chloride.

Biochemical evidence was supplied by the serum potassium levels, estimated by the usual chemical methods. The flame photometer, which makes estimation easy and rapid, was not then available. The normal amount of potassium in the serum is minute, being 4–6 m.eq. per litre (16–22 mg. per 100 ml.), and in both these techniques the slightest hæmolysis in the blood sample will lead to false high figures owing to contamination of the serum by the high concentration of potassium from the erythrocytes. The figures in the present case were only on the low side of normal and not so low as would be expected with potassium deficiency causing serious symptoms. But the essential deficiency is intracellular, and there is no way, apart from muscle analysis, of measuring the cellular potassium. Symptoms of potassium deficiency may arise although the serum potassium level is normal, and, in cases where dehydration results in the removal of intracellular fluid and the transfer of potassium to the serum, the serum potassium levels may temporarily be higher than normal before excretion in the urine has taken place. Such cases can only be detected by potassium balance experiments. Generally, the serum potassium, which accurately reflects the potassium level in the extracellular fluid bathing the cells (Folk et al. 1948), is an accurate guide to the presence of this syndrome.

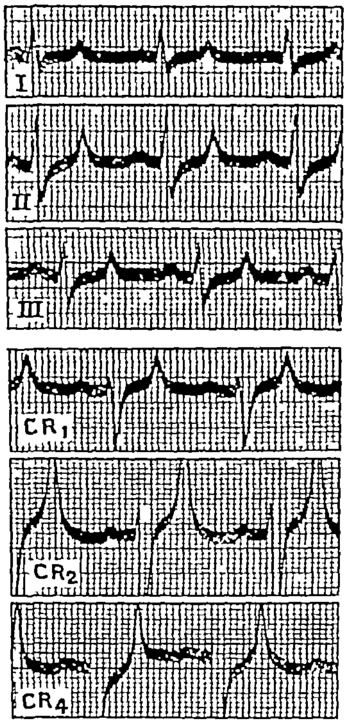


Fig. 4—Electrocardiogram indicating potassium intoxication; T waves now tall and spiky.

Electrocardiography proved to be the quickest method of detecting changes in potassium metabolism in the present case. Both rises and falls in the serum potassium level affect the cardiac mechanism, as Ringer showed when developing his solution to perfuse the isolated mammalian heart (Ringer 1883), and other workers who have studied the electrocardiographic responses to variations of serum potassium in man have shown that a low serum potassium level is associated with a flat broad T wave and a prolonged Q–T interval. Later there is further lowering of the T wave, then depression of the ST segment, eventually leading to heart block and heart failure in systole (Stewart et al. 1940, Stoll and Nisnowitz 1941). Raised levels of serum potassium produce high T waves, followed by auricular arrest, prolonged Q R S complex, and heart failure in diastole from a direct depressant action of the potassium ion on the myocardium (Winkler et al. 1938, Tarail 1948). The prolonged flat T wave (fig. 2*b*) in the present case and an associated long QT interval were typical of potassium deficiency, and returned to normal after therapy. This had been shown by Thomson (1939) who demonstrated a direct correlation between the serum potassium level and the height of the T waves. The alteration following specific therapy is important because other factors in the electrolytic pattern may play a part in the electrocardiographic changes, notably hypocalcæmia (Barker et al. 1937), which was unlikely in the present case because the serum calcium level was normal. Overdosage with potassium later produced intoxication with remarkably high peaked T waves, similar to those reported in a fatal case by Finch and Marchand (1943). The serum potassium level had then risen to 8.8 m.eq. per litre (35 mg. per 100 ml.), and the patient had severe malaise and water depletion. All these features disappeared after the administration of intravenous glucose, which lowers the serum potassium level (Fenn 1939), and physiological saline.

The sequence of events leading to symptoms of hypokalæmia probably occurred on a background of deprivation, for the intake had long been inadequate. The expenditure of cellular elements by the body for energy, heat, and repair, which occurs during starvation, probably contributed to the deficit, while further accentuation would follow the continuous vomiting and gastric aspiration, for the fasting gastric juice contains about 80–90 mg. of potassium per 100 ml. Dehydration also contributed by loss of potassium with the intracellular fluid.

The effect of treating such a patient with large quantities of intravenous sodium chloride is not only to increase any potassium deficit (Stewart and Rourke 1942) by causing a potassium diuresis (Gamble 1942), possibly aggravated by defective tubular function (Burnett et al. 1950), but also to substitute sodium for potassium in the cells, an exchange that has been shown by muscle analysis (Mudge and Vislocky 1949) to be a feature of alkalosis. There seems, in fact, to be a reciprocal relationship between sodium and potassium, and the giving of generous infusions of sodium chloride as a routine may be ill advised and even dangerous unless their amount is controlled by frequent serum potassium estimations. It is indeed surprising that hypokalæmia does not occur more often in undernourished patients with vomiting or diarrhœa who are treated with massive infusions Perhaps it goes unrecognised. That low serum-potassium levels are not uncommon in pyloric stenosis was shown by Falconer et al (1939), and Bellett (1950) mentions that among a series of 25 cases with vomiting due to intestinal obstruction there were several with symptoms similar to those in our patient which responded to potassium therapy

The details of potassium therapy have been reviewed by Howard and Carey (1949) Treatment is hazardous unless care is used, and accurate dosage is impossible unless a quick method of estimation is available An excess of potassium may cause cardiac arrest This is more likely to happen with intravenous infusions, and Howard mentions a case where the cardiac changes were being recorded on a continuous electrocardiogram when, without warning, the patient collapsed with heart failure in diastole It is not the total dose that is so important, provided renal function is adequate, but the amount of serum-potassium reaching the heart This can be controlled by the rate of injection, and the lethal threshold is about 10–12 m eq per litre In the present case the subcutaneous method was chosen because we have found subcutaneous infusion with hyaluronidase very satisfactory, and believe that it is safer than intravenous infusion The administration of potassium chloride by mouth was ineffective, probably owing to defective absorption due to the almost complete pyloric stenosis Large doses of potassium chloride (total 29 7 g) had to be given parenterally as a life saving measure before the tendency to relapse was overcome This was to be expected, and it may take fourteen days, or longer, before the potassium of the body is replenished

SUMMARY

A patient with advanced pyloric stenosis suffering from salt depletion and extrarenal uræmia was only temporarily benefited by glucose saline infusions His apathy, muscular atonia, bradycardia, and shallow respirations pointed to potassium deficiency, which was confirmed by the electrocardiographic findings and was not excluded by a serum-potassium level only on the low side of normal

Ætiological factors, such as undernutrition, vomiting and dehydration are discussed, and the dangers of infusing such a patient with sodium chloride are indicated.

Early recognition of hypokalæmia is of great importance in such cases which do not respond to the usual treatment of salt depletion and uræmia

In the present case, the subcutaneous infusion of potassium chloride resulted in dramatic improvement in the symptoms and reversal of the electrocardiographic abnormalities For a time the symptoms of hypokalæmia returned if the infusion was stopped, but ultimately the patient fully recovered

We wish to thank the electrocardiographic department, under Prof K. D Wilkinson, for invaluable coöperation in this case, and Dr Garfield Thomas for the biochemical estimations also Mr D F Cole B SC for his advice on the paper

REFERENCES

Aitken R S Allott, E. N Castleden L I. M. Walker M. (1937) *Clin. Sci* 3 47

Barker P S Johnston F D Wilson F N (1937) *Amer Heart J* 14 82

Bellett S (1950) Postgraduate Gastroenterology (ed. by Bockus H. L) London p 515

Blixenkrone-Møller N (1949) *Acta chir scand* 97 300

Brown, M. R Currens J H Marchand, J F (1944) *J Amer med Ass* 124 545

Burnett C H., Burrows, B A Commons R. R Towery B T (1950) *J clin. Invest* 29 175

Butler A M. Talbot N B MacLachlan E A (1942) *Proc Soc exp Biol., N Y* 51 378

Cayley F E de W (1950) *Lancet* i 447

Darrow D C (1946) *J Pediat* 28, 515

Continued at foot of next column

POTASSIUM DEFICIENCY IN IDIOPATHIC STEATORRHŒA

M LUBRAN
M.B , B Sc Lond
CONSULTANT PATHOLOGIST

P M MCALLEN
M.D Lond , M R C.P
SENIOR REGISTRAR IN MEDICINE

WEST MIDDLESEX HOSPITAL, ISLEWORTH

POTASSIUM deficiency in steatorrhœa has been described in 2 cases by Harrison et al (1943) and in 1 case by Engel et al (1949) All the patients had a low serum-potassium level associated with muscular weakness An increased fæcal excretion of calcium and phosphorus is well known to occur in steatorrhœa, but abnormal loss of potassium and sodium in the stools has rarely been reported (Black 1946, Harrison et al. 1947)

The case described here is one of idiopathic steatorrhœa showing low serum potassium levels and a markedly increased fæcal excretion of both potassium and sodium

Technical Methods—Sodium and potassium were determined on ashed fæces and urine after removal of interfering substances by methods essentially similar to those described by Hawk et al (1947) The sodium and potassium concentrations in the resulting clear filtrates were estimated by the same methods as for serum. Serum potassium was determined by the method of Jacobs and Hoffman (1931), and serum sodium by that of McCance and Shipp (1931)

CASE RECORD

A woman, aged 41 was admitted on May 3, 1949, with two weeks history of diarrhœa Owing to her low level of *intelligence no clear previous history could be obtained*

On admission she looked ill and wasted There was general weakness but this was in keeping with her illness The tongue was smooth and sore and there were fissures at the angles of the mouth Blood pressure 105/80 mm Hg No abnormalities were found in other systems There was no evidence of tetany From 5 to 10 fluid stools were passed daily

Investigations—Microscopy and bacteriology of the stools were normal. Sigmoidoscopy and a barium enema were also normal Radiography of the chest showed normal heart and lung fields A blood count showed Hb 87% (12 9 g per 100 ml), red cells 4 430,000 per c.mm., and white cells 10 600 per c.mm. (neutrophils 68%, lymphocytes 31%, monocytes 1%) On May 26, 1949 the blood chemistry (in mg or g per 100 ml. or m.eq per litre of serum) was sodium 301 mg (103 5 m eq), potassium 12 1 mg (3 1 m.eq), chlorides (as sodium chloride) 600 mg (102 6 m eq), calcium 7 6 mg (1 9 m eq) phosphorus 3 2 mg (1 0 m.eq), bicarbonate 69 ml CO_2 (30·8 m eq), protein 6 1 g (albumin globulin ratio = 1 3 1), urea 28 mg The electrocardiograms showed changes related to the serum-potassium level and are reported elsewhere (McAllen 1951)

Progress—The diarrhœa continued unchecked for three weeks after admission, despite routine treatment with fluids

---

DR HAWKINS AND OTHERS REFERENCES—*continued*

Falconer M. A., Osterberg A. E Bargen J A (1939) *Arch Surg* 38 869

Fenn W O (1939) *J biol Chem.* 128, 297

Ferrebee J W , Parker D Carnes, W H. Gerity M. K. Atchley, D W Loeb R F (1941) *Amer J Physiol* 135 230

Finch, C A. Marchand J F (1943) *Amer J med Sci* 206 507

Folk, B P Zierler K. L. Lilienthal, J L jun. (1948) *Amer J Physiol* 153 381

Gamble J L (1942) Chemical Anatomy Physiology and Pathology of Extracellular Fluid. Camb Mass

— Fahey K. R., Appleton, J E., MacLachlan, E. A. (1945 *J Pediat* 26 509

Holler J W (1946) *J Amer med Ass* 131 1186

Howard, J E Carey R A. (1949) *J clin. Endocrinol* 9 691

Mudge G H Vislocky K. (1949) *J clin. Invest.* 28 482

Ringer S (1883) *J Physiol.* 4, 29

Stewart, H J., Smith, J J., Milhorat, A. T (1940) *Amer J med Sci.* 199 789

Stewart J D Rourke, G M. (1942) *J clin Invest* 21 197

Stoll, B Nisnewitz S (1941) *Arch intern Med* 67 755

Talbott J H., Schwab R. S. (1940) *New Engl. J Med* 222 585

Tarail, R. (1948) *Amer J Med.* 5 828

Thomson, W A. R. (1939) *Lancet* i, 809

Willson, D M. Power M. H. Kepler E J (1940) *J clin. Invest* 19 701

Winkler A. W Hoff, H E., Smith P K. (1938) *Amer J Physiol.* 124 478

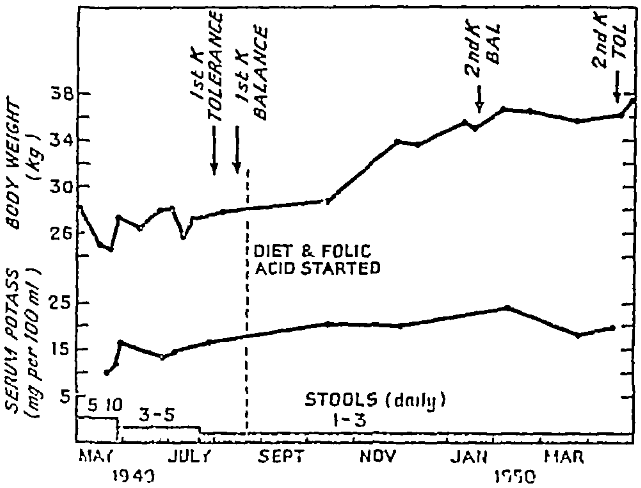


Fig 1—Serum potassium level and weight before and during treatment.

sulphaguanidine, kaolin, and vitamins There was a little improvement in the patient's condition during the next two months A three day fat balance test (233 g of fat taken) showed 77 7% absorption The fæcal nitrogen averaged 0 98 g a day A fractional test meal revealed a histamine fast achlorhydria The glucose tolerance curve after glucose 50 g by mouth was low and flat (80, 67, 83, 67, 60, 67 mg per 100 ml at half hourly intervals) A barium meal showed a pronounced deficiency pattern in the small intestine The diagnosis of steatorrhœa was thus established, and the evidence was in favour of the idiopathic type Treatment with a low fat high protein diet and folic acid 20 mg was then started There was a great improvement in the patient's condition over the next six months (fig 1) Her weight increased by 12 kg and she became more alert mentally Her tongue and lips returned to normal The frequency of her stools decreased to 1–3 a day The serum potassium level rose to 23 mg per 100 ml A second barium meal showed a normal pattern in the small intestine A glucose tolerance test gave a normal result (82, 124, 92, 76, 86, 68 mg per 100 ml) The fat balance, however, remained abnormal, showing 74% absorption

Electrolyte Studies —The first study was carried out during the acute phase of the illness, before the treatment by diet and with folic acid had been given Potassium and sodium were in great excess in the fæces, and there was a negative balance of each The second study, during the clinical remission following treatment, showed almost normal values of potassium and sodium in the fæces and a positive balance of each The results are shown in the accompanying table

Potassium tolerance Tests —Oral potassium tolerance tests were made during the acute and remission phases (fig 2) The serum potassium level was determined before, and at intervals after, the patient had been given potassium chloride 5 g by mouth The two curves are strikingly different The second (remission phase) agrees in shape with the normal curves described by Zwemer and Truszkowski (1936), Keith et al (1942), and Keith and Osterberg (1946) The first (acute phase) shows a delayed rise to a low maximum, followed by a slow fall

POTASSIUM AND SODIUM BALANCES IN ACUTE AND REMISSION PHASES

—	Amount of potassium or sodium (g per 24 hr)			
	Acute phase		Remission phase	
	Pot	Sod	Pot	Sod
Intake	3 0	1 4	3 0	3 4
Excretion				
In fæces	4 9	1 3	0 6	0 1
In urine	1 7	0 6	1 5	2 3
Balance	−3 6	−0 5	+0 9	+1 0

During both balances the patient was on a constant intake of potassium and sodium for three days before collections began The first balance period was over 24 hours the second over 72 hours

DISCUSSION

In this case there was no evidence of associated or underlying disease which could have given rise to the high fæcal potassium level during the acute phase Increased cellular loss from the bowel, as a cause, was excluded by the normal fæcal nitrogen level. The high fæcal potassium level could be explained by a defective absorption of potassium from the diet and the intestinal secretions, in view of the many absorption defects which are believed to occur in steatorrhœa This explanation is supported by the initial low flat potassium tolerance curve and by its change to a normal shape after the patient had responded clinically to treatment

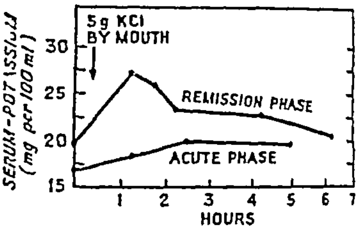


Fig 2—Potassium tolerance tests during acute and remission phases

SUMMARY

A case of idiopathic steatorrhœa is described which showed a low serum potassium level, excessive loss of potassium in the fæces, and a negative potassium balance

The potassium deficiency was thought to be caused by impairment of potassium absorption

We wish to thank Dr N F Coghill for permission to study this case, and Mr R J Hall for technical assistance

REFERENCES

Black D A K (1946) *Lancet* ii 671
Engel F L, Martin S P, Taylor H (1949) *Bull Johns Hopk Hosp* 84, 285
Harrison H E Harrison H C Tompsett R R Barr D P (1947) *Amer J Med* 2 131
— Tompsett R R, Barr, D P (1943) *Proc Soc exp Biol, N Y* 54 314
Hawk, P B, Oser B L Summerson W H (1947) Practical Physiological Chemistry 12th ed London, p 890
Jacobs H R D Hoffman W S (1931) *J biol Chem* 93, 685
Keith N M Osterberg A E (1946) *Proc Mayo Clin* 21 385
— — Burchell H B (1942) *Ann intern Med* 16 879
McAllen P M (1951) *Brit Heart J* 13 159
McCance R A Shipp, H L (1931) *Biochem J* 25, 449
Zwemer R L, Truszkowski R (1936) *Proc Soc exp Biol N Y* 35, 424

PROLONGED ABNORMALITY OF CEREBROSPINAL FLUID AFTER CISTERNAL STREPTOMYCIN

DAVID BEYNON
M B Lond, M R C.P, D C H
LATE RESIDENT ASSISTANT PHYSICIAN, THE HOSPITAL FOR SICK CHILDREN GREAT ORMOND STREET, LONDON

A BABY, aged 6 weeks, was treated for acute meningitis due to *Bact fæcalis alkaligenes* with cisternal and intramuscular streptomycin The cerebrospinal fluid (C S F) became sterile on the second day of treatment, and clinical recovery was rapid, but six months passed before the protein content of the C S F returned to normal. The patient, now aged 2½ years, appears normal and mentally forward

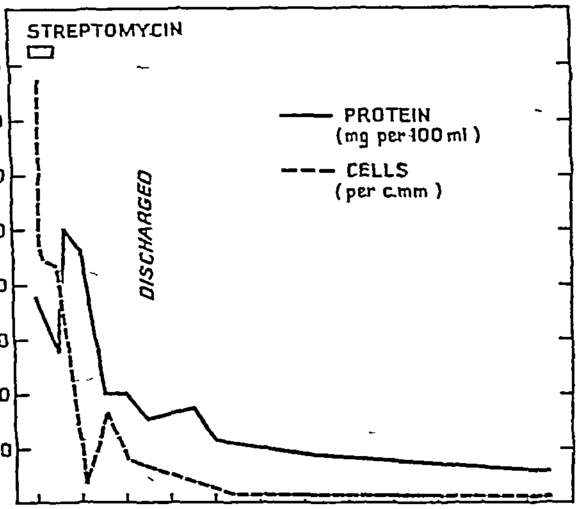
CASE RECORD

A baby girl, aged 6 weeks, was admitted to the Hospital for Sick Children, Great Ormond Street, with a history of loose stools and anorexia for five days and convulsions for four days

On admission she was ill, collapsed, and somewhat dehydrated, with rectal temperature 98°F, and weight 6½ lb There were constant fibrillary twitching of the left eyelids, spastic rigidity of the left leg and intermittent generalised convulsions No neck rigidity was present, and bulging of the fontanelle only appeared two days later when hydration had been fully restored Lumbar puncture on admission produced a dry tap, and cisternal puncture produced only a few drops of thick purulent fluid containing protein 384 mg per 100 ml sugar 6 mg per 100 ml , chlorides 540 mg per 100 ml , cells 3000 per c.mm (polymorphs 98%) A film of the c s f showed many gram negative organisms, and a culture grew *Bact fæcalis-alkaligenes* A blood count showed 50,200 white cells per c mm (polymorphs 76%) A blood culture had not grow the organism

Treatment —Intramuscular penicillin and oral sulphadiazine were started on admission and continued for ten days From the day following admission streptomycin sulphate was given intrathecally 0 05 g daily for eight days and intramuscularly 0 04 g six hourly for seven days (0 02 g per lb of body weight daily) The intrathecal streptomycin dissolved in 5 ml of physiological saline solution was injected by cisternal puncture each day owing to continued lack of flow of c s f on lumbar puncture, presumably due to spinal block Even cisternal puncture, on two occasions, produced only a few drops of thick purulent fluid, and streptomycin had to be injected under pressure

Progress —The c s f was sterile on the day after streptomycin was started and remained so thereafter The turbid fluid became clear and yellow after three days Clinical mprovement was obvious on the fourth day of treatment convulsions and twitching had stopped, the fontanelle was normal, and the appetite was good This progress was maintained until the seventh day of treatment, when a mild clinical relapse occurred Convulsions reappeared the fontanelle became tense, there was slight neck stiffness, and feeds were refused There was no corresponding change in the c s f and the white-cell count in the blood continued to show steady improvement, being now 14 700 white cells per c.mm. (polymorphs 48%) It was therefore decided to stop intramuscular streptomycin on that day and the intrathecal streptomycin was stopped on the following day On the day after that the baby again rapidly improved and no further ill effects appeared She gained weight steadily and was discharged home in the fifth week.



Alterations in cerebrospinal fluid

Follow up —When the patient was discharged from hospital the c.s.f still contained 154 mg protein per 100 ml. and 61 white cells per c mm She was therefore subsequently readmitted at intervals for lumbar puncture The c s f white-cell count fell to normal in the eighth week after the illness, but the protein was still 60 mg per 100 ml after twenty three weeks (see figure) Six months after this a lumbar puncture produced c s.f which was chemically normal, with protein 30 mg per 100 ml Clinically the child has remained quite well and her mental and physical development has been forward rather than average Her mother said that she spoke her first word at the age of 7 months and began to walk at 11 months Now at the age of 2½ years she is a healthy child, with no detectable abnormality of the nervous system. Her hearing and eyesight appear normal to clinical testing, and there is no ataxia The circumference of her head is 19¼ in (average = 19 in) Her mother considers that she is mentally more forward than was her elder sister at the same age

DISCUSSION

Bact fæcalis alkaligenes is a harmless saprophytic inhabitant of the gastro intestinal tract, and only very rarely becomes pathogenic Bischoff et al (1948) found only six previously published cases of meningitis due to this organism They described two further cases, both fatal, in newborn babies The results of treatment of four cases with streptomycin have been reported (National Research Council 1946), with one survival

The protracted high protein level and raised white cell count of the c s f in the present patient are presumed to be a direct toxic effect of the streptomycin A relatively large dose of streptomycin for an infant of this size was injected daily for eight days into the cisternal space It is interesting that the protein level rose suddenly from about 280 to 600 mg per 100 ml. on the third day after streptomycin had been stopped Cathie (1948) has demonstrated the effect on the cells and protein of the injection of streptomycin into a normal theca , his figures show an immediate cellular response but a delayed small rise in protein level Ounsted (1949), describing the treatment of ten cases of *Hæmophilus influenzæ* meningitis with streptomycin, reports that the c.s.f in several cases remained mildly abnormal for ninety days after the institution of treatment No such abnormality has been described after other forms of treatment Examination of the records of twenty cases of acute meningitis due to various organisms successfully treated with intrathecal penicillin and/or oral sulphonamides at this hospital showed no prolonged abnormality of the c s f beyond six weeks

The clinical relapse which occurred on the seventh day of treatment is considered to be significant There was a pronounced rise of intracranial pressure without any corresponding change in composition of the c.s f It is suggested that there was an increased secretion of c s.f due to irritation of the choroid plexuses by the streptomycin

Attention has already been drawn to clinical reactions following cisternal and intraventricular injection of streptomycin (Cathie 1948, Debré and Mozziconacci 1949) A report on the treatment of tuberculous meningitis (Smith et al 1948) describes an acute hydrocephalic episode which arose during the course of streptomycin treatment in two cases, and another (Medical Research Council 1948) describes dramatic clinical improvement, with cessation of meningism, in two cases when streptomycin was stopped Two of Ounsted's (1949) patients with *H influenzæ* meningitis were given intraventricular streptomycin because of spinal block. One, a baby aged 10 months, died from an acute hydrocephalic attack on the day following the first injection The other, aged 9 months, was given intraventricular streptomycin for three days and then lumbar injection for twelve days Four days after intrathecal streptomycin had been stopped the baby had an attack resembling a hydrocephalic attack This was attributed to a probable intercurrent infection, but the c s f remained sterile ; there was a slight rise in the protein level but none in that of the cells

It is suggested that streptomycin, when injected intracranially, can produce an increased outflow of c.s.f sufficient to cause signs and symptoms of raised intracranial pressure, thereby disguising the clinical course of the disease and raising the hazard of overtreatment

SUMMARY

A case is described of severe acute meningitis due to *Bact fæcalis-alkaligenes*, a very rare and fatal infection, in a baby aged 6 weeks

Treatment was with streptomycin, cisternal as well as intramuscular, because of spinal block

Recovery was rapid, but a mild abnormality of the C S F in the form of raised protein level persisted for over twenty three weeks

This is considered to be a direct toxic effect of streptomycin, but has been without any ill effects on the patient, as judged by clinical examination after an interval of nearly two and a half years

A possible effect of streptomycin in producing raised intracranial pressure is also discussed

I wish to thank Dr Bernard Schlesinger, under whose care this patient was treated for permission to publish, and Dr I A B Cathie for advice and for pathological reports

REFERENCES

Bischoff H W Reelnos A jun Anderson W R, Rice, J O (1948) *J Pediat* 32 558
Cathie I A B (1948) *Post grad med J* 24, 351
Debré R Mozziconacci P (1949) *Brit med J* ii 451
Medical Research Council (1948) *Lancet* i 582
National Research Council (1946) *J Amer med Ass* 132, 4
Ounsted C (1949) *Lancet* ii 639
Smith H V, Vollum R L Cairns, H (1949) *Ibid*, i 627

GALL-BLADDER DISEASE IN CHILDHOOD

ROLAND N JONES
M A, M Chir Camb, F R C S
CHIEF ASSISTANT, ESSEX COUNTY HOSPITAL,
COLCHESTER

DISEASE of the gall bladder in children is not commonly recognised, for Kellogg (1923) could only collect 64 cases published in the last 200 years These cases include cholecystitis alone, cholelithiasis alone, and, more often, the two in combination Potter (1928) collected and summarised 226 cases, and Sobel (1938) increased the total to 317 The incidence is higher in males, and calculi have been found in an eight month fœtus

The first reported case was under the care of Joseph Gibson, a surgeon of Leith (Swing and Bullowa 1938)

A boy, aged 12, fell sick with severe right-sided abdominal pain in October, 1721, and his condition deteriorated until death 18 months later He had hectic fever and vomited frequently After a few months the stools were white, and a mass appeared in the right hypochondrium, emaciation was conspicuous *Œdema and ascites appeared towards* the end of the illness, and two days before death 12 lb of turbid greenish fluid was removed by paracentesis

Gibson was assisted in the necropsy by James Crawford, professor of medicine, and also of Hebrew, in the University of Edinburgh The report says that 'the gall bladder was extended to a most surprising Bulk, for it contained no less than two Scots Pints, or eight pounds of Bile ' The wall was thickened, and the common duct was dilated and contained small spongy yellow stones When the slightly enlarged liver was cut, "a great number of spherical Tubercles, about the Bigness of a common Bean appeared in its Substance, some of the Gentlemen present were inclined to esteem them to be Glands, but how justly I am not to determine It was observed *that they had no vessels either entering in or growing* out of them, and seemed only to be set loose in the Substance of the Liver ' These were undoubtedly multiple liver abscesses resulting from ascending cholangitis and stones in the common duct

Acute cholecystitis, uncomplicated by stone, is usually due to bacterial infections, such as typhoid, septicæmia, and scarlet fever In children the migration of intestinal parasites, such as ascaris and protozoa, is not ordinarily accompanied by inflammation, though this is common in adults On the other hand, acute suppuration of the bile ducts and gall bladder *may* be set up by *round* worms entering the bile passages from the intestine Disease of the gall bladder is often confused with appendicitis, and often there is 5–10 years' history of undiagnosed attacks of abdominal pain (Sobel 1938) Evarts Graham is of the opinion that many cases of cholecystitis first recognised later in life had their origin in childhood, when they were regarded as catarrhal jaundice, gastroenteritis or indigestion Cholecystitis may be associated with mild inflammation of the appendix, and it has been suggested that cholecystitis may be a metastatic complication of an acute or chronic appendicitis (Farr 1932, Snyder 1925)

The primary complaint is abdominal pain, varying in intensity and usually in the right hypochondrium Many workers emphasise the fact that the pain is in the region of the umbilicus and radiates to the right subcostal angle (Lowenburg and Mitchell 1938) Nausea and vomiting are common, with pyrexia and often jaundice There is usually a moderate leucocytosis In cases associated with mild changes in the appendix the pain is often localised in the right iliac fossa

The treatment seems to depend on whether exploration has been carried out for appendicitis If disease of the gall bladder has been diagnosed, penicillin and sulphonamides should be used before having recourse to surgery (Nelson 1946) Surgical *treatment* consists in drainage or cholecystectomy

CASE RECORD

A female child, aged 3 years *was admitted* with 48 hours history of abdominal pain At the onset she appeared fretful and complained of pain in the lower abdomen on being lifted from her cot She vomited twice during the first night, but next day she seemed better however she was kept in bed During the following night she became restless, cried, and again appeared to have pain in the lower abdomen, though she did not vomit again *Her bowels* were *regular* but on the day of admission her stools were said to have been rather pale

On examination she was well nourished, with a flushed face and circumoral pallor There was rigidity with tenderness over the whole abdomen, especially on the right side, and she appeared to be in much pain Rectal examination revealed no *abnormality, and no abnormal physical signs* were found in the chest Acute appendicitis was diagnosed and operation undertaken forthwith

Operation —The appendix was approached through a muscle splitting incision in the right iliac fossa, and, when the peritoneum was opened, a thin purulent fluid *welled out of* the abdominal cavity The appendix was readily delivered and found to be *normal*, *it was removed, but* on exploration of the abdomen through this incision a very large tense gall bladder was palpated which was dusky purple all over It could not be emptied by light pressure, and the omentum was slightly adherent to it The incision in the right iliac fossa was closed, and cholecystectomy was done *through* a right upper paramedian incision No anatomical abnormality of the biliary system was *found* The abdomen was closed, and the child returned to the ward

The gall bladder was $3^{1}/_{2}$–4 in long, and its entire surface was purplish and covered with fibrin It could not be emptied by pressure even after removal, and the obstruction proved to be due to an enlarged cystic gland The mucosal surface was covered with hæmorrhagic areas, and the wall appeared very thin in places On being opened it was found to be filled with a greenish flocculent fluid, undoubtedly containing pus Unfortunately no culture was made The diagnosis of acute cholecystitis was confirmed microscopically

Progress —The child passed a satisfactory night after *operation but next day seemed to* have profound toxæmia, with cyanosis, rapid respirations, vomiting, and a rapid thready pulse Continuous gastric suction was instituted, an intravenous glucose drip was started, and *half a* pint of blood was transfused The child improved slowly for 48 hours and from then onwards *made an uninterrupted* recovery She was discharged from hospital 28 days after admission

COMMENTS

This case has many points of interest, for it presented as an acute appendicitis, which was quite properly submitted to operation, when a general acute peritonitis was discovered The gall bladder was distended and tense, seemed to be in danger of perforating, and, if left, might easily have done so Even if the correct diagnosis ad been made in this case, it would have been dangerous o treat the condition without operation With severe bdominal pain in childhood, when a confident diagnosis as not been made, it is wiser to "look and see" than to wait and see"

Acute cholecystitis in children should be treated by holecystectomy, but, if the child appears too ill for hat, cholecystotomy should be done, followed by holecystectomy later

It is well to remember gall bladder disease in the liagnosis of abdominal pain in children, and, if laparo-omy is done and a normal appendix and no obviously nlarged abdominal glands are found, the gall bladder hould be examined

REFERENCES

arr, C E (1022) *Arch Pediat* 39 574
Kellogg (1923) *Ann Surg* 77 587
owenburg H jun Mitchell, A G (1938) *J Pediat* 12 203
Nelson W E (1946) Textbook of Pediatrics London p 680
Potter A. H (1928) *Surg Gynec. Obstet* 46 795
Snyder, C C (1925) *J Amer med Ass* 85 31
Sobel I P (1938) *Arch Pediat* 55 669
wing A. T, Bullowa J G M. (1938) *Amer J Dis Child* 55, 521

TREATMENT OF ACUTE LEUKÆMIA WITH AMINOPTERIN

JOHN F WILKINSON
M.D, M Sc, Ph.D Manc, F.R C.P, F R I C
PHYSICIAN AND DIRECTOR, DEPARTMENT OF HÆMATOLOGY

C GARDIKAS
M D Athens, M Sc, Ph.D Manc
REGISTRAR

MANCHESTER ROYAL INFIRMARY

IN 1948 Farber et al noted the beneficial effects of olic acid antagonists on acute leukæmia in 50% of a group of children, various degrees of temporary improvement were noted during therapy with aminopterin or other folic-acid antagonists, such as amethopterin, Amino an fol,' 4-amino N^{10} methyl pteroylglutamic acid or 4-amino pteroylaspartic acid Later Farber (1949) reported that in 2 patients clinical and hæmatological remissions were sustained for sixteen and twenty three months, both patients being alive at the time he wrote

Several other workers have also observed the effects of folic acid antagonists in the treatment of acute leukæmia thus Dacie et al (1950) obtained various temporary remissions in 9 out of 13 patients with acute leukæmia, Dameshek (1949) in 9 out of 35, Jacobson et al. (1948) in 2 out of 10, Jimenez de Asua (1949) in 3 out of 8, Meyer et al (1949) in 2 out of 37, and Pierce and Alt (1948) in 5 out of 9 cases Sachs et al (1950) observed a considerable improvement in 2 of 14 children, and Stickney et al (1948, 1949) in 54 cases of acute leukæmia treated with folic acid antagonists reported 8 cases of complete remission, the word "complete" is used in the sense that both clinical and hæmatological (blood and/or marrow) pictures improved. A complete remission was also observed by Hart (1949) in 1 case of monocytic leukæmia Another 58 cases, with remission in 19, are mentioned in an extensive review on the subject by Thiersch and Philips (1949), according to whom about 250 cases of acute leukæmia in man have so far been treated with folic acid antagonists with temporary remissions in about 30% This percentage is much above the spontaneous remission-rate reported by Diamond and cited by Farber (1949) as approximating to 10%

Between December, 1948, and August, 1950, we treated 27 patients with acute leukæmia with the folic acid antagonist aminopterin, and we summarise our results here

MATERIAL AND TECHNIQUE

There were 14 adults and 13 children—20 males and 7 females In all cases the diagnosis of acute leukæmia was established by marrow biopsy, although the type of the dominant cell could not always be determined with certainty However, on the basis of the cytologic appearances they were classified as 19 cases of acute myeloid leukæmia, 5 of acute lymphatic leukæmia, and 3 of acute monocytic leukæmia

Aminopterin only was given to all the patients in this group except one who had previously received 'Met Fol B,' but this was superseded later by aminopterin The usual plan of treatment has been to give intramuscular aminopterin 1 mg daily or on alternate days, but this was always discontinued or given at less frequent intervals if any toxic manifestations or severe leucopenia developed Blood transfusions and antibiotics were given if the patient's condition required them, otherwise no other treatment was given

RESULTS

For the purpose of tabulation we have used criteria similar to those of other investigators Thus, partial remission is used to imply that the clinical condition showed subjective improvement with return to normal temperature and decrease in size of lymph-nodes and spleen, but the hæmatological picture either remained unchanged or the white cell count fell to normal limits although the numbers of immature cells might remain unmodified Complete remission implies both clinical improvement and remission of the hæmatological condition

In 6 cases the patient received less than 3 mg of aminopterin because the treatment was instituted at very advanced terminal stages of the disease, the patients dying before larger doses of aminopterin could be given, or because it was necessary to discontinue this treatment owing to the onset of a severe leucopenia or other severe toxic manifestation that might have been due to the aminopterin

Tables I and II give the results of the treatment in the other 21 cases No remission was maintained for long, since the marrows of all patients now alive are leukæmic

As table II shows, there were only 2 patients in whom a complete remission was brought about, one of them is given in detail since it presented interesting features

CASE 12

A girl, aged 2¼ years, entered the hospital on June 15, 1949, almost moribund She had been well until two months

TABLE I—PATIENTS WHO SHOWED NO RESPONSE TO AMINOPTERIN

Case no	Sex	Age (yr)	Length of treatment (days)	Total dose (mg)	Duration of leukæmia since treatment began (days)
		Acute myeloblastic leukæmia			
1	F	55	9	7	11
2	M	17	7	6	7
3	M	66	15	10	21
4	M	33	25	23	98
5	F	47	12	7	42
6	M	5	9	9	9
7	M	44	17	10	62
8	M	45	11	4	13
9	M	37	16	11	23
10	F	24	9	5	35
11	M	24	6	6	64
		Acute lymphatic leukæmia			
12	M	2	10	9	10
13	M	12	10	10	10
		Acute monocytic leukæmia			
14	M	72	79	25	80
15	M	45	36	20	54

TABLE II—PATIENTS WHO SHOWED PARTIAL OR COMPLETE REMISSION FOLLOWING AMINOPTERIN TREATMENT

Case no	Sex	Age (yr)	Length of treatment (days)	Total dose (mg)	Length of remission (days)	Duration of leukæmia since treatment began (days)	Type of leukæmia
				Partial remission			
16	M	6	25	17	20	75	Myeloblastic
17	M	13¾	25	Met Fol B 100 mg + aminopterin 6 mg	60	120	Myeloblastic
18	M	4	10	3	20	60	Myeloblastic
19	M	5½	28	14	60	204	Monocytic
				Complete remission			
20	M	15	51	15	30	63	Myeloblastic
21	F	2¼	2 courses {17 15	2 courses {9 5	2 remissions {62 60	187	Lymphatic

before admission, when she developed a swelling of the neck The swelling subsided within a week, and the patient was moderately well until five weeks before admission Since then she had been weak and pale, and because these symptoms became progressively worse she was admitted on May 15, 1949, to another hospital A blood count and sternal puncture were done and acute leukæmia was diagnosed She was discharged from the other hospital thirteen days before the present admission under our care

On admission she was very ill, lethargic, pale, and dyspnœic The cervical, axillary, and inguinal lymph nodes were slightly enlarged The spleen was just palpable The remainder of the examination was essentially negative A blood count showed red cells 1,750,000 per c mm, platelets 28,000 per c mm, Hb 30%, white cells 377,000 per c mm (polymorphs 2 0%, lymphocytes 6 5%, monocytes 1 0%, "blasts" 90 5%) The bone marrow was packed with blasts (99%)

Course—On the same day aminopterin treatment was started By the fourth injection the patient's condition showed a remarkable improvement, and five more injections, each of 1 mg of aminopterin, were given Four weeks after the institution of the treatment the improvement was most striking, and from that time (July 20) until the beginning of September, 1949 the child appeared well Her appetite had improved, weight increased, and peripheral blood so improved that the red cells numbered 3,500,000–3,800,000 per c mm, Hb was 65–85%, and white cells numbered 5000–7000 per c mm, with a completely normal differential count The blood picture on Aug 24 1949, showed red cells 3,890,000 per c mm, Hb 86%, and white cells 8000 per c mm (polymorphs 54 0%, lymphocytes 45 0% blasts 1 0%) A sternal marrow biopsy showed that the bone marrow picture also was completely normal

On Sept 10, 1949, the child started to relapse A blood count on Sept 14 showed red cells 4,050,000 per c mm, Hb 50% and white cells 389,000 per c mm (polymorphs 1 5%, lymphocytes 88 5% blasts 10 0%, platelets 12,000) Sternal puncture showed a bone marrow again packed with blasts The child was readmitted to hospital and had a second course of aminopterin, consisting of five daily injections of 1 mg each The response to this second course was again remarkable, and the child remained well for two months During the second remission the red cells numbered 3,500,000–4,500,000 per c mm, Hb was 70–90% and white cells 4000–7200 per c mm, the differential count being essentially normal On Oct 31, 1949, a blood count showed red cells 3,620,000 per c mm, Hb 70%, white cells 7200 per c mm (polymorphs 66 5%, lymphocytes 22 5%, monocytes 10 0%, blasts 1 0%), and platelets 300,000 per c mm On Oct 21, 1949, sternal puncture showed that the bone marrow was normal, both myeloid and erythroid series appeared active

The patient was discharged on Nov 18, 1949, but readmitted on Dec 20, 1949, because she was not at all well She was very pale, had nodules in the scalp and a few small lymph nodes in the cervical region, and her spleen was palpable 6 cm below the costal margin From that time onwards the course was progressively downhill, and she died on Jan 17, 1950 without any further remission The accompanying figure shows the course of the disease

Necropsy showed gross hæmorrhage into the right internal capsule and had ruptured into the ventricular system there was considerable subtentorial clot around the pons and medulla

The interest of this case lies in the fact that aminopterin induced two dramatic complete, although temporary, remissions from both the clinical and the hæmatological aspects All bone marrow and peripheral blood films were practically normal during the short remissions, and the child appeared entirely normal clinically

TOXIC SYMPTOMS

The toxic symptoms produced by aminopterin have been similar to those reported by others, and in 13 of our patients were as follows

Stomatitis	3	Other types of rash	1
Diarrhœa	2	Epistaxis	[illegible]
Hæmorrhagic rash	3	Alopecia	[illegible]

In many instances it has been difficult to assess whether aminopterin and not the leukæmic process should be held responsible for certain of these manifestations Wide fluctuations in the number of leucocytes are often seen in acute leukæmia, it is often impossible to be certain whether, for instance, severe leucopenia or thrombocytopenia are toxic symptoms due to the aminopterin or merely features known to occur in the terminal phase of acute leukæmia Discontinuance of treatment may often be followed by remission of the toxic symptoms

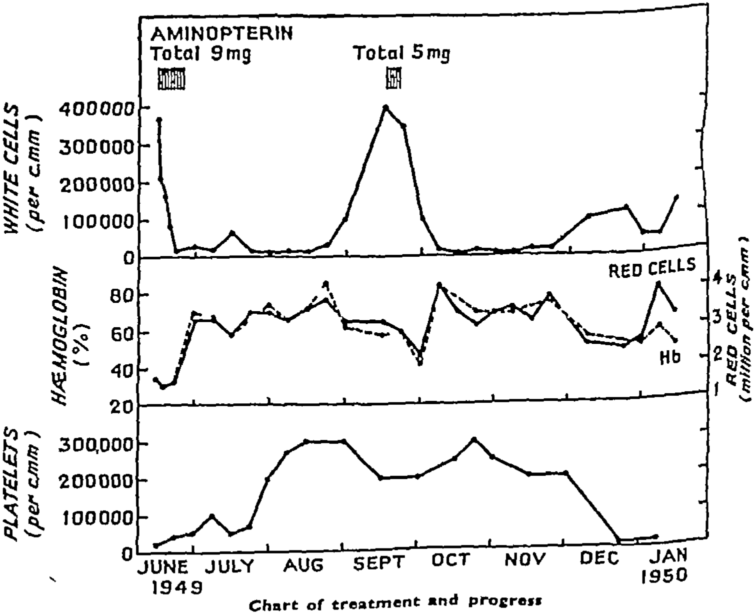


Chart of treatment and progress

DISCUSSION

The ultimate results obtained by the use of the folic acid antagonists in the treatment of acute leukæmia have so far been unsatisfactory In most patients these substances have not affected the leukæmic process to any extent, the course of the disease progressing steadily Experience has shown that the use and control of the effects of these substances is not easy for their effects in any given case are unpredictable Toxic manifestations may be numerous, and often come on with dramatic suddenness, for the margin between the therapeutic and the toxic dosages is extremely small Consequently, the use of these substances in the treatment of acute leukæmia must be restricted, they should only be used by those fully familiar with their effects and having full hæmatological facilities for the daily control that is necessary in the beginning Nevertheless, the frequent observations that some patients show complete or almost complete, although temporary, clinical and hæmatological remissions have renewed hope for future treatment of the hitherto invariably fatal acute leukæmias It is of the greatest importance that even in a proportion (greater than the spontaneous occurrences) of acute leukæmias, many of which are certainly of different ætiology, remissions can be produced for a time by known chemical agents Quite clearly much further work is required to separate the group, or groups, of acute leukæmias that may be sensitive to this form of therapy, and to follow up the clues already appearing so as to develop more suitable and less toxic chemical substances A greater proportion of acute leukæmias do not show any beneficial response to these agents, and probably fall into other groups of different ætiology, just as the chronic leukæmias do For them other types of chemical agents are required

SUMMARY

27 patients with acute myeloid, lymphatic, or monocytic leukæmia were treated with aminopterin

6 patients received less than 3 mg of aminopterin because either the treatment had to be discontinued after development of severe leucopenia or had been instituted at a very advanced stage, the patient dying before further doses could be given

Of the remaining 21 patients, the treatment produced no response in 15, partial remissions in 4, and complete remissions in 2 for relatively short periods

One case is reported to demonstrate the ability of aminopterin to induce two dramatic complete remissions in which the clinical condition, the hæmatological picture, and the bone marrow returned to normal

We wish to thank the Medical Research Council for a research grant, the Sybil Mary Pilkington Fund Trustees for a fellowship to one of us (C G), and Messrs Lederle Laboratories Division, American Cyanamid Company, for supplying the aminopterin free both directly and through the Medical Research Council

REFERENCES

Dacie J V Dresner E Mollin D L White J C (1950) *Brit med J* i 1447

Dameshek W (1949) *Blood* 4 168

Farber S (1949) *Ibid* p 160

— Diamond L K Mercer R D Sylvester R F jun Wolff J A (1948) *New Engl J Med* 238 787

Hart P L de V (1949) *Brit med J* ii 363

Jacobson W Levin W C Holt C (1948) *J Lab clin Med* 33 1642

Jimenez de Asua F (1949) *Rev Soc argent Hemat* 1 303

Meyer L M Fink H Sawitsky A Rowen M Ritz N D (1949) *Amer J clin Path* 19 119

Pierce M Alt H (1948) *J Lab clin Med* 33 1642

Sacks M S Bradford G T Schoenbach E B (1950) *Ann intern Med* 32 80

Stickney J M Hagedorn A B Mills S D Cooper T (1948) *J Lab clin Med* 33 1481

— Mills S D Hagedorn A B, Cooper T (1949) *Proc Mayo Clin* 24 525

Thiersch J B Philips F S (1949) *Amer J med Sci* 217 575

THE DANGER OF PENICILLIN THERAPY IN GONORRHŒA

A A M REEKIE
M.B Edin

PHYSICIAN I C VENEREAL DISEASE DEPARTMENTS, PRINCE OF WALES'S HOSPITAL, LONDON ASHFORD HOSPITAL, MIDDLESEX, AND MILLER GENERAL HOSPITAL, GREENWICH

THE treatment of gonorrhœa with penicillin has increased the risk that concomitant syphilis may go unrecognised

The incubation period of syphilis (9–90 days, average 3 weeks) being so much longer than that of gonorrhœa (12 hours–21 days or more, average 2–5 days), in simultaneous infections the gonococcal urethritis is being treated while the patient is in the incubation period of syphilis The small doses of penicillin which are so successful in curing acute gonorrhœa may suppress or modify primary or early generalised symptoms and signs of concomitant syphilis without curing it (Shafer and Zakon 1944, Canizares 1944, Hailey 1944, Ricchiuti 1944, Boyd et al 1944, Walker and Barton 1945, Kemp and Shaw 1946, Leifer and Martin 1946, Suter 1947)

The early treatment of syphilis decreases the opportunity for dissemination of infection both in the individual and in the community and appreciably increases the probability of cure (Moore 1948) Double infection is not uncommon—males 1 4%, females 3% (Kemp and Shaw 1946)—and whenever it is suspected the gonorrhœa should be treated not with penicillin but with another drug, such as sulphonamide which will not prevent syphilis from declaring itself

SIGNIFICANCE OF PYREXIA

Ricchiuti (1944), Walker and Barton (1945), Fromer et al (1946), and Leifer and Martin (1946) mention the development of chills, fever, and malaise, developing early in the course of penicillin therapy of gonorrhœa, as a possible indication of dual infection

The treatment of early syphilis with penicillin is accompanied by a Herxheimer reaction in 50–90% of cases (Moore 1949, Leifer and Martin 1946, Fromer et al 1946) The reaction is attributed to the liberation of toxins from the spirochætes either dead or in course of destruction by penicillin It is in fact therapeutic shock, and it may be systemic and/or focal It occurs with a penicillin dosage of 10 units per kg of body weight, or more, it usually appears from three to nine hours after the initial dose of penicillin and its incidence and severity are not related to dosage (above 10 µ per kg of body weight), or stage or duration of infection (Moore 1949) In early syphilis fever is almost an essential part of the reaction

Penicillin treatment of uncomplicated gonorrhœa, on the other hand, is very rarely accompanied by fever Leifer and Martin (1946) state that they have not observed fever "among hundreds of cases" Buchholtz (1946) says that, in the penicillin treatment of over 2000 patients with simple acute or chronic gonococcal urethritis unaccompanied by clinical evidence of syphilis, only 2 or 3 patients were observed to have a febrile reaction which could not be explained either by a toxic reaction to penicillin or by the coexistence of syphilis

Therefore unexplained fever and malaise during the early stage of penicillin therapy in acute gonorrhœa strongly suggest concomitant syphilis

ILLUSTRATIVE CASE RECORDS

Case 1 —A lorry-driver, aged 26 reported in February, 1948, with 4 days history of urethral discharge He had had gonorrhœa 9 months previously treated in London. Recent exposures had been 1 4, and 8 weeks previously with different consorts no precautions had been taken at the last two The urethral discharge was diagnosed

TABLE II—PATIENTS WHO SHOWED PARTIAL OR COMPLETE REMISSION FOLLOWING AMINOPTERIN TREATMENT

Case no	Sex	Age (yr)	Length of treatment (days)	Total dose (mg.)	Length of remission (days)	Duration of leukæmia since treatment began (days)	Type of leukæmia
				Partial remission			
16	M	6	25	17	20	75	Myeloblastic
17	M	13³/₄	25	Met Fol B 100 mg + aminopterin 6 mg	60	120	Myeloblastic
18	M	4	10	3	20	60	Myeloblastic
19	M	5¹/₂	28	14	60	204	Monocytic
				Complete remission			
20	M	15	51	15	30	63	Myeloblastic
21	F	2³/₄	2 courses {17 15	2 courses {9 5	2 remissions {62 60	167	Lymphatic

before admission, when she developed a swelling of the neck The swelling subsided within a week, and the patient was moderately well until five weeks before admission Since then she had been weak and pale, and because these symptoms became progressively worse she was admitted on May 15, 1949, to another hospital A blood count and sternal puncture were done and acute leukæmia was diagnosed She was discharged from the other hospital thirteen days before the present admission under our care

On admission she was very ill, lethargic, pale, and dyspnœic The cervical, axillary, and inguinal lymph nodes were slightly enlarged The spleen was just palpable The remainder of the examination was essentially negative A blood count showed red cells 1,750,000 per c mm, platelets 28 000 per c mm, Hb 30% white cells 377,000 per c mm (polymorphs 2 0%, lymphocytes 6 5%, monocytes 1 0% "blasts" 90 5%) The bone marrow was packed with blasts (99%)

Course—On the same day aminopterin treatment was started By the fourth injection the patient's condition showed a remarkable improvement, and five more injections, each of 1 mg of aminopterin, were given Four weeks after the institution of the treatment the improvement was most striking, and from that time (July 20) until the beginning of September, 1949, the child appeared well Her appetite had improved, weight increased, and peripheral blood so improved that the red cells numbered 3,500,000–3,800,000 per c mm, Hb was 65–85%, and white cells numbered 5000–7000 per c mm, with a completely normal differential count The blood picture on Aug 24, 1949, showed red cells 3,890,000 per c mm, Hb 80%, and white cells 8000 per c mm (polymorphs 54 0%, lymphocytes 45 0%, blasts 1 0%) A sternal marrow biopsy showed that the bone marrow picture also was completely normal

On Sept 10, 1949, the child started to relapse A blood count on Sept 14 showed red cells 4,050,000 per c mm, Hb 50% and white cells 389,000 per c mm (polymorphs 1 5%, lymphocytes 88 5%, blasts 10 0%, platelets 12,000) Sternal puncture showed a bone marrow again packed with blasts The child was readmitted to hospital and had a second course of aminopterin, consisting of five daily injections of 1 mg each The response to this second course was again remarkable, and the child remained well for two months During the second remission the red cells numbered 3,500,000–4,500,000 per c mm, Hb was 70–90%, and white cells 4000–7200 per c mm, the differential count being essentially normal On Oct 31, 1949, a blood count showed red cells 3,620,000 per c mm, Hb 70%, white cells 7200 per c mm (polymorphs 66 5%, lymphocytes 22 5%, monocytes 10 0%, blasts 1 0%), and platelets 300,000 per c mm On Oct 21, 1949, sternal puncture showed that the bone marrow was normal, both myeloid and erythroid series appeared active

The patient was discharged on Nov 18, 1949, but readmitted on Dec 20 1949, because she was not at all well She was very pale, had nodules in the scalp and a few small lymph nodes in the cervical region, and her spleen was palpable 6 cm below the costal margin From that time onwards the course was progressively downhill, and she died on Jan 17, 1950 without any further remission The accompanying figure shows the course of the disease

Necropsy showed gross hæmorrhage into the right internal capsule and had ruptured into the ventricular system there was considerable subtentorial clot around the pons and medulla

The interest of this case lies in the fact that aminopterin induced two dramatic complete, although temporary, remissions from both the clinical and the hæmatological aspects All bone marrow and peripheral blood films were practically normal during the short remissions, and the child appeared entirely normal clinically

TOXIC SYMPTOMS

The toxic symptoms produced by aminopterin have been similar to those reported by others, and in 13 of our patients were as follows

Stomatitis	3	Other types of rash	1
Diarrhœa	2	Epistaxis	[illegible]
Hæmorrhagic rash	3	Alopecia	[illegible]

In many instances it has been difficult to assess whether aminopterin and not the leukæmic process should be held responsible for certain of these manifestations Wide fluctuations in the number of leucocytes are often seen in acute leukæmia, it is often impossible to be certain whether, for instance, severe leucopenia or thrombocytopenia are toxic symptoms due to the aminopterin or merely features known to occur in the terminal phase of acute leukæmia Discontinuance of treatment may often be followed by remission of the toxic symptoms

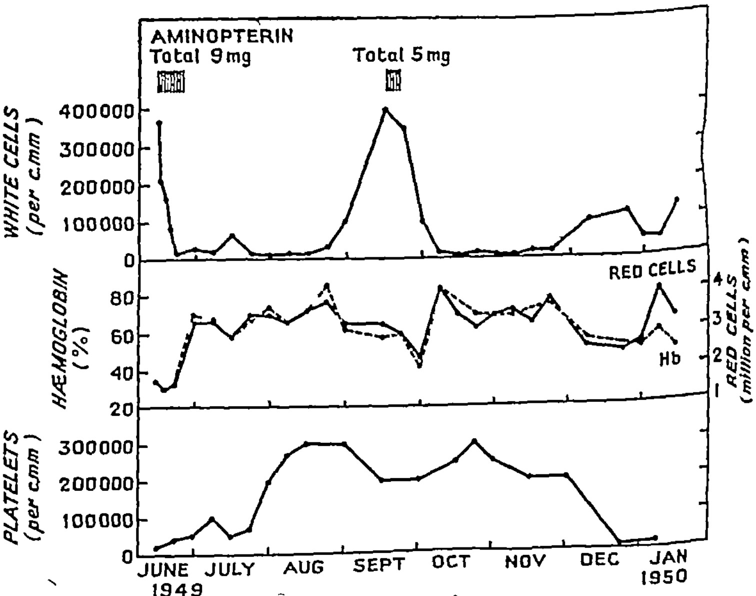


Chart of treatment and progress

DISCUSSION

The ultimate results obtained by the use of the folic acid antagonists in the treatment of acute leukæmia have so far been unsatisfactory In most patients these substances have not affected the leukæmic process to any extent, the course of the disease progressing steadily Experience has shown that the use and control of the effects of these substances is not easy, for their effects in any given case are unpredictable Toxic manifestations may be numerous, and often come on with dramatic suddenness, for the margin between the therapeutic and the toxic dosages is extremely small Consequently, the use of these substances in the treatment of acute leukæmia must be restricted, they should only be used by those fully familiar with their effects and having full hæmatological facilities for the daily control that is necessary in the beginning Nevertheless, the frequent observations that some patients show complete or almost complete, although temporary, clinical and hæmatological remissions have renewed hope for future treatment of the hitherto invariably fatal acute leukæmias It is of the greatest importance that even in a proportion (greater than the spontaneous occurrences) of acute leukæmias, many of which are certainly of different ætiology, remissions can be produced for a time by known chemical agents Quite clearly much further work is required to separate the group, or groups, of acute leukæmias that may be sensitive to this form of therapy, and to follow up the clues already appearing so as to develop more suitable and less toxic chemical substances A greater proportion of acute leukæmias do not show any beneficial response to these agents, and probably fall into other groups of different ætiology, just as the chronic leukæmias do For them other types of chemical agents are required

SUMMARY

27 patients with acute myeloid, lymphatic, or monocytic leukæmia were treated with aminopterin

6 patients received less than 3 mg of aminopterin because either the treatment had to be discontinued after development of severe leucopenia or had been instituted at a very advanced stage, the patient dying before further doses could be given

Of the remaining 21 patients, the treatment produced no response in 15, partial remissions in 4, and complete remissions in 2 for relatively short periods

One case is reported to demonstrate the ability of aminopterin to induce two dramatic complete remissions in which the clinical condition, the hæmatological picture, and the bone marrow returned to normal

We wish to thank the Medical Research Council for a research grant, the Sybil Mary Pilkington Fund Trustees for a fellowship to one of us (C G) and Messrs Lederle Laboratories Division, American Cyanamid Company, for supplying the aminopterin free both directly and through the Medical Research Council

REFERENCES

Dacie J V Dresner E Mollin D I White J C (1950) *Brit med J* i 1447

Dameshek W (1949) *Blood* 4 168

Farber S (1949) *Ibid* p 160

— Diamond L K, Mercer R D Sylvester R F jun Wolff J A (1948) *New Engl J Med* 238 787

Hart P L de V (1949) *Brit med J* ii 363

Jacobson W Levin W C Holt C (1948) *J Lab clin Med* 33 1642

Jimenez de Asua F (1949) *Rev Soc argent Hemat* 1 353

Meyer L M Fink H Sawitsky A Rowen M Ritz N D (1949) *Amer J clin Path* 19 119

Pierce M Alt H (1948) *J Lab clin Med* 33 1642

Sacks M S Bradford G T Schoenbach E B (1950) *Ann intern Med* 32 80

Stickney J M Hagedorn A B Mills S D Cooper T (1948) *J Lab clin Med* 33 1481

— Mills S D Hagedorn A B., Cooper T (1949) *Proc Mayo Clin* 24 525

S (1949) *Amer J med Sci* 217 575

THE DANGER OF PENICILLIN THERAPY IN GONORRHŒA

A A M REEKIE
M.B Edin
PHYSICIAN I C VENEREAL DISEASE DEPARTMENTS, PRINCE OF WALES'S HOSPITAL, LONDON, ASHFORD HOSPITAL, MIDDLESEX, AND MILLER GENERAL HOSPITAL, GREENWICH

THE treatment of gonorrhœa with penicillin has increased the risk that concomitant syphilis may go unrecognised

The incubation period of syphilis (9–90 days, average 3 weeks) being so much longer than that of gonorrhœa (12 hours–21 days or more, average 2–5 days), in simultaneous infections the gonococcal urethritis is being treated while the patient is in the incubation period of syphilis The small doses of penicillin which are so successful in curing acute gonorrhœa may suppress or modify primary or early generalised symptoms and signs of concomitant syphilis without curing it (Shafer and Zakon 1944, Camzares 1944, Hailey 1944, Ricchiuti 1944, Boyd et al 1944, Walker and Barton 1945, Kemp and Shaw 1946, Leifer and Martin 1946, Suter 1947)

The early treatment of syphilis decreases the opportunity for dissemination of infection both in the individual and in the community and appreciably increases the probability of cure (Moore 1948) Double infection is not uncommon—males 1 4%, females 3% (Kemp and Shaw 1946)—and whenever it is suspected the gonorrhœa should be treated not with penicillin but with another drug, such as sulphonamide which will not prevent syphilis from declaring itself

SIGNIFICANCE OF PYREXIA

Ricchiuti (1944), Walker and Barton (1945), Fromer et al (1946), and Leifer and Martin (1946) mention the development of chills, fever, and malaise, developing early in the course of penicillin therapy of gonorrhœa, as a possible indication of dual infection

The treatment of early syphilis with penicillin is accompanied by a Herxheimer reaction in 50–90% of cases (Moore 1949, Leifer and Martin 1946, Fromer et al 1946) The reaction is attributed to the liberation of toxins from the spirochætes either dead or in course of destruction by penicillin It is in fact therapeutic shock, and it may be systemic and/or focal It occurs with a penicillin dosage of 10 units per kg of body weight, or more, it usually appears from three to nine hours after the initial dose of penicillin and its incidence and severity are not related to dosage (above 10 µ per kg of body weight), or stage or duration of infection (Moore 1949) In early syphilis fever is almost an essential part of the reaction

Penicillin treatment of uncomplicated gonorrhœa, on the other hand, is very rarely accompanied by fever Leifer and Martin (1946) state that they have not observed fever "among hundreds of cases" Buchholtz (1946) says that, in the penicillin treatment of over 2000 patients with simple acute or chronic gonococcal urethritis unaccompanied by clinical evidence of syphilis, only 2 or 3 patients were observed to have a febrile reaction which could not be explained either by a toxic reaction to penicillin or by the coexistence of syphilis

Therefore unexplained fever and malaise during the early stage of penicillin therapy in acute gonorrhœa strongly suggest concomitant syphilis

ILLUSTRATIVE CASE RECORDS

Case 1—A lorry-driver, aged 26 reported in February, 1948, with 4 days history of urethral discharge He had had gonorrhœa 9 months previously, treated in London Recent exposures had been 1, 4, and 8 weeks previously with different consorts no precautions had been taken at the last two The urethral discharge was diagnosed as gonococcal by smear and culture. There was no clinical evidence of coexisting syphilis; blood Wassermann reaction and Kahn test were negative. The patient was given one injection of procaine penicillin 150 000 units.

At his next attendance, 2 days later, after inquiry, he said that about 4 hours after the injection he had felt cold and shivery and had a headache and some backache. These symptoms had passed off by the next day. He did not volunteer this information, because he thought that the symptoms "were due to the injection, and so he didn't take much notice of them." Clinical examination revealed no abnormality, and the urethritis was resolving satisfactorily. Temperature and pulse were normal.

Throughout the course of the surveillance period no further malaise occurred, and surveillance for gonorrhœa was completed in the 8th week. Blood tests were negative, and there was no clinical evidence of syphilis. He was instructed to continue reporting weekly, and did so. In the 10th week a tiny indurated painless non-tender papule was present on the dorsal aspect of the glans penis. The patient was unaware of its existence. The left inguinal glands were very slightly, almost insignificantly, enlarged. There were no other signs suggesting syphilis. Dark-ground examination of serum from the papule showed *Treponema pallidum*. Blood tests were still negative. He denied further risks of infection since his first attendance.

Case 2.—A mechanic, aged 27, reported in April, 1949, with 5 days' history of urethral discharge. He had had gonorrhœa 12 months previously and been treated in London. Recent exposures had been 1, 4 and 9 weeks previously with different consorts; soap and water had been used prophylactically after each exposure. The urethral discharge was diagnosed as gonococcal by smear and culture. There was no clinical evidence of coexisting syphilis; blood Wassermann reaction and Kahn test were negative. The patient was given one injection of procaine penicillin 150,000 units.

At his next attendance 3 days later, he said that about six hours after the injection he had had a bad attack of shivering and some frontal headache, lasting until the next afternoon. Clinical examination showed no abnormality, the urethritis was resolving rapidly, and temperature and pulse were normal.

Surveillance for gonorrhœa continued uneventfully, and was completed in the 8th week. No further malaise had occurred during this period. There was no clinical evidence of syphilis and blood tests were negative. The patient continued to attend weekly, and in the 11th week he said he had had a slight watery urethral discharge for 3 days, with smarting and tingling in the urethra localised to an area about 1 in. from the meatus. Palpation of this area revealed a small slightly tender induration. A scanty serous discharge was present at the meatal orifice. The right inguinal glands were very slightly enlarged and painless. There were no other signs suggesting syphilis. Dark-ground examination of the urethral discharge showed a few specimens of *Trep. pallidum*. Urethroscopy showed a localised elevated erosion on the roof, $1^1/_2$ in. from the meatal orifice, dusky red, and exuding serum. Serum obtained directly from the lesion by loop via the urethroscope showed *Trep. pallidum*. Blood tests were negative. He denied further risks of infection since his first attendance.

Case 3.—A man, aged 28, who had recently been a merchant seaman but was now working on shore, reported in August, 1949, with 3 days' history of urethral discharge. He had had gonorrhœa 8 months previously (treated in New York) and 18 months previously (treated in Southampton); also 12 months previously he had had malaria, treated in Bombay. Recent exposures had been 8 days (London), 5 weeks (New York), and 9 weeks (Hamburg) previously. Soap and water had been used prophylactically after each exposure. Homosexual exposure was denied. The urethral discharge was diagnosed as gonococcal by smear and culture. There was no clinical evidence of syphilis; blood Wassermann reaction and Kahn test were negative. The patient was given one injection of procaine penicillin 150,000 units.

At his next attendance, 2 days later, he said that 4 or 5 hours after the injection he had felt very cold and shivery, had a headache, and thought that his malaria had returned. He took his temperature and found it to be 101°F. He said that next day he felt much better and his temperature was normal. On examination, the urethritis was subsiding satisfactorily, temperature and pulse were normal, there was no clinical abnormality, and no explanation could be given for the febrile reaction.

In the 8th week surveillance for gonorrhœa was completed, there was no evidence of syphilis, the blood serology was negative, and no further malaise had occurred. Surveillance was continued weekly, and in the 10th week clinical signs and blood tests were still negative. Then he defaulted, to return in the 19th week with hoarseness of voice, sore throat, perineal itching and irritation, all of about 10 days' duration. On examination he showed neither penile lesions nor scars nor rash, but had a very definite generalised adenitis. His soft palate was deeply injected, and both tonsils were much enlarged but not ulcerated. On his perineum a small cluster of flat moist indurated papules was seen at the anal mucocutaneous junction. Dark-ground examination of serum from a papule showed *Trep. pallidum*. Blood tests were strongly positive. He denied further exposures since his first attendance.

DISCUSSION

These cases show once more that the manifestations of syphilis can be appreciably masked by penicillin therapy for gonorrhœa. This fact is common knowledge today, and in venereology due allowance is made for it. Leifer and Martin (1946) found in their series that, although subcurative doses of penicillin prolonged the incubation period of syphilis, syphilis was definitely diagnosed less than 90 days after the use of penicillin. In the present three cases it is impossible to pinpoint the sources of infection, but the onset of clinical signs of syphilis may well have been retarded towards the limit of the usually accepted incubation period.

All three patients had a febrile reaction shortly after receiving penicillin. Hence I would suggest that all patients undergoing treatment for gonococcal urethritis not only should be informed that there is a risk of concomitant syphilis being delayed in its appearance because of treatment, but also should be asked specifically whether any untoward reaction occurred shortly after receiving penicillin. As in case 1, they may omit to mention this information. Systemic sensitivity reactions occasionally follow injection of penicillin, but in almost all such cases there is urticaria. Except for those who later proved to have syphilis I have never seen a penicillin-treated patient develop fever without other signs.

All patients who have had penicillin treatment for gonorrhœa should be advised to report at once the presence of any lesion, no matter how seemingly trivial, during the period of surveillance and they should be warned against sexual intercourse throughout that period. They should be examined very carefully at every attendance, because very early lesions may be asymptomatic (case 1).

An unexplained febrile or other reaction a few hours after penicillin therapy should forewarn the clinician of the possibility of coexisting syphilis; and, although repeated clinical examinations may elicit no evidence, blood tests in such cases should be made at least once weekly for six months after the start of treatment.

SUMMARY

Unexplained fever and malaise occurring shortly after penicillin therapy for gonococcal urethritis strongly suggest coexisting syphilis, and the symptoms and signs of the oncoming syphilis may be suppressed, masked, or delayed. Patients displaying such reactions should be subject to very close scrutiny, both clinical and serological, for six months from the start of treatment.

REFERENCES

Boyd, G. G., Wagner, J. A., Hewson, G. F. (1944) *U.S. nav. med. Bull.* 43, 1034.
Buchholtz, M. (1946) *J. vener. Dis. Inform.* 27, 175.
Canizares, O. (1944) *Arch. Derm. Syph., Chicago*, 50, 246.
Fromer, S., Cutler, J. C., Levitan, S. (1946) *J. vener. Dis. Inform.* 27, 171.
Halley, H. E. (1944) *Arch. Derm. Syph., Chicago*, 50, 269.
Kemp, J. E., Shaw, C. (1946) *Amer. J. Syph.* 20, 56.
Leifer, W., Martin, S. P. (1946) *J. Amer. med. Ass.* 130, 202.
Moore, J. E. (1948) *Brit. J. vener. Dis.* 24, 1.
— (1949) *Ibid.* 25, 100.
Ricchiuti, J. F. (1944) *U.S. nav. med. Bull.* 43, 1031.
Shafer, B., Zakon, S. J. (1944) *Arch. Derm. Syph., Chicago*, 50, 200.
Sutor, J. M. (1947) *Virginia med. Mon.* 74, 369.
Walker, A. E., Barton, R. L. (1945) *J. vener. Dis. Inform.* 26, 241.

HÆMOPOIETIC EFFECT OF THYMIDINE IN PERNICIOUS ANÆMIA

K Hausmann
M.D Hamberg

I medizinische Abteilung, Allgemeines Krankenhaus St Georg, Hamburg

According to Shive et al (1948), Snell et al (1948), and Wright et al (1948) thymidine (desoxyribose thymine) may take the place of vitamin B_{12} as a growth promoting factor for *Lactobacillus lactis* Dorner and *L leichmannii* 313 Acting on these observations Ungley (1949) administered to a patient with pernicious anæmia 48 mg of thymidine, but it had no effect on blood regeneration Reisner (1949) also reported the ineffectiveness of thymidine therapy in doses varying from 5 to 150 mg

In two cases of addisonian pernicious anæmia I have administered a concentrate containing 85–90% of thymidine, prepared by K Mulli from the purified liver extract 'Pernical forte' The results, already briefly reported (Hausmann 1949), are here described more fully The concentrate used, according to chemical analysis, contained neither vitamin B_{12} (10 g failed to give a positive reaction with the cobalt reagent α nitroso β-naphthol) nor folic acid and thymine The small amounts of impurities present consisted of substances which in former trials had proved ineffective In quantities of 10–20 mg the thymidine concentrate exerted a growth promoting action on *L leichmannii* 313, similar to that of 1 μg of crystalline vitamin B_{12} ('Cobione,' Merck)

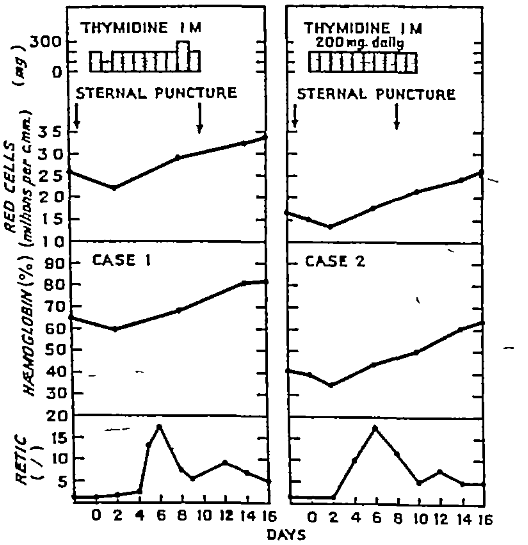


Fig 1—Quantitative changes in peripheral blood during thymidine therapy in cases 1 and 2. At the point indicated by the first arrow in each case the sternal marrow was megaloblastic, at the point indicated by the second arrow it was normoblastic.

In differentiating the material obtained by sternal puncture 500 cells were counted and the count of erythroblasts, including megaloblasts, was calculated per hundred leucocytes

CASE RECORDS

Case 1 —A woman, aged 54, had had liver therapy for pernicious anæmia since 1936 The last injection of liver extract had been given six months previously She was admitted to hospital because of coronary insufficiency

Examination of the blood revealed macrocytosis aniso cytosis, poikilocytosis and hyperchromasia of erythrocytes, and 3200 white cells per c mm, with highly segmented neutrophils Sternal puncture showed the typical bone-marrow picture, with megaloblasts of all stages, giant meta myelocytes, and a diminished count of highly segmented megakaryocytes No free hydrochloric acid was found in the gastric juice after histamine stimulation. Anorexia, paræsthesia of the hands and feet, and general weakness were present There were no signs of glossitis or of subacute combined degeneration of the spinal cord

Treatment—Thymidine was given in an average daily dose of 200 mg (100–250 mg a day) The first injection of 200 mg was tolerated without pain but caused a slight collapse shortly after the injection The following injections had no untoward effects

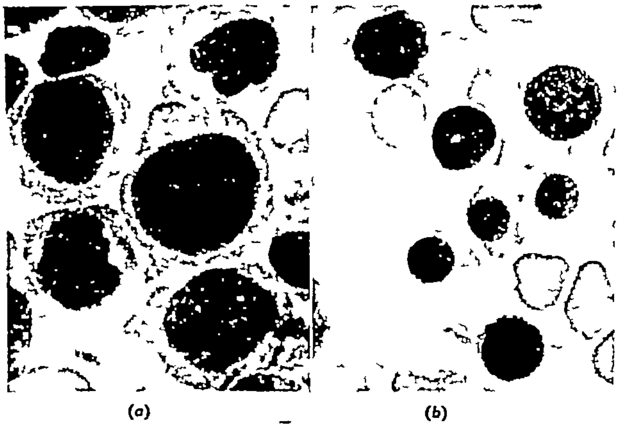


Fig 2—Qualitative changes in red and white cells in case 1 : (a) blood film before treatment (b) after treatment with thymidine.

Results—From the fourth day of thymidine therapy her appetite increased and weakness and paræsthesia became less On the sixteenth day there were no symptoms except angina pectoris The changes in the peripheral blood are shown in figs 1 and 2, and the bone marrow changes in the table The leucocytes reached a level of 5200 per c mm

Since no thymidine was available for further treatment, 25 μg of vitamin B_{12} ('Pernipur') was administered. There was no second reticulocytosis

Case 2 —A woman, aged 81 was admitted with untreated pernicious anæmia Examination of her blood revealed macrocytosis, anisocytosis, poikilocytosis, and hyperchro masia of erythrocytes with leucocytes 2300 per c.mm , and highly segmented neutrophils Her sternal marrow had the characteristic features of pernicious anæmia, with abundant megaloblasts at all stages, giant metamyelocytes, and highly segmented megakaryocytes There was no free hydrochloric acid in the gastric secretion after the administration of histamine The patient had pronounced weakness, with

STERNAL MARROW COUNTS IN CASES 1 AND 2 I WAS BEFORE TREATMENT AND II DURING TREATMENT (SEE FIG 1)

Marrow cells	Case 1		Case 2	
	I	II	I	II
Erythroid myeloid ratio	1 02 1	0 44 1	0 53 1	0 43 1
Megaloblasts per 100 white cells	78 0	0	37 5	0
Basophilic megaloblasts	20 0	0	12 5	0
Polychromatic megaloblasts	46 0	0	24 0	0
Orthochromatic megaloblasts	13 0	0	1 0	0
Erythroblasts per 100 white cells	13 5	44 0	15 0	42 5
Basophilic erythroblasts	1 0	1 0	6 5	4 5
Polychromatic erythroblasts	1 5	6 0	7 0	25 5
Orthochromatic erythroblasts	11 0	37 0	1 5	12 5
Giant forms per 100 white cells	20 0	4 5	28 0	10 0
Myeloblasts	0 5	0 5	0	0
Promyelocytes	2 0	2 0	5 0	2 5
(Giant forms)	0	0	0	0
Myelocytes	37 0	27 0	19 5	19 5
(Giant forms)	0	0	0 5	0
Metamyelocytes	22 5	10 5	19 5	18 5
(Giant forms)	17 0	2 0	13 5	5 5
Rod forms	20 0	29 5	15 0	15 0
(Giant forms)	2 5	2 0	4 5	1 5
Polymorphonuclear neutrophils	11 5	28 0	38 0	40 0
(Giant forms)	0 5	0 5	0 5	3 0
Lymphocytes	6 5	2 5	3 5	4 0

paræsthesia and anorexia but no signs of glossitis or subacute combined degeneration of the spinal cord. Some myocardial weakness.

Treatment with thymidine consisted in daily injections of 280 mg each to a total dosage of 2·5 g. The intramuscular injections were tolerated without any untoward side reactions.

Results.—Subjectively there was a striking improvement on the sixth day of therapy, the patient feeling much better with increased appetite and diminished paræsthesia. The rise of erythrocytes and hæmoglobin in the peripheral blood is indicated in fig 1 and the quantitative bone-marrow changes are shown in the table. The white cells reached a level of 6800 per c mm. After the sixteenth day of treatment the patient received 50 µg of vitamin B_{12} (permipur), no more thymidine being available. There was no second reticulocytosis.

RESULTS AND CONCLUSIONS

The foregoing studies indicate that intramuscular thymidine 200–280 mg (total dosage 2–2·8 g) changed the megaloblastic marrow to normoblastic and led to a decrease of giant metamyelocytes, and in the peripheral blood produced a reticulocytosis and a subsequent increase in the red-cell and hæmoglobin count. The doses administered, however, were too small to produce a complete remission of the blood picture. No more thymidine being obtainable we could not ascertain whether thymidine provoked nervous disturbances.

The blood-forming action of thymidine in pernicious anæmia is similar to that of corresponding doses of the various hæmopoietic active forms of vitamin B_{12} as well as folic acid and thymine. The negative results reported by Ungley (1949) and by Reisner (1949) were probably due to insufficient dosage.

In practice, the effect of thymidine in pernicious anæmia will probably be unimportant, because such large amounts of thymidine are required for blood regeneration that a depot therapy, such as is possible with vitamin B_{12} and highly purified concentrates of that substance, will be impracticable.

The value of liver extracts in pernicious anæmia cannot be ascribed to their content of thymidine, because even refined liver extracts such as pernical forte, which produce their best effects in doses of 120 mg of solid matter do not contain more than about 1% of thymidine.

The extreme nuclear alterations of bone-marrow cells in pernicious anæmia in relapse suggest the existence of far-reaching metabolic disturbances. As a growth-promoting factor for *L casei* (Stokes 1944) and in the treatment of macrocytic anæmia (Spies et al 1946) large doses of thymine, a factor in the formation of thymonucleinic acid, can be substituted for folic acid. This has led to the assumption that folic acid may function as an enzyme of nuclear metabolism. Since in tests with *L lactis* Dorner and *L leichmannii* 313 large doses of thymidine can be substituted for vitamin B_{12}, it may be assumed that vitamin B_{12} also exerts an enzyme influence on nuclear metabolism. The hæmopoietic effect of thymidine in pernicious anæmia supports this assumption.

SUMMARY

In two cases of pernicious anæmia a total dosage of 2 and 2·8 g of thymidine exerted a blood-forming action comparable to that of corresponding doses of vitamin B_{12}, folic acid, or thymine.

REFERENCES

Hausmann K (1949) *Lancet* ii 962
Reisner E H jun (1949) *Bull N Y Acad Med* **25** 120
Shive W, Ravel J M, Eakin R E (1948) *J Amer chem Soc* **70** 2614
Snell E E, Kitay E, McNutt W S (1948) *J biol Chem* **175** 473
Spies T D, Frommeyer W B, Garcia Lopez G, Lopez Toca R, Gwinner G (1946) *Lancet* i 883
Stokes J L (1944) *J Bact* **48** 201
Ungley, C C (1949) *Lancet* i 104
Wright L D, Skeggs H R, Huff J W (1948) *J biol Chem* **175** 475

Medical Societies

ROYAL SOCIETY OF MEDICINE

Cyclical Vomiting

THE section of pædiatrics of the Royal Society of Medicine met on Jan 26 under the chairmanship of Dr K H TALLERMAN, president of the section, to discuss Cyclical Vomiting and Allied Periodic Disorders of Childhood.

Dr C K J HAMILTON said that cyclical vomiting was first described by Gee under the name "fitful" or "recurrent" vomiting. Attacks started at the age of 3 years or less, and they usually ceased spontaneously around the age of 12. The patient was likely to be thin and nervous; often he was an only child, and commonly there was a family history of similar attacks, of travel sickness or of migraine. Attacks might be precipitated by shock, strain, excitement, infection, or dietary indiscretion, and a prodromal period of listlessness could often be recognised. After the first vomit, which might contain food taken many hours before, nothing taken by mouth could be retained, and the vomit consisted of gastric juice containing mucus, bile, and possibly blood. Associated symptoms were nausea, abdominal pain, headache, and giddiness; some of these manifestations might be more conspicuous than the vomiting, and occasionally there were convulsions. The patient might be pale and febrile and either drowsy or restless. The blood-pressure was sometimes raised and the urine contained acetone. A severe attack might end fatally, but usually recovery took place quite suddenly after two or three days.

The abdomen was lax and easy to palpate, so confusion with acute inflammatory abdominal diseases did not usually arise, but the condition was often difficult to diagnose from recurrent intestinal obstruction, intracranial tumour, and diabetic coma (glycosuria often being present). The first attack was, of course, always difficult to diagnose. Recurrent vomiting was closely connected with recurrent pyrexia without obvious cause, attacks of which might alternate with vomiting, and also with recurrent headache, but no relation with epilepsy or with allergy had been demonstrated.

Prof STANLEY GRAHAM said that the condition could be defined as "periodic attacks of vomiting associated with marked ketosis." The attacks were sometimes called "acidosis," but this was a bad term because acidosis did not necessarily accompany the ketosis, and indeed there might be an alkalosis. In hospital attacks did not occur spontaneously, and could not be induced by giving a ketogenic diet or ammonium chloride. Professor Graham disliked the term "cyclical," because the attacks do not have any definite rhythm.

The basis of the condition seemed to be an abnormal production of ketone bodies, and possibly this represented an abnormal response by the liver to some form of stress rather than a disease entity. Turning to treatment Professor Graham emphasised the importance of treating the child as a whole; administration of extra carbohydrate between attacks was probably beneficial, but the value of fat reduction was doubtful. There was no theoretical basis for the regular administration of alkalis.

Dr DESMOND O'NEILL spoke on the psychiatric aspect of abdominal pain. He described a study made at Guy's Hospital by Dr R C MacKeith and himself on a consecutive series of children attending the outpatient pædiatric clinic with recurrent abdominal pain as a presenting symptom, for which no physical cause could be found. In several of these children vomiting occurred in some of the attacks. The purpose of this study was to determine whether the abdominal pain could be regarded as an adaptive disorder—that is, whether it was related to emotional tension from maladaptation to stresses which the child had to meet. It was found that emotional tension was, in fact, the principal determinant of the pain in 15 out of 25 children, and that it was a contributory factor in another 6. Of this group of 21, 17 had other tension signs, such as headache, poor sleep, tics, and behaviour disorders. In 14 there was a history of nervous disturbance or stress disorder in one or both parents.

Anxiety and fear were much the most common emotional states associated with pain, fear of the teacher at school or of being bullied was often found Once the attacks had been set in motion in this way, a complaint of abdominal pain might be made in order consciously or unconsciously, to escape from an unpleasant situation The effect of simple psychotherapy, in which play therapy had an important part, was striking reduction or disappearance of the pain being achieved in a high proportion of cases In some children under treatment the pain was replaced by another symptom, such as screaming attacks, and this had in turn to be treated

Dr R E Smith, whose paper was read in his absence by Dr D V Hubble, dealt with the prognosis and sequelæ of recurrent vomiting, basing his conclusions on a study of 700 boys between the ages of 13 and 18 at Rugby School Of those who had had attacks in childhood nearly a quarter continued to do so in adolescence, but there was a well-marked decline around 15–16 years of age Acute appendicitis might be overlooked in a boy subject to these attacks, but otherwise they were not serious

Dr Hubble also described the findings in a fatal case of his own, in which there was hypertrophy of the pylorus He suggested that during life there might have been pylorospasm and reversed peristalsis, and he thought that a similar mechanism might account for the vomiting of migraine He had found ergotomine tartrate of value in recurrent vomiting as well as in migraine

Dr R C Mac Keith remarked on the interval of up to 48 hours that often elapsed between the exciting cause and the onset of the attack.

Dr J P M Tizard referred to some organic causes of recurrent vomiting, such as tonsillitis, pyelitis, œsophageal stenosis, and intestinal obstruction, and Dr H. R Jolly mentioned lead poisoning

Dr J J Kempton observed that the subjects of recurrent vomiting are often in a state of mild chronic ill health, correction of which suffices to bring about improvement

Prof A. A. Moncrieff emphasised the importance of adequate rest for these children, and the value in many cases, of a regular sedative The infections precipitating attacks might be very slight, and detectable only by careful examination Professor Moncrieff also spoke of the need for a control series in evaluating the rôle of emotional factors in causing symptoms

Dr W W Payne said that in the subjects of recurrent vomiting the glucose tolerance was normal between attacks, but there was some delay in the storage of lævulose He had often found the blood sugar raised at the beginning of attacks He had noticed that in diabetic children hypoglycæmia was often accompanied by abdominal pain, vomiting, and diarrhœa, which were presumably due to overaction of adrenaline He wondered whether recurrent attacks of vomiting might be precipitated by a similar mechanism followed by exhaustion of the glycogen reserve of the liver and hypoglycæmia and a further excessive adrenaline action Dr Payne therefore recommended repeated administration of carbohydrate during the day between attacks and a sedative to reduce sympathetic overaction

Dr G M Kerr said that in practice the best description to use was still ' bilious attacks ', he thought that these cases were as numerous as ever, but that fewer were being referred to hospital. The patient might be given a rectal sedative if nothing could be retained by mouth

The President pointed out that in organic abdominal disease the pain was likely to be more severe, and not so commonly associated with headache and pyrexia He thought " abdominal migraine ' a good descriptive title for these attacks'

Mr J T Edwards described acetonæmia " in cows, and recurrent vomiting in puppies Highly selected strains were most liable, and they were also unduly nervous and relatively infertile Replying to the discussion, Professor Graham said that he had found the blood-sugar to be normal between attacks He had also seen asthma arise as a sequel, and he believed this to be commoner than migraine

Reviews of Books

Peptic Ulcer

A C Ivy M D vice president of the University of Illinois, M I Grossman, M.D, associate professor of physiology, University of Illinois, W H Bachrach M D, research associate in physiology, University of South Carolina School of Medicine London J & A Churchill 1950 Pp 1144 96s

Here is the accumulated experience of many physicians surgeons, physiologists, and pathologists indeed Dr Ivy and his collaborators seem to have gathered together almost all our current knowledge of peptic ulcer In performing this monumental task, they have summarised clearly the great mass of often contradictory evidence, and present reasoned conclusions The result is a valuable and important book Of the four major parts that on pathogenesis is by far the largest Diagnosis gets relatively scant attention—a bare 100 pages—while treatment rightly has double as much The section on pathogenesis covers modern work on experimental production of ulcer constitutional and environmental factors, and the role of the nervous system, and there is a good discussion on psychosomatic—or as the authors prefer to call them " emotogenic "—causes There are innumerable references, and many excellent illustrations and diagrams

This is the magnum opus of an outstanding gastroenterologist. All interested in peptic ulcer will feel indebted to Dr Ivy

Surgery of the Eye Injuries

Alston Callahan, M D, F.A.C S, professor of ophthalmology, Medical College of Alabama, director, Thigpen Cater Eye Hospital, Birmingham, Alabama Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 217 84s

The experience which led Professor Callahan to write this book was gained when he was surgeon to an army ophthalmic centre, and afterwards to a civilian eye hospital As he says in the introduction the work is not an all-encompassing text of eye surgery, but is concerned only with the repair of injuries and of the deformities they produce No part of the eye or adnexa is omitted and he begins with corneal suture and ends with repair of the bony walls of the orbit, but it seems that his chief interest relates to structures outside the globe of the eye Corneal grafting, for instance, is treated with extreme conservatism as being rather dangerous, and three-quarters of the text deals with the injuries to the adnexa Nevertheless, his presentation of the methods employed in a variety of injuries is outstandingly successful, actual cases being beautifully illustrated and lucidly described Moreover, this is a delightful book to read and handle

Osteology for Dissectors

A Tutorial Pocketbook Robert King Howat, M.B, F.R C.S F.R F.P S, hon demonstrator of anatomy King's College London London Henry Kimpton 1950 Pp 292 15s

One of the objects of this book is to promote the study of the bones and soft tissues as an interdependent whole, each component of which explains the other Mr Howat therefore places considerable emphasis on living and functional anatomy Indeed, several short notes are included on subjects not strictly to be classified as osteology, such as the mechanics of respiration, the muscles of the back, and the muscles of facial expression

In the descriptions of the bones the main features are clearly and succinctly brought out, but minutiæ are left out the vexed subject of ossification dates is sensibly treated by the omission of detail. The book is illustrated by 46 rough outline drawings on which the student is expected to sketch in the various muscular and ligamentous attachments

The text is essentially in the form of notes and the arrangement of material is occasionally odd for example though an introductory section is given the various types of epiphyses are not classified until p 131, where the classification is somewhat arbitrarily introduced into the description of the femur Nor is the treatment of the skull bones wholly logical the palatine bone is described in the text, but the ethmoid is relegated to an appendix The list of contents leads one to expect a separate description of the sphenoid, but none is given, nor does the sphenoid appear in the index The index is, indeed inadequate and often capricious The terminology used is deliberately inconsistent, which may serve to accustom the student to the conditions he will encounter later in the curriculum, but which may also, at this early stage, confuse him Nevertheless, the book may *prove of value to those who find the larger osteology texts* too detailed and too far divorced from the study of the anatomy of the soft parts

The National Health Service Acts, 1946 & 1949

J A SCOTT, O B E, M D, D P H, deputy medical officer of health, London County Council, D J B COOPER, A C I S principal clerk L C C public health department, S SEUFFERT of the Middle Temple and the South eastern circuit, barrister at law London Eyre & Spottiswoode 1950 Pp 1192 55s

IN 1947 Dr Scott published a slender volume called *The National Health Service Act, 1946*, containing an informative introductory chapter, the text of the Act, and an index to the Act compiled by Mr H A C Sturgis In this new version, which bears about the same relative proportions to its forerunner as Falstaff to his page, Dr Scott has had the help of Mr Cooper and Mr Seuffert The introduction has been largely retained and expanded and a chapter has been added on the scope and structure of the National Health Service, informative and easy to follow The texts are given of the 1946 Act, the 1949 (Amendment) Act, and the Statutory Instruments Rules *and Orders (as amended)* issued up to March 31, 1950, both Acts are fully annotated in a manner which relates allied subjects fills in gaps, and throws a beam through the haze of official language Appendices include a pictorial diagram of the administrative structure of the service, the statutory rules and orders relating to regional hospital areas, a list of disclaimed hospitals an account of the prospect of health centres, the text of Ministry of Health circulars of 'particular interest and importance," and a list of Whitley Councils, and there is a comprehensive index Professional and amateur administrators who found the original volume a useful acquaintance will be quick to make friends with its larger successor

Asphyxia Neonatorum

WILLIAM F WINDLE, PH D, professor of anatomy, University of Pennsylvania Springfield Ill Chas C Thomas Oxford Blackwell Scientific Publications 1950 Pp 61 15s

THIS monograph in the series " American Lectures in Physiology " represents ' the revised text of several lectures in an elective course in ' Developmental Physiology ' at the University of Pennsylvania " It is concerned with the relation of asphyxia neonatorum to the fœtal blood, the fœtal circulation and respiration, and the effect of this condition upon the brain

The subject is introduced with a discussion of fœtal maternal relationships, and thereafter the blood of the fœtus and of the new born is considered from the aspects of development, disposition, volume, and iron content Other chapters are devoted to fœtal circulation, intra uterine respiration, fœtal respiratory activity, and the advent of in breathing Only the last chapter deals with asphyxia neonatorum as such, from experimental and pathological points of view

Professor Windle is not one to accept statements without putting them to the test of experimental proof, as the following quotation illustrates " Some are content to assume that a significant percentage of the population is born defective mentally and that this defect may be the cause rather than the effect of respiratory abnormality at birth Although clinical evidence suggests a close relationship between asphyxia at birth and late neurological defects in infants and children, adequately controlled experimental conditions are practically non existent in the human species Consequently, it is essential to turn to the laboratory and try to reproduce similar conditions in animals that give birth to two or more offspring "

This is a notable monograph on a subject of increasing importance to obstetricians, pædiatricians, physiologists, and pathologists

British Encyclopædia of Medical Practice (2nd ed. London Butterworth Medical Publications 1950 Vol 4. Pp 688 £3) —The fourth volume of this standard work in its second edition, edited by Lord Horder, goes forward alphabetically from corneal lesions (reviewed by Mr J H. Doggart) to ear diseases (by Mr Maxwell Ellis) Technically this volume is noteworthy for fine colour illustrations of the tympanic membrane

Annual Review of Medicine (Stanford University School of Medicine California Annual Reviews 1950 Pp 454. $6) —Essentially intended for those engaged in teaching or research volumes in the " Annual Reviews series are designed to cover all the principal advances in knowledge in their special subjects The present volume, edited by Windsor C Cutting and Henry W Newman and carrying an impressive list of authors, is remarkably up to date Besides quoting from large numbers of original papers, the various authors give their own views clearly, and keep a good balance between experimental and therapeutic results Some 250 reviews on medicine published between July, 1948, and November, 1949, are annotated, and the authors referred to amount to nearly 4000

Atlas d'Électrocardiographie (2nd ed Paris Masson 1950 Pp 260 Fr 2200) —This atlas, intended for beginners and for practitioners, is compiled by V Fattorusso and O Ritter, and is based on very clear tracings, which—though evidently retouched—are faithful reproductions of the originals, many of which were taken in the clinic of Dr F N Wilson at Ann Arbor In subjects which have recently advanced, particularly cardiac infarction, the book is up to date, and wherever possible an electrical anatomical explanation is given for the tracings For those who wish to go a little deeper into the matter there is a supplementary section on electrophysiology, with brief notes on vectorcardiography and on the ventricular gradient The atlas can be recommended to anyone with a little French but the price is high for a book with soft paper covers

Foot Mechanics (London Baillière, Tindall & Cox. 1950 Pp 106 6s) —Leslie R Smart, chiropodist to the Bermondsey and Southwark group of hospitals, sets out to describe the mechanics of the foot and the principles of *treatment of mechanical disorders, and to correlate chiropodial* measures with other methods of physical treatment His account of the mechanics and functions of the foot and of its common disorders is clear and straightforward though more emphasis might have been laid on the functional importance of the toes In the chapters dealing with methods of diagnosis and treatment it is disappointing to find that emphasis is laid on technique rather than principles Thus the operative treatment of hallux rigidus is described in detail, but the indications for operation, and the results that may be expected are not mentioned In a book of this kind it is surely unnecessary to discuss the technique of giving local anæsthesia, or the development of an X ray plate space would be far better given to a fuller account of the indications for the forms of treatment advocated

A Medical Handbook for Athletic and Football Club Trainers (London Faber & Faber 1950 Pp 144 10*s* 6*d*) —A certain amount of scientific and medical knowledge is desirable and indeed necessary for a correct understanding of the training of footballers and those engaged in other athletic ventures But it is far from easy to define the limits of such instruction and in this book Mr W D *Jarvis has attempted too much in some directions* and too little in others He clearly has a good superficial knowledge of anatomy and physiology , but a profound knowledge of these is required by anyone setting out to impart elementary principles to beginners, and to preserve a proper proportion in selection of material Is an athletic trainer any more efficient because he knows about the cytology of the blood, the character of the heart sounds, the gaseous changes which influence the respiratory centre, the structure of the intestinal wall, the anatomy of the brain and of the autonomic nervous system, and the anatomy and physiology of the endocrines ? The details of first aid are sound, but references to the differential diagnosis of such diseases as peritonitis are out of place A man with considerable practical experience of athletes must have many more useful things to offer than an epitome of current textbooks for the medical student.

LANCET

TURDAY, FEB 10, 1951

er Cookery

T [illegible] Working Party[1] makes two mai[illegible]endations (1) that premises used in the [illegible] should be registered with local authorities and (2) that a "standard" code of hygienic practice should be enforced. In addition it has drawn up a 'target' code at which catering establishments, great and small, are advised to aim. Not all the members of the working party could agree that a local authority should have power to prevent the proposed use of premises on the ground that the plans and plant are going to prove unsatisfactory, and members representing the trade raised the reasonable objection that the major dangers to public health arise not from failings in layout or equipment but from the dirty habits or lapses of the workers. We too are not over-fond of provisions—necessary though they be at times—which leave a citizen's livelihood to the discretion of the single expert employed by a statutory body.

The dangers to the public from the catering trade are those of food-poisoning in its many forms. Food may be dangerous when it reaches the restaurant, or while on the premises it may be rendered dangerous by human or animal contamination or by the multiplication of bacteria derived from these or other sources. At any stage, and sometimes by almost grotesque ill chance, it may adsorb metallic and other chemical poisons. The measures proposed in the "standard" code to lessen these dangers are those suggested by reason and experience. Working premises must be kept clean in every sense, and vessels and equipment should be what the good housewife calls spotless. Lighting and supplies of hot and cold water must suffice for every purpose. Perishable food must be kept at a temperature below that at which bacteria multiply freely, and viands to be eaten cold must, after cooking, be chilled as rapidly as possible. Interpreted with caution, regulations such as these could be enforced. Whether this is true of those directed against infection derived from the people who handle food we are less certain. The working party rightly rejects the proposal, so often made, that all employees should submit to medical inspection at regular intervals or at least on engagement. Even if such an inspection were limited to a search for carriers of enteric fever, such as is undertaken before men are employed in waterworks, the time and money spent to no advantage would soon bring the system into disrepute. Enteric fever is mercifully rare, while food-poisoning caused by salmonella, shigella, and staphylococcus is only too common. Cumulative experience suggests that, though a permanent carrier may occasionally be responsible for these infections, the commonest source is the person with a superficial infected wound of hand or face or with a discharging nose or one who returns to work free of symptoms after a bout of diarrhœa, or who is the unwitting family contact of an infected person.[2] We should not care for the task of framing regulations adequate to control these sources of infection, and we doubt whether this "standard" code will be of much help in this direction. Indeed the results of applying this code as a whole will deserve close attention from those interested in the science (or art) of citizenship. So long as social regulation was limited to the obvious externals of our living, enforcement was not difficult. The Elizabethan cit who did not attend his church on Sunday or the wretch who failed to obscure his house lights in the blackout, were sitting birds to the legal gun. But the kitchen-hand who fails to report to the restaurateur that he passed a fluid motion during the night (Standard Code, Sect 2b) will be elusive game. It is fair to ask whether expert knowledge is not, with the best of intentions, pushing us too deep into the brier-bush of unenforceable regulations. If these were based on facts beyond dispute we should feel less uneasy; but if this working party had met in 1940 its findings would not be what they are now, and its successor in 1960 may not accept its premises and suggestions unamended.

But, if some misgivings are permissible, no-one should make light of this report; for, applied with sense and tact, its suggestions will do much to enhance the safety of those who eat in public and those who buy cooked food. People who cynically deny the possibility of improvement in these matters would do well to consider the ice-cream trade, where a single regulation demanding pasteurisation, a practical but non-statutory test of bacterial contamination, and the wholehearted support of the makers, have together entirely changed the quality of the article sold to the public. Today food hygiene is headline news, and to make this report effective some responsibility lies with the popular expositors of hygienic living. A public which grumbles with intelligence is unlikely to come to much harm, and the critical diner-out will send the dirty plate back quicker than a ream of regulations. Perhaps, too, the sanitary inspector will learn to look more often at the waitress's finger-nails and less severely at the height of the kitchen ceiling. And every doctor will help if he notifies to the M.O.H. any outbreak of gastro-enteritis involving two or more persons.

Methods of Rat Destruction

THE war stimulated study of scientific methods of destroying rats. In Britain the centre of investigation was the Bureau of Animal Population at Oxford, and some of the work done there has been reviewed by BARNETT.[3] Poisoning remains the method of choice, but difficulties arise from the tendency of rats to avoid anything unfamiliar ("new object reaction") which leads to refusal of poison when first put down.[4] After an interval of hours or days small and often sublethal quantities are taken, and a rat which recovers from poisoning may afterwards refuse the food that caused his illness ('bait-shyness'). In the now familiar technique of "prebaiting" plain bait is laid for several days before poison is added, and the rats thus become accustomed to the new food THOMPSON[5] has shown that if the amount of bait laid each day is much less than the rats need, feeding becomes more and more concentrated into a short period immediately after the bait is put down, and when poison is eventually added the mixture is taken readily in lethal amounts Prebaiting, however, is laborious, and it is hard for organisations such as local health departments to find the labour for it Moreover, even prebaiting may leave some survivors, and these, according to official advice,[6] should be dealt with by a further course of prebaiting and poisoning, with different materials to avoid possible shyness If this is not done, or if for any reason complete or nearly complete clearance is not achieved, the rat population may restore itself rapidly by breeding

---

[1] Ministry of Food Hygiene in Catering Establishments H.M. Stationery Office 1951 Pp 50 1s 9d.

[2] Francis T jun. J Amer med Ass 1949 141 308.

[3] Barnett S A. Preservation of Grains in Storage F.A.O Agricultural Publications no 2 1948 p 129

[4] Chitty D., Shorten M. J Mammal 1946 27 63

For economic reasons, therefore, a means of doing without prebaiting is needed, and BARNETT and his colleagues have investigated this problem One possibility is a poison so toxic that rats could rarely, if ever, take a less than lethal dose, and it has been widely suggested that sodium monofluoroacetate ("1080") meets this need Of 16 carefully assessed field tests of 1080, used without prebaiting, 10 were judged successful, 4 were failures, and 2 were doubtful[7] 1080 is therefore considered better than the commonly used rat poisons (such as zinc phosphide) without prebaiting, though the results are not as reliable as those of the normal prebaiting procedure But 1080 is very dangerous, and a number of domestic animals and wild birds were killed during the tests Also it was found that rats surviving 1080 poisoning may refuse further baits containing the poison Since the LD50 of 1080 to wild *Rattus norvegicus* is 4 mg per kg or less, this is of considerable interest it shows that an increase in toxicity which would obviate prebaiting must be so great that it is probably impracticable The problem would be solved if a highly toxic, palatable poison could be found, *specific to rats*, but only one substance is known to be fairly specific to rats—namely, scilliroside, the toxic glucoside of red squill—and this poison has proved ineffective without prebaiting[8]

An alternative way to make prebaiting unnecessary would be to use a poison that did not cause shyness Such a poison could be laid continuously, in infested places, without loss of efficacy ARMOUR and BARNETT have tried the anticoagulant dicoumarol in an investigation of this possibility, which they call "chronic baiting"[9] As dicoumarol acts slowly, and has little effect after a single dose, it was thought that the rats would *not* learn to avoid it But laboratory and field tests, all on wild rats, showed that dicoumarol is capable of producing shyness, though to a less extent than strong poisons, and also that it is distasteful to rats Granted, however, that dicoumarol is not the ideal substance for chronic baiting, the fact remains that ARMOUR and BARNETT found *that in* the field it gave kills of over 70% in 6–9 weeks, laying bait only once a week And SCHEIN[10] reports briefly even higher kills in some environments with another anticoagulant, Compound 42 or 'Warfarin' Though a great deal more work needs to be done, it seems likely that chronic baiting with special poisons will be the next stage in the development of methods of rat destruction

Contaminants in the Blood-culture

COAGULASE-NEGATIVE strains of *Staphylococcus albus* are almost always harmless saprophytes, and when found in a blood culture they are therefore reported as contaminants But in the two cases reported by Dr MATTHEW three weeks ago (Jan. 20, p 146) there seemed to be no doubt that they were the cause of a fatal infective endocarditis Diphtheroids, bacilli resembling *H influenzæ*, and enterococci, as well as these white staphylococci, have on rare occasions grafted themselves on damaged heart valves and instituted *an infection which in pre penicillin days* was almost invariably fatal These cases usually have a persistent pyrexia, probably related to the continuous release of bacterial protein—an accepted pyrogen—into the blood stream, and the breaking off of friable endocardial vegetations causes the non septic infarct often found in various organs Myocardial infarction is a rarity, but it was a feature of MATTHEW's cases, where it led to a secondary pericarditis with effusion. In cases of bacterial, but not rheumatic, endocarditis this complication of pericardial effusion should make the clinician consider the possibility of infection with *Staph albus*, even though the reports on blood cultures have hitherto mentioned it *only* as a contaminant

Despite this evidence of its very occasional pathogenicity, *Staph albus* remains the commonest contaminant found in blood cultures taken by inexperienced housemen, where it may be derived from the patient's skin, the operator's hands, or the environment Students nowadays are often called upon to draw blood for various purposes, and they should be taught the correct technique of venepuncture early in their clinical training A short technical film, on the lines of *Taking a Blood-culture*, which was shown to the Royal Society of Medicine at St Mary's Hospital in November, would tell them how the risk of introducing contaminants can be reduced to a minimum The important points are to use a syringe *ready assembled with a sharp needle* and sterilised by dry heat, to have the patient's arm fully extended on a resistant surface, *and to feel* as well as see the vein chosen for puncture (avoiding the shifting superficial kind) A sphygmomanometer cuff having been applied to the upper arm and inflated just enough to make the veins stand out, the skin is painted with 2% iodine or 70% alcohol, and the operator then introduces the needle as nearly as possible parallel to the vein, *to avoid catching the opposite* wall The blood should flow into the syringe without undue suction by the piston, and without including any air bubbles After its withdrawal from the vein the needle is left attached to the syringe and the blood is slowly ejected into the appropriate culture media—bottles or tubes with screw cap and rubber diaphragm enable one to inoculate the medium without exposing it to the outside air

Besides the usual aerobic and anaerobic culture (and, where undulant fever is suspected, incubation in 5–10% CO_2), an attempt at a quantitative culture an be made if, when the blood is being collected, wo 1 ml amounts of blood are added to tubes of nelted agar which are then emptied into petri plates f this is done routinely in cases of obscure pyrexia, t will be possible for the laboratory to say whether ny dubious organism is a pathogen, for contaminant rganisms will usually number less than 1 and pathogens more than 1 per ml It will also help to differ- ntiate a temporary bacteræmia, with, as a rule, less han 10 organisms per ml, from a true septicæmia, where—for example, in subacute bacterial endocarditis —the number per ml may range from tens to undreds

---

[5] Thompson H V *Bull Anim Behav* 1948 6 26
[6] Barnett S A Infestation Control Rats and Mice London 1946
[7] Barnett, S A Spencer M M *J Hyg Camb* 1949 47 426
[8] Barnett S A, Blaxland J D Leech F B Spencer, M. M. *Ibid* p 431
[9] Armour C J Barnett, S A *Ibid* 1950 48 158
[10] Schein, M. W *Publ Hlth Rep Wash* 1950 65, 368

Annotations

INFLUENZAL PNEUMONIA

EXCEPT for rare cases which radiologically belong to the "atypical pneumonia" group of infections, influenzal pneumonia seems to be caused by pneumococci, staphylococci, streptococci, or *Hæmophilus influenzæ* We may think of these bacteria as opportunists exploiting gaps in the defences, consolidating in areas whose perimeter has been weakened by influenza virus The incidence of pneumonia differs greatly in different influenza outbreaks and even in different areas where the same strain of virus seems to be at work Many experienced bacteriologists believe that *H influenzæ* was of special importance in the 1918 pandemic of virus influenza, and there is some evidence that particular bacterial species tend to predominate in particular outbreaks The relationship of bacteria and virus is thus very important in considering influenzal pneumonia Bacteria play the main part in the later stages but both virus and bacteria have frequently been isolated in the same case Finland et al.[1] found that half of 69 cases of bacterial and other pneumonias gave positive serological tests for the virus Maxwell et al.[2] obtained serological evidence of infection or isolated the virus in 17 of 36 cases of pneumococcal pneumonia Now Stuart-Harris and his colleagues[3] in Sheffield report that at least 18 of 55 cases of pneumonia during the spring of 1949 were infected with influenza A virus In addition, 8 of 15 cases of bronchitis, 1 of 2 cases of bronchiectasis, and 4 of 6 cases of congestive heart failure also had evidence of virus A infection These positive results were confined to the period of prevalence of influenza A, and only 2 out of 158 patients, including 78 cases of bacterial pneumonia, were infected with the virus when there was no epidemic. The Sheffield workers isolated *Staphylococcus aureus* from several of their cases of influenzal pneumonia, particularly from the fatal ones and this type of infection should be constantly kept in mind

One of the striking features of certain cases of influenzal pneumonia associated with *Staph aureus* is the ease with which influenza virus may be recovered from the lungs of fatal cases Some workers believe that this indicates a special relation between the virus and the bacteria, but the rapidity with which staphylococcal pneumonia develops may also be relevant On the other hand, there may be some sort of synergism at work, and possibly a staphylococcal spreading factor plays a part From the clinical angle, synchronous virus and staphylococcal infection is particularly important because it may resist many forms of current treatment In influenzal pneumonia associated with pneumococci there is less evidence of synergism, and in such cases the clinical features and the response to treatment do not differ materially from sporadic cases of pneumococcal pneumonia Harford et al[4] showed that the power of the mouse lung to reduce its content of pneumococci was less in the presence of influenza virus infection, but in these experiments definite lung lesions were produced by the virus itself We cannot, therefore, lightly dismiss the possibility of some sort of concerted attack between virus and bacteria especially where the influenza and pneumonia infections are not separated by an appreciable interval of time

Another form of relation between the virus and bacterial agents in influenzal pneumonia is suggested by the Sheffield workers Certain organisms present in the nasopharynx as peaceful residents may be transferred and "passaged" from one person to another along with the virus. It is possible that during this transfer an epidemic strain of the bacterium might emerge, and, if this happened, more cases of pneumonia associated with this virulent strain would occur than before the outbreak, and these infections might be combined with influenza virus infection No single serological type of pneumococcus was particularly common among the Sheffield cases, but other workers have found a prevalence of one type in other outbreaks There is a suggestion that one bacteriophage type of *Staph aureus* was common in Sheffield during the epidemic, but this may not mean very much The investigation does not shed much new light on the virus-bacteria relationship in influenzal pneumonia, but it is a valuable record of what happens in a community when, as at present, influenza virus reaches it from abroad

THE WORK OF THE BORSTALS

A Home Office pamphlet, Prisons and Borstals,[5] reminds us that in 1863 a committee of the House of Lords reported in favour of a punitive regime in prisons, based on "hard labour, hard fare, and a hard bed" This was interpreted as requiring complete isolation of the prisoner at all times, and his employment on irksome, fatiguing, and useless labour at the treadmill, the shot-drill, and the crank In 1895 a departmental committee, with Lord Gladstone as its chairman, found that under this system neither crime nor recidivism had decreased, and that prisoners, far from being deterred, became degraded, embittered, and confirmed in their choice of a criminal life The committee recommended that, in future, reformation and deterrence should go hand in hand, and that "prison treatment should be effectually designed to maintain, stimulate, or awaken the higher susceptibilities of prisoners and turn them out of prison better men and women, both physically and morally, than when they came in"

Nowhere in the prison service has the attempt to apply these principles been more earnest than in the borstals, and achievement has been considerable, though it is partly limited by lack of appropriate staff and buildings There are two reception centres for boys, one at Latchmere House, Kingston, and the other in a wing of Wormwood Scrubs Prison Until recently girls were received at Holloway Prison but now they are sent directly to the borstal at Aylesbury The Howard League[6] think the continued use of a prison as a reception centre is unfortunate and so indeed do the Prison Commissioners Boys are studied for about two months at the reception centres, and are examined medically, educationally, and psychologically A woman social worker visits the home and reports on the family background of each young offender, and finally he is assessed for vocational training On the basis of these studies he is allocated to the borstal most likely to suit him Of the 13 institutions available 4 are in 'security" buildings, 7 are in camps or adapted country houses, 1 is a specially built open borstal, and 1 is in an old prison with an outlying camp, there are also a correctional borstal for absconders in a wing of Wandsworth Prison, and a recall centre at Portsmouth for the further training of those recalled from supervision Girls under borstal training are far fewer than boys (an average of 275 against 3100 in 1949), and less choice of training is open for them There are only two centres—that at Aylesbury (a "security" institution with a farm outside the walls), and an open borstal at East Sutton, where 40–50 suitable girls are trained in an adapted country house

---

[1] Finland M. Ory E M Meads M. Barnes M W *J Lab clin Med.* 1948 33 32

[2] Maxwell E S Ward T G van Metre T E *J clin Invest* 1949 28 307

[3] Stuart-Harris C H. Laird, J Tyrrell D A. Kelsall M. H Franks Z C Pownall, M. *J Hyg Camb* 1950 47 434

[4] Harford, C G Leidler V Hara M *J exp Med* 1949 89 53

[5] 2nd ed H.M. Stationery Office 1950 Pp 72 2s 6d.

[6] Borstal a Critical Survey London Howard League for Penal Reform. 1950 Pp 43 2s 6d

A statutory duty is laid on the borstals to provide continued education for the inmates, not only by class teaching but by means of hobbies and handicrafts, and in addition eight hours every day are spent at work, at first in construction and maintenance about the house and farm and later in training for a trade The boys are taught by self respecting craftsmen, vigorous and often athletic, who provide, as the Howard League survey says, a living proof that honesty is not a sign of effeminacy and weakness Small sums can be earned at work, which can be spent in the canteen For the girls there is much less choice of occupation then for the boys, until recently domestic work and sewing were the only resources offered to young women who before admission had mostly been living lives of considerable excitement Nowadays, however, they have opportunities to learn dairy farming, and at East Sutton they also help with building and maintenance, and not surprisingly many of them show much aptitude for these things The Home Office pamphlet notes that the spare time activities at borstals are valuable instruments of training A library (often a branch of the county library system), indoor and outdoor games, matches played against neighbouring teams, cadet corps, boys' clubs, young farmers' clubs, summer camps and harvesting camps, and the opportunity to go home for five days' leave, all bring these young people into touch with the community, and help them to know they have a place in it

The aim of all borstal training, as the Howard League point out, is to fit the young offender for ordinary life by giving him increasing responsibility, both in his environment and for his own self discipline The duration of a borstal sentence is, in effect, for four years, of which not less than nine months and not more than three years must be spent in the institution, the rest being a period of supervised freedom How far is the system successful ? It is generally reckoned that the approved schools are successful with over three quarters of their cases, the borstals, faced for the main part with the tougher delinquents, succeed with more than half Thus of boys discharged in the years 1942–46, 52 1% had not been reconvicted up to 1948, and 22 3% had been reconvicted once only For girls the figures were 59% not reconvicted and 21 9% reconvicted once only But about a quarter of the boys and a fifth of the girls had been reconvicted more than once in that time, and for these we must take yet more thought Among constructive measures the Howard League propose that staff should be increased by offering higher salaries, and by experimenting in the use of more women staff in the boys' institutions Special institutions should be provided, they suggest, for absconders from approved schools (especially for those children who have been sent to such schools because they needed care and protection), for children of very low intelligence, and for psychopaths No part of a borstal sentence, they think, should be served in a prison building The welfare of those who leave is now in the hands of a Central Council for Aftercare The Howard League feel that such care might well be more personal and less formal more use should be made of voluntary workers, and there should be one or more officers in every borstal to act as a liaison officer for aftercare Better aftercare, indeed, might make all the difference to some, for a boy who leaves with the knowledge that he is well on the way to becoming a skilled workman may find his way blocked by trade union regulations when he tries to get a job, and his bitterness may lead him back to crime

We have good reason to be proud of the work done by our approved schools and borstals With more staff they could probably diminish still further the residue of young people who still sink into the miserable career of the persistent offender

SEASONAL INCIDENCE OF POLIOMYELITIS

In the tropics the incidence of poliomyelitis does not vary with the seasons, but as one moves north or south of the Equator there is an increasing tendency for outbreaks to occur in the warm months of the year Exceptional seasonal outbreaks are not rare but generally speaking the rule holds The explanation which comes most readily to mind is that climate affects the means of transmission of the virus, whether we believe this to be by droplets or by food and drink If the disease is spread by contact we must explain why outbreaks occur when people are spending most time in the open air, and Armstrong[1] meets this paradox by suggesting that the portal of entry of the virus is more permeable in warm weather When it is cold the secretions of the nose and throat, which are thought to have a protective effect, are greatly increased Mucous secretion at its site of penetration may dilute or carry the virus away and at the same time make it more difficult for the virus to come into contact with susceptible cells in the nasopharynx In warm weather, when secretions are less, the opportunities for virus penetration will be better, and Armstrong has shown that there is a striking correlation between the absolute humidity, the average monthly temperature, and the incidence of poliomyelitis in the United States Similarly, in our public health section (p 355) Dr Ian Taylor's chart illustrates how London epidemics in the last few years have begun as soon as the average temperature at Kew reached 60°F But if this correlation means anything, why do mumps, influenza, and chickenpox not flourish in the same sort of weather ? The difference may be concerned with the type of cell which attracts these viruses

In search of experimental support for his hypothesis, Armstrong suspended the Lansing strain of poliomyelitis virus in varying amounts of mucin, and after centrifuging injected the supernatant fluid intracerebrally into mice Mucin appeared to snare the particles of both poliomyelitis and herpes simplex virus, since the tubes containing the highest concentrations of mucin were least infectious Next he injected mice intracerebrally with herpes virus suspended in mucin and 4 out of 30 survived whereas all 43 controls died A similar protective effect was noted when the injections were given into the pad of the foot or into the loose tissues of the groin Using a strain of rabies virus he found that 5 out of 12 mice survived when mucin was added to the intracerebral inoculum whereas all 12 control mice died. In all of these experiments mucin delayed the infection, and although only a proportion of the animals survived the results might have been better if as in the nasopharynx, there had been a continuous supply of fresh mucin The effect of this substance in the virus experiments is exactly the reverse of what happens in some experimental bacterial infections where mucin enables a feebly pathogenic organism to initiate infection In those infections mucin protects the bacteria from the host's defences, here it forms a protective barrier between virus and the susceptible tissue cell If the seasonal incidence of poliomyelitis is related to the conditions of the portal of entry or exit for the virus it is conceivable that such conditions could be altered by artificial measures Armstrong's hypothesis may not be entirely convincing but it suggests several lines for epidemiological and laboratory investigation

---

[1] Armstrong C Amer J publ Hlth 1950 40 1296

ACCORDING TO OUR CLOTH

GIVE some men a few packing cases and a packet of screws and they will make a passable dining room suite, others will split the wood for kindling, and some, giving the whole thing up, will leave it to rot in the rain These are the differences between the able, the average, and the problem outlook

That gift for improvising, of which, in war time, we are so rightly proud, has now some special opportunities in the health service The Newcastle Regional Hospital Board,[1] reviewing their charge in 1948, found a shortage of hospital buildings and great inequalities in staffing and equipment Some parts of the region had about enough hospital beds, but few had adequate X ray departments or pathology laboratories, and none had adequate outpatient departments There was nothing like enough accommodation for the tuberculous, *the mentally ill, or the mentally defective* To bring this all up to a uniformly high level, the board saw clearly, would take many years and much rebuilding They would like to be able to build 3 new general hospitals, 3 new sanatoria, and a new mental hospital, and to extend and adapt some 25 existing general and special hospitals, but they realise that for ten years or more they must spend much of their capital allowance on improving what already exists New hospitals, they say, cost £2500 or more per bed, but a bad hospital may be transformed for less than £500 per bed, and greatly improved for an outlay of only £50 per bed They have therefore given to both patients and staff the immediate benefits which come of redecorating, refurnishing, and the removal of extra beds from overcrowded wards Hospital management committees have been given the means to buy good beds and mattresses in place of very poor ones, and each committee has been given £1 2*s* per bed per year to spend on minor capital works of their own choosing The board hope to increase this allocation in the coming years

Staffing, they find, can be improved astonishingly quickly The regional nursing officer has helped management committees to develop comprehensive schemes for training nurses and nursing cadets, and as a result nursing recruitment has improved wonderfully, not only in many general hospitals of the region but in a mental hospital and a mental deficiency hospital as well Working with the dietetic officer of the Ministry of Health, she has also improved the feeding arrangements of patients and staff The main advance in staffing, however, has been in the specialist service The time given by consultants and senior hospital officers has increased by 55%—over half as much again All consultants who came into the service of the board in July, 1948, were allowed to increase their half day sessions to 9 per week, or to become whole time consultants, and additional consultants were appointed either for 9 sessions weekly or full time, at their own choice As a result, consultants are now uniformly distributed through the region—a remarkable achievement in two years—and this has been done by levelling up, not levelling down even such favoured areas as Newcastle, Carlisle, and Sunderland, which had relatively large consultant staffs before the service began, have been able to increase these staffs since 1948 Moreover, the convenience of the consultants themselves has been considered, their sessions being arranged so that they give all, or nearly all, their service in one group of hospitals, and no longer have to go from one end of the region to the other This conservation of their energy costs nothing and is much appreciated

The board have a five year plan for further expansion of the consultant service which financial stringency may prevent them from completing, but they think that, in any new appointments which are made, the tuberculosis service, the mental health service, and the backward parts of the region should have preferential treatment Where consultants are too few, they find, examination, diagnosis, and treatment are sometimes neither efficient or quick, and this leads to extravagance in the use of beds patients are taken in unnecessarily, or stay in too long

> "A hospital spending £1 10*s* weekly on its consultant service and £12 weekly per patient on all services may well be a much more economical as well as a much more efficient hospital than one spending 10*s* weekly per patient on its consultant services and £8 weekly per patient on all services "

They also believe that a regional board which expanded the consultant service to absorb an eighth of the total cost of the service would have found the quickest way to raise the quality of the service to the standard of the best hospitals in the region But they point out that the consultants in such an enlightened service would have to accept the important duty of keeping expenditure down to a minimum consistent with good care of the patients

HIRSCHSPRUNG'S DISEASE

THE American pædiatric surgeons, Swenson and Bill,[1] began to treat Hirschsprung's disease by rectosigmoidectomy at the Boston Children's Hospital over 3 years ago, and soon afterwards Mr F D Stephens, of the Hospital for Sick Children, Great Ormond Street, after visiting Boston, adopted their technique with some modifications in detail In January, 1949, Bodian and his colleagues [2] published encouraging preliminary results in 12 cases, but it was clear that the value of the treatment could not be judged until the patients had been observed for several years The surgeons at Great Ormond Street have now operated on 37 cases and have followed 23 of these patients for a minimum period of a year, and 12 for at least two years The clinical results, reported by Dr Bodian and his colleagues in this issue (p 302) are highly satisfactory There have been 3 deaths, and 2 cases have been followed for less than six months, but the remaining 32 are all in good general condition and 31 of them are having regular and spontaneous bowel actions The Boston results are equally good,[3] and these two groups of workers have undoubtedly established rectosigmoidectomy as a sound and reasonably safe operation capable of producing a lasting cure in most cases

Rectosigmoidectomy is nevertheless a serious operation, and a task for the future, as with many other congenital malformations, is to search for means of prevention This will depend on a better understanding of the interplay of the genetic and environmental factors Now that Hirschsprung's disease has been clearly defined pathologically from other types of megacolon, it has been possible to attempt a genetic analysis of the condition Bodian, Carter and Ward have made a start by investigating the families of their 40 cases and it is to be hoped that other centres will follow suit One valuable fact has already emerged that the chances of brothers of children with Hirschsprung's disease being affected are about 1 in 4 or 5—an appreciable risk—whereas for sisters the chances are much lower

What is the explanation of the remarkable absence of intramural ganglion cells found histologically in a part of the bowel which looks normal to the naked eye? Unfortunately, the early stages of the development of Auerbach's and Meissner's plexuses are not yet fully understood Some authorities suggest that the intestinal neurones have a vagal and pelvic parasympathetic origin On the other hand, van Campenhout[4] has produced evidence in favour of their development from the thoracolumbar neural crest Again, Weber[5] suggests a local differentiation of neuroblasts in the mesenchyme of the gut wall Whatever the origin of the intestinal ganglion cells may turn out to be, Bodian and Carter point out that the characteristic distribution and variable length of the lesion in Hirschsprung's disease can be explained in terms of a disturbance affecting at variable stages the differentiation of intestinal neurones in a craniocaudal direction On embryological grounds, the disturbance probably occurs between the 30th and 35th days of fœtal life, and although a definite genetic factor has been established it would be worth while keeping a close eye on the antenatal history of the mothers of these children, especially in the 4th and 5th weeks of pregnancy Some "trauma"—whether infective, nutritional, or otherwise—may play a secondary part in the ætiology

---

[1] First Report July 1948 to March 1950

[1] Swenson O Bill A H, jun *Surgery* 1948 **24** 212

[2] Bodian M Stephens F D Ward B C H *Lancet* 1949 i 6

[3] Swenson O *Surgery* 1950 **28** 371

SOME FAMOUS DUBLINERS

LET bygones be bygones," the Englishman is apt to say—or anyhow to think—when confronting an Irish patriot moved by his country's history But what bygones! There was a time, as Mr William Doolin[6] reminds us, when the Irish were specifically excluded from the Dublin Guild of Barber Surgeons, though this piece of oppression, to be sure, was less villainous than it sounds, for the guild was founded in 1446 to tend the injuries sustained by the English soldiers in the defence of Dublin against the Irish The futile device of keeping the Irish out of their own institutions reached a peak at the end of the seventeenth century when the Irish Catholics who had supported the Stuarts were finally defeated, their lands being given to English settlers, and their religion proscribed They were excluded from the franchise, from the Bar and the Bench, from a seat in Parliament, and from any office under the Crown, and they were not even allowed to cut hair The oath of admission to the Guild of Barber Surgeons contained the ordinance "You shall not take any apprentice but of the Protestant religion " The English settlers became the founders of a new class, Protestant and Liberal, the Anglo Irish

The penal code against the Irish was, Mr Doolin says, of unparalleled severity, but he manages to be very good humoured about it, weighing the outcome of those times in a steady balance "To those privileged aristocrats of eighteenth century Dublin, we—Irish as well as English—owe a lasting debt" They gave us Swift, Berkeley, Steele, Goldsmith and Sheridan, Burke and Grattan, Thomas Moore, but no great doctors, for there was no school of medicine in Ireland until 1711, when the anatomy house was built in Trinity College, largely through the energy, foresight, and generosity of an Aberdonian, Sir Patrick Dun Yet even in 1741, when three King's professorships were founded in Trinity, there was the proviso that "all Papists shall be utterly *incompetent of being elected* " An Irish answer came to that in due course Sylvester O'Halloran, of Limerick, came back from Paris to practise medicine, and in 1764 put forward proposals for the advancement of surgery in Ireland a "convenient edifice" should be erected and three professors appointed, a register of practising surgeons should be compiled, candidates should apply for public examination, and the course should be attended with no kind of expense to the candidate, and should be "free to all Irishmen *only* without distinction" In 1780 the Dublin Society of Surgeons was established, and a year or two later the Barber Surgeons Guild was dissolved The surgeons were authorised to found their Royal College (but given no Government funds for the purpose)

In the eighteenth century Dublin contributed to British medicine the idea of the voluntary hospital, and of the special maternity hospital In the nineteenth century it gave the work of two outstanding men, *Abraham Colles, an Anglo Irishman,* and James Macartney, an Armagh man of Scottish stock, and men of note among the Irish-born trained in the Dublin schools are Alcock Crampton, Houston, Jacob, Porter, Todd, and later Macalister and Wilde

HALF A CENTURY OF ORTHOPÆDICS

THE current issue of the British volume of the *Journal of Bone and Joint Surgery* is devoted to a retrospect of progress in orthopædic surgery during the past fifty years Sir Reginald Watson Jones has collected a team of contributors from the world over to trace the developing patterns in America, Great Britain, the Dominions, and continental Europe

Leo Mayer of New York, describes the founding of the American Orthopædic Association and its subsequent growth, gives us vignettes of the grand old men of the period, and reminisces on Anglo American orthopædic comradeship in the field during the first world war under the leadership of Robert Jones and Joel Goldthwait Eminent United States authorities sum up their countrymen's advances in surgical technique, in the orthopædic application of biochemical discoveries, and in orthopædic research and education, and they remind us of the vast responsibilities of public authorities and orthopædists alike to the *crippled in peace and war* Sir Harry Platt tells of the great figures and pioneers in France, Belgium, Holland, Italy, Scandinavia, and Middle Europe, and gives a glimpse, as through a glass darkly of that enigmatic and oddly named man—Henry Turner of Leningrad Canadian orthopædics is the subject of a group of authors which includes R I Harris and W E Gallie, Jackson Burrows gives a sympathetic account of the Australian scene and other reports deal with New Zealand, South Africa, and Southern Rhodesia

But it is Osmond Clarke's survey of the men and events of the half century here in Britain that will stand out for most readers at home Polished, mildly nostalgic, yet alert and forward looking, it brings the mighty names which star his pages to life in vivid word pictures Robert Jones and Agnes Hunt, Muirhead Little and T P McMurray, Tubby, Hey Groves, Arbuthnot Lane, Trethowan, Elmslie, Naughton Dunn, and Lambrinudi, these are some of the giants—joined in the shades as this volume was in the press by that great and kindly man, Gathorne Girdlestone—on whose shoulders we have climbed and whom Osmond Clarke brilliantly portrays They are summed up in two reproductions one the unforgettable painting of Hugh Owen Thomas from the National Portrait Gallery, and the other a photograph of Robert Jones and Agnes Hunt walking together in the grounds of their early cripples' hospital at Oswestry Lloyd Griffiths presents some of the classics of British orthopædic literature, and the volume concludes with a collective review of intramedullary nailing in fractures, and a study of orthopædic endocrinological interrelations by Leonard Simpson

Sir Reginald Watson Jones has re created for us at just the right moment the spirit and atmosphere of an all important period before its memories have entirely faded

---

THE next session of the General Medical Council will open on Tuesday, Feb 27, at 2 P.M, when Prof David Campbell, the president, will take the chair

---

[4] van Campenhout, E *Arch Biol* 1931 42 479 *Ibid* 1947 58 1

[5] Weber, A *Bull Histol appl* 1940 17 149

[6] Dublin's Surgeon Anatomists Thomas Vicary lecture delivered at the Royal College of Surgeons of England on Dec 13 1950 *Ann R. Coll Surg* 1951, 8 1

Special Articles

MUNCHAUSEN'S SYNDROME

RICHARD ASHER
M.D Lond, M.R C.P

HERE is described a common syndrome which most doctors have seen, but about which little has been written Like the famous Baron von Munchausen, the persons affected have always travelled widely, and their stories, like those attributed to him,[1] are both dramatic and untruthful Accordingly the syndrome is respectfully dedicated to the baron, and named after him

The patient showing the syndrome is admitted to hospital with apparent acute illness supported by a plausible and dramatic history Usually his story is largely made up of falsehoods, he is found to have attended, and deceived, an astounding number of other hospitals, and he nearly always discharges himself against advice, after quarrelling violently with both doctors and nurses A large number of abdominal scars is particularly characteristic of this condition

That is a general outline, and few doctors can boast that they have never been hoodwinked by the condition Often the diagnosis is made by a passing doctor or sister, who, recognising the patient and his performance, exclaims "I know that man We had him in St Quinidine's two years ago and thought he had a perforated ulcer He's the man who always collapses on buses and tells a story about being an ex submarine commander who was tortured by the Gestapo" Equally often, the trickster is first revealed in the hospital dining room, when, with a burst of laughter, one of the older residents exclaims "Good heavens, you haven't got Luella Priskins in again, surely? Why she's been in here three times before and in Barts, Mary's, and Guy's as well. She sometimes comes in with a different name, but always says she's coughed up pints of blood and tells a story about being an ex-opera singer and helping in the French resistance movement"

DIAGNOSIS

It is almost impossible to be certain of the diagnosis at first, and it requires a bold casualty officer to refuse admission Usually the patient seems seriously ill and is admitted unless someone who has seen him before is there to expose his past Experienced front gate porters are often invaluable at doing this

The following are useful pointers

1. (Already mentioned) a multiplicity of scars, often abdominal
2. A mixture of truculence and evasiveness in manner
3. An immediate history which is always acute and harrowing yet not entirely convincing—overwhelmingly severe abdominal pain of uncertain type, cataclysmal blood loss unsupported by corresponding pallor dramatic loss of consciousness, and so forth
4. A wallet or handbag stuffed with hospital attendance cards, insurance claim forms and litigious correspondence

If the patient is not recognised by an old acquaintance, the diagnosis is only gradually revealed by inquiries at other hospitals Some have given so much trouble elsewhere they have been placed on hospital black lists Often the police are found to know the patient and can give many helpful details Gradually the true history is pieced together and the patient's own story is seen to be a matrix of fantasy and falsehood, in which fragments of complete truth are surprisingly imbedded. Just as the patient's story is not wholly false, so neither are all the symptoms, and it must be recognised that these patients are often quite ill, although their illness is shrouded by duplicity and distortion When the whole truth is known, past history sometimes reveals drug-addiction, mental hospital treatment, or prison sentences, but these factors are *not constant*, and the past may consist solely in innumerable admissions to hospitals and evidence of pathological lying Often a real organic lesion from the past has left some genuine physical signs which the patient uses (to quote Pooh Bah) "to give artistic verisimilitude to an otherwise bald and unconvincing narrative"

SOME CHARACTERISTIC FEATURES

Most cases resemble organic emergencies Well-known varieties are

1. The acute abdominal type (laparotomophilia migrans) which is the most common. Some of these patients have been operated on so often that the development of genuine intestinal obstruction from adhesions may confuse the picture
2. The hæmorrhagic type, who specialise in bleeding from lungs or stomach, or other blood loss They are colloquially known as "hæmoptysis merchants" and "hæmatemesis merchants."
3. The neurological type, presenting with paroxysmal headache, loss of consciousness, or peculiar fits

The most remarkable feature of the syndrome is the apparent senselessness of it Unlike the malingerer, who may gain a definite end, these *patients often seem* to gain nothing except the discomfiture of unnecessary investigations or operations Their initial tolerance to the more brutish hospital measures is remarkable, yet they commonly discharge themselves after a few days with operation wounds scarcely healed, or intravenous drips still running

Another feature is their intense desire to deceive everybody as much as possible Many of their falsehoods seem to have little point They lie for the sake of lying They give false addresses, false names, and false occupations merely from a love of falsehood Their effrontery is sometimes formidable, and they may appear many times at the same hospital, hoping to meet a new doctor upon whom to practise their deception.

POSSIBLE MOTIVES

Sometimes the motive is never clearly ascertained, but *there are indications that one of the following* mechanisms may be involved

1. A desire to be the centre of interest and attention They may be suffering in fact from the Walter Mitty syndrome[2] but instead of playing the dramatic part of the surgeon, they submit to the equally dramatic rôle of the patient
2. A grudge against doctors and hospitals, which is satisfied by frustrating or deceiving them
3. A desire for drugs.
4. A desire to escape from the police (These patients often swallow foreign bodies, interfere with their wounds, or manipulate their thermometers)
5. A desire to get free board and lodgings for the night, despite the risk of investigations and treatment

Supplementing these scanty motives, there probably exists some strange twist of personality Perhaps most cases are hysterics, schizophrenics, masochists, or psychopaths of some kind but as a group they show such a constant pattern of behaviour that it is worth considering them together

ILLUSTRATIVE CASE RECORDS

Three cases of the abdominal type of Munchausen's syndrome are described below, for they show clearly the typical features of the advanced form of the disease Many other milder forms have been encountered, but it would be tedious if more were described All the names used in these case histories have been altered, though most of the names were false to start with, but doctors who have met any of the patients may find that the changed name gives a clue to the original one.

---

[1] Raspe R E et al (1785) Singular Travels Campaigns and Adventures of Baron Munchausen London Cresset Press 1948

[2] Thurber J The Secret Life of Walter Mitty My World and Welcome to It. London 1942

I

A man of 47, giving the name Thomas Beeches, was transferred to the Central Middlesex Mental Observation Ward on May 16 from Harrow Hospital. He had been admitted there on May 13 with suspected intestinal obstruction; laparotomy had shown nothing abnormal. After the operation he had accused the ward sister of tampering with his wallet while he was under the anæsthetic, he had become truculent and demanded his discharge, and because of his violence, and his foolhardiness in wanting to walk out with a day old laparotomy, he was sent for mental observation.

On examination he was rational and convincing. His abdomen was a mass of scars of various vintage. He explained that while in the Merchant Navy in 1942 he had been torpedoed, suffering multiple abdominal injuries. He was then taken prisoner by the Japanese and kept in Singapore till 1945. Throughout this time he had multiple discharging fæcal fistulæ. In 1945, after the liberation of Singapore, he had been taken to Freemantle where he had eleven operations in 7 months (to close the multiple fistulæ), since when he had been continuously at sea till 4 days previously.

The characteristic Munchausen flavour of this history led to further inquiries which revealed that only 8 days previously, while supposed to be at sea, he had been in St James' Hospital, Balham, complaining of acute abdominal pain, and that a year before that he had been in the same hospital and again behaved in the same way. It was further found that in 1943, when he should have been in Singapore, he had been admitted to the Central Middlesex Hospital complaining of "bursting open of an old torpedo wound" with a discharging sinus in the right iliac fossa. He had then told such a bewildering series of different stories that he had been transferred to Shenley Hospital as a chronic delinquent psychopath, where he was observed for 2 months and then discharged. At Shenley it was discovered that he had a long history of delinquency and had three past convictions for crime, as well as having been twice in West Park Mental Hospital. (He had escaped both times.) On this present occasion no certifiable abnormality could be found and he was discharged on May 19, 3 days after admission. No doubt he is still going from one hospital to another.

A fortnight later, a surgical registrar, knowing my interest in Munchausen's syndrome, produced the notes of a case he had encountered at the Norfolk and Norwich Hospital. It was interesting but not surprising to find that it was the same patient. The notes showed that a Thomas Beeches had been admitted on June 23, 1949, as a case of acute intestinal obstruction. He told a story of having been 33 years in the R.A.F. and of having been shot down over Mannheim in 1942, after which he needed "eight abdominal operations and three short circuits." After treatment with morphine, intravenous drip, and gastric suction, he refused a laparotomy and discharged himself against advice on June 26.

II

A woman of 29, giving the name of Margaret Coke, was admitted on June 13, 1948, complaining of 3 days' severe abdominal pain and vomiting. Her abdomen was a mass of scars. Though admitted from an Edgware address, she gave a home address in Houston, Texas, and said that all her previous operations had been done there, some of them by a "horse doctor." Clinically, she appeared to have subacute intestinal obstruction and was treated with morphine and a Miller Abbot tube, but she discharged herself on June 19 at her own request.

Three weeks later, on July 3, a woman calling herself Elsie Silverborough was admitted to another ward at the Central Middlesex Hospital, having been found collapsed in the street by the police. She gave a home address in Lancashire. It was found she had discharged herself that day from Wembley Hospital, where she had been admitted on the previous day for suspected acute intestinal obstruction. As before, she had been found by the police collapsed in the street. Elsie Silverborough told a story of having had all her previous operations at the Manchester Royal Infirmary, but a surgical registrar recognised her as the Margaret Coke who had been operated on by the Texas horse doctor, and they were proved to be one and the same person.

Inquiries at Manchester Royal Infirmary revealed no trace of either Margaret Coke or Elsie Silverborough having been there, but the day after the identities of these two persons had been merged, a surgical houseman recognised the patient as a certain Elsie Packoma whom he had encountered twice at the Royal Northern Hospital on Oct. 27, 1947, and Nov. 13, 1947. On both occasions she had arrived in casualty smelling of drink and complaining of retention of urine. On the first occasion she was catheterised and then refused all treatment, refused to sign the book or to be admitted, and said she was going to a hotel to call in her private doctor. On the second occasion, she was recognised by the casualty officer and made off before a doctor had seen her. Further inquiries at the Manchester Royal Infirmary revealed that an Elsie Packoma, with a scarred abdomen and a Manchester address, had been admitted as a case of intestinal obstruction on Nov. 15, 1947—two days after discharging herself from the Royal Northern Hospital. No operation had been performed. She had been treated with morphine, Ryle's tube, and enemata, and discharged herself against advice 2 days after admission.

The triad of Margaret Coke, Elsie Silverborough, and Elsie Packoma was discharged from the Central Middlesex Hospital on July 6, 1948, and nothing further has been heard of it. She told us before she went that she had lived in Piccadilly nearly all her life, working as a prostitute.

III

A woman of 41, giving the name Elsie De Coverley, was admitted to the Central Middlesex Hospital on Feb. 7, 1950, having collapsed on a bus. She gave a history of 2 days' melæna and 1 day's severe abdominal pain with vomiting of dark blood. On examination she was apparently in severe pain. Her abdomen was a mass of scars and her veins showed marks of many "cutting down" operations. Her heart showed a mitral presystolic murmur. She told us that in the last 5 years she had had two operations for perforation, one for gastro enterostomy and one for intestinal obstruction, all done at the Royal Devon and Exeter Hospital, where she said she was due to return for a partial gastrectomy.

At first she was diagnosed as a case of a bleeding ulcer with probably a small perforation, but despite her severe pain there was no abdominal rigidity and radiography showed no gas under the diaphragm. Her hæmoglobin was 90 % and her stools gave only a weakly positive benzidine test. A telephone message to the Royal Devon and Exeter Hospital revealed that she had only once been there in 1944 and had never had an abdominal operation there, but that many other hospitals had made inquiries about her. The patient continued to complain of severe abdominal pain, and a barium meal and gastroscopy had been arranged when she discharged herself against advice on Feb. 15, saying that nobody really thought she had pain.

Since that time an attempt has been made to find out about her past, and here the Royal Devon and Exeter Hospital have been most helpful, because they have been able to trace much of her progress round the country by noting the hospitals that asked after her. More inquiries at these hospitals have each disclosed more admissions at other hospitals, and the complexity of the patient's wanderings grew in the manner of a snowball. I had not the time or the patience to pursue the meanderings completely and the fact that she was found to use nine different names made the project more formidable. The following list of some of her activities is probably incomplete.

In February, 1944, she was admitted to the Royal Devon and Exeter Hospital as Elsie De Coverley from Exeter Prison, with epistaxis.

On April 9, 1947 she was admitted to the Croydon General Hospital as Miss Joan Morris, a shorthand typist, giving long history of dyspepsia and hæmatemesis While being reated with rest and diet she discharged herself 2 days later

From Oct 31 till Nov 16, 1947, she was in the Royal Sussex Hospital, giving the name Joan Summer, and suspected of having a bleeding leaking ulcer , but at operation the findings were subacute obstruction from adhesions and scarred duodenal ulcer Gastrojejunostomy was performed She discharged herself on Nov 16 against advice, still complaining of severe abdominal pain

On Dec 10, 1947, she was admitted to the Croydon General Hospital with acute abdominal pain, ' doubled up in agony," as Mrs Elsie Layton, a district nurse She said she was awaiting a partial gastrectomy in Birmingham Hospital Efforts made to contact her relatives showed that the names and addresses were all false and the patient discharged herself on Dec 12 She was admitted to Redhill County Hospital a few days after leaving Croydon She again gave a similar story and discharged herself within a few days

From Jan 29 to March 29, 1948, she was in Paddington Hospital, again as Joan Summer, and a laparotomy for bleeding duodenal ulcer was performed , later she complained of severe anginal pain and discharged herself after giving much trouble in the ward

In March, 1948, she was in the West London Hospital as Joan Lark with alleged pain and bleeding, and discharged herself

From April 6 to 9, 1948, she was in Fulham Hospital as Joan Summer giving a history of having all her previous operations in York (inquiries at York failed to trace her), and again presenting with alleged abdominal pain and hæmatemesis On April 9 she was recognised by a surgeon as Joan Lark of the West London and discharged herself that day

On July 10, 1948 she was admitted to Guy's Hospital as Joan Malkin, but later said this was an assumed name and gave the name Joan De Coverley, and said all her previous operations had been done at Edinburgh (Edinburgh denied knowing her) At Guy's she was suspected of having a perforated ulcer, but a laparotomy on July 10 showed nothing abnormal except a mass of adhesions, and she discharged herself on July 13, only 3 days after the operation, and never returned to have her stitches out

On Jan 6, 1950, she was admitted to the Royal Free Hospital as Elsie De Coverley, with the usual story She complained of continuous pain and discharged herself on Jan 11, saying her sister had just died (At many hospitals she has given a story of a dying sister)

On Jan 18 she was admitted to St Mary Abbots Hospital still as Elsie De Coverley, having collapsed in Kensington High Street with alleged pain and vomiting of blood On Jan 20, when told she was not going to have an operation, she pulled out her stomach tube and demanded her immediate discharge

Later the same day, she was admitted to University College Hospital, and she had a laparotomy on Jan 25 for suspected perforation Nothing was found except adhesions The usual self discharge followed on Jan 30

The same day she was admitted to St Bartholomew's Hospital and discharged herself on Feb 2

From Feb 7 till 15 she was in the Central Middlesex Hospital—see the description at the beginning of this story

Since leaving us she has remained active, because on March 7 she arrived at the Elizabeth Garrett Anderson Hospital as Jean Hops and was transferred via the Emergency Bed Service to the Royal Free Hospital The transfer was unfortunate for her because she was recognised by the ward sister and registrar at the Royal Free, where she had been under another name in January this year, and she discharged herself immediately

On March 27 she was admitted to Middlesex Hospital as Elsie De Coverley, with the usual story of pain and hæmatemesis, where she remained for three days She discharged herself when she learnt that inquiries were being made about her at the Royal Devon and Exeter Hospital

On April 12 she was admitted to the Croydon General saying she was awaiting a partial gastrectomy at the Royal Devon and Exeter Hospital, and giving a history of severe abdominal pain and bleeding The Croydon General rang the Royal Devon and Exeter Hospital and while the telephone conversation was being conducted she got out of bed, dressed, and made off

On April 17 she turned up in Hackney Hospital as Elsie Shackleton, and that is the last that has been heard of her Probably she is now careful to avoid mentioning the Royal Devon and Exeter Hospital, who have repeatedly exposed her in the past, and, with new names and a slightly different story, is continuing to deceive the few remaining hospitals which she has not yet visited

It seemed worth publishing this rather tedious itinerary in full to show the lengths to which a case of Munchausen's syndrome can develop, and also because it may be a help to surgeons and physicians who are confronted by her case in the future

CONCLUSION

The syndrome of Baron von Munchausen has been described and three typical cases reported

These patients waste an enormous amount of time and trouble in hospitals If any correspondence follows this account, exposing other cases, perhaps some good will have been done It would be even better if an explanation for the condition could be found, which might lead to a cure of the psychological kink which produces the disease

I wish to thank the many doctors and records officers who supplied information about these cases, particularly Mr K P S Caldwell who traced most of the migrations of case 3

COST OF HOSPITALS

Some Facts from Scotland

THE Department of Health in Edinburgh has been working away industriously at hospital " cost " statistics The obligation to make good use of the material now coming to hand in respect of the six Scottish regions for 1949–50 is clearly felt strongly The department deserves a good mark—not yet earned by the Ministry of Health in London, or by any of the regions in England and Wales—for coming forward and offering its efforts for publication and criticism

Much of this material is of considerable interest It is based on the first full year's figures available—i e , 1949–50, when the total bill for Scotland, including specialist services, was £21,933,000 A total showing the relative importance of the several elements in the hospital cost proper, which amounted to £17,691,000, shows the following picture

	% of total	
Patients food	9 8	
Patients clothing and laundry	3 1	
Drugs dressings surgical appliances &c	6 1	
1 COSTS ATTRIBUTABLE TO PATIENTS		19 0
Maintenance of buildings and grounds	2 7	
Domestic repairs and replacements	6 0	
Fuel light and power	8 2	
2 COSTS ATTRIBUTABLE TO BUILDINGS		16 9
3 MISCELLANEOUS—administration transport travelling amenities trading services rent and rates &c		4 9
Staff food laundry and uniforms	4 5	
Salaries and wages—junior medical staff	2 3	
—nursing staff	28 8	
—administrative staff	4 3	
—other staff	19 3	
4 COSTS ATTRIBUTABLE TO STAFF		59 2
Total		100 0

Commenting on these figures the Secretary of State has pointed out that it is thus clear that most of the money is going on staff salaries and upkeep and that control over staff establishment is therefore of decisive importance as a means of ensuring economy Expenditure, however, on the salaries of those who are solely concerned with administrative and clerical work of the hospitals represents only some 2½% " In the light of these figures," he said, " it does seem to me to be sheer nonsense to talk wildly of saving millions on the Health Services by slashing administrative waste in the hospitals "

Another total shows the costs of hospital beds per day category by category The department uses for this purpose a "composite" cost of its own devising, built up in an effort to strike a useful compromise between the cost per occupied bed and cost per bed calculated on the complement irrespective of occupancy This method no doubt has merit, but it is perhaps a pity to use it without showing also a straight cost per occupied bed, which, despite its well known defects, has been widely adopted in hospitals in Great Britain

	Composite rate s	d
General hospitals—		
1—50 beds	21	11*
51—300 beds	2[illegible]	[illegible]
301—900 beds	28	8
All general hospitals	2[illegible]	7
Infectious diseases hospitals	22	9
Maternity hospitals	37	8
Tuberculosis sanatoria	20	0
Convalescent hospitals and homes	15	4
Mental hospitals	11	6
Mental deficiency institutions	10	4
All hospitals	18	4

* To the nearest 1*d*

The department offers this table as a yardstick against which the regional boards would be wise to check the costs of individual hospitals, and by way of emphasising this examples are given of groups of presumably comparable hospitals showing wide variations from the average cost, for example, mental hospitals are compared

> "Most of them are fairly large, their functions are similar and their rates of occupancy are uniformly high There are a few wholly exceptional ones but these are all omitted from the comparisons below The composite occupied bed day rate for all mental hospitals in Scotland is 11*s* 6*d* The highest figure for any single hospital is 16*s* 9½*d*, the lowest is 7*s* 5½*d* If the national mean is taken as 100, there are two hospitals under 70 and five more under 80, there are, also, three over 130 These variations make a big difference in the annual expenditure The rate of 16*s* 9½*d* for the hospital in question represents an annual expenditure of £31,140 more than the average rate of 11*s* 6*d* would produce, the rate of 7*s* 5½*d* represents an annual expenditure of £32,374 less It is hard to believe that these wide variations can be accounted for except by substantial differences in standards of accommodation and of care and treatment and the abnormally low costs must be a matter for serious concern as well as the abnormally high"

The regions are urged to look into these matters, but here the department has to confess its bankruptcy In the absence of a system of departmental analysis it cannot offer any further help at the point at which it is really needed The Secretary of State did say that it is proposed "to tackle also the comparative analysis of expenditure in various fields" and to look first at things like *food costs, fuel, light and power*, and that another possibility would be to compare two X ray departments one with another But is this going far enough? The urgency and the fundamental importance of a proper system of departmental analysis of expenditure does not seem to have been grasped Tables similar in principle to those now offered by the department were available for the former voluntary hospitals in London through the King's Fund's statistical summary for the last fifty years, it is primarily the fact that such tables, though most useful, are no more than an unsatisfactory half way house that has led the Minister of Health to set on foot the important investigation into hospital costing now being undertaken by King Edward's Hospital Fund for London and the Nuffield Provincial Hospitals Trust

But the Department of Health has also branched out in another direction It has prepared data comparing one region with another under a variety of headings, and has ventured to set down data comparing beds to populations Ever since serious quantitative discussion of hospital affairs began in the '30s, assuming the possibility of a comprehensive service, it has been evident that what is really a new science of hospital provision was about to dawn upon us Here now at last is the first serious set of figures based on a whole year and comparing sizable areas one with another It has always been suspected that the figures when produced would show substantial variations from the norm, and so they do

—	Northern	North eastern	Eastern	South eastern	Western	Scotland
Beds per 100 000 of population	99	85	128	89	103	100 = 1[illegible]
Ratio of nurses to staffed beds	84	112	95	106	98	100 = 0[illegible]
Ratio of nurses to staffed beds excluding mental hospitals and institutions	93	114	98	107	95	100 = 0 4[illegible]
Ratio of other staff to staffed beds (excluding doctors and nurses)	81	83	112	105	100	100 = 0 43
Ratio of specialists to staffed beds	100	100	84	113	98	100 = 16·[illegible] per 1000
Ratio of specialists to population	107	97	114	99	99	100 = 1 3 per 10 000
Annual specialist costs per staffed bed	92 3	99 7	72 9	122 9	97 7	100 = £17 1[illegible]
Annual specialist costs per head of population	93 8	89 5	100 8	106 3	98 4	100 = 10s [illegible]
Composite in patient day rate	99 5	95 9	97 3	99 6	101 4	100 = 18s [illegible]

On this head the department is certainly to be congratulated, not so much for its achievement as for setting sail on an uncharted sea Who is going to be the first to devise the really instructive way of handling data such as these? Who is going to be able to say that there, and there, and there, are hospitals that work twice as effectively or twice as cheaply as the others? The Department of Health think that "unless there are special circumstances to the contrary in any particular Region it should be the first object of policy to encourage developments in those particular fields in which the Region is least favourably placed" But is this the right way to look at it? May the signs not be read to mean that these are precisely the fields in which success has been achieved or where perhaps preventive factors in their widest sense are most effectively deployed? It would be a pity if such useful tables were to be read in the light of the assumption that progress is synonymous with increasing hospital services May we hope that in each Scottish region at least one medical officer of health will fasten upon the data and try to see that they are *read the right way up and not the wrong way down*

"The influence of mind on body was recognised long before anyone began to talk of psychosomatic medicine and no doubt there were many family doctors in the nineteenth century who were just as good at treating nervous dyspepsia as anyone is nowadays with Freud or Jung behind them You may remember the heroine of Jane Austen's youthful burlesque who said 'Beware of swoons, dear Laura A frenzy fit is not one quarter so pernicious It is an exercise to the body and if not too violent is I dare say conducive to health and its consequences"—Prof E D ADRIAN, O.M., F.R.S, *Conquest*, 1951, 38, 2

Medicine and the Law

Secrecy of Service Medical Reports

EXECUTIVE councils have lately been assured that the Admiralty, War Office, and Air Ministry will continue to make available the medical reports of persons discharged on medical grounds from the Forces But, it is stated in E C N 68, the reports are supplied to practitioners in confidence for the sole purpose of helping them in their treatment of the patient, and must therefore not be disclosed either to the patient or to any other party If, continues E C N 68, a subpœna is served on the practitioner to produce a Service medical record in court, the practitioner should not return the report to the Service department, but should at once tell the department so that the responsible Minister can have an opportunity of giving him a certificate claiming "Crown privilege" for it and directing him not to produce it

A year ago we recorded[1] a refusal by the War Office to allow a coroner's court to have evidence of an Army doctor's previous medical examination of a soldier who dropped dead during a course at the Guards' depot at Caterham The coroner adjourned the inquest in the hope that the Army doctor would attend to give the evidence, but the War Office claimed privilege on the grounds of public interest

"Crown privilege," said Lord Simon in Duncan *v* Cammell Laird and Co (1942), the leading case on the subject, "is an unhappy expression" Privilege, in relation to "discovery" (i e, the litigant's obligation to disclose facts and documents which might tend to establish his opponent's case) is for the protection of the litigant and may be waived by him, but the rule that the national interest must not be jeopardised by producing documents which would injure the State is a principle quite unconnected with the interests or claims of the particular litigant Where the document contains information about a patient, there is clearly a sharp distinction between the Crown's "privilege" and the patient's

The Cammell Laird litigation arose out of the sinking of the submarine *Thetis* during her submergence trials in June, 1939 when 99 men lost their lives In a test case against the company the Crown claimed privilege in respect of several documents, including the contract for the hull and machinery, the plans and specifications, the report of the submarine s condition when raised and a foreman painter s note book The First Lord of the Admiralty testified in an affidavit that production of these documents would be injurious to the public interest In effect the House of Lords refused to interfere and the significance of Lord Simon s opinion is that he prescribes the considerations which a responsible Minister must have in mind when making such objections to disclosure It would not be a good ground he said, to contend that, if the documents were produced, the consequences might involve the department or the Government in parliamentary discussion or public criticism or might necessitate the attendance as witnesses or otherwise of officials who have pressing duties elsewhere The Minister must not refuse disclosure on the ground that it might tend to expose a want of efficiency in the department or to lay the department open to claims for compensation It was not enough that the department should want non disclosure There must be some such ground as that disclosure would be injurious to national defence or to good diplomatic relations, or that the practice of keeping a class of documents secret was necessary for the proper functioning of the public service

If a discharged soldier's medical history sheets are kept secret even from himself, the War Office presumably justifies the secrecy as "necessary" in that sense

Before the Crown Proceedings Act of 1947 came into operation, the Crown, when a party to a suit, could never be ordered by a court to make discovery of documents the Act now allows such orders to be made In confirmation, however, of the decision in the Cammell Laird case the Act allows the responsible Minister still to withhold a document on the ground that disclosure would be injurious to the public interest The Act contemplates (and the rules of court made thereunder allow) that the Minister may even conceal the existence of a document if disclosure would be thus injurious

There seems a wide difference of degree between non disclosure of a new submarine's secret plans and that of a soldier's medical record where his own interest may be at stake The Ministry of Health seems to expect that some discharged men will not consent that their Service medical history be disclosed to their doctor in civil life The doctor will have to apply to the executive council on form E C 53, which provides for the patient's consent to disclosure It is a complicated procedure, and the councils may have plenty of documents to file If the only privilege in the case were the professional privilege between doctor and patient, the profession would know how to deal with it

---

[1] *Lancet* 1950 i 186 273

Parliament

Kingston Victoria Hospital

IN the House of Commons on Jan 30 Mr C W BLACK raised once more the position of the Kingston and Malden Victoria Hospital[1] A new situation had arisen, he said, since the beginning of November, when notice had been given to the hospital authorities that no more patients were to be received That order was not complied with by the doctors or the hospital authorities Whatever the legal niceties of the position might be, the action of the doctors and the hospital staffs had been condoned by the regional hospital board, which had continued to pay the salaries and the running expenses connected with the hospital The proposal that this much-esteemed local hospital should lose its independence had been strongly criticised by local and medical opinion After outlining the course of the dispute, Mr Black said he did not ask the Minister at this juncture to override the decision of the regional hospital board, but to set up an independent and impartial inquiry

Sir IAN FRASER said this situation was parallel to that of the Victoria Hospital, Morecambe, and there were about 20 or 30 other towns in the same position He asked the Minister not to confine his answer to the local issue but to deal with the wider issues involved Mr FRED MESSER declared that if the Minister conceded what had been asked he would have trouble from one end of the country to the other The regional hospital boards had been set up to plan the health service. What did not strike Mr Black and those local people who opposed these proposals was that planning would result in an addition to the available beds Mr Messer asked the Minister to let the regional boards get on with their job

Mr H A MARQUAND the new Minister of Health, said that he assumed that they were all in favour of a health service and of a regional organisation for that purpose Reorganisation was bound to affect some of the smaller hospitals which covered the wider range of specialties and yet had few beds and perhaps lacked other facilities. In every one of these schemes such hospitals had to give up some of these specialties and become a unit for one specialty only in order that one adequate unit might be available in every committee group That was the essence of the planning of the regional hospital boards, and consequently the functions of this particular hospital had to be changed for the better service of the public There was no question of animus on the part of the regional board or the Ministry of Health against a general-practitioner hospital as such

It had been found, he continued, that in the Kingston area there was an outstanding need for a first-class gynæcological unit. He was told that there were nearly 300 women on the waiting-list which could not be cut down until the scattered gynæcological facilities were centralised and improved He was sure that the regional board had considered this matter carefully and he did not see why he should reject their opinion that the scheme could not be worked without using the exceptional facilities of the Kingston Victoria Hospital to create there this gynæcological unit That was the place chosen because it was close to the specialised skill and equipment possessed by the Kingston Hospital

---

[1] See *Lancet* 1950 ii 527 832

It was unfortunate that the plan meant that some patients would no longer be able to use this hospital, but there was no doubt that its facilities and 11 beds would be better used for the proposed purpose than in an attempt to deal in such a small compass with all aspects of medical and research work Proper safeguards for the general practitioners using the hospital at present were preserved under this scheme , they were not to be cut off from hospital work altogether and the Surbiton Annexe could, he believed, be made a satisfactory building, and he asked the general practitioners of Kingston for their cooperation The gains, Mr Marquand pointed out, would be substantial Among the six or seven hospitals in the Kingston area there would be 226 beds under the new scheme, as against 203 at present, 102 maternity beds as against 81, and 11 gynæcological beds as against 37 Apart from these increases in beds there would be an increase in facilities There had already been ample inquiry into this matter All the facts were known, and action had to be taken on the basis of those facts If, however, members would like to bring a deputation to him and allow him to explain the scheme in greater fullness he would gladly do that But he was not prepared to hold up the work on the annexe

Cleanliness in Handling Food

In the House of Commons on Feb 2, Dr A D D BROUGHTON moved that action should be taken by the Government to encourage cleanliness in the preparation and serving of food in retail shops and catering establishments One of the first essentials, he believed, was clean hands when dealing with food, but there were still food shops with no adequate washing facilities Food-poisoning was increasing , before the war there were 50 outbreaks a year , now there were nearly 1000 most of which had been traced to food eaten or prepared outside the home Communal feeding was increasing and the population were eating more and more made up foods He urged the Government to introduce a Bill requiring catering establishments to register with their local authority , to encourage local authorities to adopt a standard code of practice for catering establishments , and to encourage education in hygiene

Dr BARNETT STROSS held the figure of 1100 persons stated in the report of the Medical Research Council to have been affected by food-poisoning in 1949 to be an underestimate At a guess he thought the number of cases in an average year might be as high as 50,000 with a consequent loss of 100,000–500,000 working days Among the 1100 cases in 1949, there were 58 deaths The Medical Research Council had analysed 339 outbreaks or instances of food-poisoning in 1949 , and of these, 222 attacks, or 65%, were traced to meat dishes, and 195 of these were due to made up meat dishes Fish caused 46 outbreaks, or 14% , 30 outbreaks were due to duck eggs, and 5 outbreaks were traced to milk In school canteens there were 68 outbreaks, in works canteens 32, in restaurants and hotels 35, in hospitals and institutions 44 Workers with discharging wounds or diarrhœa must not be allowed to handle food and must be compensated for loss of earnings He believed the fullest medical supervision of workers to be impossible, and anything less was useless But premises could and should be inspected

Mr SOMERVILLE HASTINGS was sure that some of the epidemics of food-poisoning associated with minced meat and sausages occurred not because anything was wrong with the food but because the mincing machines had been imperfectly washed Washing up in public restaurants and bars was often imperfect and was a real danger Diarrhœa, ulcerated gums, and influenza, had been traced to that source Recent work suggested that if utensils were put into water at nearly boiling-point for about 30 to 60 seconds, there was little additional danger from cracked crockery Mr Hastings held that authorities should have power to inspect dish-washing as well as the preparation of food There should be two washing-up bowls, and dishes should be dried by air, as towels used for wiping were a great source of danger

Dr CHARLES HILL pointed out that it was food that had been left about, usually milk products and made-up dishes, which was most dangerous The value of refrigeration should not be exaggerated the refrigerator suspended the activities of the germs, but when the food was withdrawn into a warmer temperature the energy of the germs returned unabated For the most part the agency of contamination was flies or fingers The public had to realise that disease carried in the bowel, in the nose or throat, and on the infected skin could be imparted to foodstuffs and lead to disease in hundreds of people. The problem was a restricted one There was no need to put people off their victuals by generalised scare talk The problem arose for the most part from careless or ignorant conduct on the part of food handlers. Prevention could only take place by convincing people of the dangers and that personal conduct would solve the problem. Today, Dr Hill said, it was much easier to engage in such propaganda with candour and frankness than it was some years ago

Mr F T WILLEY, parliamentary secretary to the Ministry of Food agreed that the annual report of the Ministry of Health showed that the number of food poisoning outbreaks had increased from 422 in 1945 to 961 in 1948, and the number of individual cases of food poisoning from 6063 in 1949 to a provisional figure of 7180 in 1950 The increase might be partly due to improved diagnosis but that did not relieve us of responsibility, for if we are more aware of the dangers of food-poisoning, so much greater is the burden upon us to prevent it On the other hand, there were over a quarter million catering establishments serving a large number of meals every day Against this background the risk of food poisoning is infinitesimal Model by-laws had been adopted by 1100 local authorities, and there were many powers for local authorities to use On the question of registration of catering establishments, Mr Willey said there was a difference of opinion among the catering trade working party in the light of their recent report, and it was also too early to give an undertaking to enforce a code of practice on the catering industry It was essential that they should carry the industry with them Health departments were giving all the help they could and the Ministry of Food was doing everything possible to encourage educational activity in food hygiene Until practices which spread food infection were widely known, he thought it would be difficult to make further regulations or legislative changes effective

The motion was agreed to

Penicillin (Merchant Ships) Bill

In the House of Commons on Jan 29 this Bill which has already passed through the House of Lords was reported without amendment and read the third time and passed

QUESTION TIME

Treatment of Tuberculosis

Mr JOHN RODGERS asked the Minister of Health if he would inform all local authorities of the facilities available in the country for the rehabilitation of men and women suffering from tuberculosis and the desirability of using these facilities to their full capacity —Mr MARQUAND replied The attention of local health authorities has been drawn, most recently in July last, to the means available for this purpose, and I am sure they will share my view that they should assist in using these means to the full Mr RODGERS Is the Minister aware that the British Legion village of Preston Hall in Kent today has 50 vacancies for ambulant ex Servicemen, and will he again impress upon the local authorities their moral obligations in this matter ?—Mr MARQUAND I am sure that this exchange of question and answer will draw attention to the existence of these facilities

Tuberculosis Beds

In answer to a question Mr MARQUAND stated comparable figures are not available for these, but that at Dec 31, 1949, 28,430 beds for tuberculous patients were in commission (including about 1250 beds used in hospitals outside the health service) In England and Wales at present the waiting list as provisionally ascertained was approximately 10,400, about 600 fewer than a year ago This was the first decrease recorded since the war

In answer to further questions Mr Marquand said that the possibility of using the available beds in Switzerland was being considered He had had two officials in Switzerland looking into the matter, and for technical reasons it had been decided to send at once a senior medical officer to amplify the report already rendered Discussions were going on with the Chancellor of the Exchequer Mr Marquand added that he had no power to make grants to tuberculous patients who tried to find accommodation for treatment in Switzerland at their own expense

Certified Lunatics and the Franchise

Colonel Leonard Ropner asked the Minister on what grounds he had decided to extend the franchise to certified lunatics —Mr Marquand replied The franchise has not been extended The law is and has been for many years, that apart from idiots, a person suffering from any form of mental disability, if on the electoral register, is entitled to vote if he presents himself at the appropriate polling station and satisfies the presiding officer as to his capacity to do so

Benefactors of Voluntary Hospitals

Sir John Mellor asked the Minister if he would identify the powers by which he had instructed benefactors under covenant of voluntary hospitals to pay instalments to him, and if he would refrain from enforcing such claims in the courts —Mr Marquand replied The powers are contained in section 7 of the National Health Service Act 1946 I am advised that a person who executed a deed of covenant has himself no power to cancel it, and I hope therefore that action in the courts to enforce compliance will not become necessary

Hospital Consultants

In answer to a question, Mr Marquand, the Minister of Health, stated that at Dec. 31, 1949 1309 full time consultants were in contract with the regional hospital boards The numbers were highest in the four Metropolitan boards (161–185) and lowest in Oxford (21), Liverpool (39) and Leeds (40)

Number of General Practitioners

In reply to a question Mr Marquand stated that the number of general practitioners on the medical list in the National Health Service in England and Wales on July 1, 1950, was 18,710

Immunisation and Limb Paralysis

Mr S P Viant asked the Minister whether any record existed of the number of cases of paralysis developing in the inoculated limb, one, two, or three months after immunisation —Mr Marquand replied Details are available for 1950 In that year 46 cases of paralysis developing in the inoculated limb after immunisation were reported Of these 35 occurred within one month, 10 in the second month, and 1 in the third month after immunisation

School Dental Service

Mr George Tomlinson, Minister of Education informed Mr John Baird that the number of dental officers in the school dental service at the end of 1950 was equivalent to 717 full time officers

Cancer Research

Mr George Thomas asked the Lord President of the Council whether he was now able to arrange for an increased grant for research into the causes and cure of cancer —Mr Herbert Morrison replied Substantial sums are already allocated by the Medical Research Council to research on this important subject and further provision is made by bodies such as the British Empire Cancer Campaign and the Imperial Cancer Research Fund I am unable to recommend any further grant at this time but a constant watch will be maintained for any new and promising lines of inquiry for which present resources may be inadequate

Replying to further questions Mr Morrison said the expenditure of the Medical Research Council for the current financial year on the cause and cure of cancer is estimated at £157 400 Further expenditure was expected to be incurred during the coming financial year In so far as promising lines of research opened themselves the Government would be ready to spend money but the spending of money in advance of research would be silly

Mr Somerville Hastings Has there been any demand from responsible members of the Medical Research Council for more money to be spent on cancer research ?—Mr Morrison I think not, Sir

In England Now

A Running Commentary by Peripatetic Correspondents

These economist chaps seem agreed that, if we are to maintain our present fancy standard of living, we must increase productivity Unless my educativity has been sadly neglected, productivity doesn't mean much more than production or output, and I suppose the only way you can increase your output is by putting more time to it None of us, of course, works as hard as he thinks he does, but I have been musing on the case of my friend, patient, and fellow-worker, Fred, who drives the lorry for the Council. Fred works a 44-hour week and has a fortnight's annual holiday with pay His health is generally good but he's apt to get flu in the winter and a go of lumbago in the summer That means another 4 weeks off sick, and he rightly gets public holidays, Christmas Day, *and so forth—call it another week* Now, if my arithmetic is right, Fred works 44 hours a week for 45 weeks in the year In other words, out of every 365 days of his life he works rather less than 87 My deductivity is that he is not achieving maximum productivity

* * *

"Mad Lou,' as she was called locally, was brought to our Observation Unit by the Police and the Duly Authorised Officer, together with Exhibit A—the coal-hammer with which she had threatened her neighbours, whom she imagined to be making abusive remarks about her Since she weighed twenty stone and was muscular in proportion it was easy to understand the consternation she had created. She seemed fairly happy with us, apart from periodic outbursts due to similar hallucinations, but Sister, finding her in tears some days later, discovered that she was grieving for Peter, who turned out to be not a long-lost son but a large ginger and-white cat, abandoned in Lou's unceremonious departure from home We made inquiries and found that Peter had been handed over by the Police to the R S.P C.A, but Lou had neither family nor friends, and none of the neighbours would adopt her cat, so it seemed that he would have to be destroyed when his mistress, in a few days' time, was removed to a mental hospital under certificate

The D A O, Sister, and I asked all the hospitals in our catchment area, and finally I struck a particularly humane medical superintendent and secured a double vacancy Lou s delight on hearing that she was to have Peter with her was touching to behold, but when the day came for her transfer to hospital, the ambulance was getting ready outside, and there was still no sign of Peter, she reverted to tearful suspicion, evidently believing she was being lured to her doom by false promises Fortunately, the R S.P C.A. man arrived at the gallop, in the nick of time, with the bewildered Peter in a basket He had gone by mistake to another hospital nearby, where his breathless inquiries for an ambulance waiting for a cat had led to his being hastily re-directed to us—we felt he was lucky not to have been sent under escort

Lou, with Peter in his basket, and one of our sisters, were bundled into the ambulance, the Cockney driver remarking drily that he *hoped* his insurance covered cat-bites, and off they went On the journey, Peter miaowed so piteously that Sister let him spring out of his basket into Lou's arms, where he settled down peacefully When they reached the hospital Lou still thought the whole thing was a trap, and my friend the superintendent had to come to the ambulance and reassure her personally that Peter would not be taken away from her The last thing Sister saw of them was Lou lying on a bed in the admission ward clasping the purring Peter to her ample bosom.

Tail-piece.—On phoning a few days later I was told that Lou is settling in happily and that Peter has become the pet of the ward Lou much prefers her new quarters —"It's not like that Other Place," she remarks with a sniff, 'they wouldn't let me 'ave Peter with me *there*" Just as I am digesting this news, Sister enters the clinical room and tells me that Mrs X, an extremely paranoid patient, is now asking why she can't take her three dogs when she goes to hospital tomorrow

* * *

An interesting panorama of the contemporary French school of art has been assembled at the Royal Academy (L'École de Paris, 1900–50) and will be on exhibition until March 7 There are 162 pictures on view, about a third of them abstract The five by Matisse illustrate clearly his characteristic drawing, with its intentional distortion, and his love of clear sweeps of bright colour Kandinsky, the originator of the Abstractionists, is represented by four pictures His "Violet Dominant" will either make you feel very humble or irritate you extremely But as he paints to produce an emotion, perhaps this is a measure of his success Apparently Picasso will not allow his pictures to be shown officially in England, owing to his political convictions However, the Cubists are well represented and from these pictures, with their striving for strength through insistence on the straight line and distortion, one can understand their affinity with Communism they certainly cannot be accused of bourgeois sentimentality Among these more extreme schools there are some excellent examples of such French Realists as *Utrillo, Vuillard, and Bonnard* I found Utrillo's suburban scenes particularly effective, but Marquet's "Docks at Le Havre," Soutine's "After the Storm," Bauchant's "Asters," and Marchand's "Snow Landscape" are all delightful and show that the Paris School is not entirely concerned with Abstract Those who like searching out psychological motifs will no doubt point to Coutaud's "L'Armoire Chair de la Porteuse de Pain" as a demonstration of coprophilia and to Miro's "Bull Fight" as one of infantilism

The Academy's exhibition of "Holbein and other Masters of the 16th and 17th Centuries" is still open and will be until March 7—a magnificent collection of early English *portraits* *Medical visitors should note the* large picture of Henry VIII presenting a charter to the Guild of Barber Surgeons and Carlo Dolci's portrait of Sir Thomas Baines (1622–81) The collection includes works by Eworth, Titian, Tintoretto, Van Dyck, Rubens, Raphael, Michelangelo, and Leonardo da Vinci (one), so I need say no more I found it a welcome relaxation after the École de Paris

* * *

The series of articles appearing in *The Lancet* on the techniques in Medical Lifemanship are filling a long felt want A search through the shelves of a well-known medical bookseller has failed to reveal a single textbook on this subject, and it is indeed fortunate that my own two works—*Recent Advances* and *Students' Aids* are nearing completion Meanwhile the primary purpose of this note is to draw attention to a little known branch of which I, as a pathologist, have made a special study—namely, Labmanship Labmanship in a laboratory technician may be defined as getting one up on the pathologist, and vice versa A pretty example came my way the other day As I was examining the vibrio isolated from a patient's stools I remarked to our Senior Technician "I don't think it's a *choleræ*, Mr Hearty, do you?" Quick as thought, he replied, "No, sir, it's either a *berolinensis* or a *helcogenes*, but it's certainly not a *choleræ*" There is an effective counter-ploy which was first demonstrated by Xavier Odoreida, elder brother of the famous Old Wykehamist Xavvy spent three years as bacteriologist at St Rhoea's In the above case his counter ploy would have run something like this "I agree with you, Mr Hearty, but if it's not a *choleræ* I never bother to take it any further" These examples will show that Labmanship has its own problems and can legitimately claim to be regarded as a specialised branch of Medical Lifemanship I have felt for some time that there is room for a Section of Lifemanship at the Royal Society of Medicine, and I herewith invite any Fellows interested to communicate with me on the matter

* * *

Aphorism of the Week

We stand on our fathers' shoulders, but our children tread on our corns

Letters to the Editor

METHONIUM COMPOUNDS IN HIGH BLOOD-PRESSURE

SIR,—The statement has been made several times recently that the benefits to be derived from methonium salts in hypertension are uncertain, and that there is no strong indication that their introduction has changed the outlook for high blood pressure patients Experience here does not lead to this conclusion, and I have come to regard the benefits of effective methonium therapy in high blood pressure as of a different and higher order from those ordinarily obtainable by other methods Differences in the opinions held about the treatment seem to depend partly on the method of using the drugs

In a large hypertension clinic we have seen the results of thiocyanate,[1] salt free diets, and sympathectomy in the treatment of high blood pressure Recently with Dr Oliver Chapman a study has been made of some of the newer veratrum preparations All these measures produce some excellent results, but many failures With pentamethonium and hexamethonium salts, however, it is possible to obtain in almost all patients a much more effective control over blood pressure levels than has hitherto been practicable, and the relief of clinical manifestations secondary to the high blood pressure is correspondingly greater

In successive collaboration with Dr P A Restall[2] and Dr K S Alstad (unpublished) the effects of these substances have now been studied in 130 patients with substantial hypertension of various ætiology, and 3[illegible] patients with severe hypertension, including 9 with malignant hypertension, have been treated for one to twelve months, with no deaths The outspoken clinical improvements referred to in previous communications have been maintained

Our early results were obtained by subcutaneous injections We noted subsequently that authors reporting the effects of oral administration were less satisfied with their results than we had been with ours, therefore we continued mainly to employ subcutaneous injection

One factor which, in some instances, may have limited the degree of benefit obtained, whatever the method of administration, is that there has not been sufficient recognition of the tolerance which develops with continued administration of pentamethonium or hexamethonium salts, thus an initial dose of 15 mg subcutaneously may produce as great an effect as a dose of 80–200 mg administered by the same route after two or three months of continued treatment Hence, if a fixed routine dose is employed, the hypotensive effect of one and the same dose may prove dangerous in the early stages and ineffective later

Recently Dr. Kilpatrick and I have studied the effects of oral administration in a number of patients who, having developed the full degree of tolerance to subcutaneous injections of methonium salts, have had the desired amount of blood pressure reduction for several months without further increase in dose In such patients the effective oral dose is high, but some patients remain sufficiently sensitive to have a sufficient degree of blood pressure reduction with oral administration, even when full tolerance is established Several patients, however, could not take doses of hexamethonium bromide large enough to reduce the blood pressure, because of the prior onset of nausea, diarrhœa, or vomiting Other patients required an oral dose of 3000 mg of the drug to reduce the blood pressure Such a dose is of the order of 20 times the effective subcutaneous dose and should not be administered outside hospital, because an alteration in the rate of alimentary absorption could be dangerous, and delayed absorption is not unusual

---

[1] Alstad K S *Brit Heart J* 1949 11, 249
N Z *med J* 1950 49 200

Patients who have not been treated previously with methonium salts respond to much smaller oral doses for example, 500 mg commonly induces a fall of blood-pressure in the upright posture It would appear, therefore, that tolerance develops in the course of oral administration as well as with subcutaneous dosage With oral administration the drug action is more capricious even under rigidly controlled conditions Therefore we feel that continued effective oral therapy is sometimes impracticable , however, continued treatment by subcutaneous injection is almost always possible

In reducing blood pressure levels with methonium compounds there is more than the usual need to adjust the treatment to the individual response of the patient Without frequent observation in the initial stages it is only by chance that the patient will escape discomfort or danger on the one hand, and ineffectiveness on the other It is, however, my experience that these drugs can be used in such a way that they give unmistakable relief to a considerable proportion of hypertensive patients , and, after a period of observation in hospital, outpatient care presents no difficulty

University of Otago
Dunedin New Zealand. F H SMIRK

BROMISM ON LOW-SALT DIETS

SIR,—My attention has recently been drawn to a danger associated with the use of low salt diets

A patient who had previously been in hospital with severe hypertension and left ventricular failure and who had been sent home on a low-sodium diet was readmitted in a state of mental confusion His blood-bromide level was found to be 360 mg per 100 ml. (expressed as NaBr) He had been treated with moderate doses of ammonium bromide by his own doctor His renal function was normal.

It became evident that doses of bromide which would be well tolerated by people on normal diets might lead to bromide retention in patients on a low salt intake for the body's excretory mechanisms cannot distinguish between the chloride and bromide ions

There were in the wards at that time four patients with hypertension who were being treated with hexamethonium bromide by mouth and who were also on a low-salt diet The blood bromide level was found to be raised in all four—ranging from 120 to 300 mg per 100 ml. (as NaBr)

This problem is being investigated further, but it is clear that the salt intake of patients receiving hexamethonium bromide over long periods should not be rigorously reduced and that a watch should be kept on the blood bromide level.

University College Hospital,
London. M L ROSENHEIM

SIR,—Correspondents have emphasised the danger of indiscriminately using the methonium halides [1] In concurring with this opinion, we would draw attention to the occasional development of dangerously high levels of blood-bromide after prolonged administration of the bromide salts of methonium. Bromine comprises some 44% by weight of the molecule of hexamethonium bromide and an even higher percentage of the penta methonium salt Therapy with these compounds therefore involves administering a substantial dose of bromine, especially since, in our experience, tolerance seems to become established, necessitating a progressive increase in dosage. Unfortunately an iodide preparation for oral use is not at present available.

Goodman and Gilman [2] place the toxic level of blood bromide at 150–200 mg per 100 ml., and add that if unexplained mental or neurological symptoms are found in association with a blood level of even 75–100 mg per 100 ml bromide intoxication may be suspected as the cause

Amongst a group of six patients receiving methonium bromides, two complained of severe drowsiness and were found to have blood-bromide figures within the toxic range, the readings in the other four cases all being less than 75 mg per 100 ml. The most severe symptoms were in a man, aged 47, with malignant hypertension and cardiac failure Routine treatment of the cardiac failure included salt restriction, together with the administration of digitalis and mersalyl An intramuscular, and later an oral, preparation of pentamethonium bromide was given, in gradually increasing dosage, over a period of 7 weeks before toxic symptoms developed. He was then taking 3 g daily the blood-bromide level being 175 mg per 100 ml. Restoration of a normal salt intake, supplemented by 3 g sodium chloride daily, rapidly abolished the drowsiness, and within a fortnight the blood-bromide had fallen to 125 mg per 100 ml. although during the same period it had been necessary to increase the dosage of pentamethonium bromide to 6 g daily

It is recognised that those using salt sparingly are unduly susceptible to bromide intoxication It would therefore appear that, in the treatment of cardiac failure secondary to hypertension, severe restriction of sodium-chloride intake should be avoided if methonium bromides are to be used , and we would again stress the necessity for careful medical supervision while these drugs are being administered

St Mary's Hospital,
London W 2

MARY C HOLT
J W LITCHFIELD

SEASONAL INCIDENCE OF CONGENITAL MALFORMATIONS

SIR,—The article by Professor McKeown and Dr Record (Jan 27) illustrates two forms of statistical convention which, I suggest, would be undesirable anywhere, and are particularly out of place in a non specialist journal

The first is the lavish use of numbers like 0 70 ± 0 31, with no indication as to what the 0 31 means. I assume it is the standard error, or some multiple of it such as probable error , but whatever it is should have been stated And what are we to make of the *observed* malformation rate (table VIII) of 2 77 ± 0 76%—unless it be the authors' estimate of their error in dividing 13 by 470 ? No doubt, however, it is intended to be some measure of the uncertainty range of the true rate But what measure ?

The other bad habit is the description of findings as "significant" or "not significant" without any indication of the level of significance taken as critical , as it is, the designations are useless The proper way is to state the probability of the result occurring by chance, and furthermore to state or imply what probability hypothesis has been assumed. The responsibility is then on the reader to make up his mind whether to regard the result as true or as a chance effect If the scientist wishes to help the reader to decide, as his expert knowledge may very well entitle him to do, he should do so in the form of an opinion , but he ought not to hide behind magic words like "significant"

A degree of significance is simply a probability, calculated on a certain assumption No matter how large or small it is, by itself it tells us absolutely nothing about the truth of the proposition to which it refers It is equivalent to saying that something is as long as a piece of string A degree of significance means nothing until it is compared with another quantity of like kind —i e , another probability The other probability is the piece of string in the case, and we must know how big it is before the comparison can give any information.

---

[1] Hillis B R Kelly J C C *Lancet* 1950 ii 540 Ball J D *Ibid* p 650

[2] Goodman, L Gilman A. Pharmacological Basis of Therapeutics New York 1941 p 161

Broadly speaking, the counter probabilities are of two kinds a priori probabilities, and profit loss expectations For example, if, before trial, we regard a proposition as equally likely to be true or false, a significance of just less than 0 5 must decide us in favour of "true," *provided* we know we shall gain as much if we are right as we shall lose if we are wrong It is unfortunate that the counter probabilities usually depend upon subjective judgment, with all the uncertainty which that implies But it is surely better that the skeleton should sit visibly at the scientific feast than be hidden away in the cupboard

Psychological Laboratory
Cambridge W E HICK

SIR,—Your leading article of Jan 27 on the "Ætiology of Anencephalus" indicates that several factors may be at work in the causation of this, as of other, congenital abnormalities It may be that heredity is of importance, and possibly the other influences only operate when a suitable gene is present With regard to the other factors I should like to add the following comments

First, Duraiswami [1] has shown that insulin hypoglycæmia *may be one of the causes of fœtal abnormalities in chick embryos* It seems reasonable to infer from this that vomiting in early pregnancy, anorexia, and mild starvation may be important factors in the causation of abnormality in the human fœtus

Secondly, with this in mind it is interesting to study the data obtained by McKeown and Record [2] Their table XLII *(disability during pregnancy) contains these figures*

—	Malformation in fœtus					Controls
	Anencephalus	Spina bifida	Hydrocephalus	Others	Total	
Number of cases studied	305	309	118	23	755	742
Cases with vomiting						
Number	28	20	3	1	52	37
Percentage	9 2	6 5	2 5	4 3	6 9	5

In other words, among the mothers of anencephalic fœtuses vomiting was nearly twice as common as among mothers of normal children

Now comes the startling discovery by Professor McKeown and Dr Record that stillbirths due to anencephalus are considerably more common in December than in June, and your comment that this may be due to infection, diet, allergy, or abnormal activity during spring cleaning I was about to suggest that Lenten fasting might be another possibility, returning to the theme of hypoglycæmia But a study of McKeown and Record's paper (*Lancet*, Jan 27) shows *that the anencephalics were not born at full term but had been conceived in April, May, and June, and there was still* a high rate for July, August, and September conceptions *Even the most extreme date for Easter can hardly bring* Lent into this period, though the spring cleaning may be delayed for several months

Another line of attack, as you mention, has been on the effect of lack of vitamins, particularly vitamin A There should be enough vitamin A in our diet now that National Butter and Special Margarine are universally provided, but some pregnant women have a dislike for fat and may thus become deficient Of course there are other sources of vitamin A, such as eggs and milk, while carrots provide the precursor carotene Any gardener knows *that April to June is the one period of the year* when fresh carrots are unobtainable The old ones *have been eaten or have withered and rotted,* and the young ones are not yet grown It would be interesting to have the views of expert dietitians on the seasonal variations of the vitamins in our diet, and also to have any information that Professor McKeown and Dr Record can provide about the diets of the mothers of anencephalic fœtuses

Until more is known about these factors it would seem to be good antenatal pediatric practice to pay more attention to the rapid correction of vomiting in pregnancy and to the provision of adequate supplies of vitamins from the earliest possible moment in pregnancy

Department of Child Health
Bristol University H R E WALLL

OCCUPATIONAL THERAPY

SIR,—*I agree with much that Mr Krauss (Jan 20)* has *to say* Perhaps in my letter (Dec 30) I failed to make my point clear The crafts I had in mind restore function and by arousing interest stimulate mental recovery *They involve the extensive use of machine tools*

For many patients I see no value in a "work environment" *doing economically unproductive machine work* In many cases they are not initially fit for this work *Many workers recovering from sickness or injury* need no specifically industrial rehabilitation they merely need *rehabilitation My plea is for a wider view* Craftwork properly organised has much to offer At Farnham Park *in the Slough Industrial Health Service* an example of this type of work may be seen

Farnham Royal Bucks M E M HERFORD

APPLICATION OF PSYCHOLOGY TO DERMATOLOGY

SIR,—*I read with great interest and profit the* article of Jan 13 by Dr MacKenna and Dr Macalpine

The most controversial section of the paper, it seems to me, is that which seeks to establish a clear distinction between the mechanisms involved in psychoneurotic and psychosomatic symptom formation

> "*Somatic manifestations such as skin disease are mostly affect equivalents'—they may be a disguised discharge of* anxiety, fear, rage, or any other simple affect'

This statement, if true, would involve a reassessment of the concepts of emotion and its conative component which I accept at present This concept, which was elaborated by Rivers [1] and others, states that emotion accompanies an impulse to action, and that so long as free expression is given to the impulse emotion remains minimal Should the direct pathway of expression be denied to the impulse, then emotion will increase to an intensity which inspires the individual to seek alternative methods of satisfying the impulse This suggests that emotion does not occur per se but is always the accompaniment of a drive or impulse to action I submit *that the attempt to find alternative paths of expressing drive is the mechanism behind symptom formation,* and *not an alternative path of emotional expression*

Conscious suppression of emotion because of social *situation or out of regard* for the feelings of others is an adaptation which is called for daily in each of our lives If, as Dr MacKenna and Dr Macalpine suggest, such suppression of emotion could give rise to psychosomatic disturbance, one would expect this to be much commoner than it is But if one takes the view that it is drive that is denied expression and that seeks an alternative through symptom formation, then the psychosomatic symptom may have the same significance as the compulsive acts of the obsessional, *the tics,* and the conversion symptoms of hysteria

The example quoted *in the article as a simple affect* equivalent is of a woman, aged 45 who suffered from *blepharitis conjunctivitis,* and itching around the eyes It

---

[1] Duraiswami, P K *Brit med J* 1950 ii 384

[2] McKeown T Record R G *Brit J soc Med* 1949 3, 183

[1] Rivers W H R Instinct and the Unconscious Cambridge 1920

> is suggested that this was due to the fact that, when her father had died some nine months previously, she had out of consideration for her mother bottled up her feelings of grief and that this suppressed affect was then discharged through some psychosomatic mechanism in the symptoms of which she complained.

In order fully to understand the symptom and the total situation of which it is a part, is it not necessary to understand what drive, impulse, or wish was being denied expression, and was so producing a pressure of painful emotion? May not the symptoms around the eyes be an attempt to find an alternative channel for expressing the drive or wish rather than the emotion?

Freud in his classical paper, Mourning and Melancholia,[2] has suggested that mourning involves the withdrawal of all libido from the love object and its gradual detachment and redistribution. In this process some individuals may direct, at least temporarily, some of the displaced libido on themselves. Since all love involves ambivalence, the hostile component may thus be self-directed and in this way involve psychosomatic manifestations. I am not of course suggesting this type of mechanism for the case described, but offer it as evidence of the deeper interpretations involving libido rather than affect which might be applicable.

The fact that such symptoms as those described may be cured by abreaction does not affect the issue, since it is the painful intensity of the emotion which makes the individual seek to express libido through alternative channels. The painful affect, having been as it were artificially tapped and discharged, no longer serves as an impetus and the symptom may disappear. If the abreaction extends over that time during which the deflected drive is operating, then a good result may be obtained; but if the drive is persistent, then one must expect a further accumulation of painful affect. The bearing of this on relapse is obvious.

Dr MacKenna and Dr Macalpine refer to other examples of the miracle cure in the early stages of psychological investigation and therapy. Such dramatic improvements of symptom occur also in the psychoneuroses during the early stages of treatment, and may also involve abreaction. Others occur after the redistribution of libido accompanying the formation of the transference; and still others may be due to defence mechanisms, such as the flight into health. Whatever they may be, it is my contention that they all involve redistribution of libido rather than the discharge of affect alone.

All this bears profoundly on that part of the paper which puts forward the view that psychosomatic symptoms have no meaning and no psychic content. I have found that this is not so in the perplexing symptom variation found in patients suffering from the eczema-asthma complex. In treating such patients I have tried to relate the current psychic situation to the physical symptoms. In a number of patients I found that I could predict with a significant degree of accuracy the variation that would take place. I thought at first that this was related to certain complex formations; but I later revised this view, and I came to the conclusion that when the patient was expressing himself freely and with pleasure in the analysis, eczema was the prominent symptom, but that when defences were operating and the patient was struggling painfully through them, then asthma was the prominent symptom. This has suggested to me that eczema represents an outgoing of libido and asthma a retention or bottling up of libido.

I have quoted this particular example because Dr MacKenna and Dr Macalpine refer to infantile eczema, and suggest that the only psychological interpretation must be a correlation with adult types of conflict. It may be significant that infantile eczema occurs during that period of life when in fact there is little impediment to the free expression of libido, and asthma supervenes when the child is old enough to have developed conflicts involving the repression of libido.

Although in this letter I may have shown a bias towards the psychoanalytical approach to psychosomatic disease, I am convinced that the next advance in this field will come neither from the clinician nor from the psychiatrist but from the neurophysiologist. I feel it is essential that understanding of the neurophysiological mechanisms involved in psychosomatic symptom formation should be greatly extended to form a firm structure on which theory may be based. Such a structure would serve as a framework for the sceptical clinician and as a bridle for the enthusiastic psychiatrist. I see a real danger that in the study of psychosomatic medicine we may establish a top-heavy load of theoretical and facile explanation unfounded on accurate knowledge of the neurophysiological mechanisms involved.

I have concentrated on those parts of the paper which are, as the authors say, controversial; but I agree with a great part of the paper, which has lessened my ignorance of the subject.

Wanstead Hospital,
London, E.11 DESMOND IRWIN.

ACUTE OBSTRUCTIVE LARYNGOTRACHEITIS

SIR,—We have been interested to read the article by Dr Forfar, Dr Keay, and Dr Thomson, in your issue of Jan. 27. As these writers suggest, the condition is probably much more common than the reported cases suggest.

At this hospital there have been 26 cases in the last three years, one of which, a baby of six months, was admitted a year later with a second attack. 7 of the cases were under one year of age, 8 between one and two years, 8 between two and five years, and 3 over five years. Most of these cases were admitted with a diagnosis of laryngeal diphtheria. As regards severity, 10 of the cases were regarded as severe, and the remainder either moderate or mild and not causing any anxiety as to the outcome. Of the severe cases, 1 died on admission and 2 required tracheotomy but recovered. An autopsy on the child who died was carried out by Dr J. Hart-Mercer, who commented that, although the ulcerative condition was limited to the larynx, the similarity to the acute laryngotracheitis of infants was very marked and there was considerable destruction of the mucous and submucous tissues; and, in addition, *Staphylococcus pyogenes* and *Streptococcus viridans* were cultured from the larynx.

Hæmolytic streptococci were found in 4 other cases, 2 of which were the cases requiring tracheotomy; *Staph. pyogenes* was found in 2; and the remainder gave negative pharyngeal swabs. One child two months old, who had a moderately severe attack, continued to have stridor for a month after recovery, and bronchoscopy showed a large granulating area in the trachea which eventually resolved without sequelæ.

Treatment of most of these cases previously was by steam, antitoxin, penicillin, and sulpha drugs; but 5 recent cases have had chloramphenicol and 1 'Aureomycin,' and all seemed to respond much quicker than formerly. The cases requiring tracheotomy were a child of eleven months and an older child of nine years; and both were thought unlikely to survive without interference. In both instances the subsequent course was stormy and associated with further obstructive spasms due to necrotic tissue and secretions.

One wonders whether a similar condition may not occasionally occur in adults. A soldier, aged eighteen, was admitted in 1947 in extreme distress from laryngeal obstruction, which had commenced suddenly with pain on swallowing and talking about eight hours previously.

---

[2] Freud, S. Collective Papers. London, 1925, vol. 4.

and required tracheotomy soon after admission Swabs from pharynx and tracheotomy wound were negative The condition, which gradually cleared, was associated with a temperature of 101 8°F and considerable induration of the cellular tissues of the neck

F G BREWIS
Senior Physician

Walker Gate Hospital,
Newcastle upon Tyne

C NEUBAUER
Assistant Physician

SCHOLARSHIPS AT THE LONDON SCHOOL OF HYGIENE

SIR,—In recognition of the services of Sir George Elliston, who has just demitted office as its chairman after eleven years' tenure, the board of management of the London School of Hygiene and Tropical Medicine have decided to offer two scholarships of £150 each, with free tuition, for students taking its course for the diploma in public health commencing in October, 1951 Official intimation will be found in the advertisement columns These are additional to the Bygott scholarships, awarded by the University of London, also tenable at this school, about which official notification will appear later

The board hope that the Elliston scholars will eventually join the preventive services in the United Kingdom, the number of recruits to which has been seriously reduced by the discrepancy existing between the emoluments offered and those obtainable now in other branches of the medical profession We hope that many more of the medical officers of health of the future will become the pivotal points of the medical services of their areas All thinking people deplore the increasing tendency for each section—domiciliary, hospital and preventive—to develop and function as separate entities The medical officer of health with the proper outlook and background should, we think, be the coordinator, this implies a very adequate clinical training, and we hope that men of good quality will give careful consideration to adopting community health as their career

The modern course for the D P H is much more a cultural discipline than a technical training, and there are few young medicals who would not derive great benefit from it whatever their ultimate aim may be

London School of Hygiene and
Tropical Medicine, W C 1

ANDREW TOPPING

POLIOMYELITIS AND POLIOENCEPHALITIS WITH OPSOCLONIA FOLLOWING APPENDICECTOMY

SIR,—Dr Warren, in his interesting paper of Jan 27, remarks "The association [of poliomyelitis] with appendicectomy has only rarely been reported" Admitting the possibility and the analogous instances described, I would submit that the association is so rare that the diagnosis should be most carefully considered On the other hand, the history of "appendicular colic" followed by mental confusion and symmetrical ascending paralysis is typical of acute porphyria

This may be appreciated if the case be compared with Kinnier Wilson's description,[1] which could be read as an accurate account of Dr Warren's case, including the following features which are most unusual in poliomyelitis (1) considerable delirium at the onset (of a spinal type) with absence of pain in muscles, which were flaccid next day, (2) retention of urine at an early stage [2], (3) ascending flaccid paralysis of symmetrical distribution, (4) pyrexia continuing for five to six weeks, and (5) an encephalitic episode with convulsions five weeks after the onset I do not deny that each of these features has been described in poliomyelitis, but all are rare, whereas each is mentioned by Kinnier Wilson as a feature of acute porphyria

The only feature of the report which is against a diagnosis of porphyria is the cerebrospinal fluid It is regretted that the pressure, type of leucocyte, and number of erythrocytes present are not recorded The figures presented are compatible with poliomyelitis, though at the stage described one would have expected a greater pleocytosis and a lower protein I should like to be reassured of the absence of blood contamination Furthermore, there is no mention of inflammatory or obstructive pathology in the appendix, "a long kinked retrocæcal appendix" is a poor basis for diagnosing appendicular colic

Gardiner Institute of Medicine
University of Glasgow

J A SIMPSON

ADRENOCORTICOTROPIC ACTIVITY OF BLOOD PLASMA EXTRACTS

SIR,—The article of Dec 2 by Miss Trowbella and myself contains an ambiguity In the section "Preparation of Extract" it is stated

> "The plasma was taken off and added to 4 volumes of acid acetone, prepared by adding 25 ml of analytically pure hydrochloric acid to 975 ml of redistilled acetone The resulting precipitate was allowed to stand at room temperature for eight hours, vigorously shaken at intervals, and then centrifuged The supernatant fluid was taken off, 1 ml of saturated sodium chloride solution was added and the concentration of acetone was brought to 94%"

The last sentence should read "The precipitate was discarded, and the acetone concentration of the supernatant fluid was brought to 94% after adding 1 ml. of saturated sodium chloride solution"

Department of Chemical Pathology,
King's College Hospital London, S E 5

J BORNSTEIN

PULMONARY HYPERTENSION IN MITRAL STENOSIS

SIR,—Some clinical observations appear to support Dr Dornhorst's contention, in his letter of Jan 6, that the increase in heart rate during exercise may influence the pulmonary artery pressure in mitral stenosis Thus Gallavardin[1] in 1921 commented on the apparent precipitation of pulmonary œdema when certain patients with tight mitral stenosis developed a tachycardia More recently Harken et al [2] observed the ill effects of a tachycardia developing during operations on the mitral valve and attributed this in part to shortening of the diastolic time We also have noted that a tachycardia of emotional origin, such as may occur the night before operation, may apparently precipitate pulmonary œdema

However, some experimental evidence and our incomplete knowledge of factors affecting the circulation make it doubtful whether simple mathematical calculations can legitimately be applied to this problem If the right side of the heart can be assumed to be analogous to the left, it has been shown that atropine induced cardiac acceleration in normal subjects is associated with a fall in right auricular pressure despite a rise in cardiac output [3] Furthermore the effect of digoxin on the cardiac output and venous pressure in heart failure due to mitral stenosis does not appear to bear any relation to the degree of cardiac slowing achieved, nor does atropine acceleration following digoxin therapy reduce the cardiac output or increase the venous congestion

Thus despite theoretical considerations there is indirect evidence that tachycardia per se may not necessarily be a major factor in increasing the pulmonary artery pressure in mitral stenosis So far as I know, direct evidence on this point has not yet been reported, but an unpublished observation in this country showed

---

[1] Wilson, S A K Neurology Edited by A Ninian Bruce London 1940, vol i p 308

[2] *Ibid*, p 231

---

[1] Gallavardin L *Arch Mal Cœur* 1921 14, 262

[2] Harken D E Ellis L B Ware P F *New Engl J Med* 1948 **239** 801

[3] Kelly H G Bayliss R I S *Lancet* 1949 ii 1071

that on exercise, when there was a marked tachycardia but no increase in cardiac output, the pulmonary "capillary"-pressure rose slightly, indicating a rise in left auricular pressure, whilst there was a conspicuous increase in the pulmonary artery/pulmonary "capillary" gradient, indicating increased pulmonary vascular resistance

College of Physicians and Surgeons
Columbia University New York

R I S BAYLISS

CORONARY DISEASE AND MODERN STRESS

SIR,—Reference has been made by Professor Platt (Jan 6) and by Dr Stewart (Jan 27) to an observation in the Registrar General's Decennial Supplement for 1931, which was based upon study of the death certificates of men between the ages of 20 and 65 during the years 1930–32 This was to the effect that, whereas among men whose social conditions are most favourable degenerative heart-disease tends to express itself as angina pectoris or coronary disease, at the other end of the scale it tends to take forms described on death certificates as myocardial or cardiovascular degeneration

It is becoming a convenient expedient today to explain away unpleasant things in vital statistics—such as the rising death-rates from bronchogenic cancer, leukæmia, or mechanical suffocation of infants—by faults and changing fashions in certification, although when a death rate is falling it is readily accepted as authentic It is also possible to resort at once to this "explanation" when death statistics throw up something surprising and difficult of explanation, but if carried to its logical conclusion this would mean that vital statistics of separate causes of death are a rather futile study

In this particular instance it would seem to be more difficult to accept that explanation than to accept the figures at their face value I have often been accused of having too high an opinion of the intelligence of certifying medical practitioners, but I have never credited them with superhuman ingenuity To suppose that their vagaries in diagnosis and certification were so ordered in irregularity as to produce the figures below seems to me rather like that tiresome idea of a million monkeys producing by accident the Book of Job on their *million* typewriters

Dr Stewart prefers to think that doctors knew something about angina pectoris even in country and industrial practices in 1930–32, and he leans to the idea that the explanation lay in the differing proportions of men who were afflicted with anxiety to better themselves, or the world generally, at different levels in the social scale That might perhaps account for the social class gradient of the coronary myocardial ratio, but it will hardly explain the curious differences in this ratio between occupations whose outstanding contrast was in the physical nature of the work done rather than in the mental outlook of the workers The amount of physical energy expended in an occupation has not been considered as a factor of importance in determining the type of heart-failure which terminates life, although that would be an obvious reason for the class gradient Broadly, the social grouping used in 1930–32 was correlated in a negative way with calories expended in physical work, and if that happened to be an important factor in determining the coronary-myocardial ratio it would explain the class gradient just as well as the mental stress hypothesis At that stage of our civilisation at least, mental stress and a sedentary life tended to go together, and the second might be even more important than the first in its effect on the coronary arteries

The figures below have been taken from table 4A of the report referred to, as anyone could do who, following Professor Platt's advice, took it to bed with him and applied pencil, paper, and simple arithmetic I have tried to arrange some of the large occupations into five groups in descending order of the physical activity I think they involve, keeping apart another two groups of rural workers for separate comparison because they have low death rates from every cause

Group nos	Occupation groups	Total coronary and myocardial deaths	Coronary % of total	S.M R at 20–65	
				Cerebral hæmorrhage	Nephritis
4 48 57 87	General and dock labourers navvies, coal hewers	3495	14 8	103	100
16–19 23 44, 45	Furnacemen smiths boiler-makers bricklayers, builders labourers	1175	18 7	101	86
20 42 43 58 64 65	Metal machinists printers compositors retail salesmen potmen sorters	643	25 3	106	87
56 63	Motor drivers commercial travellers	512	36 3	79	87
67 68 74 82 83	Teachers, clerks bankers administrative officials	1242	38 6	101	103
3	Agricultural labourers	550	14 3	59	58
1	Farmers and their relatives	493	22 6	106	87

The standardised mortality ratio (S.M.R) for total heart-disease was above average (114) for the general labourer group, but was very low (68) for agricultural labourers Nevertheless, in both groups coronary disease formed one seventh of the total deaths from coronary and myocardial disease combined The proportion increased steadily with diminishing physical activity to about two fifths in the most sedentary group Farmers and their relatives gave a proportion between those for the second and third groups, which is reasonable Neither cerebral hæmorrhage nor nephritis showed differences in mortality comparable with the progression of the coronary-myocardial ratio

It is to be hoped that the occupational mortality statistics for years around the census of 1951, based as they will be upon the new International Classification of Diseases which attempts to differentiate hypertensive disease, will throw further light on this problem

World Health Organisation Centre
for Classification of Diseases
London

PERCY STOCKS

PROTRUDED INTERVERTEBAL DISCS

SIR,—May I warmly endorse Dr Jefferson's plea (Jan 20) for conservative treatment of laterally placed cervical disc lesions? Since spontaneous cure is nearly always established at the end of three to four months in 5th, 6th, and 7th root compression, and in six months at the 8th root, operation is very seldom indicated unless the spinal cord is compressed as well

Curiously enough, Dr Jefferson does not mention the swiftest conservative measure of all, which is of course manipulative reduction In the stage where there is scapular pain only (what used to be called "fibrositis") the displacement is slight, and one session often suffices, when root-pressure has supervened reduction is more difficult, but is often still possible For the past six years manipulation during traction has been the method of choice in our physical medicine department, traction in recumbency, head suspension, a collar, or waiting for spontaneous cure are reserved according to circumstances, for displacements irreducible by manual means

I was most interested to read the paper by Mr Floyd and Dr Silver, also in your issue of Jan 20 In my view, relaxation of the sacrospinalis muscle as trunk flexion proceeds is the mechanism for preventing lumbar-disc lesions It must not be forgotten that the first action of the sacrospinalis muscle is to approximate the vertebræ, only when this slack has been taken up can the muscle act as an extensor Compression of the joint while it is held in the kyphotic position is the usual cause of retropulsion of part of the disc, and the relaxation of the sacrospinalis muscle that Mr Floyd and Dr Silver describe diminishes this possibility

Mr Charnley's article (Jan 27) emphasising the importance of estimating straight leg raising is to be welcomed The range of this movement is proportionate to the pressure exerted on the nerve root, except in cases where pressure atrophy is taking place

During attempted manipulative reduction of a lumbar displacement causing sciatica, straight leg raising is a most sensitive test, varying from moment to moment as the loose fragment moves We therefore use it as an immediate measure of the success of each different manipulation A particular technique is tried, and the effect on the range of straight leg raising is estimated at *once In this way, so long as the patient is not anæsthetised,* the method best suited to him can quickly be discovered

An interesting phenomenon that we often notice is the appearance of a painful arc on straight leg-raising when reduction is almost complete This I interpret as the root catching against so small a protrusion that it glides over The main virtue of straight leg raising is that it clearly indicates the size of the protrusion at any one instant

St. Thomas's Hospital,
London S.E 1 — James Cyriax

Sir,—In last week's article by Mr Burns and Mr Young one reads that low back pain and sciatica are probably "part of the price we pay for our upright posture" This phrase is handed on from author to author It seems to me that we pay with these ailments for our civilisation Has one found these disorders in African negroes, Australian aborigines, or Polynesians? Are these disc accidents not a sequel of our wrong *posture, our wrong way of using our body, and our lost* bodysense? Are these disc operations not another example *of combating the smoke and leaving the fire burning?*

London, W C 1 — E F Meyer

*** A corrigendum for the paper by Mr Burns and Mr Young appears on p 358

TUBERCULOSIS FIGURES

Sir,—Your annotation of Jan 6, and numerous articles and letters in the medical and lay press, rightly focus attention on the apparent increase in the morbidity of pulmonary tuberculosis The facts give cause for serious anxiety, and the Glasgow figures, backed by a corresponding increase in mortality rate, are alarming None the less it is essential for a full appreciation of the position and for the initiation of steps to bring tuberculosis under control that the notification figures should have some degree of accuracy, this, at present, is plainly not the case

There is a wide divergence of *opinion as to what* cases of tuberculous infection should, and what cases should not, be notified *Apart from the clear cut instance* of active pulmonary tuberculosis with tubercle bacilli demonstrable *in the sputum, the variation in procedure* is formidable The diagnosis of erythema nodosum (a condition now recognised as usually *following closely on a primary tuberculous infection) should lead to an* intensive search for the original source of infection The necessity for this procedure is one of the chief arguments for notifying the disease, yet the majority of such cases are not notified Similarly, cases of pleural effusion are invariably notified by some, and rarely or never by others Again, should action be taken on the diagnosis of a minimal tuberculous lesion of the lung found to be healing without treatment?

The anomalies are further underlined by the official figures for pulmonary tuberculosis in children under 15 years of age The 1948 figures for Glasgow, Leeds, and Bristol, kindly supplied to me by the medical officers of health, read *510, 27, and 71 This wide variation* cannot be wholly explained by inequalities in total population, in social condition, in opportunity for infection or in degree of immunity The discrepancies must largely be due to a difference in interpretation of the regulations

In 1945 the Joint Tuberculosis Council went some way towards improving the position by advising the Minister of Health that notification should be a two stage procedure of (1) intimation, followed if necessary by (2) full notification Five years have elapsed with no apparent result, and the time is ripe for reconsideration In *formulating new regulations, whether or not "intimation"* is accepted, some lead should be given as to the criteria *for notifying such conditions as intrathoracic tuberculosis* in children, pleural effusions, and minimal tuberculous lesions of the lung

Review and subsequent modification of the notification system is essential if the morbidity figures are to provide adequate data for planning the attack on tuberculous disease

King's Lynn — G F Barras

VACCINATION AGAINST SMALLPOX

Sir,—Dr Dixon (Jan 20) has already disposed of several of the arguments against vaccination put forward by Dr Killick Millard in his article of Jan 13 There are a number of other fallacies in this article, but it is scarcely necessary to discuss these since Dr Millard himself invalidates his entire thesis when he writes "Incidentally I am all in favour of everyone who visits *the East being efficiently protected by recent vaccination* "

A little later he quotes the example of the recent outbreak of virulent smallpox at Glasgow, initiated by *the arrival of a "well vaccinated" Asian seaman from* the Far East I believe that in fact all the recent outbreaks in Britain have been originated by persons arriving from the East If Dr Millard is going to have all such travellers vaccinated, then, according to his own argument, he is going to increase the number of undetected cases and hence the number of outbreaks The only way in which such occurrences could be prevented would be to subject every arrival from the East to medical examination, and then to place in quarantine all those with slightly suspicious symptoms even if the disease did not appear to be smallpox

Arlesheim
Switzerland — A M Woolman

Sir,—In his article Dr Killick Millard says "Dr Stallybrass in the *Medical Officer* of July 29 last thinks that the danger of spread from unrecognised cases in unvaccinated subjects counterbalances my argument as to the spread from unrecognised cases in the vaccinated" In the interests of accuracy, may I observe that this suggestion emanated from me (*Medical Officer*, July 8, 1950)

I recall that correspondence for another reason In his *final* letter (*Medical Officer*, Aug 12) Dr Millard admitted that too little attention had been given to the *relative danger of smallpox in* vaccinated and unvaccinated subjects, *and* that, as his argument was based *merely on* personal belief, he proposed to devote some time to collecting definite data on the question It is disappointing, therefore, to note that he makes no further reference to this projected research Certainly his latest article contains few novel aspects, it consists in a repetition of the same old selected facts and biased evidence *It does, however,* show one new feature of great promise He concludes that, since he cannot agree with *any view which differs* from his own, he can only leave it for others to decide

More serious is Dr Millard's propagation of his views in the lay press by an article under his name which *appeared* about the same time in a popular journal The issemination of these views can have nothing but a etrimental effect on the level of herd immunity, the nportance of which was emphasised, among other oints, by Dr Dixon in your issue of Jan. 20

Health and Welfare Department,
Glasgow
J S GEMMILL

ALARMING NAMES FOR HOSPITALS

SIR,—I endorse the remarks in your annotation of)ec 30 If anyone remains doubtful of the layman's eaction to these ill conceived titles, let him see the faces f his fellow passengers when, on a number 14 bus, he sks clearly for his ticket to "the Cancer Hospital"

St Bartholomew's Hospital
London E C 1
GEORGE H DU BOULAY

ACQUIRED IDIOSYNCRASY TO SODIUM p-AMINOSALICYLATE

SIR,—The case of P.A.S sensitivity with jaundice eported by Dr Little (Jan 27) is an interesting contribuion to this subject, but we must disagree with his onclusion that the blood-P A S level may be presumed o rise steeply in such cases Reference to our own case eport[1] will show that the blood level on the first day of the reaction was scarcely any higher than during the irst week of treatment, and was actually lower than n the preceding week We would like to emphasise his point in case an erroneous impression is gained that repeated blood estimations will enable the physician to foresee and prevent such a reaction

Whether the total dose of the drug at the time of onset of the reaction is the deciding factor in determining its severity is also debatable We have had a case which developed a P A.S sensitivity reaction much less severe than the one we reported, in which the total dosage was 760 g over a period of 38 days It is now our practice to discontinue P.A.S *at once* if a patient taking this drug shows a sudden rise of temperature, which is usually if not always the first sign of idiosyncrasy In all the reported cases of severe allergic reactions to P A.S., treatment with the drug was continued for some days after the onset of pyrexia, and in our opinion this is probably more important than the total dose in determining the severity of the reaction

Lenham Sanatorium
Kent.
R LIVINGSTONE
E W STREET

TREATMENT OF THE AGED SICK

SIR,—Many of those concerned with the care of the aged sick must have been compelled by the article (Jan 20) by Lord Amulree and his colleagues to make comparisons, and to look again for new and more hopeful lines of approach. As we are constantly faced with the economic aspect, it would be interesting to know the cost, in medical and nursing man-power, of achieving the results described.

As a comparison, in one hospital group with more than 100 aged sick cases, it is found that, on a basis of 1 trained nurse to more than 20 cases, and of 1 untrained nurse to more than 3 cases, it does not seem possible to achieve the turnover quoted in the article But of course the other factors mentioned play a large part in diminishing the discharge rate

Many provincial hospitals must be having similar difficulties, perhaps some peculiar to their own locality In the Eastbourne area for example, the percentage of the population in 1947 aged 65 and over was 16 7, whereas the figure for England and Wales was 10 9 One difficulty must, however, be common to all—namely, the problem of senile mental changes Surprisingly, Lord Amulree and his colleagues make no reference to senile mental changes as a reason for a patient being confined to bed

St Mary's Hospital Eastbourne
IAN M BROWN

LEUCOCYTE-COUNTS IN THIOURACIL MEDICATION

SIR,—Many clinics have satisfied themselves that symptoms give an adequate warning of the need for action against agranulocytosis in thiouracil treatment The case described last week by Dr Holliday, in which thiouracil agranulocytosis developed during penicillin treatment for otitis media, was interesting but very unusual Surely the only, but important, lesson is During thiouracil treatment, if the patient needs penicillin or a similar antibiotic, she also needs weekly leucocyte counts, since penicillin will suppress the usual warning symptoms

Dr Holliday has made a useful tabulation of the published cases of thiouracil agranulocytosis, but the expected finding that agranulocytosis without symptoms has a better prognosis than that with symptoms gives no clue to the optimum method for supervision How many blood counts had to be done to discover these 11 cases one to three days before the onset of their symptoms? None appear to have had their symptoms averted It is unfortunate that his tables do not state the intervals between the onset of symptoms of agranulocytosis and both the cessation of thiouracil and the start of penicillin therapy I do not know of any fatal cases where these intervals have been short Only a serious risk of this outcome could justify including regular blood-counts in the routine of thiouracil treatment—excepting, of course, when an antibiotic is also being administered A thyrotoxic patient is usually sufficiently nervous because of her disease

Postgraduate Medical School of
London W 12
RUSSELL FRASER

PROSPECT OF WAR

SIR,—The correspondence initiated by Professor Penrose and his colleagues indicates considerable strength of feeling on the questions they raise, but does not by any means show the same unanimity of opinion

Dr Adair Girby (Jan 27) refers to the Society for Social Responsibility in Science, an American organisation whose activities would probably be admired by all, and he asks that a comparable lead be given in this country

I should like to draw attention to the activities of the Cambridge Scientists' Anti-War Group, which, though small, attempts to express the views of scientists who have the interests of humanity at heart Recently, for example, we organised a petition among Cambridge scientists condemning the development of the hydrogen bomb We have held a conference on secrecy in science, and are just completing a book in which are contrasted the effects on science of war and war preparations, and the possibilities that can be envisaged in a world at peace We have dealt with topics of immediate concern, including, on the one hand, biological warfare, and, on the other, the world requirements for food and the necessities for their fulfilment

In view of the seriousness of the present situation, we are calling a national conference of scientists, medical and otherwise who share our aims We hope that this will lead to the formation of similar groups in universities and laboratories elsewhere, and perhaps to the formation of a national scientists' organisation At this conference we plan to discuss those aspects of the present political situation that affect both the scientist and his science Prominence will be given to the special responsibility of scientists who are being called upon as never before to prostitute their work in the interests of a new and terrible war All scientists are affected to some extent, but in many cases the connection is quite direct and explicit The most glaring example, perhaps, is that of those physicians and their colleagues who are now being asked to make the weapons of biological and chemical warfare One session of the conference will be devoted to a discussion in more general terms of what can be done by scientists to prevent the present drive towards war

---

[1] Livingstone R Street E W *Lancet* 1950 ii 308

I hope you will allow me, through your columns, to ask medical scientists who would like to attend the conference to communicate directly with us We wish to bring together all those who feel that scientists must take a stand in defence of their science If we can find a basis for common action we will serve both our own good interests and those of all mankind

S M HILTON
8 Harvey Road, Cambridge
Secretary, Cambridge Scientists Anti War Group

SIR,—Statesmen of all countries claim to be working for the welfare of man, each claims that his is the true path of social salvation, and with even greater vehemence that all other paths lead to deserts and waste places, not to the lands of milk and honey There are three chief systems to choose from, the competitive, the compulsive, and the cooperative, and each has its sincere advocates

Nullius in verba May we not, as men of science, suggest to the disputing statesmen that they put their systems to the test of experiment The world is big enough Let Russia, China, and such other countries as wish to follow them continue to govern by the strictest Marxian principles, let the New World follow even more zestfully the American Way of Life, and let Western Europe and the British Commonwealth struggle hopefully towards the more difficult goal of voluntary cooperation After a sufficient period, say three human generations, there would be no need to argue or to assert, the facts would be plain There are measurable indices of social health, such as the infant mortality rate, the net reproduction rate, the tuberculosis death rate, the suicide death rate, the V D incidence rate, and the mental disease rate The Statistical Section of the World Health Organisation could frame schedules for the experiment, and afterwards analyse the data Interim reports could be published, say every ten years, and the participating countries could see where they were strong and where they were falling behind It would be better and wiser to compete in a health race than in another arms race, and in such a cause every doctor could give his whole strength to his country's effort

This is the scientific way of solving disputes, an appeal to reason, not to prejudices and fears, to facts, not to force, to measurement, not to argument I feel we are justified in urging its value on all who will hear us

Cragdale, Settle
D P LAMBERT

SIR,—Your correspondents of Jan 20 might have condemned war and arming for war, as human activities, even more roundly That all the "great nations" and many small ones are either fighting or arming, and that neither good will nor good sense, neither belief in goodness and justice nor enlightened self interest, stops them seems to me the final demonstration of human obliquity and folly Well may we confess, as units of humanity, that "there is no health in us" Should we catch our fellow citizens or our leaders preparing aggression I trust we should "in the spirit of our chosen profession of healing" protest

But we shall not so catch them To call this nation "peace loving" is an exaggeration, for love is a warmer, livelier emotion than we now, as a nation, seem able to feel for anything, good or bad But that we have a profound aversion from arming for or making war surely cannot be doubted by any unbiased observer seeing us from within or, I should have thought, from Moscow or Peking We went far in disarmament between wars, can any doubt that, with any practical encourageme from the East, we should go further now?

We all know that we are not preparing for aggressive war Are we justified in preparing for armed defence? Not if it is possible to reach a trustworthy "live and let live" agreement, sealed by disarmament, with the Communist powers, still less if, in our hearts, we are weary of freedom—the freedom to think, to believe or disbelieve, to choose the better or the worse But suppose we still cherish these freedoms and the real choice is between standing to arms and Communism here in our time, what then?

From Russia little news comes, but men who sound good witnesses talk to us soberly of what they have seen and heard in China and in Prague, and the story is always the same and matches the rumours from Russia and the sentiments, arguments, and slogans of our domestic Communists Thought and belief are not free, the end justifies the means, there are no absolute values in science, art, or life—no unqualified truth, beauty, or goodness "Whosoever will be saved must *thus think*" There is more besides, but this is enough Can members of our high profession stand for this?

But can arms defend us? Who can say? Doubtless real love of liberty, zeal for our free institutions, displayed not in words or votes but in work, is the best defence, but history suggests there is a place for arms At Marathon and Salamis the Greeks fought for their civilisation, of which free thought was the very heart They won, and if our medicine today is in debt to Greek thinkers, and our professional ethics to the Hippocratic standards of conduct, then they are in debt also to Greek arms and those who used them In 1588 we and the Netherlanders fought on the sea to defend our freedom to believe or to disbelieve, to decide for ourselves between right and wrong They won, and if medical research and practice here today need not swerve to avoid conflict with ecclesiastical dogma we owe it, in part, to those ships and sailors In 1914 we, and many other nations fought to keep out the philosophy of Nietzsche and Bernhardi, the doctrine that might is right We kept it out "They stood, and earth's foundations stay" But we went slack and in 1939 we had to fight again, this time against a direction of thought and enslavement of the mind, most definitely invading medicine, which seems to most of us twin brother to Communism The cost was hideous "Victory of desolation" is perhaps a fair phrase, but we do keep our freedom to believe, to think, to choose, to decide, to be kind and tolerant, not to hate or despise those of some class, nation, or economic status not our own

If only arms will defend these things must we not arm, whatever the cost?

London, N W 3
LINDSEY W BATTEN

SIR,—The possibility of doctors being able to outlaw war by concerted action is, unfortunately, a pipe dream Our opinions and ideologies cover too wide a range to allow of cooperation for any purpose—this is frequently shown, even within the bounds of this one little country

There is, however, no doubt that most people (and most doctors) detest war Most men will not work actively and voluntarily for a thing they do not want, but curiously enough, most people (and most doctors) will work for war Surely we should reorientate ourselves and work for peace?

Peace starts at home and in small communities. If even some of those who hate war will work for friendship between men at home and abroad, and will do their best to lessen or eliminate injustice, prejudice, and misunderstanding, we may slowly move towards peace I believe there is no short cut

London E 11
J BARNARD

Public Health

Influenza

In England and Wales influenza continues to be generally prevalent In many areas, including the North and North-west, the incidence is declining, in other areas, more lately attacked, the peak may not yet have been reached. The disease is usually mild, and the causative virus is now clearly A-prime

In the week ended Jan 27 influenza deaths in the great towns totalled 1239—a rate of 59 7 per million population, compared with 54 per million in the previous week In each of the weeks from that ended Dec 9 to that ended Jan 20 the totals were 34, 33, 54, 102, 458, 890, and 1099 Figures for deaths during the week ended Jan 27 in the great towns grouped regionally show decreases in the Northern and North western regions, though the rate for the North-west (104 9 per million population) is still the highest There were decided increases in the North Midland, Midland, Eastern, and South-western regions and in Wales, and less significant increases in the East and West Ridings and the London and South eastern areas, in the Southern region there was a very slight drop More than 86% of the deaths were of patients over the age of 55

Influenza Abroad—The position abroad was reviewed last week (p 286) The disease is now reported to be prevalent in Yugoslavia, and the type of virus is stated to be B Influenza reported from Israel seems to be due to virus A-prime The disease is also prevalent in Japan, but the type of virus is not yet known

Infectious Diseases in England and Wales

Disease	Week ended Jan			
	6	13	20	27•
Diphtheria	38	30	43	48
Dysentery	834	698	727	706
Encephalitis				
Infective •	3	2	3	3
Postinfectious	1			3
Food poisoning	115	65	66	143
Measles excluding rubella	21 691	18 658	15 996	15 930
Meningococcal infection	50	61	44	60
Ophthalmia neonatorum	26	19	31	11
Paratyphoid fever	1	8	2	4
Pneumonia primary or influenzal	1774	2538	3112	3572
Poliomyelitis				
Paralytic	37	27	29	20
Non paralytic	10	11	7	7
Puerperal pyrexia and fever	90	102	107	102
Scarlet fever	923	853	1015	955
Smallpox	13	11	3	2
Typhoid fever	4		4	4
Whooping-cough	5011	4980	4822	5023

• Not including late returns

Estimate of Births

The Registrar-General's[1] final estimate of live births to be expected in England and Wales during the quarter ended March 31 is 178,000, and the provisional estimate for the quarter ended June 30 is 175,000 This would bring the total for the first six months of this year to 353,000, compared with 361,846 in the first half of 1950

Poliomyelitis

Since Jan. 1, 1950, doctors notifying poliomyelitis in this country have been required to distinguish between paralytic and non-paralytic forms In charting the weekly totals for 1950 (fig 1) we have therefore included the curve for non-paralytic cases The proportion of non-paralytic cases has been found to vary widely in different parts of the country, and, as the chart shows, the proportion tends to rise as the epidemic approaches its peak.

Relation to Weekly Temperature

In fig 2 the mean weekly temperatures at Kew have been charted with the poliomyelitis notifications for the county of London in the last few years It will be seen that in all three epidemic years the epidemic began in the week when the temperature first reached 60°F, and in 1949 and 1950 the epidemic began to recede when the temperature first fell below 60°F Dr Ian Taylor, of the Public Health Department, London County Council, who compiled this chart, remarks that, despite its obvious fallacies, the curve seems to show that poliomyelitis is associated in an "all or nothing" manner with the attainment of a critical atmospheric temperature

---

[1] Registrar-General s Return for the Week ended Jan 27 H M Stationery Office Pp 20 6*d*

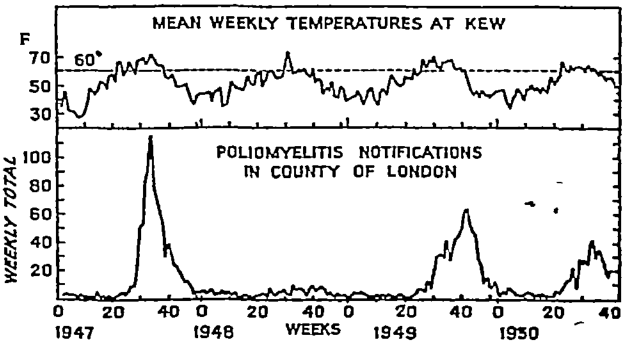


Fig 2—Poliomyelitis in County of London related to mean weekly temperatures at Kew

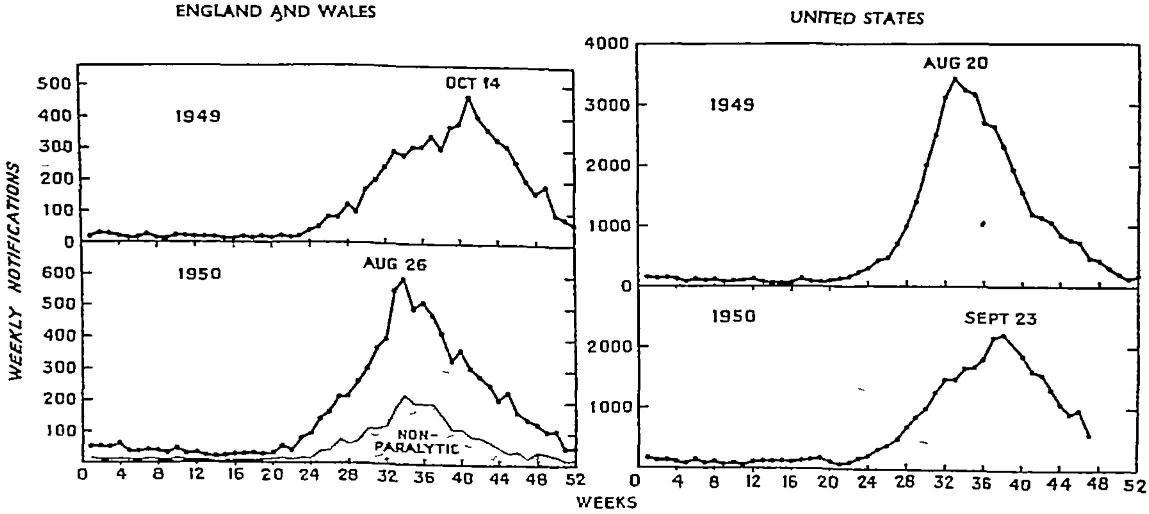


Fig 1.—Weekly notification of poliomyelitis in 1949 and 1950 showing dates of epidemic peaks. These were unusually late in England and Wales in 1949 and in the U.S A. in 1950 The chart for England and Wales in 1950 shows the proportion of non paralytic cases (stippled area)

Obituary

WILLIAM EWART BARNIE-ADSHEAD

M B Birm , B Sc , F R C S , F R C S E , F R C O G

Dr W E Barnie-Adshead, gynæcologist and obstetrician to the Birmingham United Hospitals, who died on Jan 26 at the General Hospital, Birmingham, was born at Dudley in 1901 He entered the Birmingham Medical School in 1917, and his friendliness and good nature soon made him popular with his fellow students, who elected him their representative on the Guild of Undergraduates and president of the Medical Students Union

After taking his B SC in 1920 and his M B in 1923, he held resident posts at the Queen's Hospital, the General Hospital, and the Birmingham and Midland Hospital for Women He also worked for a time in the London Hospital, before he obtained the fellowships of two Royal Colleges of Surgeons in 1926 In the same year, at an unusually early age, he was appointed assistant obstetrician and gynæcological surgeon to the Queen's Hospital at Birmingham Here he was junior to Mr Lewis Graham, on whose teaching and example he largely founded his own practice In 1929, he joined the staff of the Women's Hospital as surgeon

One of the first members of the Royal College of Obstetricians and Gynæcologists he became a fellow in 1938, and he was lately elected to the council For many years he was lecturer and examiner in obstetrics and gynæcology to the University of Birmingham, and his students appreciated the value of his straightforward and direct teaching He was also lecturer and examiner to the Central Midwives Board

As a student he was remarkably good at games He captained the university soccer and cricket teams, and he was also a member of the tennis and golf sides For a season he played cricket for Worcestershire, and he is remembered as a sound bat and a brilliant fieldsman He was one of the best amateur footballers of his time, and for two seasons he was an English international halfback Later, when he had less time for games, he still played every year in the Birmingham doctors *v* clergy cricket match But golf became his main interest As well as playing himself, he generally managed to watch the Open Golf Championship and it was a great pleasure to him to encourage his two sons in their progress in the Boys' Open Championship

" Those who knew Barnie-Adshead well," writes F S T, " recognised in him a man of the highest integrity, with deep convictions Modest about his own merits, he did not try to create an impression but tended rather to minimise his achievements His views were known to be unprejudiced and were listened to with respect One of the kindest of men, he was very reluctant to criticise or impute unworthy motives to others His charm of manner and natural sympathy and understanding made him popular with his patients, and his colleagues valued his sound clinical judgment As an operator he was reliable and safe, deliberate but quick, and with no striving after effect 'Barnie' had many friends both inside and outside the profession It was a great grief to them to learn that he, who had always seemed so full of vitality, had been stricken Those who visited him during his illness were impressed, though not surprised, by his courage and fortitude "

J F B writes ' 'Perhaps it was because of his perfect natural physical abilities that Barnie-Adshead was above all the misfortunes of ambition The affection of his patients, his successes in his surgery came as naturally as his games—for he was a first-class sportsman in football, cricket, golf, and tennis His counsel was at all times thoughtful and free from bias, and his happy outlook brought good fellowship where there might have been estrangement His memory will always be cherished by those fortunate enough to be associated with him , particularly those of us who were his fellow students and shared his confidence In the prime of his condition his astounding courage in facing the inevitable will always be an inspiration''

He leaves a widow, Dr Eileen Adshead, and two sons, both of whom hope to become doctors

Notes and News

CODE OF SURGICAL OPERATIONS

THE Registrar General announces that the first draft of a Code of Surgical Operations has been prepared with the help of his Advisory Committee on Medical Nomenclature and Statistics, and making full use of existing American classifications The 3 figure code is divided into fifteen main sections according to the surgical specialty or broad anatomical location of the operation, with subsections giving greater detail of the site Within each subsection is a grouping, according to the different operational procedures, with tabular lists of the principal ones included in each category The draft code is being tried in certain hospitals and it is hoped that, with amendments resulting from this trial, a provisional code for wider use may be issued in 1952 The provisional code will form the basis of this country's recommendations to W H O for an International Code of Operations to supplement the International Statistical Classification of Diseases, Injuries, and Causes of Death

VOLUNTARY WORK FOR OUR HOSPITALS

THE pattern of our social services is changing, and the National Council of Social Service are wisely reconsidering the proper place of the voluntary worker in the new régime With the financial support of King Edward's Hospital Fund they are making a special study of voluntary services in the new hospital system Mr John Trevelyan, former director of education for Westmorland, is the director of the inquiry, and the advisory committee consists of Lady Norman (chairman), Dr Janet Aitken, Mr S F Burman, Sir Wilson Jameson, F R C P , Mr G Mitchell, and Dr Keith Murray

TUBERCULOUS IMMIGRANTS

THE regulations for the medical examination of immigrants have lately been discussed by the Joint Tuberculosis Council They fear that among the people who come to settle in this country there may be undetected cases of tuberculosis At a recent meeting of the council Dr Sybil Horner, who is observer for the Ministry of Labour, described the procedure of that Ministry for dealing with the immigrants they sponsor, most of whom are Italians These immigrants are examined in Italy, according to standards laid down by the Ministry of Health, by doctors appointed by the Italian ministry of labour A miniature chest X ray is made followed by a full sized film where necessary, but it is not known whether the doctor who reports on the film is always of consultant status The miniature film is included in the immigrant's dossier and is available to the port medical officer, who himself examines the immigrants at the port of entry The immigrants are first sent to a reception centre in London and then to a depot in Oldham till they are dispersed to their places of employment Further medical examinations could be carried out at either of those centres if necessary The Ministry of Labour, Dr Horner said, would be glad to know of instances of people reasonably suspected of having tuberculosis before immigration who had been accepted under the scheme Some of the trouble in the past might, she thought, have been with displaced persons from other war areas who are now no longer being brought over, or with people brought over by private arrangement, for whom no special provisions exist The repatriation of tuberculous immigrants is difficult because they can only be sent home if they are fit to travel and willing to go After hearing the measures taken at present, the council remained uneasy The regulations, they thought, are not sufficiently stringent It is essential they hold, that the doctors who scrutinise the X ray films should be of consultant status Large films, as well as the miniatures, they also suggest should accompany the immigrant

BRITISH STANDARD FOR CHILDREN'S COTS

THIS standard (B S 1694/1950) covers children's metal cots suitable for use in hospitals and similar institutions The standard height of the cots to the top of the corner castings is 2 ft , but alternative heights of 2 ft 3 in and 2 ft 6 in have also been provided Similarly a standard length of 4 ft 6 in has been adopted but an alternative length of 5 ft has been standardised for use in special cases The dimensions of the gaps between the tubes and bars forming the ends and the sides are to be not less than 3 in or more than $3^1/_2$ in , in order to avoid the risk of a child being trapped or injured The standard does not prevent the incorporation of additional atures, such as a removable head end or an adjustable ack rest Copies of this standard may be obtained from the ales department of the British Standards Institution, 4, Victoria Street, London, S W 1 price 2*s* 6*d* A separate tandard covering wooden cots for domestic use is being repared

---

University of Cambridge

On Jan 27 the following degrees were conferred

M.B B Chir—L J H Arthur N B Atkin • J A C Bamford • A P Barclay M H S Bound • J W Bradbeer • A A F Bryson • W E G Buckley • A S F Butcher • E P Cadbury • Eileen H Coats • P H Crosskey • J C M Currie J M H Dickson • B O L Duke • John Fairgrieve R M Fl Fox • P H Gorodi • A T G Gunn • J M Heaton • Una M P Hill • Geoffrey Hirst • M L House, • E W Jones • A B McGrigor J J McMullan • D S H W Nicol • F S Perry, • J R H Pinkerton • P J Randle • J R Rees, • J M. G Ritchie • H B Russell • J J H Rymer • Hiran Sirikantha Kirthi P C Steel • J D E Strong • P W Tucker • P H Wheeler • R. A Williams

• By proxy

University of London

Dr Ian Donald has been appointed to the university readership in obstetrics and gynæcology at St Thomas s Hospital Medical School

Dr Donald graduated B.A at Cape Town in 1930 before beginning his medical studies at St Thomas s Hospital in London He qualified in 1937 and he held a registrarship at the General Lying in Hospital before returning to St Thomas s as first assistant in the department of obstetrics and gynæcology During the war he served with the medical branch of the R.A F and he was mentioned in despatches and appointed M.B E for his services He took the M.D Lond and the M R C.O G in 1947 At present he holds the posts of clinical tutor in obstetrics and gynæcology at St Thomas s and of chief assistant at the Chelsea Hospital for Women His published work includes a paper on Uterine Rupture

University of Manchester

Dr W H Trethowan has been appointed lecturer in psychiatry

Royal College of Physicians of Ireland

On Feb 2 the following were admitted to the membership J C Dutta, William McAdam, Mary B O Donnell

Association of Surgeons of Great Britain and Ireland

The annual meeting of the association will be held in Manchester on Thursday, Friday, and Saturday, July 19, 20 and 21 The programme will include discussions on Head Injuries (opener, Sir Hugh Cairns), Infections of the Hand (Mr R M. Handfield-Jones and Mr W Gissane), Carcinoma of the Colon (Mr C Naunton Morgan), Acute Pancreatitis (Dr H. T Howat) After history of the Amputee in Peripheral Vascular Disease (Mr W A Mackey and Prof George Perkins)

Faculty of Ophthalmologists

The annual general meeting will be held on Wednesday, March 28, at 2 30 P M

British Association of Otolaryngologists

The following have been elected officers of the association for 1950–51 president Mr V E Negus vice president, Prof F C Ormerod secretary Mr F C W Capps, treasurer, Mr W A. Mill.

Conference on Tuberculosis

The Socialist Medical Association and the London Trades Council are holding a conference on tuberculosis on Saturday, Feb 10 at 2 P M., at St Pancras Town Hall, Euston Road, N W 1 Further particulars may be had from the secretary of the council 5 Guildford Place, W C 1

Medical School for non-Europeans in South Africa

A letter on the medical education of Africans, which appeared in our issue of Nov 25, mentioned the Union government s intention to open a non European medical school It is now officially stated that the new school has been "swamped with applications from native Indian, and Coloured students from all over the Union" The aim of the school is to turn out at least 20 qualified non European doctors each year A special building is being erected to house the medical school at Durban Natal at a cost of more than £200 000, and it is to be ready by 1953 At present a few non Europeans are trained at European medical schools in the Union. When the separate school has been completed, "apartheid" will be applied to the study of medicine, and non Europeans will not be accepted in other schools

Dental Fellowships for Doctors

The Nuffield Foundation is offering fellowships of £500 to £800 to graduates in medicine and science to receive training that will qualify them to undertake teaching and fundamental research on dental health and disease Further particulars will be found in our advertisement columns

Princess Tsahai Memorial Hospital

A further £2000–£3000 is needed to complete the equipment of this hospital in Addis Ababa Donations should be sent to the hon. treasurers, Lord Horder and Lord Amulree, c/o Messrs Gould & Prideaux, 88, Bishopsgate, London, E C 2

Shortage of Hospital Beds

A deputation from the British Medical Association's General Medical Services Committee visited the Ministry of Health on Jan 30, to discuss the increasing difficulty experienced by doctors in finding hospital accommodation for acute cases According to a statement which was issued afterwards, a number of suggestions were made to the Ministry These were being considered, and discussions, to be attended by medical officers of regional hospital boards, would continue

Health Services Conference

A conference to bring together representatives from all branches of the National Health Service will be held in London at Church House, Westminster, from March 14 to 16 to discuss Administrative Problems of the Health Services Mr Henry Lesser will be in the chair, and speakers will include Dr A Talbot Rogers, Dr T Rowland Hill, Dr A Torrie, Dr J A. Scott, and Dr W G Patterson Further particulars may be had from the secretary of the Institute of Public Administration, 76A, New Cavendish Street, W 1

French Government Exchange Scholarships

Under a reciprocal arrangement with the Centre National de la Recherche Scientifique, the Medical Research Council invite applications from young graduates in medicine or science who have already had some experience in a branch of medical science, excluding clinical medicine, for two scholarships tenable at research institutions in France during 1951–52 Candidates must be of British nationality and have at least a working knowledge of French The stipend will be within the range of 40,000–60,000 francs a month, and married men will receive a supplementary allowance Forms of application, to be returned by March 31, may be had from the secretary of the council, 38, Old Queen Street, London, S W 1

Meeting of W H O Executive Board

A meeting of this board opened at Geneva on Jan. 22 with Dr H S Gear in the chair (see *Lancet*, Feb 3, 1951, p 297) On Jan 24 the board decided, in view of the international situation, to postpone the first meeting of the Committee for the Western Pacific Region, which is served at present by an office in Hong Kong the meeting was to have been held in March With regard to Europe, the board approved the convening this year of a special consultative committee, to discuss future activities On Jan 26 the International Antivenereal Disease Commission of the Rhine was formally created This, the first intergovernmental commission established within the framework of W H.O, includes Belgium, France, the Netherlands, and Switzerland, the German federal government will be represented by observers The commission, which will have its administrative centre in Strasbourg and a technical and medicosocial secretariat in Rotterdam is to coördinate the venereal disease services of the five Rhine bordering countries for the benefit of Rhine River boatmen, and, where necessary, it will establish diagnostic and treatment centres in the main river ports

On Jan. 29 the board discussed the proposed W H O budget of $8 300 000 for 1952 Several members doubted whether additional financial burdens should be imposed on governments, but Dr Brock Chisholm, the director general, declared that 1952 would be a crucial year for W H.O —a year in which the Organisation should decide whether it was going to ' become a parasite or a leader He believed that millions of people throughout the world were prepared to spend large sums of money for health rather than for defence, and in any case the small amounts asked of each government for world health could not prejudice the execution of other programmes The board, unable to agree referred the question of this budget to the Committee on Administration and Finance

Obituary

WILLIAM EWART BARNIE-ADSHEAD

M.B. Birm., B.Sc., F.R.C.S., F.R.C.S.E., F.R.C.O.G.

Dr. W. E. Barnie-Adshead, gynæcologist and obstetrician to the Birmingham United Hospitals, who died on Jan. 26 at the General Hospital, Birmingham, was born at Dudley in 1901. He entered the Birmingham Medical School in 1917, and his friendliness and good nature soon made him popular with his fellow students, who elected him their representative on the Guild of Undergraduates and president of the Medical Students Union.

After taking his B.SC. in 1920 and his M.B. in 1923, he held resident posts at the Queen's Hospital, the General Hospital, and the Birmingham and Midland Hospital for Women. He also worked for a time in the London Hospital, before he obtained the fellowships of two Royal Colleges of Surgeons in 1926. In the same year, at an unusually early age, he was appointed assistant obstetrician and gynæcological surgeon to the Queen's Hospital at Birmingham. Here he was junior to Mr. Lewis Graham, on whose teaching and example he largely founded his own practice. In 1929, he joined the staff of the Women's Hospital as surgeon.

One of the first members of the Royal College of Obstetricians and Gynæcologists he became a fellow in 1938, and he was lately elected to the council. For many years he was lecturer and examiner in obstetrics and gynæcology to the University of Birmingham, and his students appreciated the value of his straightforward and direct teaching. He was also lecturer and examiner to the Central Midwives Board.

As a student he was remarkably good at games. He captained the university soccer and cricket teams, and he was also a member of the tennis and golf sides. For a season he played cricket for Worcestershire, and he is remembered as a sound bat and a brilliant fieldsman. He was one of the best amateur footballers of his time, and for two seasons he was an English international halfback. Later, when he had less time for games, he still played every year in the Birmingham doctors *v.* clergy cricket match. But golf became his main interest. As well as playing himself, he generally managed to watch the Open Golf Championship and it was a great pleasure to him to encourage his two sons in their progress in the Boys' Open Championship.

"Those who knew Barnie-Adshead well," writes F. S. T., "recognised in him a man of the highest integrity, with deep convictions. Modest about his own merits, he did not try to create an impression but tended rather to minimise his achievements. His views were known to be unprejudiced and were listened to with respect. One of the kindest of men, he was very reluctant to criticise or impute unworthy motives to others. His charm of manner and natural sympathy and understanding made him popular with his patients, and his colleagues valued his sound clinical judgment. As an operator he was reliable and safe, deliberate but quick, and with no striving after effect. 'Barnie' had many friends both inside and outside the profession. It was a great grief to them to learn that he, who had always seemed so full of vitality, had been stricken. Those who visited him during his illness were impressed, though not surprised, by his courage and fortitude."

J. F. B. writes: "Perhaps it was because of his perfect natural physical abilities that Barnie-Adshead was above all the misfortunes of ambition. The affection of his patients, his successes in his surgery came as naturally as his games—for he was a first-class sportsman in football, cricket, golf, and tennis. His counsel was at all times thoughtful and free from bias, and his happy outlook brought good fellowship where there might have been estrangement. His memory will always be cherished by those fortunate enough to be associated with him, particularly those of us who were his fellow students and shared his confidence. In the prime of his condition his astounding courage in facing the inevitable will always be an inspiration."

He leaves a widow, Dr. Eileen Adshead, and two sons, both of whom hope to become doctors.

Notes and News

CODE OF SURGICAL OPERATIONS

THE Registrar General announces that the first draft of a Code of Surgical Operations has been prepared with the help of his Advisory Committee on Medical Nomenclature and Statistics, and making full use of existing American classifications. The 3-figure code is divided into fifteen main sections according to the surgical specialty or broad anatomical location of the operation, with subsections giving greater detail of the site. Within each subsection is a grouping, according to the different operational procedures, with tabular lists of the principal ones included in each category. The draft code is being tried in certain hospitals, and it is hoped that, with amendments resulting from this trial, a provisional code for wider use may be issued in 1952. The provisional code will form the basis of this country's recommendations to W.H.O. for an International Code of Operations to supplement the International Statistical Classification of Diseases, Injuries, and Causes of Death.

VOLUNTARY WORK FOR OUR HOSPITALS

THE pattern of our social services is changing, and the National Council of Social Service are wisely reconsidering the proper place of the voluntary worker in the new régime. With the financial support of King Edward's Hospital Fund they are making a special study of voluntary services in the new hospital system. Mr. John Trevelyan, former director of education for Westmorland, is the director of the inquiry, and the advisory committee consists of Lady Norman (chairman), Dr. Janet Aitken, Mr. S. F. Burman, Sir Wilson Jameson, F.R.C.P., Mr. G. Mitchell, and Dr. Keith Murray.

TUBERCULOUS IMMIGRANTS

THE regulations for the medical examination of immigrants have lately been discussed by the Joint Tuberculosis Council. They fear that among the people who come to settle in this country there may be undetected cases of tuberculosis. At a recent meeting of the council Dr. Sybil Horner, who is observer for the Ministry of Labour, described the procedure of that Ministry for dealing with the immigrants they sponsor, most of whom are Italians. These immigrants are examined in Italy, according to standards laid down by the Ministry of Health, by doctors appointed by the Italian ministry of labour. A miniature chest X ray is made followed by a full-sized film where necessary, but it is not known whether the doctor who reports on the film is always of consultant status. The miniature film is included in the immigrant's dossier and is available to the port medical officer, who himself examines the immigrants at the port of entry. The immigrants are first sent to a reception centre in London and then to a depot in Oldham till they are dispersed to their places of employment. Further medical examinations could be carried out at either of these centres if necessary. The Ministry of Labour, Dr. Horner said, would be glad to know of instances of people reasonably suspected of having tuberculosis before immigration who had been accepted under the scheme. Some of the trouble in the past might, she thought, have been with displaced persons from other war areas who are now no longer being brought over, or with people brought over by private arrangement, for whom no special provisions exist. The repatriation of tuberculous immigrants is difficult because they can only be sent home if they are fit to travel and willing to go. After hearing the measures taken at present, the council remained uneasy. The regulations, they thought, are not sufficiently stringent. It is essential, they hold, that the doctors who scrutinise the X ray films should be of consultant status. Large films, as well as the miniatures, they also suggest should accompany the immigrant.

BRITISH STANDARD FOR CHILDREN'S COTS

THIS standard (B.S. 1694/1950) covers children's metal cots suitable for use in hospitals and similar institutions. The standard height of the cots to the top of the corner castings is 2 ft., but alternative heights of 2 ft. 3 in. and 2 ft. 6 in. have also been provided. Similarly a standard length of 4 ft. 6 in. has been adopted, but an alternative length of 5 ft. has been standardised for use in special cases. The dimensions of the gaps between the tubes and bars forming the ends and the sides are to be not less than 3 in. or more than 3½ in., in order to avoid the risk of a child being trapped or injured. The standard does not prevent the incorporation of additional

MYOCARDIAL ISCHÆMIA AND ITS SURGICAL RELIEF *

GEORGE A. MASON
V.R.D., F.R.C.S
SENIOR SURGEON, REGIONAL THORACIC SURGERY CENTRE, SHOTLEY BRIDGE HOSPITAL, NEWCASTLE UPON TYNE

THE term cardiac ischæmia, or preferably myocardial ischæmia, conveniently denotes anæmia of the heart muscle, generally due to degenerative and obstructive changes in the coronary vessels—coronary artery sclerosis.

Morgagni recognised coronary-vessel sclerosis post mortem in 1707 and described it in his *De Sedibus et Causis Morborum* (1761):

> "As I examined the external surface of the heart the left coronary artery appeared to have been changed into a bony canal to the extent of many fingers breadth, where it embraces the greater part of the basis. And part of that very long branch, also, which it sends down upon the anterior surface of the heart, was already become bony to so great a space, as could be covered by three fingers placed transversely."

Attention may be drawn very forcibly to the presence of myocardial ischæmia by an attack, or attacks, of angina pectoris, a term usually associated with the name of Heberden, who named and described it in 1772. The description which follows is taken from his *Commentaries*, published in 1802, and is as good as any which has been given since:

> "But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it and not extremely rare, which deserves to be mentioned more at length. The seat of it, and the sense of strangling and anxiety with which it is attended may make it not improperly called angina pectoris.
>
> "They who are afflicted with it are seized while they are walking (more especially if it be up hill and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or to continue but the moment they stand still, all this uneasiness vanishes.
>
> "In all other respects the patients are, at the beginning of this disorder perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated in the upper part, sometimes in the middle sometimes at the bottom of the os sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxysm. Males are most liable to this disease, especially such as have past their fiftieth year.
>
> "After it has continued a year or more it will not cease so instantaneously upon standing still and it will come on not only when the persons are walking but when they are lying down, especially if they lie on the left side, and oblige them to rise up out of their beds. In some inveterate cases it has been brought on by the motion of a horse, or a carriage, and even by swallowing, coughing going to stool, or speaking, or any disturbance of mind. The termination of angina pectoris is remarkable. For if no accident intervene but the disease go on to its height, the patients all suddenly fall down and perish almost immediately. Of which indeed their frequent faintness, and sensations as if all the powers of life were failing, afford no obscure intimation."

Jenner (cited by Gibson 1898) is said to have suggested that the symptoms of myocardial ischæmia might be due to coronary disease. Brunton (1867), considering that angina might be due to vascular spasm, relieved it with amyl nitrite inhalations.

The coronary vessels when sclerosed are particularly liable to thrombosis, and the resulting increased or even completed obstruction causes necrotic changes or inflammation in the heart muscle—coronary thrombosis. Herrick (1912) showed that the severity of coronary thrombosis varied in different patients, that it could often be diagnosed during life, and that a patient could and often did recover from an attack.

John Hunter is an early reminder that this is often a "doctor's disease," and his suffering from it, the manner of his death, and the necropsy findings were fully described by his brother-in-law Edward Home (1794).

Angina is now generally regarded as due to myocardial anoxæmia; this is almost always a consequence of coronary sclerosis and, though occasionally it may be due to such causes as severe anæmia, paroxysmal tachycardia, or hyperthyroidism, there is often an associated vascular disease.

Levine (1936) and others have emphasised that "angina pectoris" and "coronary sclerosis" are not synonymous. The absence of the former does not exclude the presence of the latter. Though there are almost always associated structural changes in the coronary vessels if angina is present, it cannot be too strongly emphasised that they are often present without angina—just as the absence of claudication does not necessarily exclude peripheral sclerosis.

Clinically, though myocardial ischæmia is often manifested acutely and even dramatically by angina or coronary thrombosis, in many cases its indications are more insidious: there may be shortness of breath on exertion, a sense of oppression in the chest, or other sign of cardiac dysfunction, such as congestive failure, auricular fibrillation, or heart block.

Thrombotic obstruction of certain large vessels is constantly associated with characteristic areas of infarction. The descending branch of the left coronary artery is a favourite site for occlusion, and infarction of the anterior wall of the left ventricle and of the apex results.

The infrequency with which an area of infarction (or subsequent fibrosis) extends through the whole thickness of the wall, but rather extends some distance along it, has been emphasised by King (1941). If this were not so, ventricular aneurysm and rupture would occur more often. The main vessel may escape, and thromboses in the smaller branches tend to be multiple. Sometimes these are difficult to detect by the naked eye, and microscopical examination is required. The affected muscle degenerates and its place is taken by sclerotic tissue; hence irregular areas of fibrosis may be found throughout the heart.

By escaping thrombosis the narrowing of the larger vessels may proceed more slowly, and a diffuse replacement fibrosis of the heart muscle in the affected area results. Death eventually takes place, either slowly from progressive heart failure or suddenly from a fatal "heart attack." Beck (1943a) has sought to reproduce the latter experimentally, and describes the mechanism graphically:

> "The fatal heart attack is similar to a convulsive seizure. It is now recognised that an area of anoxemia in the brain gives rise to a convulsion. This focus on the brain has been referred to as a trigger. The trigger discharges and from it emanate impulses to other parts of the brain. These produce a generalised convulsion. An analogous condition exists in the heart. A trigger can be made by ligation of four or five coronary channels supplying an area of heart muscle two or three centimetres in diameter. This area of myocardium becomes cyanotic after these arteries are ligated and suddenly something happens which destroys the coördinated heartbeat. Some fibres are contracted while others are elongated and the ventricles become a writhing squirming mass of muscle which does not pump out any blood. The term ventricular fibrillation is applied to this condition and, as you know, it is fatal. It is similar to a convulsion of skeletal muscle and the term

---

* A guest lecture given in the department of surgery, Post-graduate Medical School of London, on June 9, 1950.

Scholarships Abroad

The British Council has published a handbook describing some seventy scholarships, mostly for postgraduate study, which are offered by fifteen foreign governments and universities to British students for the academic year 1951–52 The headquarters of the British Council are at 65, Davies Street, London, W 1

CORRIGENDUM

Surgery in Sciatica and Low Back Pain

Owing to the omission of a sentence from their typescript, the final section of the article by Mr Burns and Mr Young last week (p 245) may convey an impression very different from the conservative views expressed in the rest of the article The missing sentence was the first, and the section should read

"*Summing up*

When operation has been decided on, the choice of operation is made as follows

If there are well marked physical signs indicating a protrusion *the disc should be exposed and removed* If the physical signs are slight, as in many cases of chronic lame back the lesion will be neither well defined nor what we have called 'ripe , in these patients grafting will usually be preferred In a few cases the decision will be difficult , then one may choose to inspect the disc and, if the findings are indefinite, do a fusion at the same operation "

Appointments

BERESFORD C C M B Lond D P M director and consultant psychiatrist The Retreat York

BURRELL P S R M B Leeds D P H asst county M O Harrogate public health division of Yorkshire

COCKCROFT FRANK M A Camb M R C S D P H M O H Littlehampton and Worthing, and asst county M O West Sussex

EWALD DAVIDSON LINDE M D Belf D C H asst county M O H South Essex

FRANCIS W J L M B CH M Glasg F R C S , M RAD Lpool D M R T consultant radiotherapist Norfolk and Norwich Hospital

KNIGHT GWENDOLINE M R C S D P M deputy medical superintendent The Retreat York

KNOX W A M B Belf D P H asst county M O H Gloucestershire

MAKIN ROBERT M B Edin M O to South Eastern Gas Board

STOAKLEY RUTH M B Dubl asst county M O Settle public health division of Yorkshire

SUNDERLAND ELAINE M B Leeds, D OBST asst county M O Northumberland

TORRIE ALFRED M A M B Aberd D P M medical superintendent, The Retreat York

WALKER BETTY M D Lond D P H chief asst M O for maternity and child welfare Bristol

Births, Marriages, and Deaths

BIRTHS

CHILDS —On Jan 26, at Southsea Hants the wife of Dr H K Childs—a daughter

GAMMIE —On Jan 30 the wife of Dr J L Gammie—a son

LEES —On Jan, 17 the wife of Dr George Lees—a daughter

SEYMOUR JONES —On Jan 20 at Southsea Hants the wife of Mr Anthony Seymour Jones F R C S —a daughter

SOLOMONS —On Jan 27 in Dublin the wife of Dr Bethel Solomons jun —a son

TIBBETTS —On Jan 29 in Birmingham, the wife of Dr R W Tibbetts—a daughter

WALWYN JONES —On Jan 23 the wife of Dr E O Walwyn Jones —a daughter

MARRIAGES

DILLON—CAMERON —On Feb 2 in London Frederick Dillon M D to Dorothy Cameron

DU HEAUME—GIFFIN —On Jan 29 at Ballymena co Antrim, Brian Herbert du Heaume M R C S to May Giffin

LASK—ORASMAE —On Jan 25 in London Samuel Lask M D to Salme Orasmäe

DEATHS

BARNIE ADSHEAD —On Jan 26 in Birmingham William Ewart Barnie Adshead F R C S F R C S E F R C O G

BEARBLOCK —On Jan 31 Peter Esdaile Bearblock M R C S aged 80

BRETT —On Jan 30 at Canterbury Arthur Granville Brett, M R C S

HEMMING —On Feb 1 at Brighton, Charles Harold Hemming M R C S aged 83

KELLER —On Jan 28 Nicholas Joseph Keller F R C S I

OLIVER —On Jan 28 at Maidstone, Charles Pye Oliver C B C M G T D M D D P H aged 89

O RORKE —On Feb 1 in London Frederick John William Trench O Rorke L R C P I

Diary of the Week

FEB 11 TO 17

Monday, 12th

MEDICAL SOCIETY OF LONDON 11 Chandos Street W 1
8 30 P M Mr Hedley Atkins Dr Ralston Paterson Carcinoma of the Breast

Tuesday, 13th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Mr Harvey Jackson Tumours of the Orbit (Hunterian lecture)

UNIVERSITY OF LONDON
5 P M (Westminster Medical School, Horseferry Road, S W 1) Mr C J O R Morris PH D Adrenocorticotrophic Hormone of the Pituitary Gland

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene, Keppel Street W C 1 Dr Russell Fraser Antithyroid Drugs

INSTITUTE OF DERMATOLOGY, St John s Hospital Lisle Street, W C 2
5 P M Dr J O Oliver Sedimentation Rate in Dermatology

INSTITUTE OF NEUROLOGY National Hospital Queen Square W C 1
5 P M Prof M Bleuler (Zürich) Psychopathology of Cerebral Disease

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Mr Hugh Davson D SC Nervous Aspects of the Control of the Intra-ocular Pressure

CHELSEA CLINICAL SOCIETY
7 P M (South Kensington Hotel, 47 Queen s Gate Terrace S W 7) Dr S Wand Mr Lawrence Abel Dr J L Gorsky Impact of Politics on Medicine

Wednesday, 14th

ROYAL COLLEGE OF SURGEONS
5 P M Sir Max Page The Hunterian Heritage (Hunterian Oration)

UNIVERSITY OF LONDON
5 30 P M (St Mary's Hospital Medical School W 2) Mr S R M Reynolds PH D Uterine Accommodation of the Products of Conception (First of two lectures)

INSTITUTE OF DERMATOLOGY
5 P M Dr R W Riddell Medical Mycology

INSTITUTE OF PSYCHIATRY Maudsley Hospital Denmark Hill, S E 5
2 45 P M Professor Bleuler Acromegaly and Acromegaloid States—Psychiatric and Genetic Aspects

Thursday, 15th

ROYAL COLLEGE OF SURGEONS
5 P M Mr Denis Browne Congenital Deformities of Mechanical Origin (Hunterian lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Dr G W Harris Neural Control of the Pituitary Gland

CHARING CROSS HOSPITAL MEDICAL SCHOOL, Chandos Place W C 2
6 P M Lord Horder T H Huxley—Humanist (Huxley lecture)

WESTMINSTER MEDICAL SCHOOL
5 P M Dr R D Tonkin Postoperative Pulmonary Collapse

BRITISH INSTITUTE OF RADIOLOGY, 32 Welbeck Street W 1
8 15 P M Dr J F Brailsford Relative Value of Radiology in the Prevention of Tuberculosis

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr M Langham Physiological Factors Affecting the Penetration of Antibiotics into the Eye

INSTITUTE OF PSYCHIATRY
3 P M Dr W Mayer-Gross Experimental Psychoses and Other Abnormal Mental States Produced by Drugs

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place W 1
7 30 P M Dr J Newsome Recent Investigation into the Treatment of Schistosomiasis by Miracil D in Egypt

LIVERPOOL MEDICAL INSTITUTION 114, Mount Pleasant Liverpool, 3
8 P M Dr J S Fulton Present Scope and Limitations of Radiotherapy

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small s Wynd Dundee) Dr George MacFeat Family Doctor and the Future

Friday, 16th

FACULTY OF RADIOLOGISTS 45 Lincoln s Inn Fields W C 2
2 15 P M *Diagnosis Section* Dr C J Hodson Behaviour of Lipiodol in Bronchial Tree Dr J W McLaren, Dr G M Ardran Radiological Studies of Movements of the Duodenal Cap Duodenum and Jejunum in Man (Film)

EUGENICS SOCIETY
5 P M (26 Portland Place W 1) Mr G C L Bertram, PH.D. Eugenics and Human Ecology (Galton lecture)

LIBRARY ASSOCIATION
7 P.M *Medical Section* (11 Chandos Street W 1) Dr W R Bett Problem of Medical Language and Jargon

Saturday, 17th

BIOCHEMICAL SOCIETY
11 A.M (London School of Hygiene) Symposium on Biochemistry of Fertilisation and the Gametes

coronary artery. Fauteux and Palmer (1941), recalling work in the 1914–18 war which demonstrated the increased safety attending ligation of a main artery when its corresponding vein was tied, experimented with ligation of the great cardiac vein. Ligation of this protected dogs from subsequent infarction after ligation of the coronary branch. This finding was applied to the treatment of coronary disease in 10 persons, of whom 9 had severe angina and the 10th had several attacks of coronary thrombosis; he was the only one to die soon after the operation, and death was said to be due to a tension pneumothorax. The 9 other patients were entirely freed from their anginal pain except 1, and he was much improved. 2 died, 1 three months later and the other thirty months later, and the remaining 7 were all well and working at their old jobs four to six years after operation.

It is suggested that mechanical distension of the direct arteriovenous communications, said to be present in the human heart, is the most important factor in Fauteux's operation. He later increased the scope of this to include removal of sympathetic and parasympathetic plexuses at the roots of the great vessels, thus interrupting impulses to and from the myocardium via the coronary vessels but not interfering with the pacemaker (Fauteux 1946). In 10 of these combined operations, 7 of the patients were free from pain and returned to work, but 2 were tired and complained of tightness in the chest. There were 3 postoperative deaths—2 from thrombophlebitis and 1 from coronary occlusion three months later. It is not known to what extent pericardial adhesions (which might in themselves be beneficial) have formed in these cases.

Beck (cited by Blalock 1949) has done a great deal of new experimental work in which he has attempted, by anastomosing a systemic artery to the coronary sinus, to reverse the coronary circulation. He has found it possible to apply this procedure to patients with coronary insufficiency and success has been claimed. As severe and hazardous operations are entailed, and as the possibility of such a circulatory reversal has not yet been generally accepted, further knowledge of this work is required before its utility can be assessed.

Operations to Improve Vascularity of Heart Muscle by Initiating Surface Inflammation and Provision of Extracardiac Collateral Vessels

This is where my own interest has particularly lain. Neurectomy and thyroidectomy both imply acceptance of a vascular status quo in the myocardium; the proposition of bringing an additional blood supply thereto, or of insuring against further vascular catastrophes therein, seems much more attractive.

A close friendship with Laurence O'Shaughnessy enabled me to follow this work from the beginning. Like Beck he was one of the pioneers in both the experimental work (O'Shaughnessy 1936) and its clinical application. It has been proved, I think beyond question, that a collateral extracardiac circulation can be established, whether intercostal muscle, substernal fat, omentum, or lung be grafted or an artificial pericarditis alone be provoked. O'Shaughnessy's greyhound (O'Shaughnessy 1936), a host of injection pictures in the literature, and the protocols of experiments demonstrating the immunity with which coronary vessels can be tied after grafting, demonstrate the value of this method in the laboratory animal.

Beck's beautifully detailed experiments show that the provision of what he describes as a "blood bath" can prevent a myocardial trigger from discharging. This blood bath can be provided by improving the intercoronary anastomosis in the myocardium both by provoking inflammation on the surface of the heart and by grafting on to that surface some vascular tissue such as mediastinal fat, parietal pericardium, parietal muscle tissue, lung, or omentum. The experimental work referred to has shown that with a good successful graft innumerable small vessels, often minute, establish vascular continuity between the vessels of the graft and the coronary circulatory system rather than by the formation of large new vessels. However, it has been shown that the formation of these vessels seems to be, to some extent, in proportion to the degree of obstruction present in the original coronary vessels. It is, for instance, easier, in the experimental animal, to demonstrate formation of vessels after grafting, if the coronary artery to the grafted area has already been tied. Beck's work also seems to show that the new vessels, as well as the pre-existing anastomoses between the adjacent coronary arteries, can increase in size with slowly progressive occlusion of the coronary artery (Beck 1943b).

All O'Shaughnessy's results—and he had accumulated a considerable volume of material—are not available. After he was killed at Dunkirk, the key to his material was held by H. E. Mansell, the enthusiastic physician who coöperated with him. Mansell unfortunately died early in the war, and the records now seem to have been scattered. His latest figures in my possession are those published by Davies et al. (1938). Of 20 cases reported, 15 had angina, and 5 had other symptoms of cardiac ischæmia. Of the first group 5 died within three months of operation—1 of these from rupture of the ventricle during operation. Of the 10 who lived 8 resumed more or less normal life. In the second non-anginal group of 5 cases, 1 death was recorded; all 5 were much improved. The operations employed were cardio-omentopexy both transpleural and extrapleural, pericardiotomy with introduction of 'Aleuronat' paste, and cardiopneumopexy (Lezius 1937).

Strieder (1941) reported a case of a man, crippled by angina, who obtained very great, but not complete, relief from cardio-omentopexy but died suddenly six months later after the operative correction of partial herniation of the stomach through the diaphragm:

> "At autopsy, the graft was securely in place and on injecting the specimen through the superior mesentery artery, it was evident on section and on X-ray that there was a rather rich vascular ingrowth from the raft into the myocardium. There was diffuse fibrosis throughout the myocardium."

The latest results I have of Dr. Beck's are those published by Feil (1943). Among 37 cases treated by Beck's technique there were 14 postoperative deaths. 9 patients who survived the operation but died from four months to six years later were studied after death: 4 showed little improvement, and in 5 the results had been excellent. Of the 14 patients who survived at the time of publication 9 were definitely improved, 5 showing an increase in exercise tolerance and diminution of symptoms.

Feil classified the results of the 23 who survived the operation as excellent 14, good 5, and little or no improvement 4. He says the operation gave relief to the 14 surviving when he wrote, and that 5 others had been greatly benefited. One of Beck's patients underwent successfully a course of convulsion therapy for depression—a pretty good rest.

Thompson and Raisbeck (1942) described as especially suitable for "poor risk" cases the insufflation of sterilised talc into the pericardial sac whereby an adhesive pericarditis might produce similar benefit. Thompson (1949) has reported a series of 36 seriously handicapped patients. Of these, 6 died and 26 of the remainder were improved, being classified as good or excellent; in 4 the results were poor, but 8 were completely relieved of their angina and considered themselves practically normal. The criteria of rehabilitation were relief of anginal pain,

> convulsion of the heart might well be applied to this condition I believe if we could actually observe the heart in fatal attacks we would prefer to use the term convulsion of the heart rather than ventricular fibrillation
>
> "I should like to return to the experiment in which we ligated arterial channels to produce a trigger I should like you to visualise an experiment in which we ligate four small channels to a small area of myocardium We can observe the cyanosis of this small area of myocardium Now if we go no farther with our ligation we can close the operative wound and the animal will recover If we go ahead and ligate the fifth channel to this small area of myocardium the trigger will discharge, destroy the coördinated beat, and produce death This fifth small channel then can be regarded as the 'last straw' It makes the difference between life and death This vessel carries a small amount of blood, and a small amount of blood can make the difference between life and death This small amount of blood can be looked upon as a blood bath I do not think we can overemphasise the importance of a small amount of oxygenated blood delivered to that part of the heart where the blood supply is deficient Those who are adversely critical of this research will please bear in mind that a small amount of oxygenated blood can be significant It can save the life of the individual who has a trigger zone developing in the heart I need scarcely remind you that when death occurs from a heart attack it is usually sudden and unexpected Usually there are no signs of heart failure This is a physiological derangement and it is as effective as turning the ignition switch in a smoothly working motor The trigger zone may be important anatomically No doubt it could be excised experimentally if one cared to do so and the animal would be left with a good heart A new set of coronary arteries is not necessary to prevent a small localised trigger from discharging A blood bath can be effective '

Beck found repeatedly that the ligation of four or five small arteries over the left ventricle was a fatal procedure, the ventricle going into fibrillation Then he narrowed the two main coronary arteries, reducing their bore by about a third, and this degree of obstruction was tolerated In the second series of experiments a generalised anoxæmia was produced, compared with a localised but severe anoxæmia of a small part of the myocardium in the first series the former was tolerated, although the entire coronary circulation was reduced to a greater extent, and the latter was not

Injection experiments demonstrate the existence of anastomoses between the right and left coronary vessels, and these must provide some protection against the consequence of coronary occlusion These probably increase in number as well as in capacity when an inflammatory focus, such as that after an infarction, develops in the myocardium Pericardial adhesions are another source of vascular protection against the consequences of coronary occlusion , but King remarked on the astonishing infrequency with which they are found in view of the frequency of pericardial friction

Even so, clinically, I believe that the development of pericarditis in a case of coronary thrombosis is often welcomed as of good prognostic import Thus it may be that surface inflammation in disease has some beneficial effect on "deep" vascularity, as it does in experimental work

Feil (1943) has compiled a table from the literature showing the average duration of life *after* onset of the symptoms in several series of cases of coronary sclerosis The grave prognosis is obvious—in some 1728 cases the duration of life was 3 7 years His analysis of 256 cases in which death took place in Lakeside Hospital, Cleveland, from myocardial infarction and which had received conventional medical treatment, shows how short was the course run by the disease in most of the cases He says that medical therapy "does not in any way alter the underlying progress of these changes"

Palmer's (1937) statement, however, that 73% of patients may expect to be still alive at the end of four years, and 38% at the end of ten years, must be borne in mind We all know of people who have lived for many years after coronary thrombosis, but Palmer's figures presumably refer to survivors (after initial recovery), and my impression has always been that the prognosis is much worse than this—more approaching Feil's figures

SURGICAL TREATMENT

Probably almost as many people die of coronary disease as die of cancer and, as medical treatment is of little avail, it is important to see whether surgery has anything to offer At least it can offer an opportunity for the further study of "living pathology," and the taking of such opportunities elsewhere in the body has usually led to progress As Beck (1943a) says

> "If a car does not run, someone has to lift up the hood and look We are now entering the era of direct examination and manipulation in the cardiovascular field"

Surgical treatment to date can be considered under the following headings

(1) Attempts to reduce metabolic activity and thus the demands made on the heart

(2) Interruption of nervous pathways to eliminate pain.

(3) Stimulation of intercoronary compensating circulation by obstructing the flow in the cardiac veins

(4) Operations to improve the vascularity of the heart muscle by the provision of extracardiac collateral vessels

Attempts to Reduce Metabolic Activity

Attempts to reduce the strain on the heart by reducing the level of thyroid activity were made in the years between the wars (Blumgart et al 1933) Such treatment is really only palliative and condemns the patient to a reduced level of existence I have no experience of it and believe that it is now discarded Actually one of my better grafting results has been in a lady who could not, because of angina, take the thyroid extract necessary to control her (idiopathic) myxœdema

Interruption of Nervous Pathways

Jonesco's (1920) cervical sympathectomy, Leriche's stellate ganglionectomy (Leriche and Fontaine 1927) Mandl's (1925) injection and White's (1929) excision of the upper dorsal chain, Singer's posterior and Raney's (1939) anterior rhizotomy, and now Fauteux's peri coronary neurectomy are proceedings which have all had their advocates , indeed some are still practised Again, however, they are *only palliative* and cannot properly compensate the heart for its diminished blood supply—the essence of the condition—at any rate if anything like normal function is required of it.

Injections of the sympathetic ganglia may be indicated on humanitarian grounds and often relieve the distressing pain of a patient who is unsuitable for other procedures and resigned to a quiet life Great skill and accuracy is needed to "site" these injections and probably anæsthetists used to paravertebral and sympathetic injections are most suited to do this work The method is not altogether free from risk, and I have seen, especially where bilateral injection has been necessary, the consequent fall in blood pressure apparently initiate coronary thrombosis After injection neuritic intercostal pain may persist and may be extremely severe Palmer (1937) cites a patient who said that when he had his angina he was afraid he might die from it, but when he had neuritis he was afraid he might *not* die

Obstruction of Venous Return from Heart Muscle

Gross et al (1937) have shown that occlusion of the coronary sinus in the dog causes an increase in the coronary tree and in the intercoronary anastomotic vessels Preliminary preparations of a dog's heart in this way made it well nigh impossible to produce infarction by tying the anterior descending branch of the left

TABLE II—CASES UNRELIEVED

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Post operative survival	Comment
13	53	F	9 months	Severe progressive angina on slightest exertion or excitement latterly bedfast	180/100	March 5 1937 general anæsthesia transpleural cardio omentopexy, graft stitched to heart	2 months	No relief necropsy showed graft diffusely adherent pericardial sac obliterated and chronic interstitial nephritis
12	58	M	18 months	Gross hypertension angina of effort (50 yards)	240/135	April 1 1941 general anæsthesia, pericardium opened through Larrey's angle, omentum applied to heart after application of aleuronat paste	2½ years	Slight relief only and eventually pain as bad as ever necropsy showed gross coronary atheroma large fatty heart with dilated right side, pulmonary congestion, and graft only adherent over small area
13	58	M	18 months	Angina of effort and breathlessness very neurotic and hypertensive	230/110	April 17 1949 general anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	14 months	No relief admitted widespread pains breathless, gross hyperplesia very anxious difficult to assess no beneficial effect

liable to cause arrhythmias, hence for a while we preferred ether oxygen anæsthesia Latterly we have used light general anæsthesia with thiopentone, nitrous oxide, and oxygen, with curare to control excessive respiratory movements Cardiac irregularities due to manipulation of the heart are minimised by instilling 1% procaine into the pericardium and a continuous intravenous infusion of procaine in 0 2% or 0 1% solution

SURGICAL METHODS

The operative techniques used have varied with the condition of the patient and with increased experience Where the patient's general condition has been bad, an extrapleural pericardiotomy (Davies et al 1938) through Larrey's angle after removal of the 7th costal cartilage has been used, and either aleuronat paste smeared over the pericardial sac or asbestos powder insufflated into it In the earlier cases the original O'Shaughnessy anterolateral thoracotomy and transpleural exposure of the heart were used, and a pedicled graft of great omentum was brought up and applied to the heart In one of these cases a loop of colon passed up the centre of the omentum and became strangulated, now we pass "obstructing" stitches across the omentum between the margins of the diaphragmatic defect to obviate this

Later Beck's (1943b) revised approach was used With this the 3rd, 4th, and 5th left costal cartilages are removed, the pericardium being opened extrapleurally and between the intercostal bundles, which should be preserved The parietal pericardium was abraded with Beck's raspatories and then either smeared with aleuronat paste or asbestos powder insufflated into the sac However, if the condition of the patient permitted, the omentum was first brought up either through the linea alba or through the front of the medial part of the diaphragm—i e, either in front of or behind the costal margin, as convenient—and next piloted into the sac deep to the intercostal bundles, spread over the heart surface, and tacked to the pericardium For a long time we avoided suturing directly to the heart in these cases, but it is now felt that this probably need not be feared

If the pleura has been opened, either deliberately or accidentally, during the operation the lung should be fully inflated before the wound is closed

POSTOPERATIVE MANAGEMENT

Anoxæmia must be avoided Adequate oxygenation during the postoperative period is essential, for this purpose the B.L B mask is convenient, but the patient must be well watched lest any obstruction of the airway with consequent anoxæmia occurs In this connection the importance of radiographic control may be emphasised, an X ray photograph of the chest should be obtained as soon as possible after the operation, by this a pneumothorax or even an atelectasis may be detected and, if present, dealt with promptly Such examinations should be repeated frequently during the recovery period, because respiratory complications are particularly embarrassing in such cases

It is our custom to block the appropriate intercostal nerves in all our thoracotomy cases to minimise post operative pain and so encourage the early use of breathing exercises Even so it has been our experience that these patients suffer an unusual amount of pain after operation, possibly associated with pericarditis Hence adequate sedation must be provided, for this purpose morphine is used freely, and intravenous procaine seems to be helpful

Vascular thrombosis, coronary or cerebral, has been the cause of death in a significant proportion of cases in this series (table I) Rehn and Halse (1949) and others have shown that anticoagulation therapy has had apparently a definite prophylactic effect in preventing embolism and thromboses after surgical operations generally Accordingly at present we give heparin after the first twelve or eighteen hours for two days and thereafter rely on dicoumarol for two or three weeks Even though our incidence of complicating thromboses has fallen, as a result presumably of somewhat better selection of cases and the definitely improved handling of these in the light of experience, it seems worth while using these anticoagulants

Breathing exercises and active muscular movements, within the limits of the preoperative exercise in tolerance, are practised from the day after operation until the patient is allowed up, usually after an interval of at least a month Resumption of activity must only be gradual, otherwise patients attributing their freedom from pain to some miraculous effect of the graft may undertake too much, sometimes with serious consequences Such early freedom from pain is unlikely to be due to the graft but only to the rest in bed and perhaps to an improved intercoronary circulation such as occurs in the laboratory animal as a consequence of pericardial reaction

REVIEW OF CASES

The present series consists of 30 cases operated on during the past fourteen years The great majority of these were dealt with in the Newcastle upon Tyne Regional Thoracic Surgery Centre, formerly at the Newcastle General Hospital and now at Shotley Bridge Of these patients 11 died within a few weeks of operation, but 1 of the deaths was in a private case, operated on elsewhere in unsatisfactory circumstances, and it has increase of exercise tolerance, and ability of the patients to fend for themselves and return to gainful occupation †

SELECTION OF CASES

Most physicians still being sceptical about the utility of these operations, we have not been able to pick and choose our patients Most of those with whom we have been concerned have been bad risks and often, rendered desperate by their disability, have pleaded for operation Strangely enough, some of the worst cases have been most successful, whereas some of the "early" deaths occurred among the comparatively fit At necropsy, however, even these latter were always found to have had a more severe degree of coronary disease than had been appreciated clinically

Feil (1943) remarked that the operation mortality was highest among the first patients operated on, because these, who had angina on slight exertion, had serious coronary disease and associated cardiovascular changes In our series, although the type of case latterly has not much improved, the mortality has, however, we feel that the improvement has been due rather to improved technical handling Gross hypertension has not necessarily been regarded as a contra indication, and this possibly may have been an unfavourable factor in some of our cases, but, on the other hand, some of our favourable results have been in this group We have learnt to avoid cases showing gross cardiac enlargement, renal changes, or pulmonary infection Similarly, it seems better at present to reject those who have had multiple coronary infarctions and those in whom there is clinical, radiological, kymographic, and possibly electrocardiographic evidence of severe myocardial damage

Ideally, and in principle, grafting seems to be indicated for the relief of anginal pain and, in those who have had an infarction, as an insurance against the consequences of further thromboses

ANÆSTHESIA

I am indebted to Dr Joan Millar, our senior anæsthetist, for the following details of our current anæsthetic practice The choice of suitable anæsthetic agents for patients who have had coronary thrombosis is often difficult Many of these patients belong to the older age group and are apprehensive about the condition of their heart and its ability to withstand the strain of a major operation On the other hand, some of the worst operative risks are desperately anxious to avail themselves of any chance of relief and a return to something approaching normal existence Hypertension is often a complicating factor Immediate postoperative deaths in these patients are usually the result of a further coronary thrombosis or of cerebral thrombosis, hence a marked fall in blood pressure should be avoided On the one hand the circulation must not be overloaded with large quantities of intravenous fluids, on the other there must be no dehydration during the period when the patient cannot drink freely

We have found local anæsthesia unsuitable, the injection of local anæsthetic solutions and consequent delay in starting the operation have a demoralising effect, often making these patients grey, anxious, and liable to "anginal attacks" General anæsthesia is preferable, especially when the proposed operation involves opening the pleura or diaphragm Premedication should be light but adequate for a smooth induction with a cautious dose of thiopentone The subsequent anæsthetic technique must provide high concentrations of oxygen and light anæsthesia without excessive respiratory movements Cyclopropane seems to have many advantages but is

TABLE I—EARLY POSTOPERATIVE DEATHS

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Date of operation	Date of death	Cause of death
1	34	M	3–4 years	Unable to work angina of effort (100 yards) due to emotion and sometimes at rest	140/90	General anæsthesia transpleural cardio omentopexy graft sutured	July 19 1937	July 20, 1937	Pulmonary œdema and atelectasis
2	45	F	4 years	Angina with any effort (even at rest in bed) and emotion	245/160	General anæsthesia, transpleural cardio omentopexy graft sutured	Oct 18, 1937	Nov 26, 1937	Cerebral thrombosis
3	38	F	2 years	Constant attacks of angina even at rest	135/100	General anæsthesia transpleural cardio omentopexy	July 5 1938	July 6 1938	Syphilitic aortitis &c.
4	73	M	2–3 years	Severe anginal pain sometimes at rest or with emotion	190/90	General anæsthesia transpleural cardio omentopexy abrasion with aleuronat paste	Aug 19 1938	Aug 23 1938	Broncho pneumonia and angina pectoris
5	53	M	6 months	Increasing dyspnœa and cardiac asthma after coronary thrombosis bedridden	130/75	Local anæsthesia cardio omentopexy through Larrey's angle and abrasion with aleuronat paste	Nov 1 1943	Nov 8 1943	Coronary thrombosis and pulmonary infarction
6	37	M	8 years	Angina after a few yards	210/150	Local anæsthesia anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	Nov 10 1944	Nov 10 1944	Coronary thrombosis
7	58	M	$3^{1}/_{4}$ years	Following coronary thrombosis angina of effort (100 yards) after meals or even turning in bed	164/98	Local anæsthesia anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	May 10 1945	May 31, 1945	Cerebral thrombosis
8	47	M	4–5 years	Almost bedridden with angina and claudication following attacks of coronary thrombosis	170/110	Local anæsthesia anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	June 20 1945	June 22 1945	Cerebral thrombosis
9	58	M	1 year	Angina following coronary thrombosis on least exertion unable to work	170/90	General anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	July 21 1947	Aug 11, 1947	Pulmonary embolism
10	47	M	9 months	Coronary thrombosis followed by angina of effort unable to work	152/79	General anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	Jan 31 1948	Feb 1 1948	Coronary thrombosis

---

† Since this lecture was delivered Forrester-Wood (1950) has reported 4 cases of angina apparently benefited in this way

TABLE II—CASES UNRELIEVED

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Post-operative survival	Comment
13	53	F	9 months	Severe progressive angina on slightest exertion or excitement latterly bedfast	180/100	March 5 1937 general anæsthesia transpleural cardio omentopexy, graft stitched to heart	2 months	No relief necropsy showed graft diffusely adherent pericardial sac obliterated and chronic interstitial nephritis
12	58	M	18 months	Gross hypertension angina of effort (50 yards)	240/135	April 1 1941 general anæsthesia, pericardium opened through Larrey s angle, omentum applied to heart after application of aleuronat paste	2½ years	Slight relief only and eventually pain as bad as ever necropsy showed gross coronary atheroma large fatty heart with dilated right side, pulmonary congestion and graft only adherent over small area
13	58	M	18 months	Angina of effort and breathlessness very neurotic and hypertensive	230/110	April 17 1949 general anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	14 months	No relief admitted widespread pains breathless gross hyperpiesia, very anxious difficult to assess no beneficial effect

liable to cause arrhythmias, hence for a while we preferred ether oxygen anæsthesia Latterly we have used light general anæsthesia with thiopentone, nitrous oxide, and oxygen, with curare to control excessive respiratory movements Cardiac irregularities due to manipulation of the heart are minimised by instilling 1% procaine into the pericardium and a continuous intravenous infusion of procaine in 0 2% or 0 1% solution

SURGICAL METHODS

The operative techniques used have varied with the condition of the patient and with increased experience Where the patient's general condition has been bad, an extrapleural pericardiotomy (Davies et al 1938) through Larrey's angle after removal of the 7th costal cartilage has been used, and either aleuronat paste smeared over the pericardial sac or asbestos powder insufflated into it In the earlier cases the original O'Shaughnessy anterolateral thoracotomy and transpleural exposure of the heart were used, and a pedicled graft of great omentum was brought up and applied to the heart In one of these cases a loop of colon passed up the centre of the omentum and became strangulated, now we pass 'obstructing" stitches across the omentum between the margins of the diaphragmatic defect to obviate this

Later Beck's (1943b) revised approach was used With this the 3rd, 4th, and 5th left costal cartilages are removed, the pericardium being opened extrapleurally and between the intercostal bundles, which should be preserved The parietal pericardium was abraded with Beck's raspatories and then either smeared with aleuronat paste or asbestos powder insufflated into the sac However, if the condition of the patient permitted, the omentum was first brought up either through the linea alba or through the front of the medial part of the diaphragm—i.e, either in front of or behind the costal margin, as convenient—and next piloted into the sac deep to the intercostal bundles, spread over the heart surface, and tacked to the pericardium For a long time we avoided suturing directly to the heart in these cases, but it is now felt that this probably need not be feared

If the pleura has been opened, either deliberately or accidentally, during the operation the lung should be fully inflated before the wound is closed

POSTOPERATIVE MANAGEMENT

Anoxæmia must be avoided Adequate oxygenation during the postoperative period is essential, for this purpose the B.L B mask is convenient, but the patient must be well watched lest any obstruction of the airway with consequent anoxæmia occurs In this connection the importance of radiographic control may be emphasised, an X ray photograph of the chest should be obtained as soon as possible after the operation, by this a pneumothorax or even an atelectasis may be detected and, if present, dealt with promptly Such examinations should be repeated frequently during the recovery period, because respiratory complications are particularly embarrassing in such cases

It is our custom to block the appropriate intercostal nerves in all our thoracotomy cases to minimise post operative pain and so encourage the early use of breathing exercises Even so it has been our experience that these patients suffer an unusual amount of pain after operation, possibly associated with pericarditis Hence adequate sedation must be provided, for this purpose morphine is used freely, and intravenous procaine seems to be helpful

Vascular thrombosis, coronary or cerebral, has been the cause of death in a significant proportion of cases in this series (table I) Rehn and Halse (1949) and others have shown that anticoagulation therapy has had apparently a definite prophylactic effect in preventing embolism and thromboses after surgical operations generally Accordingly at present we give heparin after the first twelve or eighteen hours for two days and thereafter rely on dicoumarol for two or three weeks Even though our incidence of complicating thromboses has fallen, as a result presumably of somewhat better selection of cases and the definitely improved handling of these in the light of experience, it seems worth while using these anticoagulants

Breathing exercises and active muscular movements, within the limits of the preoperative exercise in tolerance, are practised from the day after operation until the patient is allowed up, usually after an interval of at least a month Resumption of activity must only be gradual, otherwise patients attributing their freedom from pain to some miraculous effect of the graft may undertake too much, sometimes with serious consequences Such early freedom from pain is unlikely to be due to the graft but only to the rest in bed and perhaps to an improved intercoronary circulation such as occurs in the laboratory animal as a consequence of pericardial reaction

REVIEW OF CASES

The present series consists of 30 cases operated on during the past fourteen years The great majority of these were dealt with in the Newcastle upon Tyne Regional Thoracic Surgery Centre, formerly at the Newcastle General Hospital and now at Shotley Bridge Of these patients 11 died within a few weeks of operation, but 1 of the deaths was in a private case, operated on elsewhere in unsatisfactory circumstances, and it has increase of exercise tolerance, and ability of the patients to fend for themselves and return to gainful occupation †

SELECTION OF CASES

Most physicians still being sceptical about the utility of these operations, we have not been able to pick and choose our patients Most of those with whom we have been concerned have been bad risks and often, rendered desperate by their disability, have pleaded for operation Strangely enough, some of the worst cases have been most successful, whereas some of the " early " deaths occurred among the comparatively fit At necropsy, however, even these latter were always found to have had a more severe degree of coronary disease than had been appreciated clinically

Feil (1943) remarked that the operation mortality was highest among the first patients operated on, because these, who had angina on slight exertion, had serious coronary disease and associated cardiovascular changes In our series, although the type of case latterly has not much improved, the mortality has, however, we feel that the improvement has been due rather to improved technical handling Gross hypertension has not necessarily been regarded as a contra indication, and this possibly may have been an unfavourable factor in some of our cases, but, on the other hand, some of our favourable results have been in this group We have learnt to avoid cases showing gross cardiac enlargement, renal changes, or pulmonary infection Similarly, it seems better at present to reject those who have had multiple coronary infarctions and those in whom there is clinical, radiological, kymographic, and possibly electrocardiographic evidence of severe myocardial damage

Ideally, and in principle, grafting seems to be indicated for the relief of anginal pain and, in those who have had an infarction, as an insurance against the consequences of further thromboses

ANÆSTHESIA

I am indebted to Dr Joan Millar, our senior anæsthetist, for the following details of our current anæsthetic practice The choice of suitable anæsthetic agents for patients who have had coronary thrombosis is often difficult Many of these patients belong to the older age group and are apprehensive about the condition of their heart and its ability to withstand the strain of a major operation On the other hand, some of the worst operative risks are desperately anxious to avail themselves of any chance of relief and a return to something approaching normal existence Hypertension is often a complicating factor Immediate postoperative deaths in these patients are usually the result of a further coronary thrombosis or of cerebral thrombosis, hence a marked fall in blood pressure should be avoided On the one hand the circulation must not be overloaded with large quantities of intravenous fluids, on the other there must be no dehydration during the period when the patient cannot drink freely

We have found local anæsthesia unsuitable, the injection of local anæsthetic solutions and consequent delay in starting the operation have a demoralising effect, often making these patients grey, anxious, and liable to " anginal attacks " General anæsthesia is preferable, especially when the proposed operation involves opening the pleura or diaphragm Premedication should be light but adequate for a smooth induction with a cautious dose of thiopentone The subsequent anæsthetic technique must provide high concentrations of oxygen and light anæsthesia without excessive respiratory movements. Cyclopropane seems to have many *advantages* but it

---

† Since this lecture was delivered Forrester Wood (1950) has reported 4 cases of angina apparently benefited in this way

TABLE I—EARLY POSTOPERATIVE DEATHS

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Date of operation	Date of death	Cause of death
1	34	M	3–4 years	Unable to work angina of effort (100 yards) due to emotion and sometimes at rest	140/90	General anæsthesia transpleural cardio-omentopexy, graft sutured	July 10, 1937	July 20 1937	Pulmonary œdema and atelectasis
2	45	F	4 years	Angina with any effort (even at rest in bed) and emotion	245/160	General anæsthesia transpleural cardio omentopexy, graft sutured	Oct 18 1937	Nov 26 1937	Cerebral thrombosis
3	38	F	2 years	Constant attacks of angina even at rest	135/100	General anæsthesia transpleural cardio omentopexy	July 5 1938	July 6 1938	Syphilitic aortitis &c
4	73	M	2–3 years	Severe anginal pain, sometimes at rest or with emotion	190/90	General anæsthesia transpleural cardio-omentopexy abrasion with aleuronat paste	Aug 19 1938	Aug 23 1938	Broncho pneumonia and angina pectoris
5	53	M	6 months	Increasing dyspnœa and cardiac asthma after coronary thrombosis bedridden	130/75	Local anæsthesia cardio omentopexy through Larrey's angle and abrasion with aleuronat paste	Nov 1 1943	Nov 8 1943	Coronary thrombosis and pulmonary infarction
6	37	M	8 years	Angina after a few yards	210/150	Local anæsthesia anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	Nov 10 1944	Nov 10 1944	Coronary thrombosis
7	58	M	3½ years	Following coronary thrombosis angina of effort (100 yards) after meals or even turning in bed	164/98	Local anæsthesia, anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	May 10 1945	May 31 1945	Cerebral thrombosis
8	47	M	4–5 years	Almost bedridden with angina and claudication following attacks of coronary thrombosis	170/110	Local anæsthesia anterior pericardiotomy abrasion of pericardium and insufflation of asbestos (Beck)	June 20, 1945	June 22 1945	Cerebral thrombosis
9	58	M	1 year	Angina following coronary thrombosis on least exertion unable to work	170/90	General anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	July 21 1947	Aug 11 1947	Pulmonary embolism
10	47	M	9 months	Coronary thrombosis followed by angina of effort unable to work	152/79	General anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	Jan 31 1948	Feb 1 1948	Coronary thrombosis

his death Although there was no recurrence of his anginal pain after operation, the incapacity imposed by the trigeminal neuralgia made it impossible to test his exercise capacity

Two patients who had considerable relief from anginal pain and some increase in their exercise tolerance died five months after operation.

Case 16 —This man, who was thought to have syphilitic aortitis with aortic incompetence, died in another part of the country No necropsy was done, but his doctor informed us that he seemed to be doing well and was improving gradually until four days before his death, when he developed a severe precordial pain—unlike his previous angina—which was unrelieved by nitrites and was thought at the time to be due to his aortitis

Case 20 —This man was a severe case of myocardial ischæmia who possibly abused his newly found freedom from pain and attempted too much activity His dyspnœa, but not his pain, recurred, congestive heart failure developed, and he died At necropsy gross coronary atheroma and myocardial fibrosis were found The lung, which had been encouraged to adhere to the heart after removal of part of the pericardium on the left side and smearing with aleuronat paste, was diffusely adherent, and the pericardial sac obliterated The histological records cannot now be traced

Case 27 —This similar case is that of a female private patient who enjoyed her freedom from pain following operation so much that when discharged from hospital she at once resumed full activity, despite the protestations of her medical advisers Presumably as a consequence she developed, just two months after operation, a severe precordial pain, which was diagnosed as coronary thrombosis, and died within a few hours

Case 22 —A priest, aged 57, with gross hyperpiesia (230/130) who had had severe angina for three years, became much more comfortable after grafting and resumed some of his parochial duties Two years later, however, he began to have frequent severe attacks, each one resembling a major coronary thrombosis Only slight relief from the pain of these attacks followed a left-sided sympathectomy (Raney), and he died, four years after the original operation, from cerebral thrombosis No necropsy was done, but it seems possible (to put it at its lowest) that, apart from giving some relief for two years, the presence of the graft may well explain his long survival despite the many attacks regarded as major coronary thromboses

Case 21 —This lady, now aged 75, who was grafted in 1938, is another case from which a little encouragement may be derived Although pain was never completely absent it was considerably reduced during the early postoperative years The patient, however has gross hyperpiesis (340/240) and as long ago as 1947 had albuminuric retinitis Her doctor and her family are emphatic that she has undoubtedly benefited from the operation

Cases Deriving Benefit

Although 4 of the patients in this group are now dead, the circumstances of their deaths or the dispersal of pathological material and other records unfortunately make it necessary to rely on their clinical histories for final assessment

Case 14 —A joiner and general labourer, aged 63, had had angina for nine years and latterly been unable to work. After transpleural cardio omentopexy he was freed from disability and resumed work He remained free from any symptoms

TABLE III—*continued*

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Post-operative survival	Comment
22	57	M	3 years	Severe angina precipitated by exertion heavy meals and emotion, unable to work as parish priest	230/130	June 23 1939 general anæsthesia transthoracic cardio-omentopexy graft sutured to heart	$3\frac{3}{4}$ years	Considerable relief of symptoms and resumed duty for 2 years then repeated attacks resembling severe coronary thromboses died from cerebral thrombosis no necropsy
23	59	M	20 months	Coronary thrombosis in 1943 followed by anginal attacks on slight exertion almost confined to bed	210/130	Oct. 17, 1945 local followed by general anæsthesia abrasion of pericardium and insufflation of powdered asbestos (Beck)	$4\frac{1}{2}$ years +	Complete freedom from pain operated on for recurrent inguinal hernia in 1947, works as coalminer digging, and lifting girders &c
24	56	M	18 months	Coronary thrombosis followed by angina and dyspnœa on slight exertion	190/120	Dec 5 1946 general anæsthesia abrasion of pericardium and insufflation of powdered asbestos (Beck)	$3\frac{1}{2}$ years +	Free from pain and resumed work for 4 months pain and dyspnœa recurred with increasing obesity, now comparatively well after reducing weight
25	52	M	8 months	Coronary thrombosis followed by angina on exertion (2 or 3 steps) unable to work	210/130	Jan 2 1947 general anæsthesia anterior cardio omentopexy abrasion and insufflation of asbestos powder	$3\frac{1}{2}$ years +	Complete freedom from pain, can walk 7 miles runs to catch bus resumed work as colliery checkweighman
26	61	F	20 months	Angina of effort (10 yards), unable to take thyroid (required for myxœdema) without causing angina	150/100	Dec 5 1946 general anæsthesia transthoracic cardio-omentopexy graft fixed to heart by suture and asbestos powdering	$3\frac{1}{2}$ years +	Completely freed from pain can take necessary thyroid extract and lead ordinary life
27	53	F	2 years	Angina of effort (20 yards)	120/80	June 13 1947 general anæsthesia intercostal bundle sutured to heart, pericardium abraded and insufflated with asbestos (Beck)	2 months	Complete freedom from pain resumed too much activity too quickly and died with coronary thrombosis (presumed) 2 months after operation no necropsy
28	49	M	$3\frac{1}{2}$ years	Dizziness and angina of effort (100 yards) shortness of breath almost confined to bed unable to work	102/72	Nov 24 1949 general anæsthesia anterior cardio-omentopexy omentum applied to heart abraded by asbestos powder	7 months +	Complete freedom from pain can walk 2 miles, going to Australia for holiday
29	41	M	8 months	Anginal pain brought on by exertion ($\frac{1}{4}$ mile) cold weather or heavy meals no relief by nitrites no improvement after a month s rest in bed	130/80	Jan 5 1950 general anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	6 months +	Still has some pain on hurrying thinks he is better than before operation no dyspnœa improving on June 27 1950 reported complete recovery anxious to resume work exercise tolerance much improved

proved impossible to ascertain the cause of death or obtain any clinical details Except in so far as it weights the mortality figures, this case must be discarded from further consideration here

Details of the remaining 10 early postoperative deaths are set out in table I 7 patients died within the first three or four days, and, apart from 1 who died from œdema of the right lung and atelectasis of the left, and 1 patient with syphilitic aortitis, the deaths were due either to coronary or cerebral thrombosis Cerebral thrombosis was also the cause of death in 2 other patients dying three or four weeks later Another died from massive pulmonary embolism, originating from the calf, after a similar period It seems likely that subsequent improvements in anæsthesia and operative technique as well as in general management, would have enabled some of them to recover

3 patients (cases 11–13 in table II) definitely obtained no relief Fourteen months after operation 1 of these is still alive Another died two months and the third two years after operation, and in these the grafts had only the most slender attachment to the heart

Significant benefit to the myocardium from grafting is thought to have been derived by 16 patients (cases 14–29 in table III, where they are arranged in chronological order of date of operation)

Of these 16 patients there are 6 of whom at best it can only be said that there is possibly evidence of the graft having played a beneficial role, on the other hand, the 10 other cases show why I feel strongly that these grafting procedures can be of benefit to myocardial ischæmia It is necessary to consider both these groups in some detail

Cases Deriving Problematical Benefit

Case 18 —This man developed a virulent frontal herpes on the day after operation, and this was succeeded by severe trigeminal neuralgia, which persisted and completely incapacitated the patient until his death sixteen months later from congestive heart failure His heart fibrillated after the induction of the anæsthetic and again intermittently until

TABLE III—CASES PROBABLY DERIVING BENEFIT

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Post-operative survival	Comment
14	63	M	9 years	Presternal pain inability to work as joiner and general labourer breathlessness on exertion (80 yards) or emotion	120/70	Nov 4, 1936 general anæsthesia transthoracic cardio-omentopexy, graft sutured to heart	9 years	Complete freedom from pain for 5 years and resumed work, some pain during past 4 years died of pancreatic carcinoma with metastases necropsy showed coronaries almost occluded graft generally adherent and communicating vessels involved in growth
15	47	F	7 years	Anginal attacks precipitated by emotion and exertion and occasionally at rest breathless on slight exertion	130/80	March 25 1937 general anæsthesia transthoracic cardio-omentopexy graft sutured to heart	4½ years	Normal life with freedom from pain for 4 years some recurrence of pain for last 6 months, died from pneumonia following sloughing pharyngitis necropsy showed gross coronary sclerosis and graft diffusely adherent
16	54	M	8 years	Severe anginal pain brought on by cold, straining at stool &c specific aortitis with incompetence suspected but Wassermann reaction negative	160/30	March 25 1937 general anæsthesia transthoracic cardio omentopexy graft sutured to heart	5 months	Relief from pain and improved exercise tolerance 5 months died after 4 days illness suggesting specific aortitis, no necropsy
17	51	M	2 years	Inability to work as brass founder because of severe anginal pain brought on by exertion (stairs) and emotion and occasionally at rest virtually confined to house	160/90	May 7, 1937 general anæsthesia graft fixed to heart	7 months	Complete freedom from pain and resumed work 7 months, died of paralytic ileus and bronchopneumonia 4 days after operative relief of colon strangulated through graft (unrecognised 48 hr)
18	59	M	2 years	Anginal pain brought on by emotion and exertion (700–800 yards)	158/90	June 4 1937 general anæsthesia graft fixed to heart	16 months	Free from angina but intermittent fibrillation died from congestive failure after 16 months impossible to assess exercise capacity because of trigeminal neuralgia following malignant frontal herpes no necropsy
19	62	M	12 years	Unable to work because of angina and shortness of breath on exertion Wassermann reaction positive	135/80	Feb 1 1938 general anæsthesia, precordial pad of fat laid against aleuronated surface of heart and pericardium transpleurally	4 years	Freedom from pain and dyspnœa with resumption of work for 2 years then retired with some recurrence of dyspnœa died in sleep, no necropsy
20	57	M	5 years	5 years' breathlessness on exertion angina on walking (200 yards) and occasionally on walking in morning claudication	170/90	Feg 18 1938 general anæsthesia pericardium and heart smeared with aleuronat lung sutured to pericardium and left to adhere to heart	5 months	Free from pain but dyspnœa on exertion resumed activity too soon and died of congestive failure necropsy showed gross coronary sclerosis and lung heart, and pericardium diffusely adherent
21	63	F	1 year	Continuous anginal pain brought on by emotion and exertion (¼ mile) several syncopal attacks		May 1938 general anæsthesia transthoracic cardio omentopexy	12 years +	Considerable reduction in pain during early postoperative years now gross hypertension 340/240 but relations and doctor emphasise undoubted benefit from operation

his death Although there was no recurrence of his anginal pain after operation, the incapacity imposed by the trigeminal neuralgia made it impossible to test his exercise capacity

Two patients who had considerable relief from anginal pain and some increase in their exercise tolerance died five months after operation

Case 16 —This man, who was thought to have syphilitic aortitis with aortic incompetence, died in another part of the country No necropsy was done, but his doctor informed us that he seemed to be doing well and was improving gradually until four days before his death, when he developed a severe precordial pain—unlike his previous angina—which was unrelieved by nitrites and was thought at the time to be due to his aortitis

Case 20 —This man was a severe case of myocardial ischæmia who possibly abused his newly found freedom from pain and attempted too much activity His dyspnœa, but not his pain, recurred, congestive heart failure developed, and he died At necropsy gross coronary atheroma and myocardial fibrosis were found The lung, which had been encouraged to adhere to the heart after removal of part of the pericardium on the left side and smearing with aleuronat paste, was diffusely adherent, and the pericardial sac obliterated The histological records cannot now be traced

Case 27 —This similar case is that of a female private patient who enjoyed her freedom from pain following operation so much that when discharged from hospital she at once resumed full activity, despite the protestations of her medical advisers Presumably as a consequence she developed, just two months after operation, a severe precordial pain, which was diagnosed as coronary thrombosis, and died within a few hours

Case 22 —A priest, aged 57, with gross hyperpiesia (230/130) who had had severe angina for three years, became much more comfortable after grafting and resumed some of his parochial duties Two years later, however, he began to have frequent severe attacks, each one resembling a major coronary thrombosis Only slight relief from the pain of these attacks followed a left-sided sympathectomy (Raney), and he died, four years after the original operation, from cerebral thrombosis No necropsy was done, but it seems possible (to put it at its lowest) that, apart from giving some relief for two years, the presence of the graft may well explain his long survival despite the many attacks regarded as major coronary thromboses

Case 21 —This lady, now aged 75, who was grafted in 1938, is another case from which a little encouragement may be derived Although pain was never completely absent it was considerably reduced during the early postoperative years The patient however, has gross hyperpiesis (340/240) and as long ago as 1947 had albuminuric retinitis Her doctor and her family are emphatic that she has undoubtedly benefited from the operation

Cases Deriving Benefit

Although 4 of the patients in this group are now dead, the circumstances of their deaths or the dispersal of pathological material and other records unfortunately make it necessary to rely on their clinical histories for final assessment

Case 14 —A joiner and general labourer, aged 63, had had angina for nine years and latterly been unable to work. After transpleural cardio omentopexy he was freed from disability and resumed work He remained free from any symptoms

TABLE III—*continued*

Case no	Age (yr)	Sex	Duration of symptoms	Disability	Blood pressure (mm Hg)	Operation	Post operative survival	Comment
22	57	M	3 years	Severe angina precipitated by exertion heavy meals and emotion, unable to work as parish priest	230/130	June 23 1939 general anæsthesia transthoracic cardio-omentopexy graft sutured to heart	$3^3/_4$ years	Considerable relief of symptoms and resumed duty for 2 years then repeated attacks resembling severe coronary thromboses died from cerebral thrombosis, no necropsy
23	59	M	20 months	Coronary thrombosis in 1943 followed by anginal attacks on slight exertion almost confined to bed	210/130	Oct 17 1945 local followed by general anæsthesia abrasion of pericardium and insufflation of powdered asbestos (Beck)	$4^1/_2$ years +	Complete freedom from pain operated on for recurrent inguinal hernia in 1947 works as coalminer digging, and lifting girders &c
24	56	M	18 months	Coronary thrombosis followed by angina and dyspnœa on slight exertion	190/120	Dec 5 1946 general anæsthesia abrasion of pericardium and insufflation of powdered asbestos (Beck)	$3^1/_2$ years +	Free from pain and resumed work for 4 months pain and dyspnœa recurred with increasing obesity, now comparatively well after reducing weight
25	52	M	8 months	Coronary thrombosis followed by angina on exertion (2 or 3 steps) unable to work	210/130	Jan 2 1947 general anæsthesia anterior cardio omentopexy abrasion and insufflation of asbestos powder	$3^1/_2$ years +	Complete freedom from pain, can walk 7 miles runs to catch bus resumed work as colliery checkweighman
26	61	F	20 months	Angina of effort (10 yards), unable to take thyroid (required for myxœdema) without causing angina	150/100	Dec 5, 1946 general anæsthesia transthoracic cardio-omentopexy graft fixed to heart by suture and asbestos powdering	$3^1/_2$ years +	Completely freed from pain can take necessary thyroid extract and lead ordinary life
27	53	F	2 years	Angina of effort (20 yards)	120/80	June 13 1947 general anæsthesia intercostal bundle sutured to heart, pericardium abraded and insufflated with asbestos (Beck)	2 months	Complete freedom from pain resumed too much activity too quickly and died with coronary thrombosis (presumed) 2 months after operation no necropsy
28	49	M	$3^1/_2$ years	Dizziness and angina of effort (100 yards) shortness of breath almost confined to bed unable to work	102/72	Nov 24 1949 general anæsthesia anterior cardio-omentopexy omentum applied to heart abraded by asbestos powder	7 months +	Complete freedom from pain can walk 2 miles, going to Australia for holiday
29	41	M	8 months	Anginal pain brought on by exertion ($^1/_4$ mile) cold weather or heavy meals no relief by nitrites no improvement after a month s rest in bed	130/80	Jan 5 1950 general anæsthesia anterior cardio omentopexy omentum applied to heart abraded by asbestos powder	6 months +	Still has some pain on hurrying thinks he is better than before operation no dyspnœa improving, on June 27 1950 reported complete recovery anxious to resume work exercise tolerance much improved

referable to his heart for just over five years Nine years after operation he was admitted to a medical clinic, dying with abdominal symptoms, and stated that during the previous four years there had been some return of the precordial pain At necropsy a pancreatic carcinoma with many metastases was found The omentum was firmly and widely adherent to the heart and pericardium The omental vessels in it, including those apparently communicating with the heart, were extensively invaded by carcinomatous deposits Both coronary arteries were almost completely occluded by extensive calcareous changes

Case 15 —A woman, aged 47, had had angina for seven years, the attacks being usually precipitated by emotion and exertion but occasionally occurring at rest She was completely relieved of her symptoms by a transpleural cardio omentopexy and resumed full activity Four years later she was readmitted to hospital for assessment because of slight recurrence of pain and dyspnœa Unfortunately she developed sloughing pharyngitis and died from bronchopneumonia At necropsy the coronary arteries were found grossly thickened and the graft extensively adherent to the heart and pericardium

Case 4 —A brass founder, aged 51, had had angina for two years and latterly been unable to work and been virtually confined to the house After a transpleural cardio omentopexy he resumed full activity, walking up hills, working, &c, without disability Seven months later a hernial prolapse of the colon through the centre of the omentum into the chest became strangulated This remained unrecognised for forty eight hours and the patient died from paralytic ileus and bronchopneumonia five days after operation for its relief The graft was extensively adherent to the heart, and there was gross coronary atheroma, both arteries being almost obliterated

Case 6 —A man, aged 62, had had angina for twelve years and latterly been severely incapacitated After grafting of the precordial pad of fat on to the heart he was completely relieved of his symptoms and resumed ordinary activity for two years, at the end of which he died in his sleep—i e, *four years after grafting*

The 6 remaining patients are still alive and are even more encouraging

Case 23 —A miner, aged 59, whose blood pressure was 210/130, had had angina for twenty months following an attack of coronary thrombosis He was unable to work or to take more than two or three steps without having an anginal attack After grafting by the anterior route in October, 1945, he resumed full activity, working underground He was successfully operated on under spinal anæsthesia in April, 1947, for recurrent left inguinal hernia In a film illustrating this lecture (made in 1949) he is shown undertaking vigorous "P T," digging with pick and spade loading and wheeling a barrow, and running round a "Nylin" staircase without distress ‡

Case 11 —A miner, aged 56 with a blood pressure of 190/120, had had angina for eighteen months following an attack of coronary thrombosis Only able to walk a short distance without pain he was freed from pain and resumed work after grafting by the anterior route in December, 1946 Subsequently he became very fat from overeating and beer drinking, and after four months was readmitted to hospital with recurrence of pain and dyspnœa These symptoms cleared on a reducing diet This has happened now on three occasions, and when last admitted, the patient was said to require constant morphinisation to control the pain, in hospital, however, it was found that injections of distilled water gave the necessary relief, and again a reducing diet and abstinence led to his discharge from hospital comparatively fit The functional element and the obesity make it difficult to assess this case but it is thought that considerable benefit has resulted from grafting

Case 12 —A miners' checkweighman aged 52, with a blood pressure of 210/130 had had angina for eight months following an attack of coronary thrombosis Almost completely incapacitated, he could only walk twenty yards without having an anginal attack After grafting by the anterior route in January, 1947, he has resumed full activity at work, he can run to catch a bus and walk seven miles He also gave the same demonstration as case 23 in a film of his exercise tolerance

Case 25 —A lady, aged 61, with a blood pressure of 150/100, had been taking thyroid tablets for myxœdema for about two years Twenty months before admission to hospital she had had an attack of what was probably coronary thrombosis after which she could neither walk more than ten yards nor take the thyroid tablets without having an anginal attack. Since a transpleural cardio omentopexy in December, 1946, she has been able to take the thyroid tablets required and resume household duties, shop, and go upstairs, &c, without discomfort She has removed to another part of the country but has written saying that she is now very well

Case 28 —A man, aged 49, with a blood pressure of 102/79 and diagnosed clinically as having aortic stenosis, had had angina and "dizzy bouts" for three and a half years. He could not work as a miner or walk on the flat for more than 100 yards, being virtually confined to bed After grafting by the anterior route in November, 1949, he is now free from pain and can walk two miles He is about to visit Australia for six months

Case 29 —A miner, aged 41, with a blood pressure of 130/80, had had angina for eight months Attacks were brought on by exertion (he could only walk a quarter of a mile without pain), cold, and heavy meals They were not relieved by nitrites or a month's rest in bed Electrocardiograms suggested definite myocardial ischæmia and possibly infarction of the anterolateral part of the left ventricle After cardio omentopexy through an anterior approach in January, 1950, the patient has improved, at first gradually but latterly to such an extent that he is now anxious to resume work. On June 27, after this lecture was delivered, he stated that he could lead a normal life Only occasionally after running does he feel anything like the old pain His exercise tolerance is much improved, he can now run round the "Nylin" staircase five times without distress

DISCUSSION OF RESULTS

A series of 30 patients operated on, of whom 11 did not survive the first month, 3 were not relieved of their angina, and 16 are thought to have benefited from grafting, including 6 in whom the relief is admittedly very problematical, may not be impressive It must be remembered, however, that nearly all the patients were cardiac derelicts for whom there was little, if any, alternative hope To restore only a third of such patients as these to full activity, even temporarily, as well as to relieve them of their painful disability seems to have been worth while Experience and better facilities for treatment now available, through development of thoracic anæsthesia and surgical methods, would almost certainly improve these results

Exact pathological proof of the efficacy of grafting in this series is lacking, but it is extremely difficult to deny that something very striking has probably happened to the myocardium in the clinically successful cases It is not unreasonable to suppose that, as in the laboratory animal and in certain of Beck's, Strieders, and O'Shaughnessy's cases, a collateral circulation has been established In view of the extreme degree of bilateral coronary disease likely to be present in comparable cases coming to necropsy, it is almost impossible to explain the clinical relief obtained solely by an improvement in the intercoronary circulation

My indebtedness must be acknowledged to Dr A G Ogilvie, consulting physician, and to Dr W G A Swan, consulting cardiologist, to the Regional Thoracic Surgery Centre, for their help with the investigation and medical management of these cases, as well as to Mr W C Barnsley, assistant surgeon, and Dr Christopher Strang, senior medical registrar, for their help in following up these cases and obtaining useful information from scattered and often inadequate records

REFERENCES

Beck C S (1943a) Proc Inter-State postgrad med Assembly N Amer Chicago
— (1943b) *Ann Surg* 118 788
Blalock A (1949) *J thorac Surg* 18 849
Blumgart H L Levine S A Berlin, D D (1933) *Arch intern Med* 51 866
Brunton, T L (1867) *Lancet*, ii 97
Davies D T Mansell H E O'Shaughnessy L (1938) *Ibid*, i, 1

Continued at foot of next column

---

‡ This patient had an anterior infarction in December 1950, from which he is now (February, 1951) making a good recovery

ANÆMIA OF PREGNANCY TREATED WITH INTRAVENOUS IRON

JEAN M SCOTT
M D Glasg
ASSISTANT PATHOLOGIST

A D T GOVAN
M B Glasg, Ph.D Birm, F R.F P S
DIRECTOR OF RESEARCH

GLASGOW ROYAL MATERNITY AND WOMEN'S HOSPITAL

SOME anæmic women attending the antenatal clinic at this hospital responded in a rather peculiar way to iron given by mouth (Scott and Govan 1949)   These 14 cases (10% of our series) showed an initial rise of hæmoglobin of 2 g per 100 ml in the first month of treatment, but thereafter improvement was only slight, though treatment with iron and hydrochloric acid by mouth was continued   At that time we could not explain this tendency of the hæmoglobin level to "plateau," but we pointed out that two factors were common to the group—namely, anæmia and a mild form of gastro intestinal disorder

Later (Govan and Scott 1949) we reported 25 cases of anæmia treated with intravenous iron   This series included 2 cases of the above mentioned type, and both of them reacted to intravenous iron though they had not responded to iron given by mouth for three months   Since then we have studied the results of treatment with intravenous iron in a larger series, including cases of this type

To date we have treated 150 patients with intravenous iron, using three proprietary preparations   The biggest dose advised by the makers of two of these products is equivalent to 100 mg of elemental iron, whereas double this dose is recommended by the manufacturers of the third product

The patients formed three main groups   78 antenatal cases of uncomplicated iron deficiency anæmia, 59 cases of puerperal anæmia, and 13 antenatal cases of anæmia resistant to iron by mouth   All the antenatal patients were in the last trimester of pregnancy when intravenous iron was administered

ANTENATAL IRON DEFICIENCY ANÆMIA

Of the 78 patients in this group 29 had a moderate degree of anæmia, with Hb more than 8 g per 100 ml. (average 8 9 g per 100 ml.) and 3,600,000 red cells   All 29 responded to intravenous iron but not at a uniform rate   19 responded with an increase of at least 1 g (average 1 5 g) of Hb per 100 ml. at the end of the first week, after receiving the equivalent of 490 mg of elemental iron, and the remaining 10 showed an average increase of only 0.2 g of Hb per 100 ml at the end of a week   During the second week these 10 patients still lagged behind the others, but by the third week their response was more satisfactory (I and II on figure)

The remaining 49 patients all had severe anæmia with an average value of 6 7 g of Hb per 100 ml and 3,590,000 red cells   Of this number, 35 responded satisfactorily within a week to intravenous iron therapy with an average increase of 1 3 g of Hb per 100 ml   In the following two weeks the response progressively diminished.   The remaining 14 patients had a delayed response, and their hæmoglobin readings only increased by 0 3 per 100 ml during the first week, but in the second week the increase was slightly more than that shown by the other patients during the first week (III and IV on figure)

It is clear that many of the patients in this group showed a delayed response to intravenous iron, irrespective of the severity of the anæmia   The plasma protein levels were estimated in all our antenatal patients, and it was found that in all the patients the plasma protein levels tended to fall as the hæmoglobin increased   The fall in plasma protein level was greater in those patients who showed a delayed response   At the end of treatment the plasma protein levels of the patients who responded immediately were 5 9 g per 100 ml. or more, whereas in the patients showing a delayed response the value was just over 5 g per 100 ml   This fact suggests that the amount of available protein or protein reserve was limited in these cases

Daily hæmoglobin readings were made in some cases during the first week of treatment   It was found that the amount of hæmoglobin tended to decrease during the first three days of treatment but thereafter increased steadily   The decrease was most pronounced in severe cases   Where response to treatment was delayed the fall in the hæmoglobin curve was more prolonged, and the reading at the end of seven days was often less than at the start of treatment   The decrease in these cases was sometimes as much as 1 4 g per 100 ml.   These changes were almost certainly the result of hæmodilution

PUERPERAL ANÆMIA

There were 59 patients in this group   Only 6 had moderate anæmia (more than 8 g of Hb per 100 ml)—a number too small for analysis, and therefore they are included with the severe cases   In 47 patients anæmia was the only complaint   All showed an immediate and striking response to intravenous iron (V in figure)   Within three weeks the average amount of hæmoglobin had increased by 5 3 g per 100 ml (1 6 g per 100 ml a week)   For comparison 56 cases of uncomplicated puerperal anæmia were treated with ferrous sulphate gr 5 t.i d or ferri et ammon cit gr 30 t i d by mouth   These patients also responded promptly, but, although considerable, their increase in hæmoglobin was not comparable with that obtained with intravenous iron   At the end of four weeks the average increase of hæmoglobin was 3 4 g per 100 ml (0 8 g per a week)

The remaining 12 patients all had severe anæmia complicated by some other factor   7 of them had had severe shock at delivery, from placenta prævia, retained placenta, cervical lacerations, or cæsarean section, 4 had a secondary puerperal infection, and 1 was a grade IV cardiac   In all these cases the response to treatment was delayed, and during the first week of treatment the average increase of hæmoglobin was only 0 3 g per 100 ml.   During subsequent weeks, however, the response was similar to that of the other patients (VI in figure)

ANÆMIA RESISTANT TO IRON BY MOUTH

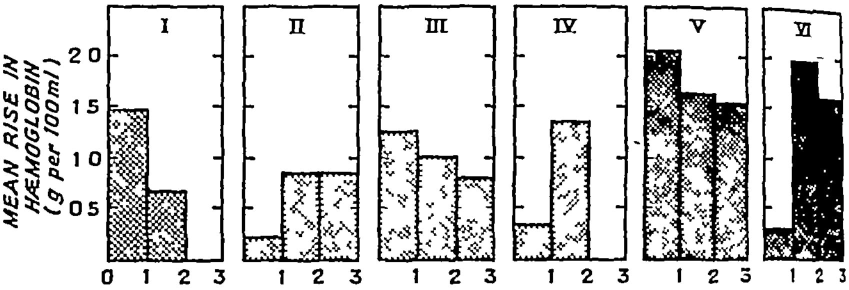
In this group 13 patients received iron and hydrochloric acid by mouth for one to five months (average

---

MR MASON   REFERENCES—*continued*

Fauteux, M. (1946) *Amer Heart J* 31 260
— Palmer J H (1941) *Canad med Ass J* 45 295
Fell H (1943) *Ann Surg* 118 807
Forrester Wood W R (1950) *Lancet*, i 1132
Gibson, G A (1898) Diseases of the Heart and Aorta   London
Gross L   Blum L   Silverman G (1937) *J exp. Med* 65 91
Heberden W (1802) Commentaries on the History and Cure of Diseases   London
Herrick J B (1912) *J Amer med. Ass* 59 2015
Home E (1794) preface to John Hunter s Treatise on the Blood, Inflammation and Gunshot Wounds   London
Jonesco T (1920) *Bull Acad Méd Paris*, 84 93
King E S J (1941) Surgery of the Heart.   London   p 419
Leriche E   Fontaine L (1927) *Arch Mal Cœur* 20 513
Levine S A (1936) Clinical Heart Disease   Philadelphia
Lezius A. (1937) *Arch klin Chir* 189, 342,
Mandl F (1925) *Wien klin Wschr* 38 759
Morgagni J B (1761) De Sedibus et Causis Morborum   Venice   Trans Benjamin Alexander   London 1769
O Shaughnessy L (1936) *Brit J Surg* 23 665
Palmer J H (1937) *Quart J Med* 6 49
Raney R B (1939) *J Amer med Ass* 113 1619
Rehn, von E.   Halse T H (1949) *Dtsch med Wschr* 74 1552
Strieder J W (1941) *J thorac Surg* 10 540
Thompson S A (1940) *Ibid* 18 848
— Raisbeck M. J (1942) *Ann intern. Med* 16 495
White J C (1929) *Arch Neurol Psychiat* 22 302

2–4 months). Of these 5 had moderate anæmia and 8 severe anæmia, the average hæmoglobin reading being 7·5 g. per 100 ml. After treatment the average hæmoglobin value had only increased to 7·8 g. per 100 ml. The peripheral blood picture was still that of a microcytic hypochromic anæmia. The plasma protein level averaged 5·5 g. per 100 ml. Test meals on 4 of these patients showed achlorhydria. Marrow biopsy was also performed, but there was no evidence of pernicious anæmia, although the picture is one which appears to be diagnostic of this type of anæmia (unpublished work). Intravenous iron produced an immediate response in 11 cases, the hæmoglobin rising 1·2 g. per 100 ml. in the first week. In the remaining 2 cases improvement was delayed, but during the second week of treatment the hæmoglobin rose by 1·9 g. and 2·1 g. per 100 ml. respectively.



Responses to intravenous iron. I: immediate in 19 cases of moderate anæmia. II: delayed in 10 cases of moderate anæmia. III: immediate in 35 cases of severe anæmia. IV: delayed in 14 cases of severe anæmia. V: in 49 cases of puerperal anæmia. VI: in 12 cases of puerperal anæmia complicated by some other condition.

The average increase of hæmoglobin for the whole group during the first week was 1·2 g. per 100 ml. and in the second week 1 g. per 100 ml.

DOSAGE

In general we have adopted the following regime. On the first day the equivalent of 30 mg. of elemental iron is given, on the second day 60 mg., and on the third day 100 mg. Thereafter 100 mg. is given daily until the end of the first week. During the second week 100 mg. is given every second day, so that by the end of this week 790 mg. of elemental iron has been given. This is sufficient to raise the "moderate" cases above the anæmia level, and they may then be given iron by mouth if necessary. Patients with severe anæmia may continue with intravenous iron 100 mg. every second day in subsequent weeks, or the dose may be reduced to 100 mg. once a week according to the severity of the anæmia.

We have been unable to use larger doses than 100 mg. of any of the three products, because of the frequency of reactions when that figure is exceeded.

REACTIONS

Minor reactions, such as pain in the arm, are fairly common, occurring in about 20% of cases. This reaction seems to be common to many types of intravenous injection and is not specifically due to iron. The most alarming reaction in pregnant women only occurs in about 1 or 2% of cases, and takes the form of a vasovagal attack, which we have described previously (Govan and Scott 1949). This type of reaction appears in some cases to depend on the amount of iron given in a single injection. It occurred in a few patients to whom we attempted to give more than the usual dose of 100 mg. of elemental iron. It may be seen, however, in some patients even with the usual dosage. In these cases its occurrence is irregular and does not follow any particular number of injections, but seems to be related more to the patient's condition at the time of injection. We have investigated some of these cases and hope to report on them later.

UTILISATION OF IRON BY PREGNANT PATIENT

According to many workers—e.g., Heath et al. (1932), Goetsch et al. (1946), and Nissim (1947)—intravenous iron is used quantitatively by the non-pregnant anæmic patient, the hæmoglobin increasing by 4% for every 100 mg. of elemental iron injected. We have shown that during pregnancy the average increase in hæmoglobin per 100 mg. of elemental iron is about half that—i.e., 0·3 g. per 100 ml. It has always been assumed that there is a considerable maternal storage during the early part of pregnancy, and that during the later months there is deviation of iron to the fœtus. We have previously suggested (Govan and Scott 1949) that the difference between the figures cited above, which is very considerable, was the result of maternal storage or transport of the iron to the fœtus.

We have investigated this point and, although our work is still in the preliminary stages, it is possible to make a definite statement indicating that maternal storage and fœtal demands are not entirely responsible for the limited response of the anæmic pregnant patients to intravenous iron. Serial estimations of serum-iron level were made following the injection of 100 mg. of iron, and in the average case the plotted values formed a steep curve. Ten minutes after injection the serum-iron level rose from 95 µg. per 100 ml. to about 325 µg. per 100 ml., but an almost equally rapid fall took place within the next two hours. It seemed to us that the iron was disappearing too quickly from the serum to be explained on the basis of storage, and the urine was found to contain iron. In this particular instance the specimen of urine passed two hours after injection contained 2·6 mg. of iron. In the twenty-four hours following injection 5·2 mg. of iron was excreted. The urine was collected in acid-washed china containers, and no specimen passed with fæces was included. Before estimation the urine was passed through acid-washed filter papers. It was next digested with concentrated sulphuric acid, and the iron was titrated in the usual way with thiocyanate.

Urine from 10 normal controls and from untreated patients with anæmia gave negative results. Up to now we have found that iron does not always appear in the urine after the initial injections but that it regularly appears later in the course of therapy. In 2 cases of anæmia in non-pregnant patients iron appeared in the urine after intravenous therapy, and we have also found it in the urine of puerperal cases undergoing treatment.

DISCUSSION

Our previous findings (Govan and Scott 1949) have been confirmed. Intravenous iron therapy is a useful means of treatment of anæmia in pregnancy, especially when time is short. It is apparent, however, in this extended series that all cases of iron-deficiency anæmia do not respond in the same way. Most of the patients respond rapidly, and in moderate anæmia the hæmoglobin is increased in the first week by 1·5 g. per 100 ml. on the average, whereas in severe cases the increase is 1·3 g. per 100 ml. These figures compare fairly well with that of 1·3 g. per 100 ml. reported in our first series. The difference of 0·2 g. per 100 ml. between the response of moderate and that of severe anæmia was puzzling until we examined the hæmoglobin level daily. In all degrees of anæmia iron therapy seems to initiate hæmodilution, which, however, is more severe and lasts longer in severe cases This causes a fall in hæmoglobin percentage and obscures the response to treatment Hæmodilution is most important in the puerperium, when there are fairly rapid and well marked changes in blood volume which may mislead the observer in making a diagnosis and assessing treatment

Delay in response until the second week of treatment was noted in 34 5% of moderate cases and 40% of severe cases No difference was detected between the blood or marrow pictures of the patients who responded immediately and of those in whom the response was delayed, but in the latter patients the plasma protein levels were uniformly low at the end of treatment Superficially at least this suggests that the delay in hæmoglobin regeneration may be related to the availability of protein In this respect it is interesting to note that Hahn and Whipple (1939) have found that the rate of hæmoglobin regeneration in anæmic animals is influenced by the intake of dietary protein

In the puerperium the response to intravenous iron is even greater than in the antenatal period It has been shown by many workers—e g, Heath et al (1932), Goetsch et al (1946), and Nissim (1947)—that intravenous iron is used quantitatively by non pregnant women, 100 mg of elemental iron leading to an increase of hæmoglobin of 4% (0 6 g Haldane) The highest response in our antenatal series was 0 4 g per 100 mg of elemental iron (average 0 3 g) In postnatal cases, however, the average hæmoglobin increase per 100 mg of elemental iron was 0 6 g, the highest individual response being 0 8 g per 100 mg The last named figure represents an abnormal increase, but it is more apparent then real, since the gradual hæmoconcentration starting about the third day of the puerperium must be taken into consideration (Crawford 1940) The same applies to the pronounced increase in the average hæmoglobin, 2 1 g per 100 ml., during the first week of treatment The calculated hæmoglobin increase of 0 6 g per 100 mg of iron during the puerperium is therefore probably greater than the actual, and it seems that even puerperal patients do not use the injected iron quantitatively

It will be noted that some puerperal patients did not respond immediately to treatment In 5 cases the cause was infection and cardiac failure The remainder had all suffered severe shock at delivery, this condition seems to depress the response to intravenous iron for a considerable time after delivery Although hæmorrhage initiated the shock in some of these cases, the delay in response was not due to blood loss, because many of the patients who responded normally had lost a considerable quantity of blood but none had suffered shock

Cases of anæmia resistant to iron given by mouth are comparatively common during pregnancy The number of such cases in our series is unknown, because most of the patients were treated with intravenous iron from the start The 13 cases we report here, however, are typical Achlorhydria was present in every case we examined, but routine treatment with dilute hydrochloric acid made no difference to their response to iron by mouth, and it seems very unlikely that a simple lack of acid could be the sole factor responsible According to Granick (1946) iron combines with apoferritin in the intestinal mucosa to form ferritin Thereafter the iron diffuses into the plasma, where it is probably linked with globulin Copp and Greenberg (1946) have shown that the diffusion of iron into the plasma is inversely proportional to the serum iron level and ceases when a certain saturation point is reached Repeated serum iron estimations were made in 3 of our patients receiving iron by mouth The results were uniformly low, varying from 5 to 45 μg per 100 ml. There was therefore no question of saturation of the plasma with iron in these cases

A possibility which must be considered is the availability of protein for the transport of iron In these cases, however, the plasma protein levels were relatively high and the serum iron level was low, and all the patients reacted to intravenous iron It seems likely that lack of response to iron by mouth is entirely related to the absorptive mechanism in the intestine Whether the intestinal environment is such that the iron is transformed into some compound which is incapable of being absorbed or the more intimate mechanism involving the apoferritin ferritin complex is upset is not known

Our finding of iron in the urine after intravenous therapy raises a number of interesting problems If, as seems likely, the iron is derived from the material injected, it would appear that either the capacity of these patients to deal with injected iron is limited or a renal threshold exists above which iron enters the urine It remains to be seen whether this urinary excretion is related to the modified response of these patients to intravenous iron It is just possible that the urinary iron is derived from some source other than the material injected However, the finding of iron in the urine of patients in the puerperium and of non pregnant patients undergoing treatment indicates that some revaluation of this mode of therapy is required

According to Hahn (1937), iron is only excreted in the urine in insignificant amounts in normal conditions A similar statement has been made by Barer and Fowler (1937) Cartwright (1946) states that only 1 5% at most of the original intravenous dose is excreted by the kidneys Most workers seem to assume that iron is never excreted in the urine after any mode of administration Our findings are in direct contrast to this, and we have even found iron in the urine of two patients undergoing treatment with iron by mouth

SUMMARY

The results of intravenous iron therapy in 150 cases of anæmia of pregnancy and the puerperium are recorded

During the antenatal period most of the cases responded immediately, and with the dosage used there was an average increase of 1 5 g of hæmoglobin per 100 ml in a week

About a third of the patients showed a delay in response until the second week of treatment This delay seemed to be related to the availability of protein

During the later months of pregnancy the highest response increase of hæmoglobin was 0 4 g per 100 mg of elemental iron

Treatment with intravenous iron at this period induced a temporary hæmodilution lasting three days in moderate anæmia and four or more days in severe anæmia

During the puerperium the average response to intravenous iron almost reached the calculated level of 4% per 100 mg of elemental iron In a few cases this figure might be exceeded, probably owing to the normal hæmoconcentration which begins usually about the third day after delivery

Response was delayed in the puerperium in infections, in systemic diseases, and in patients who had suffered shock at delivery

Iron deficiency anæmia which had proved resistant to iron by mouth improved rapidly under intravenous therapy The possible causes of resistance to oral iron are discussed

A dosage scheme is given, and it is recommended that in the treatment of anæmia of pregnancy no single dose should exceed 100 mg of elemental iron Severe reactions tend to develop when higher doses than this are given

Iron appears in the urine after intravenous injection This may be partly responsible for the modified response to intravenous iron during pregnancy

REFERENCES

Barer, A P , Fowler, W M (1937) *J Lab clin Med* **23**, 148
Cartwright G E (1946) *Blood*, **2** 111
Copp D H , Greenberg, D M (1946) *J biol Chem* **164**, 377
Crawford M D (1940) *J Obstet Gynæc* **47**, 63
Goetsch, A T Moore, C V , Minnich V (1946) *Blood*, **1**, 129
Govan, A D T , Scott, J M (1949) *Lancet*, i, 14
Granick S (1946) *J biol Chem* **164** 737
Hahn, P F (1937) *Medicine Baltimore* **16** 249
— Whipple, G H (1939) *J exp Med* **69**, 315
Heath, C W , Strauss, M B , Castle, W B (1932) *J clin Invest* **11**, 1293
Nissim, J A (1947) *Lancet* ii 49
Scott, J M Govan, A D T (1949) *Brit med J* ii 1083

INCIDENCE OF TUBERCULIN SENSITIVITY IN HOSPITAL CHILDREN

RELATED MORTALITY

Marguerite J Lunn
M B Glasg
From the Department of Child Health, University of Glasgow, and the Royal Hospital for Sick Children, Glasgow

A GREAT deal has been written about the incidence of tuberculosis in adults, but less is known of the frequency of tuberculous infection in children, as Miller (1949) has recently pointed out Watkins (1945) found that the tuberculin sensitivity rate in the medical unit of a children's hospital in Cardiff was in the region of 22% , but the unit did not admit known cases of tuberculosis, and tuberculin skin tests were performed only in selected cases Thompson (1947) reported on children in the Acton and Ealing districts of London who were tested in 1942–45 , but here too the series was not representative, since the children were attending tuberculosis clinics because of suspected infection or as contacts In 66 2% of the contact group, and 49 6% of the others there was a positive reaction to tuberculin jelly or to intradermal tuberculin

Brieger (1943) quotes the results obtained by Stott in the Papworth children, using the Moro test The reaction was positive in 63% of the children in their second year of life and in 56 8% of those aged one to five years Brieger also quotes some Continental observations For example, Heynsius van den Berg (1936) in Holland found that 71 5% of children under one year of age in contact with open tuberculosis were infected, the rate varying from 31 2%, under good hygienic conditions with slight exposure, to 100% under bad hygienic conditions with massive exposure. In Germany Seiffert (1935) reported that of children under five years of age who had been exposed to infectious tuberculosis 71 6–79 3% gave a positive reaction At the Royal Hospital for Sick Children, Glasgow, of 1470 children up to thirteen years old admitted to one medical unit in the years 1948 and 1949 116 gave a history of contact with open tuberculosis, and 68 of these proved to be tuberculin positive That is to say, 58% of these contacts had become sensitised

The following observations are presented to give an indication of the incidence of tuberculous infection, as measured by tuberculin sensitivity, in all children from birth to thirteen years admitted to the wards of one medical unit of the Royal Hospital for Sick Children, Glasgow, over the ten year period 1940–49 As no selection was exercised, the field surveyed is distinctly wider than in the above reports It must be emphasised, however, that these children do not represent a cross section of the juvenile population of Glasgow, or even of any one of its social classes The findings relate only to those admitted to a general children's hospital suffering from medical diseases

MATERIAL AND METHODS

Cutaneous sensitivity to tuberculoprotein was first demonstrated by Pirquet in 1907 It can be taken as evidence of infection with tubercle bacilli, and provides the best means of estimating the incidence of such infection in children

In the medical unit concerned, all children, except infants under four weeks of age, are on admission subjected, as a matter of routine, to two different tuberculin skin tests From 1940 to 1945, the Mantoux and the Pirquet tests were used, but after 1945 the latter was replaced by the tuberculin jelly test The figures presented here are based entirely on the results of the Mantoux intradermal reaction, because this is generally accepted as the most reliable of all the tests for tuberculin sensitivity (Hart 1932) No attempt is made to compare the merits of the various tests

In performing the Mantoux test, a weal was produced by the intradermal injection on the forearm of 0 1 ml. of a dilution of Old Tuberculin, fresh solutions being prepared every two weeks A 1/5000 solution was used for the first test, followed by a 1/1000 solution if the first test was negative and tuberculous disease was suspected clinically, and by injection of a 1/100 solution if the reaction was still doubtful The result of each test was read twenty four and forty-eight hours later It was assessed in most cases by two independent observers, erythema and induration both being required for a positive result The precise extent of the erythema and induration were not recorded, but broadly speaking the result was regarded as positive when the diameter of the reaction was 10 mm or more, and doubtful or negative when it was less than 10 mm

Changes in the staff performing and reading the tests have been unavoidable during the ten year period, and the different batches of tuberculin used must obviously have varied in potency , but these are variations which must occur in any large unselected series extending over a number of years

RESULTS

Annual Incidence

In the period 1940–49 7555 children were admitted to the unit Of these 1071 (14 7%) were Mantoux positive and 5175 (68 5%) were Mantoux negative (table I) The remaining 1309 (17 3%) comprise a group in which no results are available It consists of newborn and young infants on whom skin tests were not performed , some children who were allowed home, or transferred to a fever hospital, before their skin tests were due to be read , some who died within forty eight hours of admission , and a few in whom the results of the test were equivocal This group entitled " results not available " is included in the table because the figures are intended to show the incidence of tuberculin sensitivity in all the patients admitted to the unit It must be pointed out, however, that 1074 of the 1309 children in this group were under one year of age, and 83% of these were under three months It may be assumed that the tuberculin sensitivity rate at this age

TABLE I—RESULTS OF MANTOUX TESTS (YEARLY)

Year	Total admissions	Positive reactors	Negative reactors	'Results not available'
1940	683	95 (*14 0%*)	470 (*68 1%*)	118 (*17 3%*)
1941	642	84 (*13 1%*)	466 (*72 6%*)	92 (*14 3%*)
1942	813	116 (*14 4%*)	581 (*71 5%*)	116 (*14 3%*)
1943	895	115 (*13 0%*)	612 (*68 4%*)	168 (*18 9%*)
1944	942	96 (*10 2%*)	687 (*73 0%*)	159 (*16 9%*)
1945	683	88 (*12 9%*)	490 (*71 8%*)	105 (*15 4%*)
1946	666	122 (*18 3%*)	440 (*66 1%*)	104 (*15 6%*)
1947	761	102 (*13 4%*)	512 (*67 3%*)	147 (*19 3%*)
1948	753	153 (*20 3%*)	464 (*61 6%*)	136 (*18 1%*)
1949	717	100 (*13 9%*)	453 (*63 2%*)	164 (*22 9%*)
Totals	7555	1071 (*14 7%*)	5175 (*68 5%*)	1309 (*17 3%*)

TABLE II—RESULTS OF MANTOUX TESTS (AGE GROUPS)

Age (years)	Total admissions	Positive reactors	Negative reactors	' Results not available
0–1	3395	79 (2 3%)	2242 (66 0%)	1074 (31 6%)
1–2	900	112 (12 4%)	738 (82 0%)	50 (5 6%)
2–3	589	93 (15 8%)	458 (77 8%)	38 (6 4%)
3–4	413	75 (18 2%)	318 (77 0%)	20 (4 8%)
4–5	321	79 (24 6%)	222 (69 2%)	20 (6 2%)
5–6	335	86 (25 7%)	234 (69 9%)	15 (4 5%)
6–7	282	77 (27 3%)	193 (68 4%)	12 (4 3%)
7–8	277	83 (30 0%)	173 (62 5%)	21 (7 5%)
8–9	250	76 (30 4%)	160 (64 0%)	14 (5 6%)
9–10	227	80 (35 2%)	136 (59 9%)	11 (4 8%)
10–11	248	91 (36 7%)	143 (57 7%)	14 (5 6%)
11–12	196	89 (45 4%)	98 (50 1%)	9 (4 6%)
12–13	122	51 (41 8%)	60 (49 2%)	11 (8 9%)
Totals	7555	1071 (14 7%)	5175 (68 5%)	1309 (17 3%)

is very low, so no attempt has been made to introduce a correction in respect of these children

The incidence of positive reactors varies from year to year, the lowest was 10 2% in 1944, and the highest 20 3% in 1948 It is perhaps more significant that in 1940 it was 13 9% of all admissions, and by 1949 it was still at the same level Thus the incidence apparently did not rise during the ten years

A feature of the annual incidence is the relatively high level in 1946 (18 3%) and 1948 (20 3%) This is difficult to explain It might be suggested that the advent of streptomycin brought more tuberculous children to hospital, but this is ruled out by the fact that in 1947, the year between the two peaks, the rate was normal (13 4%). Nor does the incidence correspond to that of adult respiratory tuberculosis in Glasgow, which began to rise during the war and reached its peak in 1947 On the other hand, whereas in 1940 a family history of tuberculosis was obtained in only 20% of the positive reactors, in 1949 this figure had risen to 42 3%

Age incidence

Table II shows the number of positive reactors in each year of life from birth to thirteen years As one would expect, the percentage increases with age, but when the 12–13 age group is reached it unexpectedly falls This is most easily explained by saying that because the total number of admissions in the 12–13 age group is relatively small it may not be a representative sample Another factor, however, is the slightly higher proportion among them of " results not available," which makes the percentage of both negative and positive reactors lower than in the preceding age group

Mantoux Reversion

It is now universally accepted that Mantoux reversion does occur, and in the Prophit Survey Report Daniels et al. (1948) think it important enough to modify considerably the incidence of tuberculin sensitivity in a given community Lloyd and MacPherson (1933), in 303 urban children, found a reversion rate of 2% after an interval of two years Horan (1935) found a reversion-rate of 14% after eighteen months in 197 schoolboys aged fourteen and fifteen years Keller and Kampmeier (1939), working with students, found that 21% had reverted after four years Dahlström (1940) reported a reversion rate of 11 1% among 2828 persons after periods of five to fifteen years Madsen et al (1942) noted the influence of bovine tuberculosis on the reversion rate in 1000 Danish school-children In districts where there was a great deal of tuberculosis among cattle the rate was only 0 3%, whereas in districts where the cattle were free from tuberculosis it was 3%

In this country the phenomenon of reversion has received little attention, from which it may be inferred that it is not regarded as important But reversion may well be growing commoner now that tuberculin testing of cattle and pasteurisation of milk are eliminating the intermittent sensitivity sustaining doses of bovine tubercle bacilli in milk The theory that repeated small doses of tubercle bacilli are responsible for the persistence of allergy is supported by the work of Dahlström (1940) who found that reversion was commonest in families whose members had been least exposed to tuberculosis, and became less common as the probable exposure to tuberculosis increased On the other hand Crimm and Short (1939) were impressed by the number of patients who lost their allergy despite continued contact with tuberculosis, and suggested that desensitisation might result from "frequent subreactionary doses of tubercle bacilli"

In a small series of 40 children re tested at the Royal Hospital for Sick Children three to ten years after a known positive reaction, 6 were negative to 1/100 tuberculin This series is too small to be significant but the subject obviously requires further investigation The question also arises whether Mantoux reversion indicates bacterio logical healing of the primary lesion, just as calcification is taken to indicate clinical healing, and it would be of interest to attempt to correlate calcification and the subsequent resorption of calcium with loss of cutaneous tuberculin sensitivity

Mantoux reversion probably reduces to some extent the tuberculin sensitivity rate in the older age groups, but *until it is more fully understood no further conclusions* can be drawn

Negative Reactors Among Tuberculous Children

Some observations have been made on another well recognised group of children—those who remain Mantoux negative despite conclusive evidence of active tuberculosis During the ten year period under survey, 37 such children were seen They were all suffering from acute progressive tuberculosis, diagnosed clinically and radiologically or bacteriologically, or confirmed at necropsy, and at the time of skin testing were in an advanced stage of the disease Of these 37, 33 died during their stay in hospital, 2 were transferred to other hospitals for streptomycin therapy, and 2, with tuberculous peritonitis, survived and were allowed home

The ages of these children ranged from five months to ten years and reflected the usual high death rate in children under three years 21 of them had not reached their third birthday when they developed fulminating tuberculosis from which they died The types of lesions in these 37 Mantoux negative children were

Tuberculous meningitis	27
Miliary tuberculosis	3
Tuberculous bronchopneumonia	4
Tuberculous peritonitis	2
Spinal caries and meningitis	1
Total	37

Whether or not these children were at any stage of their illness sensitive to tuberculoprotein we do not know, but it seems more likely that the original dose of bacilli was so massive, and the organism so virulent, that they did not have the opportunity to develop sensitivity They also failed to develop the immunity required to localise the disease process

Mortality Related to Age

Table III shows the deaths from tuberculosis in hospital during the ten year period it also includes a few children discharged home with tuberculous meningitis The total number of deaths was 251, or 22 7% of the whole group of "infected children" which comprises positive reactors, children dying of tuberculosis within forty eight hours of admission to hospital, and the 37 Mantoux negative children referred to above who had acute progressive tuberculosis without tuberculin sensitivity

TABLE III—TUBERCULOSIS DEATHS (AGE GROUPS)

Age (years)	"Infected children"	Deaths	Percentage deaths of infected children
0–1	87	54	62
1–2	117	58	50
2–3	101	37	37
3–4	81	32	39
4–5	81	15	18
5–6	87	14	16
6–7	79	7	9
7–8	86	13	15
8–9	76	5	7
9–10	81	8	10
10–11	92	5	5
11–12	89	1	1
12–13	51	2	4
Totals	1108	251	22 7

"Infected children comprises those who were (a) Mantoux positive (b) tuberculous but Mantoux negative (c) tuberculous and dying within forty-eight hours of admission

The number of deaths in hospital does not of course represent the total number of deaths from tuberculosis in these children, a late follow up of whom is now in progress Most children, however, with evidence of a recent primary infection were watched for several months at least after discharge Wallgren (1943) found that the danger period in childhood lies between the fourth and twelfth weeks after the development of tuberculin sensitivity, and it might therefore be assumed that there were only a few deaths subsequently Nevertheless, the fact remains that the mortality rate of 22 7% bears no relation to the mortality from childhood tuberculosis in general, and depends entirely on the type of case admitted to this unit

Table III shows that the mortality is highest, by far, during the first year of life, when 62% of the cases prove fatal, but this high figure falls off rapidly, particularly between the third and fourth years, when it is reduced to less than half This is in keeping with the usual belief that meningitis is more likely to occur in children infected during the first three years of life than in those infected later Of the 251 deaths occurring in hospital during the ten year period, 88% showed evidence of meningitis This preponderance of meningitis over all other lesions in the fatal cases obtains at all ages above six months, below that age, meningitis was present in only 8 of 19 cases Far behind meningitis come bronchopneumonia (13 cases), miliary tuberculosis without meningitis (8), peritonitis (4), tuberculomata (2), and enteritis (1)

SUMMARY

A survey has been made of the tuberculin sensitivity of all children from birth to thirteen years of age admitted to the wards of a medical unit of a children's hospital in the ten years 1940–49

The proportion of positive reactors varied from 10 2% in 1944 to 20 3% in 1948 (average 14 2%)

The tuberculin sensitivity rate in different age groups is shown, starting at 2 4% in the 0–1 year age group and rising to 41 8% in the age group 12–13 Mantoux reversion occurred in 6 of 40 cases which were followed up There were 37 cases of tuberculosis in Mantoux-negative children

The mortality from tuberculosis in the various age groups is shown It varied from 62% in infected infants under one year to about 5% in the higher age groups The greatest reduction in mortality occurred between the third and fourth years The average mortality rate in all age groups of infected children in hospital was 22 7%

The various tuberculous lesions responsible for death are enumerated, evidence of meningitis was present in 88% of the children dying of tuberculosis.

I wish to express my thanks to Prof Stanley Graham for permission to use the case records of his unit in the Royal Hospital for Sick Children, and for his encouragement and advice during the preparation of this paper The work was done during tenure of the Walter K Hunter Research Fellowship in Medical Diseases of Children

REFERENCES

Brieger I M (1943) *Arch Dis Childh* 18 178
Crimm P D Short D M (1939) *Amer Rev Tuberc* 39 64
Dahlström A W (1940) *Ibid* 42, 471
Daniels M Ridehalgh F Springett V H Hall I M (1948) Report on Prophit Tuberculosis Survey London
Hart P D A (1932) *Quart J Med* 1 49
Heynsius van den Berg M R (1936) *Maandschr Kindergeneesk*, 5 133 (cited by Brieger)
Horan T H (1935) *Amer Rev Tuberc* 32 166
Keller, A A Kampmeier R H (1939) *Ibid* 39 657
Lloyd W E MacPherson A M C (1933) *Brit med J* 1 818
Madsen T Holm J, Jensen K A (1942) *Acta tuberc scand* suppl 6
Miller F J W (1940) *Lancet* ii 274
Seiffert E (1935) *Z Tuberk* 73 162 (cited by Brieger)
Thompson B C (1947) *Arch Dis Childh* 22 1
Wallgren A (1943) *J Pediat* 5 291
Watkins A G (1945) *Arch Dis Childh* 20 186

PERSISTENT HYPOKALÆMIA REQUIRING CONSTANT POTASSIUM THERAPY

K KJERULF-JENSEN
M D Copenhagen
ATTENDING PHYSICIAN

N B KRARUP
M D Copenhagen
PHYSICIAN-IN-CHIEF

A WARMING LARSEN
M D Copenhagen
ATTENDING PHYSICIAN

BLEGDAMS HOSPITAL, COPENHAGEN

IN the last few years many clinically important conditions have been described in which there is an acute or at any rate transitory lack of potassium on the blood serum (these are well reviewed by Danowski 1949) Chronic persistent hypokalæmia, however, has only occasionally been reported (Albright and Reifenstein 1948) Hadorn (1948) described a case of osteomalacia complicated by a tendency to œdema and by hypokalæmia, which slowly recovered spontaneously

The present case is reported because the patient was found to need permanent potassium therapy

CASE RECORD

A married woman, aged 33, was transferred to the medical department from the surgical wards on Oct 4 1948 because she had had two severe heart attacks accompanied by collapse with muscular weakness and hypotension. There was no history of familial muscular paralysis The patient had been healthy as a child, menstruation had begun at the age of 15, and apart from a year's amenorrhœa when she was 18 had been regular until 1945 She had had three normal pregnancies, in 1938, 1940, and 1945, and her children were healthy In August 1943, she had had a brief feverish illness accompanied by neck stiffness and extensor plantar reflexes, which was diagnosed as lymphocytic meningitis because there was an epidemic of such cases at the time, though the patient had not been investigated Since then, at regular monthly intervals starting about fourteen days before menstruation she had become generally œdematous, without any albuminuria, and these attacks had been treated with mercurial diuretics Since her delivery in 1945 she had not menstruated but the œdema had appeared as before, so that she was having about a fortnight with œdema and then about a fortnight without Gynæcological examination revealed only slight genital hypoplasia

In February, 1948, the patient became pregnant again, and in the early months of this pregnancy her periodic œdema ceased for the first time In June, the fifth month of her pregnancy, she had peritonsillitis, which was treated at home with penicillin. This was followed by severe anorexia, dehydration, and loss of weight and energy On July 16 she went into labour and was admitted to hospital where she gave birth to a stillborn female fœtus weighing 2 lb After delivery her temperature was at first subnormal, after which it rose to slightly above normal and remained so for some weeks During this period various signs and

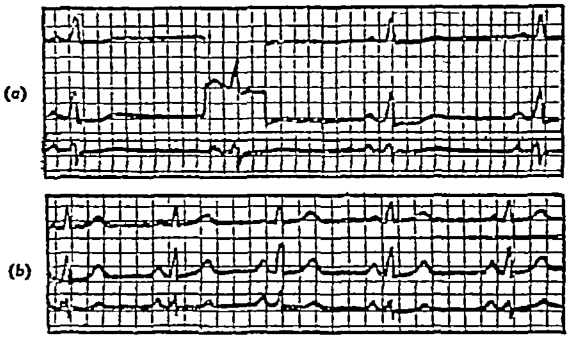


Fig. 1—Electrocardiogram (a) during period of severe potassium deficiency and (b) after treatment with potassium phosphate by mouth

symptoms which had been present since her delivery became accentuated these were hypotension, bradycardia severe thirst, diuresis muscular weakness a feeling of extreme tiredness, paræsthesiæ, and a fall in weight from 8 st 2½ lb to 6 st 5½ lb Her excretion of 17 ketosteroids mineralo-steroids and glucocortico steroids was abnormally low, and there was no demonstrable excretion of gonadotropic and œstrogenic hormones Electromyography and serum acetyl choline were normal

Her condition was interpreted as the onset of a crisis in Addison s disease, and she was therefore given intramuscular injections of 10 mg of deoxycortone acetate ('Percorten,' Ciba) daily for ten days, after which she had two or three severe heart attacks, with an irregular rapid heart-beat and a feeling of anxiety The last attack occurred an hour after she had received a litre of physiological saline with 5% glucose intravenously she collapsed, with imperceptible pulse and respirations for 1½ min. Her serum potassium level was found to be seriously low (1 38 m eq per litre) and she was transferred to the medical department

Condition on Admission to Medical Wards—There was pronounced prostration. She was emaciated (weight 6 st 8 lb, height 5 ft. 3 in.), her skin was dry but not abnormally pigmented and her hair distribution was normal There was extreme muscular weakness, so that she could not lift her outstretched legs from the bed No further abnormality was found on clinical examination and the optic discs and central nervous system were normal In the laboratory findings (see table) the only abnormality was a pronounced hypokalæmia (2 m.eq per litre) and a low serum chloride level The urea clearance was 30 and 24 c cm, and diuresis 1 12 and 0 72 ml per min (After potassium therapy the urea clearance was 75 and diuresis 3 4 ml per min.) Electrocardiography on numerous occasions showed changes characteristic of hypokalæmia (fig 1) The X ray appearances of the cranium, lungs, and urinary tract were normal

LABORATORY FINDINGS BEFORE AND DURING POTASSIUM THERAPY

—	Before potassium therapy (Oct. 6 1948)	During potassium therapy	
		(March 15 1949)	(March 15 1950)
Body weight (kg)	42	43	46
Fluid intake (ml.)	1600	2100	—
Urine			
Daily output (ml)	1140	1300	1720
Specific gravity	1008	1009	1012
Potassium (g per day)	0 09	0 26	—
Sodium (g per day)	1·09	1·09	—
17 ketosteroids (mg per day)	0 90	1 80	1 80
Blood			
Hæmoglobin (%)	100	1 05	1 02
Hæmatocrit (%)	44	44	40
Red-cell count (million per c.mm)	4 23	4 48	4·40
E.S R (mm in 1 hr)	12	6	—
Red-cell *potassium (m.eq* per litre)	101	100	91
Serum levels (m eq per litre)			
Sodium	141	138	140
Potassium	2·00	3 20	4 00
Total cation	150	140	—
Calcium	4 75	5 60	4 70
Phosphorus	—	—	2 50
Chloride	79	98	—
Bicarbonate	32	27	—
Plasma proteins (g per 100 ml)			
Albumin	4 10	5 20	—
Globulin	2 10	2 20	—
Total	6 20	7·40	—
Serum-cholesterol (mg per 100 ml)			
Free	73	86	—
Total	206	269	—
Blood-sugar fasting (mg per 100 ml)	77	80	—
Blood urea (mg per 100 ml)	32	40	—
Basal metabolic rate	− 9%	—	—

Progress—A few days after her admission the patient became œdematous, she said that the œdema was less than she had formerly but was of the same type It disappeared quickly and spontaneously In the next few months the patient was free from symptoms, except for anorexia, general weakness, and amenorrhœa Her serum potassium was persistently low (about 2 5 m.eq per litre) Since it was thought that the hypokalæmia *might* be a sequel to the treatment with deoxycortone potassium therapy was postponed for six months to see if there would be a spontaneous remission and it seemed certain that by then the deoxycortone injected would have been eliminated (see fig 3) During these six months the patient was kept in bed on an adequate, varied, and appetising diet and her condition improved slightly as her appetite increased she gained 5 lb in weight and her tiredness and weakness waned a little though she could still get out of bed only with difficulty and for short periods

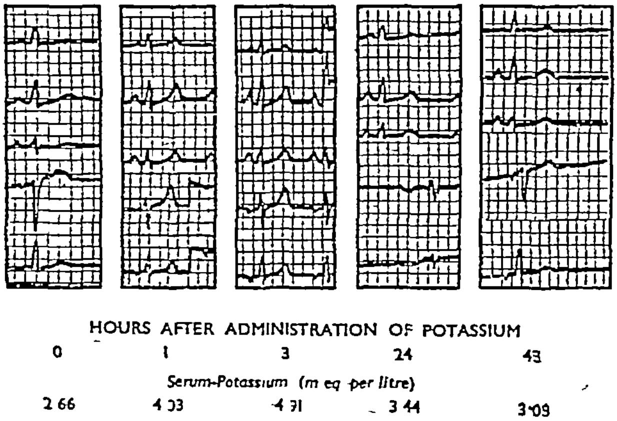

HOURS AFTER ADMINISTRATION OF POTASSIUM
0
1
3
24
43
Serum-Potassium (m eq per litre)
2 66
4 03
4 91
3 44
3·09

Fig 2—Electrocardiographic changes during administration of potassium The amount of potassium excreted in the urine in the first twenty-four hours was 1·69 g Potassium phosphate (15 g of potassium) was given by mouth at 0 hr

Potassium Treatment—Potassium was given for the first time on March 22, 1949 when the patient s serum potassium was 2 84 m eq per litre After 15 g of potassium, in the form of neutral potassium phosphate (KH$_2$PO$_4$, 52 4 g K$_2$HPO$_4$, 33 5 g water to 300 g) had been given by mouth, her serum potassium rose to 4 9 m.eq per litre in three hours (see fig 2) The potassium had a powerful effect producing transient palpitations and later a temporary collapse, with a suggestion of tetany in the position of the fingers The considerable quantity of phosphate which this solution contained caused a fall in serum-calcium In the next twenty-four hours only 1 69 g of potassium and 0 04 g of sodium was excreted in the urine The neutral potassium phosphate solution by mouth was continued in the dosage shown in fig 3 In the subsequent period a considerable retention of potassium was demonstrated—more than 87% (2 7 g a day) of the potassium phosphate given, over and above the potassium in her food, was retained After ten days' treatment her serum potassium was 5 13 m eq per litre, and the proportion of the potassium retained in a three-day period was 96% (2 9 g a day) Excretion of sodium remained abnormally low (0·02–0 83 g a day) When the patient s serum potassium had become normal, the dose was reduced to 1 5 g of potassium a day (neutral potassium phosphate solution 15 ml in one daily dose) In addition 0 8 g of sodium (2 g of sodium

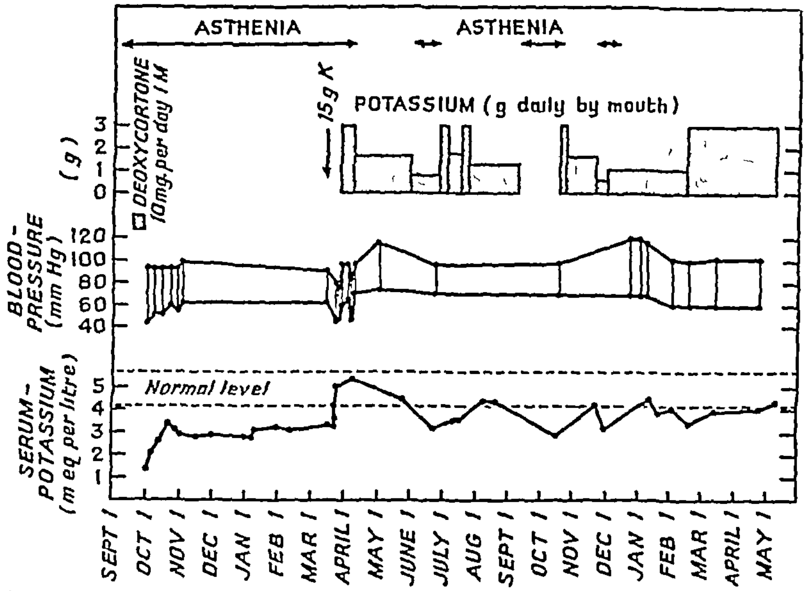


Fig 3—Variations in serum potassium blood pressure, and muscle function before and after treatment with potassium phosphate by mouth

chloride) was given daily It had been observed previously that the patient's cyclic œdema was independent of her intake of sodium chloride Thereafter her serum potassium remained subnormal or normal, and her serum sodium was 133 m eq per litre (see fig 3) The average volume of urine excreted over a three day period was 1720 ml, with a daily excretion of 3 g of potassium and 0 6 g of sodium The patient's appearance and general condition improved strikingly in this period, and she was discharged feeling reasonably well on April 15, 1949 Her tiredness and weakness had disappeared menstruation was normal, and she resumed her work

Course after Discharge—On June 1 the patient of her own accord reduced her daily dose to 0 5 g of potassium (5 ml of the solution), and after this she became worse and her serum potassium fell The dose was therefore increased (fig 4) whereupon her symptoms again disappeared

On Aug 16 her serum potassium was 4 07 m eq per litre and her electrocardiogram still normal On her own initiative she stopped her potassium altogether on Sept 10, because she felt completely well A few days later she felt tired and weak and had palpitations On Oct 14 her serum potassium was 2 76 m eq and her serum sodium 134 m eq per litre When she resumed her treatment she recovered completely in a few days At the end of November she again experimented by halving her daily dose, taking 0 5 instead of 1 g of potassium Her health gradually deteriorated, and her serum potassium fell to 3 06 m eq per litre The previous dosage of potassium had to be resumed and again she fully and rapidly recovered Her tendency to intermittent œdema and retention of fluid, with increase in weight, particularly before menstruation, did not seem to be affected by the therapeutic intake of potassium (see fig 4) A glucose tolerance test with 25 g of glucose by mouth gave the characteristic fall in serum potassium but did not produce pareses such as occur in familial muscular paralysis (fig 5) After two months, during which she regularly took 3 g of potassium daily by mouth, her average daily excretion of urine over a three-day period was 2267 ml, containing 5 65 g of potassium and 2 70 g of sodium daily

The potassium treatment has been continued since January, 1950, with a neutral *aqueous solution of potassium* salts containing KH_2PO_4 45 g, K_2HPO_4 45 g, and KCl 130 g, in a litre of distilled water Each 10 ml of this solution contains potassium 1 g (25 0 m eq), phosphorus 0 18 g (8 5 m eq of PO_4), and chloride 0 62 g (17 4 m eq)

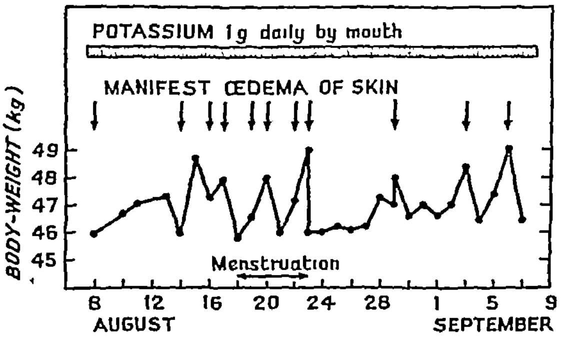


Fig 4—Variations in fluid content of body in relation to changes in body weight

DISCUSSION

It seems clear that this patient cannot maintain the normal level of potassium in her extracellular fluid without a regular supplementary intake of potassium The reason for this is obscure Theoretically, such a defect might arise (1) in the kidneys, where there might be a reduced reabsorption of filtered potassium and/or increased tubular excretion of potassium, (2) in the muscles, if they were not assimilating potassium in the normal way, as happens in familial muscular paralysis, or (3) in the hypothalamus, where the chemosensitive electrolyte regulating centres might be insufficiently sensitive to the plasma potassium level.

The considerable retention of potassium that followed its administration by mouth points away from loss through the kidneys as the cause of the hypokalæmia, but it suggests that a lack of intracellular potassium deficiency is an essential factor in her condition In this respect the case resembles familial muscular paralysis, in which Danowski et al (1948) found that the muscle potassium was deficient and that the paralysis could be relieved by suddenly reducing the potassium level in the extracellular fluid—e g, by increasing the intake of glucose The present patient, however, never had any acute attacks of paresis

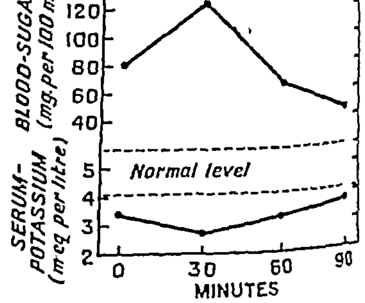


Fig 5—Glucose-tolerance test. Note absence of paresis and of any dangerous fall in blood pressure during the accentuated hypokalæmia.

A disturbance of central regulation seems the most likely explanation, and this might have arisen from the patient's lymphocytic meningitis some years before

For the present the patient's chronic potassium deficiency *must* be *classed* as cryptogenic, but it is important to recognise that such cases exist, that the condition may be hard to differentiate from Addison's disease, anorexia nervosa, and familial periodic muscular paralysis, and that potassium phosphate by mouth will relieve all the symptoms of hypokalæmia over long periods and may be life saving

SUMMARY

A woman of 33, who had had lymphocytic meningitis five years before, developed severe anorexia and muscular weakness after an attack of peritonsillitis and a six-month abortion. She was at first thought to have Addison's disease, but treatment with sodium chloride and deoxycortone produced severe cardiac disturbances and she was then found to have a very low serum-potassium level.

Her hypokalæmia and weakness lasted for six months and could only be relieved by giving potassium phosphate regularly by mouth, her condition relapsing whenever the potassium therapy was discontinued.

REFERENCES

Albright, F., Reifenstein, E. C. jun. (1948) Parathyroid Glands and Metabolic Bone Disease. Baltimore; p. 253.

Danowski, T. S. (1949) *Amer. J. Med.* 7, 525.

— Elkinton, J. R., Burrows, B. A., Winkler, A. W. (1948) *J. clin. Invest.* 27, 65.

Hadorn, W. (1948) *Schweiz. med. Wschr.* 51, 1238.

TREATMENT OF CHRONIC RENAL POTASSIUM DEFICIENCY

H. Gösta Davidsen
M.D. Copenhagen
PHYSICIAN

K. Kjerulf-Jensen
M.D. Copenhagen
ATTENDING PHYSICIAN

N. B. Krarup
M.D. Copenhagen
PHYSICIAN-IN-CHIEF

BLEGDAMS HOSPITAL, COPENHAGEN

In the hope of throwing some light on the treatment of patients with severe potassium deficiency we are reporting the following case of chronic renal hypokalæmia, with the blood-electrolyte findings during several forms of potassium therapy. Some studies of the inter-relation of serum electrolytes in rabbits are also described.

CASE-RECORD

A married woman, aged 44, was admitted on Oct. 1, 1949, to Blegdams Hospital with several days' history of nausea and vomiting, anuria, and constipation. She had been well until January, 1947, when a cancer of the uterus was diagnosed and treated with radium. She then developed a vesicovaginal fistula, which had not been closed despite four operations. In June, 1949, the right ureter was transplanted into the pelvic colon (Coffey's operation). No excretion from the left kidney was found on intravenous urography. Diuresis became normal after the operation, but no urine was passed in the natural way. The blood-urea, which had previously been normal, rose immediately after the operation to 192 mg. per 100 ml. and later fell to about 100 mg. The patient had several bouts of fever which were ascribed to ascending urinary infection and treated with penicillin, streptomycin, and sulphamethylthiodiazole. After the operation the patient had complained of constant tiredness.

First Admission.—The patient was very ill, cold, and cyanotic, with uræmic fœtor. Her skin and mucosæ were dry and flabby. Her temperature was normal, pulse-rate 64 per min., and blood-pressure 100/65 mm. Hg. It was suspected—or rather certain—that she had a negative potassium balance even before the potassium analyses were made, because of the type of respirations and the electrocardiogram. Her respirations were slow at first, but after elimination of the acidosis they became frequent and irregular without being of the Cheyne-Stokes type; they corresponded to the type found in hypokalæmia and described by Bodansky (1949) and others as "fish-mouth" respiration. The electrocardiogram (fig. 1) showed changes characteristic of hypokalæmia: low or iso-electric T waves, depression of P–Q and S–T intervals, prolonged Q–T interval, and ventricular extrasystoles (compare fig. 2, an electrocardiogram taken after her serum-potassium had become normal).

Her potassium and bicarbonate serum levels were very low, but sodium chloride and calcium were within normal limits (fig. 3). The administration of isotonic solution of sodium bicarbonate and neutral potassium phosphate in the first few days—the potassium solution had originally been prepared for the treatment of diabetic coma and contained 36 m.eq. of potassium and 120 m.eq. of sodium per litre (Kjerulf-Jensen 1949)—restored the serum-bicarbonate to normal without having much effect on the potassium level. On the other hand, the serum-calcium fell to 1·8 m.eq. per litre (3·6 mg. per 100 ml.), which caused tetany and prevented the blood from coagulating unless calcium chloride was added. The serum-phosphorus was twice the normal value. These great changes in calcium and phosphorus were attributed to the parenteral administration of too much phosphate. Similar changes were subsequently produced experimentally in animals. The removal of calcium from the plasma was thought to be due to its deposition in the bones. The large amount of isotonic solutions given caused severe over-hydration, the hæmatocrit falling from 32 to 23%, and generalised œdema and severe lung œdema developing. For the hydræmia two transfusions of whole blood and two intravenous infusions of 100 ml. of 50% glucose were given, which led to slight improvement. Despite the severe hydration diuresis was still too small to be measured. The patient seemed moribund, but in view of the severe hypokalæmia still present a hypertonic solution (10%) of potassium chloride was given by mouth as a last resort, 10 ml. every quarter of an hour for fourteen doses. Within an hour there was profuse diuresis, the œdema vanished, and the patient's general condition improved remarkably. A few hours later, however, she had a slight attack of collapse accompanied by tetany, which rapidly disappeared after an intravenous injection of calcium gluconate. The patient continued to improve under treatment with hypertonic potassium chloride solution and calcium lactate by mouth. Her potassium, calcium, and phosphorus levels returned to normal, and her blood-urea fell from 317 to 133 mg. per 100 ml. During this time in hospital her temperature was unstable, but after a four-day course of streptomycin it fell to normal and remained so. Radiography on the day before her discharge revealed bilateral lung infiltrations resembling old tuberculous lesions; there had been no cough or sputum. On her discharge at her own request, after twenty-two days in hospital, she had regained her normal weight of 8 st. 4½ lb. (53 kg.).

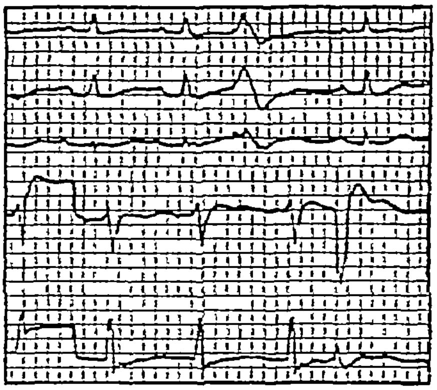


Fig. 1—Electrocardiogram in untreated hypokalæmia: serum-potassium 1·12 m.eq. and serum-calcium 5·1 m.eq. per litre; P–Q 0·20 sec.; Q–R–S 0·03 sec.; S–T negative; T waves iso-electric or negative; ventricular extrasystoles present.

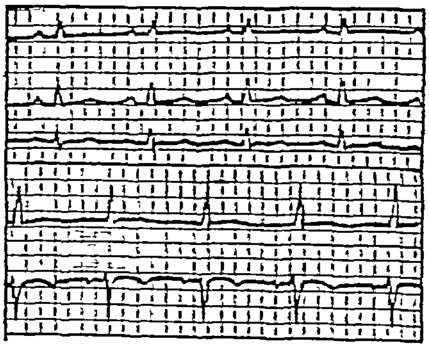


Fig. 2—Electrocardiogram after correction of hypokalæmia with potassium salts: serum-potassium 4·8 m.eq. and serum-calcium 4·1 m.eq. per litre; R–R 0·7 sec.; P–Q 0·18 sec.; Q–R–S 0·05 sec.; Q–T 0·3 sec.; T positive in leads II and III; no extrasystoles.

Second Admission.—Seventeen days after her discharge she was readmitted for a relapse after two or three days' vomiting and anuria. She was not quite so ill as on the first

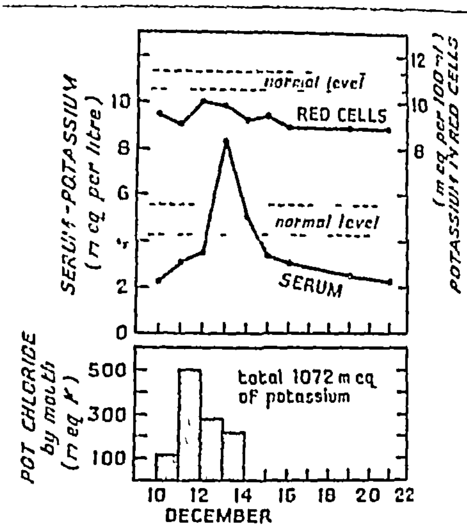


Fig 5—Potassium levels in serum and in red cells and treatment with potassium salts during second stay in hospital

admission and her serum potassium was not quite so low On the other hand, her serum bicarbonate was extremely low (fig 4) No potassium phosphate was given, but a 10% solution of potassium chloride and sodium bicarbonate powder were given by mouth In two days her serum bicarbonate became normal and her serum potassium rose slowly There was a considerable retention of fluid (hæmatocrit fell from 30 to 21%) and her serum phosphorus fell almost to zero, but her serum calcium remained normal and there were no clinical manifestations of calcium deficiency Continued administration of potassium chloride, in smaller daily doses, led to a sudden rise in the serum potassium on the fourth day (by which time 1072 m eq of potassium had been given) to well over normal values The potassium curve indicates that in the first few days of treatment the cells had assimilated a considerable amount of potassium (diuresis had not yet begun) and that the serum potassium did not rise until the supply of potassium exceeded this cellular assimilation From this time her serum phosphorus began to rise without any form of extra phosphate administration Her blood urea varied from 71 to 112 mg per 100 ml Her red cell potassium level was estimated every day in the hope of obtaining some idea of the intracellular potassium deficit The results (fig 5) show that throughout her stay the potassium content of her red cells was below normal, even during intensive administration of potassium when her serum potassium was higher than normal, this finding is in accordance with the conception that the exchange of potassium is slower in the red cells than in most other cells

It was soon possible to re-establish her electrolyte balance but this time the anticipated improvement in her general condition did not follow, and the patient gradually developed a continuous high fever and began to cough up sputum containing numerous tubercle bacilli, X-ray examination now showed rapid progression of the lung infiltration with cavity formation Her condition was hopeless, and despite penicillin and streptomycin she died 14 days after the start of the pyrexia

Necropsy Findings—Recent tuberculous pneumonia and cavities were found in the left lung and older proliferative tuberculous processes in the right lung There was a bilateral hydronephrosis, the left kidney tissue being only 3–4 mm thick The left ureter was dilated and ended blindly in fibrous scar tissue in the lesser pelvis, the right ureter, which had been implanted in the colon was dilated to the thickness of a finger Microscopy of the kidney tissue revealed no tuberculosis The suprarenal glands were normal There was no sign of recurrence in the uterine cancer, and no internal metastases were found A fat-free piece of iliopsoas muscle tissue was analysed, with the following results

Content	*Findings in iliopsoas*	*Normal range (Mudge and Vislocky 1949)*
Total solids (%)	22·6	19·8–21·6
Potassium (m eq per kg)	51	81·0–88·0
Sodium (m eq per kg)	107	35·0–44·9

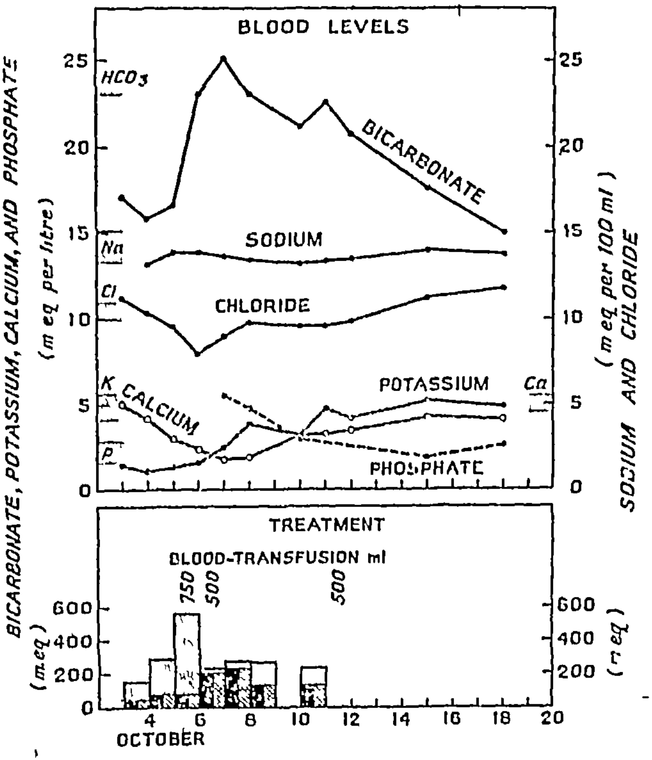


Fig 3

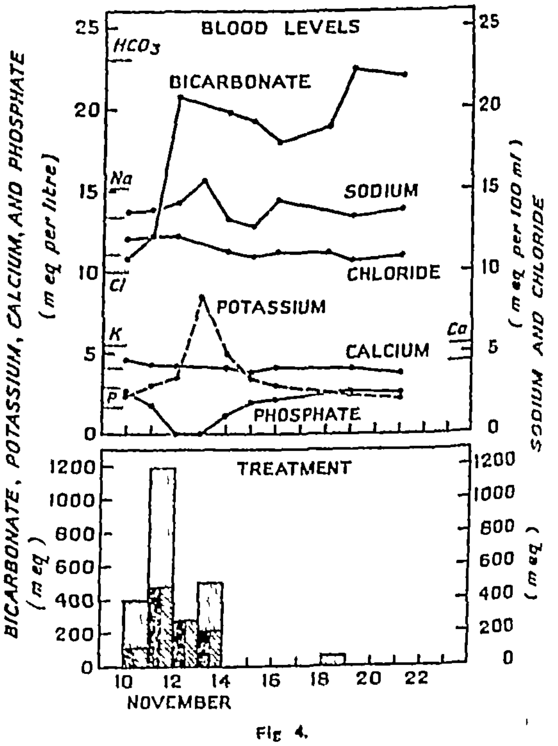


Fig 4.

■ POTASSIUM
▨ PHOSPHATE
▦ CHLORIDE
☐ CALCIUM LACTATE
☐ SOD BICARBONATE
☒ NORMAL LEVELS

Fig 3—Electrolytes in patient's blood and treatment with electrolytes during first stay in hospital

Fig 4—Electrolytes in patient's blood and treatment with electrolytes during second stay in hospital

It will be seen that the potassium content of the muscle was low whereas the sodium was significantly above normal This fits in with the well known view that during potassium deficiency sodium may act as a substitute for potassium in the cells

EXPERIMENTS ON ANIMALS

Experiments were performed in an attempt to reproduce in animals some of the changes observed in the patient's electrolyte balance during treatment

The effect of giving neutral sodium phosphate solution was studied in two normal rabbits weighing 3 kg Phosphate corresponding to 0 4 g of phosphorus was given, first (fig 6) through an œsophageal tube, and secondly (fig 7) by continuous intravenous infusion for 50 minutes In both experiments the serum phosphorus rose while the serum calcium fell from the normal of about 6 m eq to 3 6 and 2 2 m eq per litre, whereas the levels of glucose and potassium were unaffected

Continuous intravenous infusion of 3 m eq of potassium per kg of body weight into a normal rabbit for 40 minutes did not demonstrably affect the serum phosphorus level (fig 8)

DISCUSSION

There were probably several causes for the patient's severe potassium deficiency The supply of potassium was low because of reduced food intake The vomit contained 13 m eq of potassium per litre (50 mg per 100 ml) The renal potassium loss was not measurable, because implantation of the ureter in the intestine made it impossible to collect urine free from fæces, but since it was certain that the patient lost potassium even when she was not vomiting, and when her food intake was normal, it must be assumed that the renal loss was the most important factor in her deficiency Ferris and Odel (1950) found that 79% of 141 patients with bilateral ureterosigmoidostomy showed a tendency to acidosis and hyperchloræmia, with symptoms corresponding to those of our patient, but they do not mention potassium depletion in their patients In their opinion acidosis is caused by reabsorption of chloride through the intestinal mucosa Protracted acidosis is known to be accompanied by a loss of calcium, potassium, and phosphorus from the tissues, and that the rapid correction of acidosis may be accompanied by extremely low extracellular concentrations of these electrolytes and severe clinical symptoms (Rapoport et al 1947)

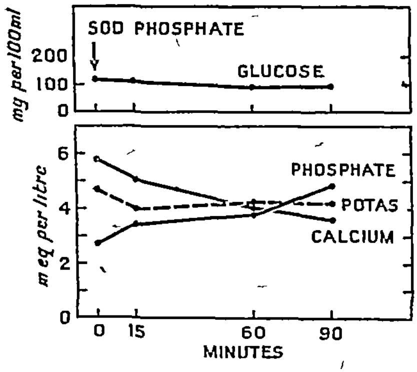


Fig 6—Calcium potassium phosphate and glucose levels in serum of normal rabbit dosed with neutral sodium phosphate solution by mouth.

The total potassium deficit seems to have been considerable in the present case Most of the potassium (1072 m eq) administered in four days must be regarded as having been retained, because in the first three days of this treatment the patient neither vomited nor excreted urine or fæces Her lowest serum potassium level was 1 12 m eq per litre (4 4 mg per 100 ml)

During the first three days of the first stay in hospital (fig 3), potassium was administered in the form of neutral potassium phosphate solution The result was hyperphosphatæmia and hypocalcæmia During the second stay in hospital potassium was administered without previous or simultaneous administration of phosphate The result was hypophosphatæmia Though the hypophosphatæmia produced no clinical symptoms, it must be desirable, in order to encourage assimilation of potassium by the cells, to supply an optimal quantity of phosphate relating to the amount of potassium given The relation between the amounts of potassium and of phosphate (in equivalents) required by the organism is not 1 : 1 The optimal ratio between the ions is about 3 eq of potassium to 1 eq of phosphate to 2 eq of chloride or bicarbonate in the present case, according to our calculations Butler et al (1946) and Reyersbach et al (1948) have used a solution containing 5 eq of potassium to 1 eq of phosphate The optimal relation is, however, subject to individual variation The fact that in the experiment on the rabbit (fig 8) no fall in plasma phosphorus level was demonstrable during infusion with potassium chloride is in accordance with the assumption that the disappearance of phosphate from the plasma was connected with the assimilation of potassium and phosphorus by the cells An increase in the extracellular potassium level alone does not affect the plasma phosphorus level.

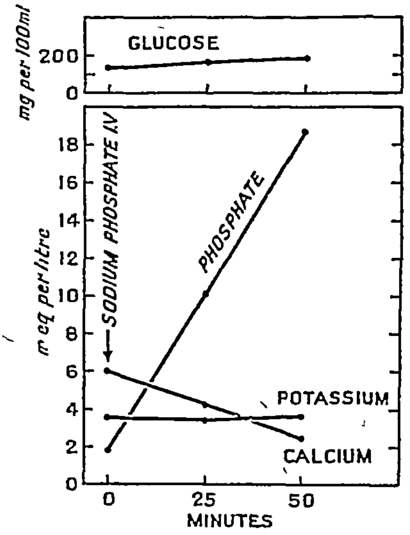


Fig 7—Calcium potassium phosphate and glucose levels in serum of normal rabbit infused intravenously with neutral sodium phosphate solution continuously for 50 min at a rate of 0·49 m eq of phosphorous an hour

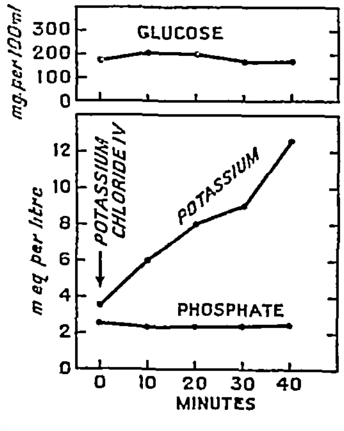


Fig 8—Potassium, phosphate, and glucose levels in serum of normal rabbit infused intravenously with potassium chloride solution continuously for 40 min to a total of 9 m.eq of potassium

CONCLUSIONS

Severe intracellular potassium deficiency should be treated with concentrated solution of potassium salts, even in the presence of severe dehydration These solutions should be given by mouth only

The initial dose of potassium salts should be accompanied by phosphate The optimal ratio (in equivalents) suggested is 3 of potassium to 1 of phosphate The remaining 2 equivalents of anion may be given as chloride or bicarbonate. Too much phosphate tends to produce hypocalcæmia, with the risk of tetany

During intensive treatment with potassium there is always a risk of acute hyperkalæmia, which develops when the amount of potassium given exceeds the amount which the cells can assimilate This risk can be reduced by giving potassium salts by mouth and by making frequent estimations of the plasma potassium level

SUMMARY

Acute hypokalæmia (plasma potassium level 1 12 m eq per litre) developed in a woman of 44 with chronic kidney disease It was combated successfully with parenteral and oral potassium salts In four days the patient retained 1072 m eq of potassium and was dramatically relieved

The administration of neutral potassium phosphate caused hyperphosphatæmia and hypocalcæmia, with temporary tetany and inhibition of blood clotting

The administration of a concentrated solution of potassium chloride without a simultaneous supply of phosphate reduced the serum phosphate to zero There were no demonstrable changes in serum calcium or any clinical symptoms

In experiments on normal rabbits the administration of sodium phosphate lowered the serum calcium while the serum potassium remained constant The infusion of potassium chloride solution in normal rabbits did not lower the serum phosphate These findings agree with the conception that the fall in serum phosphate is intimately connected with the assimilation of potassium by the potassium deficient cells

REFERENCES

Bodansky, O (1949) *Amer J med Sci* 218 567
Butler A M Talbot N B Crawford J D MacLachlan, E A, Appleton, J (1946) *Amer J Dis Child* 72 481
Ferris D O Odel H M (1950) *J Amer med Ass* 142, 634
Kjerulf Jensen K (1949) *Ugeskr Laeg* 111 773
Mudge G H, Vislocky K (1949) *J clin Invest* 28, 482
Rapoport S Dodd K Clark, M Syllm, I (1947) *Amer J Dis Child* 73 391
Reyersbach G C Butler, A M Talbot, N B (1948) *Ibid* 75, 450

FINGERPRINT DETECTION AND MERCURY POISONING

T H Blench
M D, B Hy Durh, D P H
CITY POLICE SURGEON, LECTURER IN FORENSIC MEDICINE

Harry Brindle
M Sc Manc, B Sc Lond, F R I C, Ph C
PROFESSOR OF PHARMACY
UNIVERSITY OF MANCHESTER

Metallic mercury and mercurial salts are handled and used in various industries, and as a result considerable attention has been paid to the risk of chronic mercurial poisoning A comparatively recent development is the use of grey powder (hydrargyrum cum creta) in the investigation of fingerprints

The chief drawbacks which have confronted investigators of industrial mercury poisoning have been (1) the difficulty of accurately determining minute amounts of mercury, (2) the fact that the three main manifestations of chronic mercurial poisoning—erethism, tremor, and stomatitis—are, particularly in mild cases, difficult to distinguish from conditions which arise fairly commonly in people who have no contact with mercury in any form, and (3) the apparently considerable quantitative differences in the reaction of different people to mercury, since it has generally been impossible to trace any correlation between the presence or severity of the symptoms and the probable amounts of mercury absorbed

The difficulty of accurately determining minute quantities of mercury may now be regarded as having been overcome, since Milton and Hoskins (1947) have published a method by which it is possible to determine mercury in urine in concentrations as low as 0 005 part per million The other difficulties still remain.

PREVIOUS INVESTIGATIONS

A comprehensive survey of the historical aspect of chronic mercury poisoning in industry was made by Buckell et al (1946) They also investigated workers in a thermometer factory, and the amount of mercury excreted in the urine in twenty four hours ranged from 136 to 3478 µg The three characteristic symptoms (erethism, tremor, and stomatitis) were looked for and their presence or absence was apparently independent of the urinary mercury level The average mercury level was about the same in the symptomless workers as in those found to have any or all of these three

One employee had at work an excretion of 2360 mg After seventeen days' absence he had an excretion of 1290 mg indicating that mercury was probably still being absorbed from the clothing Estimation of the mercury content of the air showed that the rate of excretion was very much more than could be absorbed by respiration Washings from the hands contained up to 9800 µg per worker It was concluded that absorption took place largely through the skin or the alimentary tract In one case the daily excretion of mercury during two separate weeks ranged from 96 to 1000 µg In a further week in the same case the range was 66–270 µg In 14 controls free from any contact with mercury the highest excretion of mercury was 90 µg and the lowest 5 µg, the average being 31 5 µg

Agate and Buckell (1949) examined 32 police officers who used grey powder in the demonstration of fingerprints In their series only two symptoms were manifest —tremor and erethism—and 4 of the 32 police officers showed both symptoms Again there seemed to be no relationship between the symptoms and the amounts excreted The average excretion was higher in the officers without symptoms than in those with one or both symptoms

At first sight these two investigations seem to indicate that there is no relationship between the presence or severity of the symptoms and the amount of mercury ingested or excreted There are, however, several factors to consider before such a conclusion is drawn

The chief difficulties in interpreting the figures seem to be

(1) Except in 2 cases in the thermometer factory, the amount of mercury excreted by each person was estimated during one day only,

(2) The symptoms are not easily diagnosed and assessed, particularly in mild cases

The second difficulty may not have been of much significance because the observers were skilled and were well aware of the pitfalls, but an indication of what is considered an excessive or toxic dose, apart from idiosyncrasy, would help in other cases It is clear from the published findings in the above investigations that the first difficulty cannot be neglected We have found that the amount of mercury excreted varies considerably from day to day, and this is illustrated in the one case reported by Buckell et al (1946) in which repeated daily determinations were made In one week the daily variation was from 96 to 1000 µg, and in another week from 66 to 270 µg It is evident that care must be exercised in drawing deductions from the excretion on a single day This must be remembered when interpreting the results of Agate and Buckell (1949), since they also determined the excretion on one day only for each police officer

PRESENT INVESTIGATION

We felt that further information was advisable before condemning the use of mercury with chalk (*B.P.*) in the detection of fingerprints, particularly since, in spite of the practice being world wide, no severe case of mercurial poisoning from this cause could be traced. This work was undertaken to find out whether any effect could be detected clinically in men investigating fingerprints with the mercury powder. The best indication of the probable amount of mercury ingested seemed to be the amount excreted in the urine. Buckell et al. (1946) and other workers have concluded that the bulk of the mercury is probably absorbed through the skin or finds its way into the body by the mouth. The mouth is probably the main source of the intake, and one may assume that the mercury gets to the mouth mainly from the hands via the food. No reliable published figures could be found to correlate the amount excreted in the urine with the quantity ingested, but probably at least a rough relationship exists. Even in cases where the excretion and therefore probably the intake are comparatively large the actual amounts are really very small. Large variations in the daily intake are therefore to be expected, since 1000 μg. of mercury with chalk, containing 330 μg. of metallic mercury, is a scarcely visible quantity, and the contamination of the hands and therefore possibly of the food is largely accidental and must be extremely variable. Obviously the amounts of mercury ingested and excreted may bear little relationship to the total amount of exposure to the powder, especially when judged by a single test of the excretion. Much must depend on the technique of using the powder, cleaning the hands and clothes, &c.

Two officers, A with twelve years' and B with nine years' experience in "dusting," volunteered to help in the investigation and agreed to provide material for examination. Twenty four hour specimens of urine were taken from both at intervals over a few months to find whether the absorption of mercury, judged by the excretion, could be related to the amount of work done, and whether the amount found could be classed as excessive. It was also decided to try simple means to reduce the intake and to determine if the effect of such means would be demonstrable. No erethism, stomatitis, or tremor was found in either volunteer. This was confirmed by Prof. R. E. Lane, of the department of occupational health in Manchester University, and Dr. J. F. Wilkinson, of the department of hæmatology, Manchester Royal Infirmary, who made independent examinations. Specimens of handwriting and free line drawing were without fault. The twenty four hour samples were taken during ordinary working periods except where otherwise indicated. The process for the determination of the mercury was substantially that given by Milton and Hoskins (1947). The results were as follows:

Date	Mercury (μg.) excreted in 24 hours		Comments
	Subject A	Subject B	
Nov. 8, 1949	—	99	
Nov. 11, 1949	396	182	
Nov. 17, 1949	394	284	
Nov. 25, 1949	214	96	
Dec. 1, 1949	697	100	Busy week previously
Dec. 28, 1949	85	53	A, six days' holiday, B four days' holiday
Feb. 13, 1950	208	93	Overalls worn, and more careful attention to washing of hands from Feb. 7, 1950
Feb. 22, 1950	99	40	
March 14, 1950	78	42	

It was thought possible that the higher figures of A were due to the fact that he performs duty in civilian clothes and visits scenes of crime during the day, with probable further absorption from the clothes he continues to wear. B, on the other hand, does most of his work in uniform inside police headquarters.

DISCUSSION

From Nov. 8 to Dec. 28, 1949, no special precautions during "dusting" were taken, the methods being those used by these officers for many years previously. These figures therefore give a picture of the absorption which had been taking place for years. In the case of subject A four samples taken during ordinary working periods gave an average daily excretion of 425 μg., and subject B five samples similarly taken gave 152 μg. daily. It should be emphasised that, though these figures probably represent fairly closely the average excretion, excluding holiday periods, over many years, there were no clinical signs of mercurial poisoning. It is evident that the rate of excretion rapidly follows the rate of intake, since the excretion fell to almost normal proportions after six days' holiday in the case of A and four days' holiday in the case of B.

After a week's wearing of overalls during the actual use of the powder and with more careful washing of the hands the findings for each officer were lower than any previously obtained during full working periods. In the case of A the figure was less than half of the previous average, and in the case of B it was two thirds. The two further samples taken fifteen days and thirty five days after the start of these simple precautions gave very low figures. Probably the powder previously deposited on the clothes, &c., had been removed by this date. The excretion of A was then about the same as the higher results found by Buckell et al. (1946) in normal people who had no known contact with mercury, and in the case of B well below that of many persons with no known contact.

Mercury can cause chronic poisoning but, apart from hypersensitivity and/or idiosyncrasy, only when the intake or absorption exceeds a certain, as yet undetermined, amount. It is evident from the work of Buckell et al. (1946) that mercury in appreciable quantities is excreted by most, if not all, the population, and therefore there must be an intake of mercury, probably in the food. The quantitative factor therefore becomes of paramount importance. Buckell et al. (1946) found in fourteen normal persons with no known contact with mercury in any form a daily range of excretion from 5 to 90 μg., average 31.5 μg. These figures are similar to those observed by us, who obtained a figure of 21 μg. for the average daily excretion in one person.

Mercury in various forms has been and is often used medicinally, often over very long periods. A normal dosage for certain purposes would be about gr. 1 (64,800 μg.) weekly for twelve weeks, a total of about 800,000 μg. Symptoms of mercurial poisoning which then occasionally occur are regarded as indicating hypersensitivity. It is therefore evident that the normal human body detoxicates small quantities of mercury throughout life, and can for fairly long periods deal with comparatively large amounts.

We do not wish to belittle the danger of chronic mercurial poisoning in those who regularly handle mercury in any form. We feel, however, that valuable information about the probability of such poisoning can be obtained by estimating fairly often the daily excretion of mercury by such people. The two police officers who were examined have been responsible for all the fingerprint work in the area, and have used grey powder exclusively for many years. They have shown no clinical sign of chronic mercurial poisoning in spite of an average daily excretion of 425 μg. and 152 μg. Simple precautions reduced this excretion to daily averages of 89 μg. and

41 µg, which are within the limits observed in persons without any known contact with mercury. We consider it desirable that clinical observations should be made and the urinary excretion of mercury estimated over a considerable period in each of a large number of cases before conclusions are drawn about the possible dangers of chronic mercurial poisoning, particularly in fingerprint detection.

SUMMARY

Two police officers heavily engaged for years in fingerprint detection with mercurial powder were examined. No clinical signs of mercurial poisoning were detected by several independent observers.

The average daily urinary excretion of mercury over a period of two months with no precautions was 425 µg and 152 µg, excluding holiday periods. By care in washing the hands and the wearing of overalls these amounts were reduced by three quarters.

It is suggested that, before the use of mercurial powder for fingerprint detection is considered as representing a definite risk, fairly protracted observations should be made on each of a large number of people who are prepared to exercise care in taking simple hygienic measures.

There is some evidence that the urinary excretion of mercury can be used to supply information about the amount ingested.

REFERENCES

Agate, J. N., Buckell, M. (1949) *Lancet*, ii, 451.
Buckell, M., Hunter, D., Milton, R., Perry, K. M. A. (1946) *Brit. J. industr. Med.* 3, 55.
Milton, R. F., Hoskins, J. L. (1947) *Analyst*, 72, 6.

EFFECT OF VENOUS OCCLUSION ON PERIPHERAL ARTERIAL BLOOD-FLOW

JESSE E. THOMPSON* JOHN R. VANE†
M.D. Harvard B.Sc. Oxfd

From The Nuffield Institute for Medical Research, Oxford

INTERMITTENT venous occlusion, by means of a pneumatic cuff placed round the thigh was introduced in 1936 by Collens and Wilensky for the treatment of patients with obliterative vascular disease. The rationale was that the reactive hyperæmia which follows release of the occluding pressure (Lewis and Grant 1925) might promote the development of the collateral circulation. Collens and Wilensky used intermittent venous occlusion pressures of 30–90 mm. Hg, with a cycle of two minutes on and two minutes off, and they reported beneficial results in a high proportion of their 124 patients.

Since its introduction numerous other investigators have examined the therapeutic effects of intermittent venous occlusion in man, yet there does not seem to be any unanimity about its efficacy. Whereas Collens and Wilensky (1937), Brown and Arnott (1937, 1938), Evoy and de Takats (1948), and Linton (1949) have found it beneficial in the treatment of vascular disease, Allen et al. (1946) and Smithwick (1949) consider it to be of little or no use. Among those who use the method and find it helpful some believe it is of value only in acute arterial emergencies, such as embolism and thrombosis, while others use it also in chronic conditions.

SUPPOSED EFFECTS

Two types of vascular change have been supposed to result from intermittent venous occlusion: (1) the acute effects, which include the changes occurring during the period of occlusion and immediately after its release; and (2) the chronic effects, which may include the changes occurring in the collateral circulation to the limb over a long period.

The acute effects have been investigated in man and animals with conflicting results. The chronic effects have been observed only in patients with obliterative vascular disease, again with conflicting results, and have not been subjected to direct experiment. Direct measurement of changes in the collateral circulation in patients has not yet proved feasible, and in animals such long-term investigations are admittedly difficult and have not been undertaken.

PREVIOUS INVESTIGATIONS

Methods used for examining acute effects of intermittent venous occlusion on arterial blood-flow are of two types: (1) the first has been designed to study the circulation in man by various indirect methods when venous occlusion is applied for a limited time; and (2) the second has been designed to study the circulation in laboratory animals by measuring the arterial blood-flow directly during and after short periods of venous occlusion.

Allen and McKechnie (1937) studied the effect of intermittent venous occlusion on the surface temperature of 19 patients with and without arterial disease, and could find no evidence of significant or consistent vasodilatation resulting from the procedure.

Veal and McCord (1939), testing blood-oxygen changes in 11 healthy males after intermittent venous occlusion, concluded there was no increase in the rate or volume of blood-flow, and that a true reactive hyperæmia was not produced.

Abramson et al. (1941), using a plethysmographic method, found no increase in blood-flow either during or after venous occlusion in the leg or forearm, but sometimes observed a slight increase in the hand and foot.

Friedland et al. (1943) and Halperin et al. (1948) using capillary microscopy, skin temperature readings, plethysmography, and venous blood-oxygen differences in human patients, concluded that blood-flow in the limbs is not increased during venous occlusion but is usually decreased. They postulated two causes for this observation: (1) a reduction in the pressure gradient from artery to vein, due to increased venous pressure; and (2) a decrease in the calibre of small vessels in the compressed area causing an increased resistance to flow.

The evidence obtained by indirect methods in man suggests that there is no increase in mean arterial blood-flow during venous occlusion.

Linton et al. (1941) reported changes in arterial flow during venous occlusion in dogs. They used a thermostromuhr method. Venous occlusion was produced either with a pneumatic cuff placed round the thigh or by clamping the major veins. During venous occlusion the arterial inflow to the hind limb increased, and immediately after release of the occlusion the arterial flow decreased. The changes were greater when the pneumatic cuff was used than when the major veins were occluded directly. On the basis of this rather surprising result Linton et al. recommended that the period of venous obstruction be longer than the period of release when intermittent venous occlusion was to be used for therapy in man. As it did not appear logical that arterial inflow should increase during venous obstruction, Gregg et al. (1948) studied the problem again.

They used three different types of instruments to measure arterial blood-flow in the dog's hind leg: (1) a Baldes-Herrick thermostromuhr; (2) an orifice meter; and (3) an optically recording rotameter. With the thermostromuhr they obtained the same results as Linton—i.e., an apparent increase in arterial flow during venous occlusion, and an apparent decrease following its release. With the other two methods they consistently found a decrease in arterial flow during venous occlusion and an increase on release.

The thermostromuhr is a complicated device which relates the rate of blood-flow to changes in the differential temperature between two thermojunctions, the flowing blood being heated by a unit situated between the two thermojunctions. Tests by Gregg et al. (1948) have revealed serious inaccuracies in the Baldes-Herrick thermostromuhr method of measuring blood-flow, since many factors other than blood-flow influence the results significantly. "The amount of backflow in the flow pattern is particularly important since the flow pattern in most arteries either normally contains backflow or it can be induced and the instrument is so sensitive that such a change can cause the device to indicate incorrectly the directional change in flow "

---

* During the tenure of a Rhodes scholarship and a Fulbright grant.
† During the tenure of a grant from the Medical Research Council.

Since the rotameter and orifice meter are not subject to the same criticisms as the thermostromuhr, Gregg et al (1948) concluded that the results obtained with the thermostromuhr during venous occlusion were diametrically opposed to the truth They therefore stated that the arterial blood flow decreases during venous occlusion and increases after release of the occlusion

PRESENT METHODS

In the present investigation we studied the acute effects of venous occlusion on the rate of arterial flow in animals by two direct methods not previously used for this purpose

Cats weighing 1 8–3 5 kg were anæsthetised with chloralose 70 mg per kg of body weight or with pentobarbitone 30 mg per kg of body weight In some experiments the hind legs were denervated either before or during the perfusion One hind leg was perfused through the iliac artery, the hypogastric and caudal arteries being tied, occasionally, in small cats both hind legs were perfused from the aorta. The rate of blood flow and the perfusion pressure were both measured directly A carotid and a brachial artery were cannulated, and blood was taken from these into the perfusion pump through a resistance The blood, kept at 37°C by a hot-water jacket, was pumped into the leg and returned by the normal venous channels The rate of blood flow was recorded by direct measurement with a volume recorder attached to the pump, and was registered as a series of vertical lines on a smoked drum. At the end of each experiment the recorder was calibrated Tested with an artificial circulation the greatest error found was + 4% at 45 ml per min (the highest rate of flow obtained in this work) It is important to emphasise that the actual volume of blood entering the leg was measured, so that the errors associated with indirect methods (such as the thermostromuhr) were eliminated Full details of the perfusion method will be published elsewhere

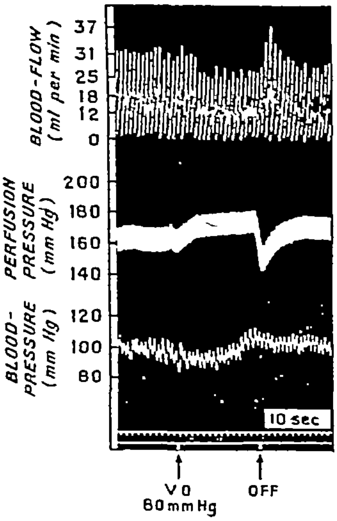


Fig 1—Cat (1 9 kg) Nembutal anæsthesia with bilateral lumbar sympathectomy Both hind legs perfused from bifurcation of aorta. Blood pressure recorded from left brachial artery Flow before occlusion was 32 ml per min At first mark, cuffs round both legs were inflated to 80 mm Hg the flow was reduced to 26 ml per min On release of the occlusion the rate of flow rose to a peak of 37 ml per min but rapidly fell again to a level of 28 ml per min Thus the flow after occlusion was lower than that before.

Serial radiographs were taken at intervals of 0·5–1 5 sec after the injection of 'Thorotrast' (2–3 ml) into the abdominal aorta The injections were made through a 'Polythene' tube tied into the stump of the inferior mesenteric artery

Venous occlusion was achieved by wrapping a pneumatic cuff round the thigh and inflating it to known pressures measured with a mercury manometer

RESULTS

The effect of venous occlusion on the rate of blood-flow in the perfused leg was studied in 12 cats

When the cuff round the perfused hind limb was inflated to a fixed pressure of 20–80 mm Hg (27 observations), 80–100 mm Hg (11 observations), and 100–200 mm Hg (17 observations) for two or three minutes, the arterial inflow always decreased (figs 1 and 2) In not one of these 55 occlusions was an increased flow recorded during the occlusion Sometimes, immediately after release of the pressure, reactive hyperæmia was observed, but this never lasted longer than twenty to thirty seconds and in no instance compensated for the reduced flow during occlusion The reactive hyperæmia, when present, was followed by a reduction in blood flow to the rate before occlusion or, in several experiments, even further (fig 1)

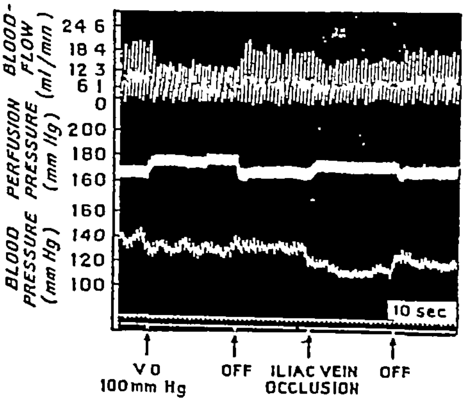


Fig 2—Cat (2 6 kg) chloralose anæsthesia. Right hind leg perfused Venous-occlusion cuff inflated to 100 mm Hg for 3 min Blood-flow reduced from 20 ml per min to 13 ml per min. After release rate of flow was 19 ml per min this was reduced to 15 ml per min by clamping the iliac vein for 3 min Note fall in blood-pressure characteristic of this type of occlusion indicating pooling of blood in the leg

To study further the effects of venous occlusion, individual veins were clamped with 'Bulldog' clips The arterial inflow decreased in all of the 21 instances where the vena cava, the common iliac, the external iliac (fig 2), or the femoral vein was clamped

Thus it became obvious that, if any over all increase in blood flow was to be obtained during intermittent venous occlusion, it must be through the reactive hyperæmia overcompensating for the reduction in flow during the occlusion A cycle of occlusion and release was therefore adopted, with the cuff inflated for 30 seconds, and deflated for 30 seconds Under these conditions an over all increase in flow during intermittent venous occlusion was never observed Nine experiments made with intermittent venous occlusion pressure of 60–300 mm Hg were made, each run lasting for five to ten minutes The reactive hyperæmia in no instance compensated for the decreased blood-flow during occlusion, although reduced blood flow was observed on all occlusions, no reactive hyperæmia followed occlusions at the lower pressures (fig 3) The rate of blood flow after intermittent venous occlusion was never greater than the rate before, in some instances it was less. In all these varieties of occlusion removal of the lumbar sympathetic trunks or cutting the sciatic and femoral nerves, or both, did not sensibly alter the results

To study the circulation visually during venous occlusion, and to confirm the results obtained on the perfused legs, radiographs were taken of both hind legs, one of which was occluded with the cuff for two minutes before the injection of thorotrast In each of the 5 cats studied the radiographs showed that filling of the vessels below the cuff on the occluded leg was much delayed, compared with the control leg There was also a considerable decrease in the number of small arterial vessels seen under the occluding cuff Fig 4 is taken from a typical series and shows both these effects

DISCUSSION

The hypothesis that intermittent venous occlusion promotes the development of collateral circulation has been based on two alleged effects during and immediately after release of the occlusion

1 An increase in arterial inflow during venous occlusion (Linton et al 1941)

41 µg, which are within the limits observed in persons without any known contact with mercury We consider it desirable that clinical observations should be made and the urinary excretion of mercury estimated over a considerable period in each of a large number of cases before conclusions are drawn about the possible dangers of chronic mercurial poisoning, particularly in fingerprint detection

SUMMARY

Two police officers heavily engaged for years in finger print detection with mercurial powder were examined No clinical signs of mercurial poisoning were detected by several independent observers

The average daily urinary excretion of mercury over a period of two months with no precautions was 425 µg and 152 µg, excluding holiday periods By care in washing the hands and the wearing of overalls these amounts were reduced by three quarters

It is suggested that, before the use of mercurial powder for fingerprint detection is considered as representing a definite risk, fairly protracted observations should be made on each of a large number of people who are prepared to exercise care in taking simple hygienic measures

There is some evidence that the urinary excretion of mercury can be used to supply information about the amount ingested

REFERENCES

Agate J N, Buckell, M. (1949) *Lancet* ii 451

Buckell M Hunter D Milton R Perry, K M A (1946) *Brit J industr Med* 3, 55

Milton R F, Hoskins, J L (1947) *Analyst* 72, 6

EFFECT OF VENOUS OCCLUSION ON PERIPHERAL ARTERIAL BLOOD-FLOW

JESSE E THOMPSON* JOHN R VANE†

M D Harvard B Sc Oxfd

From The Nuffield Institute for Medical Research, Oxford

INTERMITTENT venous occlusion, by means of a pneumatic cuff placed round the thigh was introduced in 1936 by Collens and Wilensky for the treatment of patients with obliterative vascular disease The rationale was that the reactive hyperæmia which follows release of the occluding pressure (Lewis and Grant 1925) might promote the development of the collateral circulation Collens and Wilensky used intermittent venous occlusion pressures of 30–90 mm Hg, with a cycle of two minutes on and two minutes off, and they reported beneficial results in a high proportion of their 124 patients

Since its introduction numerous other investigators have examined the therapeutic effects of intermittent venous occlusion in man, yet there does not seem to be any unanimity about its efficacy Whereas Collens and Wilensky (1937), Brown and Arnott (1937, 1938), Evoy and de Takats (1948), and Linton (1949) have found it beneficial in the treatment of vascular disease, Allen et al (1946) and Smithwick (1949) consider it to be of little or no use Among those who use the method and find it helpful some believe it is of value only in acute arterial emergencies, such as embolism and thrombosis, while others use it also in chronic conditions

SUPPOSED EFFECTS

Two types of vascular change have been supposed to result from intermittent venous occlusion (1) the acute effects, which include the changes occurring during the period of occlusion and immediately after its release, and (2) the chronic effects, which may include the changes occurring in the collateral circulation to the limb over a long period

The acute effects have been investigated in man and animals with conflicting results The chronic effects have been observed only in patients with obliterative vascular disease, again with conflicting results, and have not been subjected to direct experiment Direct measurement of changes in the collateral circulation in patients has not yet proved feasible, and in animals such long term investigations are admittedly difficult and have not been undertaken

PREVIOUS INVESTIGATIONS

Methods used for examining acute effects of intermittent venous occlusion on arterial blood flow are of two types (1) the first has been designed to study the circulation in man by various indirect methods when venous occlusion is applied for a limited time, and (2) the second has been designed to study the circulation in laboratory animals by measuring the arterial blood flow directly during and after short periods of venous occlusion

Allen and McKechnie (1937) studied the effect of intermittent venous occlusion on the surface temperature of 19 patients with and without arterial disease, and could find no evidence of significant or consistent vasodilatation resulting from the procedure

Veal and McCord (1939), testing blood oxygen changes in 11 healthy males after intermittent venous occlusion, concluded there was no increase in the rate or volume of blood flow, and that a true reactive hyperæmia was not produced.

Abramson et al (1941), using a plethysmographic method, found no increase in blood flow either during or after venous occlusion in the leg or forearm, but sometimes observed a slight increase in the hand and foot

Friedland et al (1943) and Halperin et al (1948), using capillary microscopy, skin temperature readings, plethysmography, and venous blood oxygen differences in human patients, concluded that blood flow in the limbs is not increased during venous occlusion but is usually decreased. They postulated two causes for this observation (1) a reduction in the pressure gradient from artery to vein due to increased venous pressure, and (2) a decrease in the calibre of small vessels in the compressed area causing an increased resistance to flow

The evidence obtained by indirect methods in man suggests that there is no increase in mean arterial blood flow during venous occlusion

Linton et al (1941) reported changes in arterial flow during venous occlusion in dogs They used a thermostromuhr method Venous occlusion was produced either with a pneumatic cuff placed round the thigh or by clamping the major veins During venous occlusion the arterial inflow to the hind limb increased, and immediately after release of the occlusion the arterial flow decreased The changes were greater when the pneumatic cuff was used than when the major veins were occluded directly On the basis of this rather surprising result Linton et al. recommended that the period of venous obstruction be longer than the period of release when intermittent venous occlusion was to be used for therapy in man. As it did not appear logical that arterial inflow should increase during venous obstruction, Gregg et al (1948) studied the problem again

They used three different types of instruments to measure arterial blood flow in the dog's hind leg (1) a Baldes Herrick thermostromuhr, (2) an orifice meter, and (3) an optically recording rotameter With the thermostromuhr they obtained the same results as Linton—i e, an apparent increase in arterial flow during venous occlusion, and an apparent decrease following its release With the other two methods they consistently found a decrease in arterial flow during venous occlusion and an increase on release

The thermostromuhr is a complicated device which relates the rate of blood flow to changes in the differential temperature between two thermojunctions, the flowing blood being heated by a unit situated between the two thermojunctions Tests by Gregg et al (1948) have revealed serious inaccuracies in the Baldes Herrick thermostromuhr method of measuring blood flow since many factors other than blood flow influence the results significantly 'The amount of backflow in the flow pattern is particularly important since the flow pattern in most arteries either normally contains backflow or it can be induced, and the instrument is so sensitive that such a change can cause the device to indicate incorrectly the directional change in flow '

---

* During the tenure of a Rhodes scholarship and a Fulbright grant

† During the tenure of a grant from the Medical Research Council

Since the rotameter and orifice meter are not subject to the same criticisms as the thermostromuhr, Gregg et al (1948) concluded that the results obtained with the thermostromuhr during venous occlusion were diametrically opposed to the truth They therefore stated that the arterial blood flow decreases during venous occlusion and increases after release of the occlusion

PRESENT METHODS

In the present investigation we studied the acute effects of venous occlusion on the rate of arterial flow in animals by two direct methods not previously used for this purpose

Cats weighing 1 8–3 5 kg were anæsthetised with chloralose 70 mg per kg of body weight or with pentobarbitone 30 mg per kg of body weight In some experiments the hind legs were denervated either before or during the perfusion. One hind leg was perfused through the iliac artery, the hypogastric and caudal arteries being tied, occasionally, in small cats both hind legs were perfused from the aorta. The rate of blood flow and the perfusion pressure were both measured directly A carotid and a brachial artery were cannulated, and blood was taken from these into the perfusion pump through a resistance The blood, kept at 37°C by a hot water jacket, was pumped into the leg and returned by the normal venous channels The rate of blood flow was recorded by direct measurement with a volume recorder attached to the pump and was registered as a series of vertical lines on a smoked drum At the end of each experiment the recorder was calibrated Tested with an artificial circulation, the greatest error found was – 4% at 45 ml per min. (the highest rate of flow obtained in this work) It is important to emphasise that the actual volume of blood entering the leg was measured so that the errors associated with indirect methods (such as the thermostromuhr) were eliminated Full details of the perfusion method will be published elsewhere

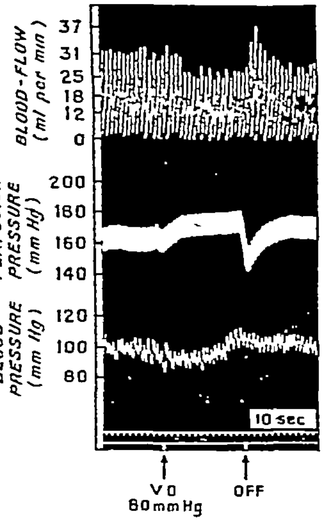


Fig 1—Cat (1 9 kg) Nembutal anæsthesia with bilateral lumbar sympathectomy Both hind legs perfused from bifurcation of aorta. Blood pressure recorded from left brachial artery Flow before occlusion was 32 ml per min. At first mark cuffs round both legs were inflated to 80 mm Hg the flow was reduced to 26 ml per min On release of the occlusion the rate of flow rose to a peak of 37 ml per min but rapidly fell again to a level of 28 ml per min Thus the flow after occlusion was lower than that before.

Serial radiographs were taken at intervals of 0·5–1 5 sec after the injection of 'Thorotrast' (2–3 ml.) into the abdominal aorta The injections were made through a 'Polythene tube tied into the stump of the inferior mesenteric artery

Venous occlusion was achieved by wrapping a pneumatic cuff round the thigh and inflating it to known pressures measured with a mercury manometer

RESULTS

The effect of venous occlusion on the rate of blood-flow in the perfused leg was studied in 12 cats

When the cuff round the perfused hind limb was inflated to a fixed pressure of 20–80 mm Hg (27 observations), 80–100 mm Hg (11 observations), and 100–200 mm Hg (17 observations) for two or three minutes, the arterial inflow always decreased (figs 1 and 2) In not one of these 55 occlusions was an increased flow recorded during the occlusion Sometimes, immediately after release of the pressure, reactive hyperæmia was observed, but this never lasted longer than twenty to thirty seconds and in no instance compensated for the reduced flow during occlusion The reactive hyperæmia when present, was followed by a reduction in blood flow to the rate before occlusion or, in several experiments, even further (fig 1)

To study further the effects of venous occlusion, individual veins were clamped with 'Bulldog' clips The arterial inflow decreased in all of the 21 instances where the vena cava, the common iliac, the external iliac (fig 2), or the femoral vein was clamped

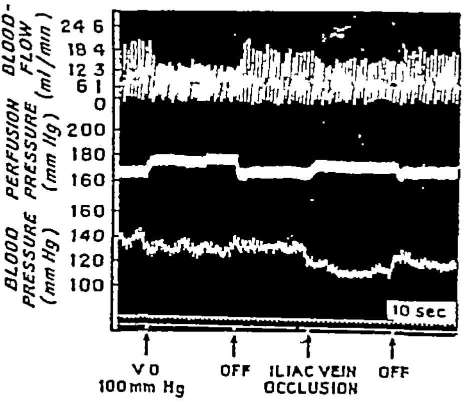


Fig 2—Cat (2 6 kg) chloralose anæsthesia. Right hind leg perfused. Venous-occlusion cuff inflated to 100 mm Hg for 3 min Blood flow reduced from 20 ml per min to 13 ml per min. After release rate of flow was 19 ml per min this was reduced to 15 ml per min by clamping the iliac vein for 3 min Note fall in blood pressure characteristic of this type of occlusion indicating pooling of blood in the leg

Thus it became obvious that, if any over-all increase in blood flow was to be obtained during intermittent venous occlusion, it must be through the reactive hyperæmia overcompensating for the reduction in flow during the occlusion A cycle of occlusion and release was therefore adopted, with the cuff inflated for 30 seconds, and deflated for 30 seconds Under these conditions an over-all increase in flow during intermittent venous occlusion was never observed Nine experiments made with intermittent venous occlusion pressure of 60–300 mm Hg were made, each run lasting for five to ten minutes The reactive hyperæmia in no instance compensated for the decreased blood flow during occlusion, although reduced blood flow was observed on all occlusions, no reactive hyperæmia followed occlusions at the lower pressures (fig 3) The rate of blood-flow after intermittent venous occlusion was never greater than the rate before, in some instances it was less. In all these varieties of occlusion removal of the lumbar sympathetic trunks or cutting the sciatic and femoral nerves, or both, did not sensibly alter the results

To study the circulation visually during venous occlusion, and to confirm the results obtained on the perfused legs, radiographs were taken of both hind legs, one of which was occluded with the cuff for two minutes before the injection of thorotrast In each of the 5 cats studied the radiographs showed that filling of the vessels below the cuff on the occluded leg was much delayed, compared with the control leg There was also a considerable decrease in the number of small arterial vessels seen under the occluding cuff Fig 4 is taken from a typical series and shows both these effects

DISCUSSION

The hypothesis that intermittent venous occlusion promotes the development of collateral circulation has been based on two alleged effects during and immediately after release of the occlusion

1 An increase in arterial inflow during venous occlusion (Linton et al 1941)

2 A reactive hyperæmia following release of the occlusion, a concept based on the work of Lewis and Grant (1925) and put forward by Collens and Wilensky (1936)

The final proof of reactive hyperæmia rests on the demonstration of increased circulation to an extremity after prolonged intermittent venous occlusion over weeks The clinical evidence on this point is conflicting, the necessary experimental data are lacking altogether

As regards the increase in arterial inflow during venous occlusion, it is clear from the data presented here and by Gregg et al (1948) that arterial inflow considerably *decreases* during venous occlusion It is unfortunate that the vagaries of the Baldes Herrick thermostromuhr should have led to an enthusiastic acceptance of a false rationale by many clinicians It seems logical that venous occlusion by a cuff should lead to a decrease in arterial flow (1) as was pointed out by Halperin et al (1948) the pressure gradient decreases from the arterial to the venous side because of the increased venous pressure, and (2) the calibre of the vessels under the cuff decreases with an accompanying retardation of flow This is demonstrated directly in our radiographs The pressure drop across arterioles is usually about 40 mm Hg, hence at their peripheral end the mean pressure is only some 30 mm Hg It is clear, therefore, that even very low occlusion pressures, far below the diastolic level, will obliterate small arterioles under the cuff, though leaving the main arteries comparatively unaffected

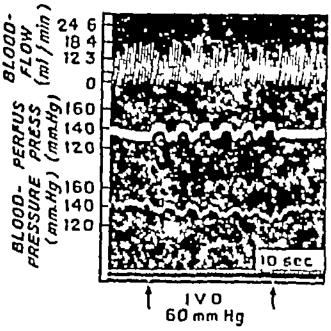


Fig 3—Cat (2·6 kg), chloralose anæsthesia. Right hind leg perfused Blood pressure recorded from left brachial artery Intermittent venous occlusion at 60 mm Hg was applied for 6 min in a cycle of 30 sec. occlusion and 30 sec. release Before occlusion, rate of flow was 18 ml per min Over the period of intermittent venous occlusion the average rate of flow was 14·5 ml per min and after release 16 ml per min

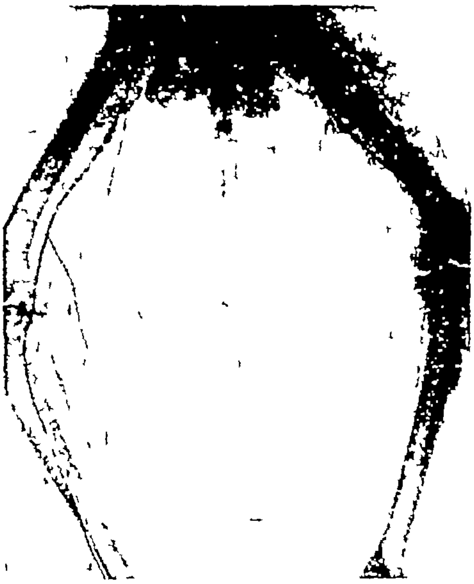


Fig 4—Cat (2·6 kg), nembutal anæsthesia. Blood pressure 120 mm Hg recorded from right carotid artery Cuff round left leg inflated to 80 mm Hg for 2 min before injection of thorotrast. The fourth exposure is shown, taken at 3·2 sec. after the injection Note filling of main arteries in right leg down to ankle but only just past knee in occluded leg Arteries of the smallest visible size in the control limb are not visible under the cuff on the occluded side Note also the compression of soft tissues and displacement of medium sized arteries under the cuff (Left leg is on right of figure)

It is even possible that the presence of the inflated cuff may induce active constriction in the vessels of the occluded leg Slight evidence in favour of this is the fact that in some of our experiments the blood flow following release of the occlusion was lower than the flow preceding occlusion The presence or absence of nerve supply had no effect on this phenomenon

It is well known that the higher the level of the occluding pressure, the greater will be the reactive hyperæmia following release In our experiments the compensatory hyperæmia never approached the amount of blood prevented from entering the limb during the period of occlusion In fact, at the lower occlusion pressures—i e, 60 mm Hg (fig 2)—no significant compensatory rise in flow was observed to follow release of the pressure Further, even when a compensatory hyperæmia did occur it lasted only twenty to thirty seconds, and the subsequent rate of flow was either the same as the pre-occlusion rate or lower, it was never higher It thus appears that there is no direct experimental evidence, in man or in animals, in favour of using venous occlusion to increase the arterial blood flow to an extremity Further, the results obtained in acute experiments by both direct and indirect measurements of blood flow point to a decrease in supply of blood to the extremity during the occlusion and no persistent increase after its release Whether repeated venous occlusion increases collateral circulation over a long period has not been proved, no alternate case reports have been published The long term effect of intermittent venous occlusion will not be known until such data are available

SUMMARY

The acute effects of venous occlusion on the rate of arterial inflow to the hind limbs of cats have been studied directly by perfusion and by serial radiography

During venous occlusion the arterial inflow to the extremity decreases

After release of the occlusion, there is commonly a transient increase in arterial flow above the pre-occlusion level, but this reactive hyperæmia does not compensate for the decreased flow during occlusion The rate of flow following release is equal to, or less than, the rate preceding occlusion—never higher

Serial radiography showed a delay in the filling of the vessels on the occluded side, and a considerable reduction in the number of visible small arterial vessels under the inflated cuff

There is no direct experimental evidence in man or in animals to substantiate the view that venous occlusion increases the arterial blood flow to an extremity

We wish to thank Dr G S Dawes for guidance in this work, Dr G M Ardran for help in interpreting the radiographs, and Mr N C Shirley and Mr H Elvidge for technical assistance

REFERENCES

Abramson D I Zazeela, H Schkloven N (1941) *Amer Heart J* 21, 756
Allen E V Hines E A jun Barker N W (1946) Peripheral Vascular Diseases Philadelphia and London
— McKechnie R E jun (1937) *J Lab clin Med* 22 1260
Brown J J M Arnott W M (1937) *Brit med J* 1 1106
— — (1938) *Ibid* 1 616
Collens W S, Wilensky N D (1936) *Amer Heart J* 11, 705
— — (1937) *J Amer med Ass* 109, 2125
Evoy, M H de Takats, G (1948) *Arch intern Med* 81, 292
Friedland C K Hunt, J S Wilkins, R W (1943) *Amer Heart J* 25 631
Gregg D E, Pritchard W H Shipley, R E (1948) *Amer J Physiol* 153, 153
Halperin M H Friedland C K Wilkins R W (1948) *Amer Heart J* 35, 221
Lewis T Grant, R (1925) *Heart* 12 73
Linton R R (1949) *New Engl J Med* 240 645
— Morrison P J Ulfelder H Libby, A L (1941) *Amer Heart J* 21 721
Smithwick R H (1949) Personal communication
Veal J R McCord W M (1939) *Amer Heart J* 17, 401

RECURRENT KAPOSI'S VARICELLIFORM ERUPTION

IN AN ADULT

W. C. BOAKE
M.B., B.Sc. Melb.
NUFFIELD DOMINIONS DEMONSTRATOR, SIR WILLIAM DUNN SCHOOL OF PATHOLOGY, UNIVERSITY OF OXFORD; LATELY RESIDENT MEDICAL OFFICER, ROYAL MELBOURNE HOSPITAL

J. A. DUDGEON
M.C., M.D. Camb.
ASSISTANT PATHOLOGIST, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON; LATELY RESEARCH ASSOCIATE, WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH

SIR MACFARLANE BURNET
M.D. Melb., Hon. Sc.D. Camb., F.R.S.
DIRECTOR, WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH, MELBOURNE

Kaposi (1887) originally described the vesicular eruption that now bears his name as a complication of eczema in infants and young children. The cases published in the last sixty years indicate that the condition is most common in early childhood but that adults are sometimes affected. Thus Ruchman et al. (1947) found that 75 of the 96 cases previously recorded (i.e., 79%) were in children, a quarter of whom were under a year old, the remainder being in adults.

Two distinct ætiological types are now recognised: the herpetic, due to the virus of herpes simplex, which is the commoner type; and the vaccinial (eczema vaccinatum), due to vaccinia virus.

Most of the herpetic cases, whether in infants or adults, occur as a manifestation of primary herpetic infection—a systemic illness, often severe, which is accompanied by the first appearance of specific herpetic antibodies in the blood-stream. Thereafter the virus remains latent in the body, producing from time to time, in response to some stimulus, a local infection, such as labial herpes. Recurrent herpes rarely if ever becomes generalised, and second attacks of Kaposi's varicelliform eruption are rare (Scott et al. 1949). Ruchman et al. (1947) reported a case in a patient aged 25, in whom neutralising antibodies were present in the acute stage of the disease but who developed a second attack six weeks after the onset of the first.

In the case reported here, attacks of a vesicular eruption recurred for some years, and the diagnosis of recurrent Kaposi's varicelliform eruption of herpetic type was confirmed by clinical and laboratory findings.

CASE RECORD

A man, aged 36, was admitted to hospital with diabetic acidosis, bilateral basal pneumonia, and a herpetiform eruption of 3 days' duration. For 25 years he had been known to have diabetes mellitus, and about twice a year there had been recurrences of labial and facial eruptions consisting of a group of vesicles usually localised to the lips but often involving the cheeks, ears, and eyebrows. The lesions reappeared intermittently at the same site, though not as a rule in consecutive attacks. The patient's mother and daughter gave a history of labial herpes extending over many years.

There seemed to be a relation between the severity of the eliciting stimulus and the extent of the subsequent facial eruptions. After a mild common cold with no pyrexia herpes did not usually develop. A more severe stimulus, such as a febrile illness, was followed by localised herpes with one or more groups of discrete lesions. A severe systemic illness such as pneumonia was followed by a generalised cutaneous eruption of the type now under discussion.

Nineteen years earlier, after the onset of the facial herpes, the patient had developed generalised atopic eczema, which persisted despite intermittent treatment. Twice in the last three years he had been admitted to the Royal Melbourne Hospital with a facial eruption similar to that now described. In December, 1946, the condition was called 'infected impetigo' and in November, 1948, 'pustular dermatitis,' but on both occasions it was essentially the same as the present illness. Each attack had been associated with pneumonia and diabetic imbalance. In the present illness he developed a corneal ulcer on the left eye, and in the previous year there had been one on the right eye; each ulcer appeared three days after the facial eruption.

The present illness commenced with chest pain, pyrexia, cough, and bloodstained sputum. On the second day vesicular lesions appeared on the face. These began as itchy papules on the nasolabial folds, and in a further 24 hours similar vesicles appeared on the cheeks, eyelids, ears, forehead, neck, and upper part of the chest.

On examination the patient had atopic eczema involving his face, chest, and arms. Superimposed was an irregular eruption strictly localised to the eczematous area and consisting of multiple, discrete, and in places confluent lesions with areas of unaffected skin in between. The single lesions were circular, averaging 3 mm. in diameter; most of them were flat, glistening, yellow, and easily broken, yielding purulent fluid; some were umbilicated with a surrounding erythema, and contained clear serous fluid; others had red bleeding bases. The whole condition was irritating but not painful. In this attack, according to the patient, lesions appeared for the first time on the forehead. In addition there was inflammation of the pharynx and tonsils, but the mucosa of the mouth was free from ulceration. The eyelids were œdematous and ulcerated, and there was a shallow ulcer on the lower and outer quadrant of the left cornea. The urine contained glucose and acetone.

Diagnosis.—On the history and clinical examination a diagnosis of recurrent facial herpes was made, together with diabetic acidosis and resolving basal pneumonia.

In the past 3 years, when intensive but unsuccessful efforts had been made to control the atopic eczema and the diabetes had been unstable, it was noted that acidosis was not followed by herpes unless there was an accompanying cold or febrile illness, but it invariably led to a rapid and severe flaring up of the eczema. Thus a worsening of the eczema associated with an intense stimulus such as pneumonia was followed by a generalised cutaneous eruption.

LABORATORY INVESTIGATIONS

Bacteriology.—A stained film from the vesicular exudate showed numerous gram-positive cocci in clusters; culture produced a coagulase-positive penicillin-sensitive *Staph. aureus.*

Isolation and Identification of Virus.—The chorio-allantoic membranes of 12-day-old chick embryos inoculated with fluid taken from vesicles on the face and chest developed lesions closely resembling those of the virus of herpes simplex after 48 hours' incubation. The lesions produced by vesicle fluid from the face and from the chest appeared to be identical. The infective agent was identified by the neutralisation test (Burnet and Lush 1939) and by a direct complement-fixation test using the membranes as antigen and a positive herpes serum (Dudgeon 1950). The membranes showing confluent lesions were ground into a 20% suspension in calcium magnesium saline (pH 7.4) and centrifuged at 2500 r.p.m. for 15 minutes. The supernatant fluid was used as the antigen in complement-fixation and neutralisation tests. This suspension fixed complement at a titre of 1 in 16 in the presence of the positive herpes antiserum; no fixation occurred with a normal uninoculated chorio-allantoic membrane of the same age. The neutralisation test showed that the chorio-allantoic lesions were inhibited to the same extent by the control herpes serum as by the patient's own serum (3rd day), thus establishing herpes simplex virus as the causal agent.

Serological Tests.—Sera collected from the patient on the 3rd and 21st days of his illness were tested for complement-fixing and neutralising antibodies. Complement-fixing antibodies were present to a titre of 1 in 16 in the acute phase (3rd day) and 1 in 16 in the convalescent phase (21st day). Neutralising antibodies were present in both specimens.

Other Investigations.—On the 3rd day of his illness the patient's white-cell count was 8000 per c.mm. with 70% polymorphs, and his fasting blood-sugar level was 370 mg. per 100 ml. On the 10th day there were 6000 white cells per c.mm. and the fasting blood-sugar was 170 mg. per 100 ml.

TREATMENT AND PROGRESS

Treatment with 'Sulphamerazine' and penicillin led to rapid resolution of the pneumonia A mild acidosis, as shown by acetone and sugar in the urine, was corrected by adjusting the diet and insulin dosage 'Benadryl' 50 mg three times a day was given on empirical grounds, and local treatment with starch poultices quickly cleared the facial lesions, which by the 12th day had almost completely healed

DISCUSSION

Isolation of the herpes simplex virus from this man's facial and neck lesions, and the demonstration of antibody in his serum in the acute stage (3rd day) as well as in convalescence, established the diagnosis of a recurrent herpetic process The extensive distribution of the lesions and their association with eczematous areas makes it legitimate to describe the condition as recurrent Kaposi's varicelliform eruption

The identification of herpes virus by Seidenberg (1941) and Esser (1941) as a common causal agent in the typical infantile form of Kaposi's syndrome has since been confirmed by many workers in different parts of the world In early childhood the eruption is essentially a manifestation of primary infection with herpes virus, but the numerous reports of Kaposi's syndrome in adults (Barton and Brunsting 1944, Lynch et al 1945, Ruchman and Dodd 1948) show that, if primary infection is delayed, infection of eczematous areas can occur later in life Not all of these adult cases were investigated in detail, but Ruchman and Dodd showed by serological tests that in 8 out of their 9 cases (4 infants and 5 adults) the infection was accompanied by a rise in antibody, thus identifying them as primary infections

The two characteristic features of primary herpes, which normally takes the form of gingivo stomatitis, are (1) the initiation of an infection which will probably persist, mainly in latent form, throughout life, and (2) the *first appearance of circulating antibody*, which will also remain in the blood for life Infected people are liable to recurrent attacks of herpes which vary in degree, frequency, and relation to the stimulus required to produce them The commonest site for recurrent herpes is the lips or nasolabial folds It is reasonable to suppose that these areas of skin are involved secondarily by extension from the original stomatitis, though this has not been clearly demonstrated Recurrent herpetic lesions rarely involve the mucosa of the mouth The recurrent stomatitis seen in many adults and often attributed to herpes simplex almost certainly has a different ætiology Dodd and Ruchman (1950) report laboratory investigations of several cases of recurrent aphthous or ulcerative stomatitis in adults, but no direct evidence of association with herpes simplex virus was obtained

It is difficult to determine the frequency of recurrent attacks of Kaposi's eruption The published reports suggest that recurrence is rare, though a few cases have been recorded by Scott et al (1949) Of about 10 children with this disease seen at the Hospital for Sick Children in the last few years, none has returned with a recurrence of the eruption, nor with any form of recurrent herpes, although many of them have continued to attend the hospital for treatment of the eczema (Brain 1950, *personal communication*)

In the present case the history indicates that ordinary labial herpes was observed before the onset of eczema It is therefore likely that the primary infection with the virus occurred in early childhood and that, with the development of eczema, affected regions of the skin were infected by transfer of virus from the labial lesions It is impossible to be certain from the patient's history when this transfer took place, but it seems necessary to assume that in the major episodes recurrence in a previously affected region occurred as well as transfer to new vulnerable areas

Cases of this type provide special opportunities not yet explored for the study of a unique and interesting problem in the general pathology of virus infection—the nature of the latent infection and its relation to circulating antibody Burnet's (1945) interpretation of the labial localisation normally seen is that the area involved is infected at the time of the primary stomatitis, that virus continues to exist "symbiotically" in the basal epidermal cells, and that only in such areas can recurrent herpetic lesions appear There are, however, no records of persons having been followed from the time of infantile infection to adult life to establish whether the primary skin involvement occurs in the same site as the subsequent recurrent lesions Cases such as the present one could provide evidence of the extent to which secondarily infected eczematous areas are subject to recurrence. Both aspects should be studied

Epidemiological evidence suggests that, after a primary stomatitis, a child is immune against any further attack of this type, and that maternal antibody can protect most infants up to the age of 12 months (Anderson and Hamilton 1949) It is known, however that a herpetic person can be infected with his own virus by scarification on the skin of the arm, so that circulating antibody is not a complete protection against extrinsic reinfection An eczematous area of a person with circulating antibody presents a complex *situation in* which cells abnormally accessible to infection are present as well as inflammatory exudative changes which will bring antibody into a position to prevent infection Whether infection occurs or not will probably depend on the *particular stage* that the eczematous process in a given area has reached when it is contaminated with virus In any case the process will be more limited than when a similar surface is infected in a person without any active immunity

There are still no real clues to the conditions which determine whether an area infected either primarily or secondarily will become the site of recurrent lesions. The fact that Kaposi's eruption in infants rarely gives rise to recurrent herpetic lesions in the eczematous skin area is in contrast to the present case, where an eczematous area was first involved in young adult life. It may be that a very severe primary attack resulted in the elimination of virus from the area, just as it appeared to be eliminated from the buccal epithelium, which bears the brunt of a primary stomatitis A combined study by dermatologists and virologists of the phenomena associated with herpetic infections in eczematous subjects of all ages would probably help to clarify the situation

SUMMARY

A case of recurrent Kaposi's varicelliform eruption is reported in an adult

Herpes simplex virus was identified as the infective agent, and antibody was detected throughout the course of the disease

The rarity of the condition in contrast to other forms of recurrent herpes is discussed

Our thanks are due to Dr Leslie Hurley for permission to publish this case, and to Dr A. Isaacs for assistance in the investigation

REFERENCES

Anderson S G Hamilton J (1949) *Med J Aust* 1 308
Barton R L Brunsting L A (1944) *Arch Derm Syph Chicago* 50 99
Burnet, F M (1945) Virus as Organism Cambridge Mass, p 50
— Lush D (1939) *Lancet* i 629
Dodd K, Ruchman I (1950) *Pediatrics* 5 883
Dudgeon J A (1950) *J clin Path* 3 239
Esser M (1941) *Ann pædiat* 157 156
Kaposi M (1887) Pathology and Treatment *of Diseases of the Skin* New York p 346
Lynch F W Evans C A Bolin, V S Steves R J (1945) *Arch Derm Syph Chicago* 51 129
Ruchman I Welsh A L Dodd K (1947) *Ibid* 56 846
— Dodd K (1948) *Pediatrics* 1 304
Scott T F M Coriell L L Blank H (1949) The Diagnosis of Viral and Rickettsial Infections New York p 83
Seidenberg S (1941) *Schweiz Z Path u Bakt* 4, 398

CLINICO-ANATOMICAL STUDY OF A SUCCESSFUL LEUCOTOMY

S DESMOND MCGRATH
M.R C P.I , D.P M
REGISTRAR, MAUDSLEY HOSPITAL, LONDON

From the Department of Neuropathology, Institute of Psychiatry, Maudsley Hospital, and the Department of Clinical Research, Crichton Royal, Dumfries

MANY successful results have been claimed for surgery of the brain in the treatment of mental disorder, and a considerable number of the patients so treated must have died since of intercurrent illness Attempts to determine whether there are optimal lesions for each type of case will require systematic correlation of the clinical data with the anatomical results of the operation in a considerable series of successful cases It is therefore a matter of great regret that up to now only one such case has been investigated and published (Freeman and Watts 1947)

I report here a second such case in the hope that it will not only contribute to a series of cases in the literature from which refinements in brain surgery may in due course be derived but will also draw the attention of doctors, especially pathologists in general hospitals, to the potential value of systematic investigation, at suitably equipped laboratories, of the brains of patients in whom leucotomy has been successful and who have died later from some other cause

CASE RECORD

Miss A, then aged 39, was admitted as a certified patient to Crichton Royal Hospital on July 26, 1937

Clinical History—Her mother had died after nine years' stay in a mental hospital because of a paranoid psychosis which had started with the menopause No other mental illness was known in the family The patient's development as a child was believed to have been normal She was a good scholar, rather reserved, and inclined to worry She was described as venturesome, difficult to advise, and self willed After some years at home she took up work in a public library, where she remained ten years In 1932 when aged 34 she left, because she thought that people were talking about her and were antagonistic to her She next trained and worked as a secretary for a short while, but in 1933 was admitted to a mental hospital for the first time with delusions of persecution auditory hallucinations impulsive behaviour, and incongruous affect She recovered sufficiently to be discharged in January 1934 She then worked as a typist, changing jobs frequently until March, 1936, when she had to be readmitted to a mental hospital, from which she was transferred to Crichton Royal in 1937

On admission she presented a typical picture of paranoid schizophrenia At first she seemed to have some insight into her illness, but soon she became overwhelmed by her delusional ideas which she extended to the hospital and the persons around her She was openly hostile towards her environment, accused her presumed persecutors of ill treatment, and was most of the time angry and withdrawn, often aggressive and violent She neglected her appearance and showed other signs of deterioration After a course of insulin coma therapy in 1939 she showed transient improvement and was well enough to index the medical library After a few months, however she relapsed into her former condition being completely self absorbed, inaccessible, and ill disposed towards everybody Electrical convulsion treatment applied in 1942 and 1943 produced only transient relief and was finally included in the patient's delusional system and refused

Leucotomy was done on May 16 1943, by Mr Alexander, using the standard technique of Freeman and Watts Immediate progress was smooth On the evening of the operation she was lucid and not confused She said she could still hear voices and that she had not changed at all After ten days she became incontinent of urine and fæces This persisted for two or three weeks and then gradually cleared Though the patient at first retained her delusions and hallucinations, she was less troubled and became noticeably more cheerful At times she was irritable and had rows with the staff and other patients By July of that year she could be given parole, and in October she went to work in the medical library However, owing to memory difficulties she could not carry out a projected revision of the library properly By February, 1944, she was efficiently doing secretarial work in the hospital and visiting her family at home for week ends She no longer expressed delusional ideas, and though when questioned she admitted that she still heard voices she said they were very faint and that she did not take any notice of them

After discharge on March 31, 1944, she got a job in a public library, where she worked satisfactorily Subsequently she was several times dismissed because of unpunctuality and lack of precision in her work, but on each occasion she very soon found a similar occupation For a time she was a librarian of a university institute, where she had much time to herself She decided to take her qualifying examination as a librarian and studied for matriculation, though now aged 47 She failed, but took this in good humour

Her condition improved progressively By the middle of 1946 she had become much more punctual and reliable, aggressive and unexpected changes in behaviour which she had shown after discharge became rare She led a happy and active life, and kept up an extensive correspondence with relatives and friends The long and chatty letters she wrote to her sister described her daily life with lively satisfaction She was considerate, friendly, and good company Only once, in 1947, did she mention in a letter her hallucinations, saying that she heard the voice occasionally but could ignore it

Though she had some difficulty in managing her money, being inclined to over generosity with presents and to sharing unduly expensive holidays, her sister said that the patient's ability to look after her affairs, and adapt to the great changes which had taken place in everyday life during her stay in hospital, was truly remarkable

She was disinclined to live and work in the small town near the hospital where she had been treated for many years, though her family would have preferred her to stay in the neighbourhood She came home, however, for short visits and was seen several times by the psychiatrist She was friendly and always willing to give information about herself, being neither over talkative nor reticent, and had full insight about her illness and the senselessness of her ideas of persecution For her treatment at the hospital she was thankful, but she attributed her recovery to the insulin therapy, not to the leucotomy Her memory of the sequence of events during the last few years of her stay in hospital was somewhat hazy

After leaving her last job as a librarian she became a secretary in the large outpatient department of a London teaching hospital, a post she held until her death from coronary thrombosis in December, 1948, at the age of 50, five and a half years after the leucotomy

Pathological Investigation

The brain displayed no abnormality of leptomeninges or superficial blood vessels The convex surface of the prefrontal region of each frontal lobe appeared moderately

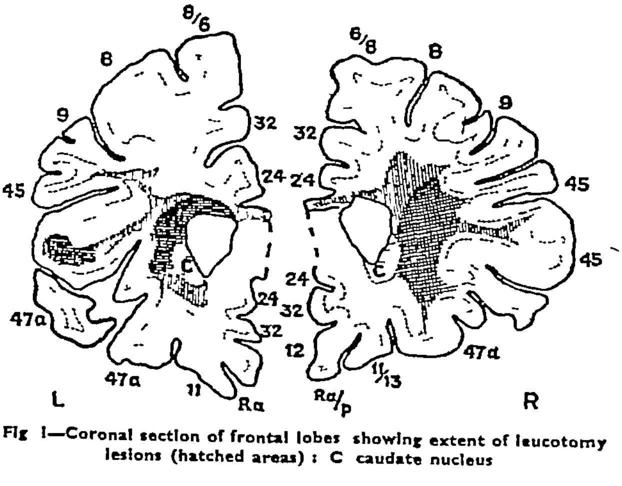


Fig 1—Coronal section of frontal lobes showing extent of leucotomy lesions (hatched areas) : C caudate nucleus

shrunken Otherwise the convolutions showed no abnormality beyond marks of the leucotome's entry on either side just rostral to the perpendicular branch of the sylvian fissure (anterior ascending ramus of the lateral cerebral sulcus) Coronal section through the two entry marks showed that the centre of each leucotomy scar lay at the level of the tip of the caudate nucleus (fig 1) On the right side the lesion took the form of a smooth walled cavity It cut at this level the whole of the central white matter external to the lateral wall of the anterior horn of the lateral ventricle, and the more superficial white matter related to Brodmann's areas 45 and 47 * The subcallosal fasciculus was damaged at the tip of the caudate nucleus The dorsal and cingulate segments of the white matter were not directly involved by the lesion, but the whole of the anterior thalamic radiation to the more rostral parts of the dorsal convexity were interrupted at the head of the caudate nucleus, which was only slightly damaged The ventricle and the main substance of the caudate nucleus had been spared

On the left side the lesion consisted of a more narrow slit The same regions of white matter as on the right side were involved, with the addition of damage deep to area 46 Both lateral ventricles were moderately dilated

Fig 2 indicates the extensive retrograde degeneration of nerve cells in the anterior, ventrolateral, and dorsomedial nuclei of the thalamus on either side as seen on examination of Nissl stained serial sections Reference to the scheme of parcellation of the thalamofrontal radiation described by McLardy (1950) shows that fibres to cortical areas 6, 8, 9 10, 11, 24, 45, 46, and 47 of Brodmann were cut Most of the fibres were cut as they emerged from the internal capsule, and the damage to the above mentioned thalamic nuclei was strikingly symmetrical The other thalamic nuclei were essentially intact, and there was no evidence of degeneration in the hypothalamus

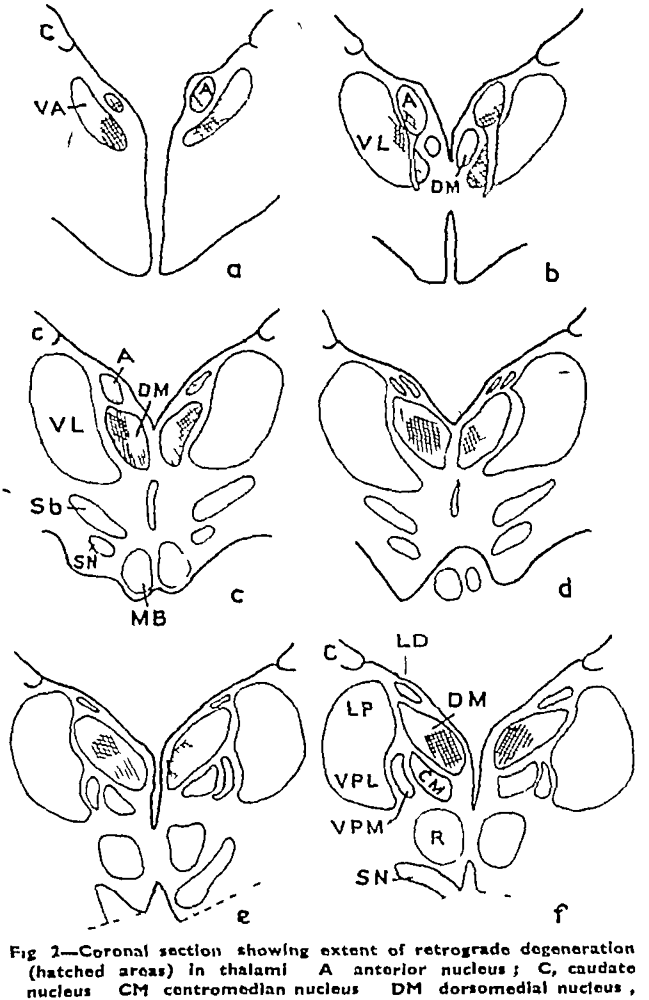


Fig 2—Coronal section showing extent of retrograde degeneration (hatched areas) in thalami A anterior nucleus ; C, caudate nucleus CM centromedian nucleus DM dorsomedial nucleus , LD, dorsal lateral nucleus ; LP, posterior lateral nucleus ; MB, mamillary body R, red nucleus Sb, subthalamic nucleus SN, substantia nigra VA anterior ventral nucleus VL, lateral ventral nucleus VPL posterolateral ventral nucleus VPM, posteromedial ventral nucleus

DISCUSSION

The leucotomy seems clearly to have been mainly responsible for this patient's recovery from a paranoid schizophrenic illness of eleven years' duration, sufficiently severe to have required her continuous detention in hospital for six years before the operation Unlike her response to insulin coma and electric convulsion therapy her post leucotomy recovery of mental health was progressive and sustained The clinical change for the better was about as dramatic as has ever been reported in the literature The retrograde degeneration of nerve cells in the dorsomedial nucleus of the thalamus is about as complete, bilaterally, as has been described in any case of leucotomy The clinical result and anatomical findings are therefore fully consistent with the tentative conclusions reached by McLardy and Meyer (1949), from analysis of a series of cases with generally low grade improvement, that the quantity of prefrontal cortex isolated from thalamic and other long fibre connections should be directly proportional to the severity of the illness The general validity of such a " quantitative principle " has been confirmed for most of the other forms of surgical treatment of mental disease

That undesirable personality change was not a striking feature in the present case despite the posterior level of the cuts may be further evidence in support of Frankl and Mayer Gross's (1947) conception that the amount of damage should be calibrated to produce ' enough frontal symptoms to combat the symptoms of the psychosis—enough euphoria against distress and depression , enough extraversion and distractibility against introspection and withdrawal " Only a larger series of successful cases to compare with others developing undesirable personality changes can determine whether such a " neutralisation of symptoms " is the main factor in determining the final state A previous good personality which was a feature of this case, has been emphasised by Stengel (1950) and Partridge (1950) as a favourable prognostic factor

A considerable series of such successful cases must be anatomically as well as clinically followed up in detail if any principles are to be discovered of optimal lesions to create maximal improvement with minimal undesirable side effects On the anatomical side it is almost indispensable that the assessment of the lesions be made post mortem Meyer and his associates (Meyer and McLardy 1949) have repeatedly shown enormous discrepancies between surgical intention and necropsy findings after blind leucotomy, and now have some early evidence (personal communication) that even in the various open operations the surgeon's estimate of the extent of damage is not absolutely reliable for such correlation

SUMMARY

The clinical history of a severe case of schizophrenia of eleven years' duration, with recovery and survival for five and a half years after leucotomy, is reported together with a description of the primary lesions and the retrograde degeneration in the thalamus

The consistency of the findings with the general " quantitative " principle in the surgical treatment of mental disease is discussed briefly

This is only the second clinico anatomical study of a successful leucotomy that has been published The attention of doctors, especially pathologists in general

---

* Brodmann's map of cortical areas is used here simply in virtue of its convenient topographical subdivision of the surface of the hemisphere

hospitals, is drawn to the potential value of the brains of leucotomised patients who die outside mental hospitals.

I wish to thank Prof A Meyer and Dr T McLardy for their interest and valuable criticisms, Dr W Mayer Gross for clinical notes, Mrs E Beck for advice, and Dr P K McCowan for permission to publish this case.

REFERENCES

Frankl L. Mayer-Gross W (1947) *Lancet* ii 820
Freeman W Watts J W (1947) *J comp Neurol* 86 65
McLardy T (1950) *J Neurol Neurosurg Psychiat* 13 198
— Meyer A (1949) *J ment Sci* 95 182
Meyer A McLardy T (1949) *Ibid* 95 403
Partridge M. (1950) Pre-Frontal Leucotomy Oxford
Stengel E (1950) *J ment Sci* 96 633

DELAYED PULMONARY COMPLICATIONS OF BRONCHOGRAPHY

PHILIP W ROBERTSON
M.D Lpool M.R.C.P

K. D FORGAN MORLE
M.B St And D.M.R.D

From the Department of Radiology, Royal Infirmary Liverpool

IN the course of investigations into various chest diseases between March, 1949, and December, 1950, we have done 220 bronchograms, mostly on young men the method used being the introduction of iodised oil by cricothyroid puncture. No instance of classical iodism was seen but 16 of the patients developed a delayed reaction one to two weeks after the bronchography. The reactions were pulmonary in type and were characterised by fever, cough, chest pain, and malaise. Five of the reactions were associated with pleural effusion. Urticaria followed the reaction in 4 cases, 1 of which also had transient swelling of the joints of the hands.

Few published references to this type of reaction have been found. Bass (1949) reports one similar case and he and Kooperstein (1946) had previously described 3 cases of delayed pneumonia following bronchography with iodised oil in asthmatic patients. Since so little has apparently been written about these reactions it seemed worth while to describe the clinical picture in detail, choosing the most severe case as an example. This bronchogram was done for control purposes on a healthy subject (one of us) and was entirely normal.

CASE REPORT

No ill effects whatever were felt after the left sided bronchography until the early hours of the seventh day when the patient was awakened by a rigor. This was followed almost at once by abdominal pain, nausea and vomiting indeed for the next few days abdominal discomfort and anorexia were the predominant symptoms. The patient felt extremely ill and had a temperature of 104°F.

Examination within a few hours of the onset of symptoms revealed signs suggestive of a pleural effusion on the left side. Cough developed in the next few hours, with scanty golden yellow watery sputum in which no pus or mucus was seen microscopically. The most striking feature of the sputum was the peculiarly uniform chemical yellowness. Laboratory examination showed that it did not contain any free iodine but on spectroscopy it gave iodine absorption bands and the yellow material was proved biochemically to be an iodoprotein.

Chest radiography twenty four hours after the onset revealed a moderate left-sided pleural effusion with a considerable residue of iodised oil. In this case evidence of any associated inflammatory change in the left lung field in the vicinity of the iodised oil would have been obscured by the effusion.

Aspiration produced opalescent fluid of the same yellow colour as the sputum containing a moderate number of eosinophils and a considerable amount of fibrin, sufficient to produce clotting and found to be sterile on culture.

The blood white-cell count was 14,000 per c mm. with a slight polymorphonuclear leucocytosis no preponderance of eosinophils was reported.

After three or four days there was no longer any fever or constitutional upset. The fluid was gradually absorbed and no trace was detectable radiologically after two and a half weeks. Furthermore, as the fluid was absorbed the residual iodised oil also disappeared, leaving a normal lung field. Subsequently there has been an entirely uneventful recovery.

OTHER CASES

The other cases have followed similar but less violent courses. Pleural pain, cough, yellow sputum, &c, have all occurred, and small pleural effusions were noted in 4 patients. In those cases which had an X-ray examination during the reaction, evidence of inflammatory change around the iodised oil was seen. In some, this consisted of a complete and uniform opacity maximal in the areas showing the most residual oil. In all cases there has been spontaneous, rapid, and complete recovery.

Several of these patients required a second bronchogram and it is interesting to note that where bronchography was repeated there was no recurrence of the complication. Indeed, a delayed reaction never followed a repeat bronchogram whether or not the first procedure was complicated.

We believe that careful observation of all patients after bronchography would reveal fever on or about the ninth day in an appreciable number. By retrospective examination of the temperature-charts of those patients who were retained in hospital for a sufficient length of time we have found that several had a short mild fever about the ninth day, with no significant symptoms.

DISCUSSION

The mechanism of these delayed reactions has not been determined, but despite the absence of any convincing allergic history, they are probably a manifestation of allergy. The constant time interval, resembling that of penicillin reactions the eosinophils in the pleural fluid, and the urticarial eruptions are all suggestive. In view of the presence of an iodoprotein in the sputum of the affected patients, there may be an individual tendency to form this compound from the iodised oil, and it may then act as the allergen. In very few cases was there any associated lung sepsis and there was no evidence that a "stirring up of infection" occurred.

It is clear that patients should be carefully observed for a fortnight after bronchography. When the investigation is performed on outpatients they should be seen at the end of one and two weeks.

There does not appear to be any indication for treatment other than general nursing, in these cases. Antihistamine drugs may be tried but it is difficult to assess their effect owing to the rapid spontaneous improvement in untreated cases. Prophylaxis would presumably include immediate and efficient postural drainage after bronchography. All the patients in this series were given preoperative potassium iodide and no reaction to it was noted. Skin sensitivity tests were not performed.

SUMMARY

In 220 consecutive bronchograms there were 16 examples of delayed reactions, characterised by fever, cough, and malaise starting about nine days after the bronchography and lasting three or four days. In 5 cases there was a pleural effusion.

Rapid and spontaneous recovery was seen in all cases. It is suggested that the reactions are allergic.

All patients submitted to bronchography should be watched during the following fortnight.

We wish to thank Dr W S Sutton and Dr P H Whitaker for their helpful advice and criticism.

REFERENCES

Bass. H E (1949) *New Engl J Med* 240 505
Kooperstein S I Bass H E (1946) *Amer J Roentgenol* 56, 569

FATAL THYROID CRISIS

COMPLICATING TOXIC GRANULOPENIA DURING THIOURACIL THERAPY

A B Pollard
M D Lond , M R C P
PHYSICIAN, ESSEX COUNTY HOSPITAL, COLCHESTER

In a case of moderately severe thyrotoxicosis treated with methyl thiouracil a previous course of thiouracil had been given Shortly after the start of the second course toxic symptoms appeared, but thiouracil therapy was continued until three weeks later, when granulopenia developed In spite of appropriate measures the patient died within thirty six hours The clinical course of the final stage of the illness was remarkable in that the thyrotoxic symptoms were violently exacerbated, suggesting a thyroid storm or crisis

CASE RECORD

An unmarried woman, aged 25, was admitted to hospital on March 30 1949 Three years previously, after an emotional shock, she had had a nervous breakdown, with tremor of hands, fainting attacks, and outbursts of weeping At this time her neck was not swollen, nor were her eyes prominent Sedatives were prescribed, and after three months she improved considerably

A year later she had again become nervous and had noticed that her eyes were prominent and aching Her doctor diagnosed thyrotoxicosis, and for a year she was given thiouracil with no adverse reaction She improved greatly, losing her nervousness and gaining weight , but later, as her face became puffy, her hair fell out, and her neck was swollen, thiouracil was discontinued

Shortly afterwards a relapse had occurred, with return of the nervousness and loss of weight On this occasion she was given Lugol's iodine for a few months However, loss of weight continued in spite of a good appetite, occasional attacks of diarrhœa occurred, palpitations were troublesome, and weakness noticeable The exophthalmos and swelling of the neck persisted unchanged

The past history revealed nothing of note An interesting fact in the family history was that a sister had died of myasthenia gravis at the age of 24 This sister had had no goitre

On admission the patient was nervous and tremulous, of average nutrition, weight 7 st 13 lb , and height 5 ft 2 in , with a warm moist skin , bilateral exophthalmos with lid retraction , thyroid moderately enlarged (right lobe more than the left), smooth and firm, with no murmur or thrill , regular tachycardia with pulse rate 120, blood pressure 155/75, and sleeping pulse rate 116 Her heart was not enlarged , there was a short soft systolic murmur at the apex Nothing abnormal was found in the respiratory system or the alimentary system No weakness was detected in the central nervous system the reflexes were brisk and equal, the plantar reflexes being flexor

Investigations —Nothing abnormal was found in the urine The serum cholesterol was 140 mg per 100 ml The basal metabolic rate was + 40 (Benedict-Roth) A white cell count showed 7000 leucocytes (polymorphs 4200) per c mm Radiography of the neck showed a slight anteroposterior compression of the trachea at the level of D1, with possibly slight deviation to the left, but no side to side compression. No intrathoracic thyroid extension was visible The lung fields were clear, and the heart was normal in size and shape

Treatment and Progress —In view of the previous apparent good response to thiouracil, it was decided that further therapy with this drug should be given and that after a time the case should be reviewed particularly with reference to the advisability of surgical treatment On admission phenobarbitone gr $^1/_2$ t d s and a barbiturate sedative at night, if required, were prescribed From April 5 methyl thiouracil 200 mg t d s was given. Next day the patient's temperature rose to 101°F and she developed a generalised macular rash A white-cell count made at this time showed 5000 leucocytes (polymorphs 3450) per c mm On April 7 the temperature was normal and the rash had completely faded Methyl thiouracil was continued throughout in the same dosage

Over the next three weeks some improvement took place The tremor was less and the skin cooler The patient slept better and gained 4 lb in weight The sleeping pulse-rate was now about 100 The thyroid swelling and exophthalmos were unchanged However, she remained susceptible to the slightest emotional disturbance, and it was clear that at this stage she was by no means under the control of the antithyroid drug Further white cell counts made during this period gave the following results April 13, 6000 leucocytes (2300 polymorphs) per c mm , April 14 5000 leucocytes (2300 polymorphs) , and April 16, 5000 leucocytes (2[illegible] polymorphs)

On the evening of April 26 the patient's temperature was 99°F Next morning she complained of a sore throat and headache Methyl thiouracil was discontinued forthwith. A blood count taken on the morning of April 27 showed Hb 75%, red cells 4,200,000 per c mm , white cells [illegible] (polymorphs 705) per c mm , platelets 150 000 per c.mm. Intramuscular penicillin 250,000 units was given four hourly By the evening of April 27 the patient s temperature had risen to 103 8°F and her pulse rate to 140 She was restless and agitated with respirations 40 a minute During the night the restlessness continued and her general condition showed a rapid deterioration Lugol's iodine 60 minims by mouth was given together with sedatives and an intravenous infusion of plasma Her restlessness became extreme urinary and fæcal incontinence developed, and her extremities became cold and cyanosed Her pulse, the rate of which had risen to 160, became increasingly weaker, and she died in the early hours of April 28 from cardiac failure During the last few hours of life the exophthalmos had become more pronounced The pulse throughout was quite regular

Necropsy —The body was that of a well nourished young adult female with protruding eyes The right side of the heart was slightly dilated The air passages contained blood stained mucus The lungs were emphysematous, with some areas of hæmorrhage and collapse, especially on the right side The bone marrow in the femur was slightly increased The spleen was somewhat enlarged, and the malpighian bodies were prominent The lymph glands were enlarged, and Peyer s patches in the gut were conspicuous The thymus was large, soft, and milky The thyroid was large and devoid of colloid The suprarenals contained little lipoid and showed an increase of brown pigment The bladder was empty, and the kidneys were slightly œdematous The uterus contained menstrual blood, and a small hæmorrhagic cyst was present in the right ovary No abnormalities were found in the central nervous system The orbital fat was much increased

Histological Examination —The heart muscle showed an increase of brown pigment Scattered groups of fibres had shrunken nuclei and hyaline sarcoplasm There were also scattered foci of chronic inflammatory cells, including numerous foamy multinucleated giant cells These were mainly distributed in the connective tissue and fat in the vicinity of blood vessels The kidneys showed cloudy swelling, with hyaline droplet degeneration in some tubules The thyroid was hyperplastic, with vesicles usually of small size, mostly devoid of colloid, and lined by large and often columnar epithelium The orbital contents were composed of adipose tissue with scattered lymphocytes The lacrimal glands showed considerable lymphoid infiltration. The spleen was congested, and the malpighian bodies were enlarged The thymus was lymphoid Cultures made from material taken from the spleen at necropsy did not show any growth.

DISCUSSION

This unfortunate case is worthy of comment on two aspects The first question is the nature of the terminal illness The second is the wisdom of continuing the methyl thiouracil after the appearance of toxic symptoms —i e , fever and rash—a day after the start of the second course

The terminal stage of the illness was ushered in with fever, headache, and a sore throat These symptoms arising in a patient under treatment with thiouracil suggest a developing agranulocytosis with a throat infection In this case a severe granulopenia was in fact present Usually, after the administration of large doses of penicillin any infection is controlled, and this therapy, together with a complete withdrawal of the thiouracil, leads to a spontaneous and complete recovery, with a return of the granulocyte count to normal within a few days The rapid downhill course could have been due to a fulminating septicæmia, the organism being insensitive to penicillin in the doses given At necropsy, however, there were no signs of such septicæmia The extreme restlessness, tachycardia, and increase in exophthalmos suggested an acute exacerbation of thyrotoxicosis—the thyroid storm or crisis—and I suggest that this was the cause of death The crisis was probably precipitated by the throat infection which coincided with the granulopenia

The fatalities which have occurred with thiouracil have been due to agranulocytosis and infection Moore (1946), who reviewed a large series of cases of thyrotoxicosis treated with thiouracil with special reference to the toxic effects, found the incidence of agranulocytosis to be 1 74% and the fatality rate to be not more than 0 5% Since the general introduction of penicillin therapy the fatality-rate is probably even less Toxic symptoms are commoner with second and third courses of thiouracil, and tend to occur at an earlier stage of treatment They rarely appear before the seventh day, and 80% appear during the first six weeks' treatment with thiouracil (Himsworth 1948)

The thyroid storm or crisis is a highly fatal complication of thyrotoxicosis which has fortunately become much less common of late Himsworth (1948) states that the fact that the response to thiouracil is so good has meant the virtual disappearance of deaths from this highly fatal exacerbation of thyrotoxicosis McArthur et al (1947) describe 36 cases of thyroid storm out of 2033 cases of thyrotoxicosis admitted to their ward in twenty five years Of these, 25 cases followed operations on the patients, the remaining 11 cases occurred, in the non operated patients, from less easily identifiable causes. Psychological trauma or infection appeared to be the initiating factor in most of the cases These workers found that most cases of storm occurred in patients who had had the thyrotoxicosis for a relatively short time—i e , five years or less They were usually severe cases characterised by malnutrition and previous neglect Means (1948) considers that psychotic manifestations are ominous, and states that crises occurred particularly in those patients who did not show the expected improvement after treatment of their thyrotoxicosis

In the present case the patient had had the disease for about three years, and it was moderately severe Emotionally she was extremely unstable and she became further disturbed when she realised that a complication—i e toxic granulopenia—had set in Further, though it is well known that patients given a second course of thiouracil respond more slowly three weeks with methyl thiouracil in fairly high dosage had produced only slight improvement in her condition In retrospect it seems that an acute exacerbation of the thyrotoxicosis was not at all unlikely

Of the complications of thiouracil therapy, agranulocytosis is said to be the only dangerous one As regards skin rashes and fever due to it, Himsworth (1948) advises that thiouracil should be continued unless there is also a significant decrease in the number of polymorphs, and states that if the thiouracil is continued the fever disappears permanently Moore (1946) finds that drug fever and skin rashes occur in about 10% of cases and may be accompanied or followed by agranulocytosis McArthur et al (1945) consider that both fever and rash are certainly manifestations of drug idiosyncrasy, and Means (1948) states that the re exhibition of an anti thyroid drug to a patient who has shown a toxic reaction is contra indicated In the present case, since no granulopenia accompanied the fever and rash which developed twenty four hours after the start of the second course of thiouracil, the drug was continued Both fever and rash had gone within twenty-four hours, and no further trouble arose until three weeks later, when the granulopenia developed

SUMMARY

A fatal thyroid crisis in a thyrotoxic patient treated for a second time with thiouracil is described The crisis was associated with, and apparently precipitated by, a toxic granulopenia with a throat infection

Certain signs and symptoms suggested that an acute exacerbation might ensue , in the absence of granulopenia early toxic signs were disregarded, in accordance with current medical opinion in this country

In thyrotoxicosis that is at all refractory, or that seems likely to develop an acute exacerbation, any toxic symptoms from thiouracil should call for an immediate withdrawal of the drug and a recourse to iodine therapy followed by skilled surgery and more iodine

I am grateful to Prof G W Pickering for permission to publish this case, and to Dr D M Pryce for the necropsy report

REFERENCES

Himsworth H P (1948) *Brit med J* ii, 61

McArthur J W Rawson R W Means, J H (1945) *Ann intern. Med* 23 915

— — — Cope O (1947) *J Amer med Ass* 134 868

Means J H (1948) The Thyroid and Its Diseases 2nd ed , Philadelphia

Moore F D (1946) *J Amer med Ass* 130, 315

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THIS association held a meeting in London between Jan 25 and 27

Amidopyrine Agranulocytosis

Dr **George Discombe** said that amidopyrine agranulocytosis was commonly caused by prescribing the drug in a proprietary mixture, the prescriber being ignorant of or forgetting its presence He had encountered 4 fatal cases , in 3 sulphapyridine was at first thought to be responsible, but amidopyrine had been taken at the same time It seemed probable that the action on the bone-marrow of sulphonamides and amidopyrine was synergic Three series of hospital and of rheumatic patients who received amidopyrine had been reported. Among altogether 960 patients in these three groups, there were 11 cases of agranulocytosis—an incidence of 1 1% This indicated that there was no justification for using amidopyrine in ordinary practice as an analgesic In Denmark the distribution of proprietary mixtures containing amidopyrine was forbidden , and it seemed probable that the same action should be taken in Britain Official figures did not provide an adequate guide to the frequency of drug agranulocytosis His impression was that there were about 50 deaths per annum in this country, although the Registrar-General s figures were somewhat lower He would say that some fatalities were undoubtedly misdiagnosed

Dr **E N Davey** referred to two cases The first was believed to be diphtheria but turned out to be an instance of absolute granulopenia, which was attributed to the taking of 'Novalgin' for ovarian pain , the patient fortunately recovered At that time Dr Davey had listed the proprietary preparations containing amidopyrine and had filled a whole sheet of foolscap The second case was in a school teacher who had all the appearance of having agranulocytic angina but turned out to have the anginose type of glandular fever This disease should be considered in the differential diagnosis

Dr **J C Ford** referred to the case of a ward sister who had been taking 'Cibalgin' for myopic headache She was admitted with severe sacro-iliac pain, was apyrexial, and had a white-cell count of 5200 per c mm , of which 35% were neutrophils This patient was allowed by her doctor to have some cibalgin for her pain, having previously been sensitised to this drug She died eleven days later, the hæmoglobin and red-cell count being unaffected throughout, but the total white-cell count falling to 400 per c mm

Dr C J C Britton could not reconcile the statement that commercial manufacturing firms were dissuading people from using drugs containing amidopyrine with the fact that he regularly received samples through the post Dr C W Taylor suggested that the best way to discourage the use of these dangerous drugs was to ensure that fatalities were properly reported at inquests Dr N Schuster suggested that the simplest action would be to disallow proprietary names for amidopyrine Doctors should prescribe it individually so that they, and nurses, would know exactly what the patient was having Dr Discombe had considered approaching the chairman of the Pharmacopœia Commission with this suggestion

Prof R J V Pulvertaft said that he would advise prohibiting the use of any proprietary name As far as he knew there was nothing to prevent a firm changing the constitution of a preparation bearing a trade name He instanced a preparation which at one time had contained amidopyrine and had been responsible for several deaths It now no longer contained amidopyrine, but a preparation known by the same name was still on the market In almost every case of severe blood disease, and particularly in cases with purpura or aplastic anæmia it was essential to inquire whether a proprietary preparation had been taken

Prof D F Cappell agreed that the inclusion of amidopyrine in proprietary preparations should be prohibited by law He had met with fatal instances of agranulocytosis associated with the taking of a proprietary preparation before amidopyrine was dropped from its formula and he had seen others due to 'Allonal'

Other Subjects

Leucocyte Changes in Burns

Dr S Sevitt reported a study of the quantitative changes in the eosinophil, lymphocyte, and neutrophil counts in 26 patients suffering from burns involving from 0 1 to 80% of the body surface Soon after burning the eosinophil count fell, reaching low or zero values in a few hours This was often accompanied by lymphocytopenia and usually by neutrophil leucocytosis (primary wave) The eosinopenia, which persisted from a half to seven days, lasted longer in those more extensively burned, and there was a statistical correlation between the percentage of skin-surface burned and the duration of eosinopenia Dr Sevitt concluded that eosinopenia was a sensitive index of adrenocortical activity in burns Other leucocyte changes described were the onset in some patients of eosinophilia following the eosinopenic stage, later or delayed eosinophilia probably being due to allergy, and a secondary neutrophil wave

Fallacies in Platelet counts

Dr W K Taylor said that platelet counts in cases of hæmolytic anæmia, using Lempert's method [1] were found to be unduly raised The error was assumed to be due to staining of the fragmented reticulum following lysis of the erythrocytes Elimination of the cresyl-blue resulted in platelet-counts which agreed with those obtained by the magnesium sulphate film method Lempert's urea-citrate mixture without the addition of dye should be generally used for platelet-counts If the field was not too bright, counting was quite simple

Normoblastic and Megaloblastic Erythropoiesis

Dr L G Lajtha said that work with bone marrow cultures had yielded evidence of an inhibitory factor in the serum and cerebrospinal fluid (C S F) of patients with pernicious anæmia This factor inhibited the ripening of megaloblasts into normoblasts and produced megaloblasts from normoblasts in vitro Folic acid overcame the action of the inhibitory factor in vitro, and so did folinic acid (citrovorum factor) Crystalline vitamin B_{12} had no such effect

Biopsies in Rectal Disease

Dr C E Dukes pointed out that malignant disease of the rectum was seldom diagnosed without evidence of infiltration, and therefore some mucosa should be included in the biopsy In some cases of well differentiated tumours without infiltration a diagnosis of malignancy might not be possible

Kaposi's Varicelliform Eruption

Dr A Dick and Dr N R Grist described 10 cases of Kaposi's varicelliform eruption which appeared at the time of the widespread vaccination occasioned by an outbreak of smallpox in Glasgow Of these 10 patients 4 were unrelated, 2 were members of the same household, and 4 were infected while in hospital No case had been vaccinated previously, and all had been in contact with recently vaccinated subjects and had suffered from skin damage In 5 cases which were investigated fairly fully the vesicle fluid showed numerous elementary bodies, cultivation of this fluid or of crusts yielded a coagulase positive *Staphylococcus pyogenes* in all, while in 3 the infection was mixed The material from crusts or smears was used to inoculate the chorio-allantoic membrane of 11 day chick embryos The vaccinia virus was isolated in 5 of the cases The evidence suggested that the causative virus (vaccinia in this series) was inoculated directly into previously damaged areas of skin 2 patients appeared to benefit by 'Aureomycin'

"*Adamantinomas*"

Dr K S Thompson and Dr L B Manley described normal tooth development briefly as a downgrowth from the ordinary squamous epithelium from the maxilla and mandible, and they drew attention particularly to the difference between the cells of the internal dental (enamel) epithelium and ameloblasts Many tumours, as in the tibia and pituitary, were wrongly called adamantinomas owing to the œdematous prickle cells, which superficially resembled stellate reticulum, the diagnosis of adamantinoma should rest on the developmental cell —the cells of the internal dental epithelium Since ameloblasts were present only with enamel, they objected to the name "ameloblastoma" for these tumours preferring "Thoma's adamantinoma", but because of long usage the term "adamantinoma" was better

Penicillin in Inflamed Tissues

Dr J Ungar recalled that penicillin could be detected considerably longer in inflamed subcutaneous tissue than in blood In a further study bronchopneumonia was produced in mice and guineapigs by intranasal instillation of a virulent suspension of *Hæmophilus pertussis* When penicillin of different types (aqueous solutions of penicillin G or suspensions) was injected into the infected animals, it could be detected in the lungs in considerably higher quantities and for longer than in the lungs of normal control animals The peak of penicillin levels in the inflamed lungs was significantly higher than that of the blood-levels The tissue levels of penicillin depended on the type of penicillin injected (water soluble or water-insoluble) and the degree of infection in the lungs, the heavier the infection, estimated by the extent of lung consolidation, the higher were the levels of penicillin in the lung This was further evidence for the efficacy of single massive doses of penicillin in the treatment of acute infections One explanation of these findings was the increased binding of penicillin on the proteins (particularly the globulins) of inflamed tissue

Diagnosis of Weil's Disease and Canicola Fever

Dr J C Broom described the customary methods for the laboratory diagnosis of leptospirosis These were isolation of the organism and the demonstration of antibodies, but with neither could the diagnosis be established early in the disease It had been found that, in the early days of the illness (1) the erythrocyte-sedimentation rate was greatly increased, (2) the C.S.F. contained an increased number of cells, even in cases which showed no symptoms of meningitis, (3) in the meningeal form of canicola fever the glucose content of the C.S.F. was increased, (4) biopsy specimens of gastrocnemius muscle showed the characteristic degenerative changes in single muscle-fibres or groups of fibres, (5) biopsy specimens of liver showed the characteristic loss of cord structure and also signs of regeneration. Sometimes the antibody titre for the infecting species was at first much lower than the corresponding titre for some heterologous species. This might lead to complications if a hitherto unrecorded species appeared to be implicated. In a recent case, however, the presence of heterologous antibodies helped to establish the diagnosis of Weil's disease in a patient who died while being treated with large doses of leptospiral antiserum, and who showed only a low agglutination titre to *Leptospira icterohæmorrhagiæ*.

---

[1] Lempert H *Lancet* 1935 i 151

[2] Ungar J *Ibid* 1950, i, 56

Epidemiology of Leptospirosis

Dr. J. M. **Alston** said that the illnesses and deaths in the British Isles known to be due to *L. icterohæmorrhagiæ* (Weil's disease) were roughly half those due to typhoid fever. The causal organism was excreted in great profusion by rats and, less, by dogs. Leptospiras did not survive long after excretion, and that was probably why the disease was limited to those people who, usually by occupation, were repeatedly or heavily contaminated by rat's urine. There was a seasonal increase of the disease in the autumn. The mortality-rate for 1949 and 1950 was 12% of observed cases. Death did not occur without obvious jaundice, and nephritis was the most lethal feature. In the non-fatal meningitic form of the disease, the glucose content of the C.S.F. was normal; infection during bathing tended to lead to meningitis. Reduction of case-mortality required early diagnosis so that penicillin and antiserum could be used to kill the leptospira before hepatitis and nephritis became severe.

The known incidence of infection by *L. canicola* in the British Isles in 1949 and 1950 was 25 and 33 cases. The source of infection was the urine of dogs. In man the disease was usually mild, with or without meningitis. Incidence was much higher in the second half of the year. The incubation-period and natural routes of infection were not certain.

Iron Metabolism

Dr. A. **Klopper** and Dr. S. **Ventura** showed that the serum-iron fell significantly in late pregnancy. The changes in normal pregnancy were not nearly so gross as those demonstrated for the hypochromic anæmias of pregnancy, but they tended to show that the drain of iron during pregnancy caused latent iron deficiency. Serum-iron curves after oral and intravenous administration of iron showed that during pregnancy the intestinal mechanism of iron absorption was orientated toward a maximal transfer of iron to the blood stream, and that, when this mechanism was short-circuited by the intravenous injection of iron, the serum of the pregnant woman still showed enhanced power and speed in dealing with the influx of iron.

Myelomatosis

Dr. J. H. O. **Earle**, Dr. N. H. **Martin**, and Prof. N. F. **Maclagan** described atypical flocculation tests in several cases of myelomatosis. Using a wide spectrum of flocculation tests, including the zinc sulphate (Kunkel) and ammonium-sulphate (Popper) tests, they found that, despite the raised globulin, only two cases of myelomatosis gave a positive thymol turbidity test, but seven gave positive ammonium sulphate tests, and two further cases gave completely negative flocculation tests. Cases with increased globulin but with negative thymol turbidity or other flocculation tests should suggest a diagnosis of myelomatosis.

Potassium Deficiency

Dr. G. K. **McGowan** said that the main clinical indications of potassium deficiency were: (1) muscle weakness leading to paralysis; (2) prostration, anorexia, and paralytic ileus; (3) alkalosis resistant to sodium chloride; and (4) electrocardiographic changes. He demonstrated particularly the shift from intracellular to extracellular potassium with the balance maintained by excretion in the urine and gastro-intestinal secretions; and he pointed out that potassium should not be given unless the renal function was satisfactory.

Estimation of Thyroid Function

Dr. J. B. **Foote** and Prof. N. F. **Maclagan** described an apparatus for estimating thyroid function by a modified radioactive test using iodine (I^{131}). By taking thigh counts and neck-counts they produced an index which appeared to have diagnostic significance in thyrotoxicosis.

Sir Lionel Whitby's presidential address and a paper by Sir Henry Cohen on the limitations of laboratory investigations have already been summarised in these columns.[3]

MANCHESTER MEDICAL SOCIETY

Oral Sepsis and Chest Infection

At a meeting of the society's section of odontology on Jan. 22, Mr. R. H. R. **Belsey** said that pulmonary suppuration and dental sepsis presented three separate problems: (1) pulmonary suppuration occurring spontaneously in patients with dental sepsis; (2) pulmonary suppuration following general anæsthesia in patients with dental sepsis; and (3) pulmonary suppuration following dental operations, with or without a retained foreign body in the bronchial tree.

By dental sepsis was meant "open" sepsis. The pulmonary lesions that might result were suppurative bronchitis, suppurative pneumonitis, lung abscess, empyema, and pyopneumothorax due to rupture of a lung abscess into the pleural cavity. The association was first emphasised by John Alexander, who stated that "no edentulous patient ever developed a lung abscess." The solitary lung abscess with sudden onset of symptoms that sometimes arose from dental sepsis suggested bronchial embolism by infected, particulate matter from the mouth.

The onset of pulmonary symptoms after a general anæsthetic or dental operation might be acute and fulminating; often there was a latent period of three weeks before these symptoms appeared, and this had masked the association of the two conditions. The diagnosis was confirmed by X-ray examination and bronchoscopy. Early diagnosis and prompt chemotherapy and physiotherapy might avert the need for surgical treatment, and greatly improve the prognosis. Modern anæsthesia with the commoner use of intratracheal tubes might have increased the risk of pulmonary infection from the mouth.

The falling incidence of lung abscess might be due to improved dental hygiene, and to educational and other factors such as the school dental service.

As a routine, dental sepsis should be eliminated at least three weeks before every elective surgical procedure under general or local anæsthesia. Intensive preoperative and postoperative physiotherapy, and chemotherapy were also important. Emergency operations should be preceded by thorough removal of all debris and infected tartar from the gums and teeth.

The elimination of pulmonary infection after dental operations could be attempted by careful preoperative oral toilet, by operating with the patient in the head-low position, by avoiding drugs that depress the laryngeal and bronchial reflexes, and by a penicillin "screen." Any patient suspected of having inhaled a foreign body should be examined radiologically as soon as possible, and if necessary submitted to bronchoscopy. Early diagnosis and treatment of pulmonary complications would prevent permanent lung damage. The removal of foreign bodies impacted in the bronchial tree for some days or weeks was rendered safer and easier by a preliminary course of intrabronchial penicillin. Awareness of the severity of the pulmonary complications that might follow dental operations should lead to greater attention to their prevention and to early diagnosis and treatment.

---

[3] *Ibid*, Feb. 3, 1951, p. 279

Reviews of Books

Thrombo-embolic Conditions and their Treatment with Anticoagulants

CHARLES D MARPLE, M D, assistant clinical professor, division of medicine University of California San Francisco, IRVING S WRIGHT, professor of clinical medicine, Cornell University Medical College New York Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 418 £3 5s

HERE is a remarkably comprehensive and up to date account of the clinical use of anticoagulants The authors get off to a good start by emphasising the importance of thorough laboratory work Properly critical and sceptical, they nevertheless succeed in demonstrating how valuable anticoagulants can be if properly controlled and used, and it is to this clinical use of anticoagulants that the greater part of their book is devoted The contra-indications to anticoagulant treatment are given 17 pages The difficulties and disadvantages of treatment with heparin and dicoumarol are fairly considered and ways of dealing with them are clearly indicated, the fact that there are occasional failures is admitted and the reasons for them are adequately discussed In a final section of 100 pages on "recent advances" the use of anticoagulants in coronary thrombosis is fully dealt with, and there are short but pleasantly didactic and adequately detailed appendices on the laboratory methods used A list of 681 references shows that the published work has been adequately sorted, and altogether the reader could not find a better and safer guide through the jungle of anticoagulant practice

Recent Advances in Ophthalmology

(4th ed) Sir STEWART DUKE ELDER, K C V O, D SC, F R C S, director of research, Institute of Ophthalmology, University of London, and ophthalmic surgeon, St George s Hospital, London, A J B GOLDSMITH, M D, F R C S, surgeon, Moorfields Westminster and Central Eye Hospital, and lecturer in ophthalmology, University of London London J & A Churchill 1951 Pp 372 28s

SIXTEEN years have elapsed since the previous edition of this book appeared, and the text has been completely rewritten Dropping some older interests and theories, the authors have chosen a number of subjects in which great progress has been made These subjects are the physiology and pathology of the aqueous humour, the use of the gonioscope and the fundus contact-lens in examining the eye, glaucoma, bacterial and virus infections, chemotherapy and antibiotics, physiology and pathology of the cornea, cataract, and endocrine exophthalmos Their approach is by way of physiology and pathology rather than surgery, and in each subject the present state of knowledge is summed up in lucid and readable style The profession will be grateful to them for this presentation of new thought—so much in so small a compass

Muscular Contraction

W F H MOMMAERTS, PH D, established investigator of the American Heart Association, Department of Biochemistry, Duke University School of Medicine, Durham, North Carolina New York and London Interscience Publishers 1950 Pp 191 33s

THE last ten years have seen the most spectacular advances in the physiology and biochemistry of muscle This is largely due to work on the molecular form and behaviour of the structural proteins, but also to the extensive studies of the enzymes of the muscle cell and of adenosine triphosphate and all that has followed from its discovery Those who began to learn their physiology in the '20s were not taught about these matters, yet many of them are still keen to learn Dr Mommaerts's little monograph is just the thing for all who like to keep abreast of their subject, for it is short, clear, simple yet not dogmatic and delightfully historical in approach

The author first draws a picture of the metabolism of striated muscle as it has been worked out over the last thirty years, though he never hesitates to point out the unfinished appearance of parts of the canvas He goes on to deal with the muscle proteins in a similar way, describing their extraction, properties, size, shape, interactions—in short, their function as revealed by inspection and analysis A useful little summary ends many of the chapters Some of the terms—such as birefringence, and double refraction of flow—could be more simply explained when they are first mentioned and discussed, and a little more might have been said about contractile systems other than those of striated muscle But those who read the introduction are likely to finish the book, and they do not need a profound knowledge of the subject to enjoy it

Developments in Diphtheria Prophylaxis

LEWIS B HOLT, M SC, Wright Fleming Institute of Microbiology, St Mary's Hospital, London London Heinemann Medical Books 1950 Pp 181 42s

THE production of diphtheria prophylactic of consistent antigenicity and constant composition is of great importance, and Mr Holt s book illustrates the immense amount of painstaking work this involves He has his own views about many of these problems, and on Glenny's depot theory of the action of alum precipitated toxoid he suggests that alum toxoids are physiologically excluded from the rest of the body fourteen days after inoculation Much of the book is concerned with P T.A.P (purified toxoid, aluminium phosphate precipitated) and there is an account of its use by Bousfield The book is too technical for the average reader, and the method of presentation does not make a difficult subject easier

The Neural Crest

Properties and Derivatives in Light of Experimental Research SVEN HORSTADIUS, professor of zoology, University of Uppsala London Oxford University Press 1950 Pp 110 15s

IN five short chapters, based on lectures given at University College, London, in 1947, Professor Hörstadius tells an absorbing story of experimental methods in embryology Most of us think of the neural or ganglionic crest as that part of the primitive embryo which goes to make the spinal root ganglia, but this is only one of its functions, for not only does it contribute to other parts of the nervous system but it also takes a diverse part in structural development elsewhere Thus excision and implantation experiments, as well as older methods depending on staining and serial section, show that it makes a major contribution to cartilage and cartilaginous bone, and even to membrane bone in the cranium. Experimental studies of the pigmentation of small amphibia and fowls are fascinating Professor Hörstadius describes how, when chick-embryo limb buds are transplanted, the development of a pigmented or a non pigmented limb depends on the presence or absence of neural crest cells in the transplant The colour of plumage is also locally affected by later transplantations of cells of similar origin This dynamic embryology is far removed from the study of serial sections of our student days

---

Moveable-Removeable Bridgework (London Henry Kimpton 1950 Pp 221 56s) —This semi technical book, by Mr J O McCall, Mr I M Hugel, and Prof C F Bodecker is based largely on the writings of Herman Chayes, who was one of the foremost exponents of movable removable types of bridge for the replacement of teeth Part of the book is given up to Chayes's arguments and suggestions in favour of this type of bridgework, and technical procedures for making such types of bridge are described There is a great deal to be said for this kind of work, but its expense rather rules out its general application to the normal dental practice in this country

Bakteriologie und Serologie (Stuttgart Thieme 1950 Pp 644 D M 29 70) —This German textbook, one of the first on the subject to be published in that country since the war has excellent illustrations and makes wise use of numerous diagrams Lother Hallmann is bacteriologist to the Heidberg Hospital Throughout the book he gives instructions in great detail and thus should be of special value to the beginner Many technical methods, such as how to use a microscope micrometer or how to do a complement-fixation test for trichina infection, will not be found in English textbooks of comparable size and descriptions of the pathogenic protozoa and viruses are included

THE LANCET

LONDON SATURDAY, FEB 17, 1951

Potassium Deficiency

WE have learnt a lot in twenty years about the changes that occur in the body electrolytes in disease An enormous literature has grown up from the early work on the inorganic metabolism in Addison's disease and our ideas on sodium metabolism and the state of hydration of the body have certainly become clearer But in the last few years potassium has come to occupy the centre of the picture In 1940 the clinician's interest in potassium metabolism did not extend beyond the recognised changes in familial periodic paralysis and Addison's disease, and some isolated pieces of information such as the low serum-potassium in cases of alkalosis from pyloric obstruction, and the association of Cushing's syndrome with an alkalosis resistant to ordinary saline therapy and a low serum-potassium. Then in 1944 BROWN et al [1] described attacks of paralysis with low serum-potassium levels in chronic nephritis, and a similar low-potassium paralysis was later described by HOLLER [2] in treated diabetic coma in both these conditions the paralysis was relieved by administration of potassium salts, and recent work has shown that the loss of potassium in treated diabetic coma is constant though paralysis is rare In 1946 GOVAN and DARROW [3] demonstrated a heavy loss of potassium in infants with gastro enteritis and claimed that treatment with potassium salts greatly improved their recovery rates Since then a wide range of conditions have been shown to cause a loss of potassium from the body These include uræmia treated with a Borst diet,[4] *p* aminosalicylic acid therapy,[5-7] partial gastrectomy [8] and many other surgical operations not always involving an escape of gastro intestinal fluids,[9] the use of ion exchange resins,[10] and those reported in these columns—idiopathic steatorrhœa (Dr LUBRAN and Dr McALLEN last week, p 321), as a sequel to abortion and tonsillitis (Dr KJERULF-JENSEN and colleagues, this issue, p 372), and chronic nephritis (Dr DAVIDSEN and colleagues, p 375). In Birmingham, Dr COOKE tells us on p 413, some 20% of patients with steatorrhœa develop hypokalæmia at some stage, and potassium lack seems to be a common immediate cause of death in the fatal cases The potassium lost in the stools comes, he suggests, from intracellular stores and is actively excreted into the gut

The major part of the body's store of potassium is in the cells, and the cells may be lacking in potassium when the serum potassium is normal, or even above normal if there is oliguria In severe cases of deficiency of cell potassium, particularly if a diuresis is produced by any means, the serum-potassium will also be low, it is probably the low serum potassium rather than any lack of muscle potassium that produces the electrocardiographic changes characteristic of potassium deficiency, the most notable being depression of the S-T segment and diminution disappearance, or occasional inversion of the T wave These E C G changes may be rapidly reversed if serum-potassium is restored to normal, long before the body potassium is fully replaced The E C G findings are the most constant sign of either potassium deficiency or potassium intoxication, and their value in diagnosis was strikingly illustrated by Dr HAWKINS and colleagues last week (p 318) in their case of pyloric stenosis The other clinical manifestations of potassium deficiency are much less clear

In the light of all this evidence, how are we to recognise potassium deficiency, and if we find it, how should it be treated ? The important factor in recognition is that we should bear in mind that it may arise in a large variety of clinical conditions, particularly those involving any disturbance of electrolytes or body water Potassium deficiency should be suspected whenever an unexpectedly poor response is obtained to saline therapy and any evidence of muscular weakness will reinforce the suspicion ELIEL et al [11] describe a postoperative potassium-deficiency syndrome consisting in apathy, lethargy, nervousness, muscular weakness, abdominal distension and occasional ileus, disorientation, delirium, muscular twitching, and tetany, which is relieved by potassium therapy However, ELKINTON and TARAIL,[12] in a well-balanced review, say

> " It is difficult to establish the exact disorders of function which result from deficiency of potassium "
>
> " The evidence to date is inconclusive in respect to the specific benefit of potassium therapy to cellular function. The rationale of such treatment, therefore, depends principally on the ground that it is desirable to replace a substance in which the body is deficient. Potassium, like protein, is an essential constituent of the cells of the body, and replacement and prevention of loss of potassium is as logical as similar procedures in the case of protein Proof of this is difficult to obtain in clinical conditions with highly unpredictable prognoses

Chemical estimations of serum-potassium take several hours, where the laboratory is equipped with a flame photometer the result can be obtained quickly, but there are still not many hospitals in this country which have one, and an electrocardiogram will then often provide the answer most readily If suspicious symptoms are present and the serum-potassium is found to be low it seems reasonable to restore the serum-level to normal by the administration of potassium, but whether potassium should be given as a routine in all cases where deficiency is a possible complication, even when there are no clinical symptoms, is not yet certain where proper biochemical control is impracticable, the theoretical advantages of replacing the missing element rapidly must be weighed against the risk of potassium intoxication In any

---

1 Brown M R., Currens J H Marchand J F *J Amer med Ass* 1944 124 545

2 Holler J W *Ibid* 1946 131 1186

3 Govan C D Darrow D C *J Pediat* 1946 28 541

4 Kolff W J *J Lab clin Med* 1950 36 719

5 Cayley F E de W *Lancet* 1950 i 447

6 Nagley M. M. *Ibid* p 592

7 Heard, K H. Campbell A H Hurley J J *Med J Aust* 1950 ii 606

8 Wilkinson A. W Billing B H Nagy G Stewart C P *Lancet* 1950 i 533

9 Evans, E I *Ann Surg* 1950 131 945

10 Dock, W Frank, N R *Amer Heart J* 1950 40 638

11 Eliel L P Pearson O H Rawson R W *New Engl J Med* 1950 243 471 518

12 Elkinton J R., Tarail R *Amer J Med.* 1950 9 200

case, if the patient appears to be making normal progress, ordinary diet will replenish the body potassium within a reasonable time

When treatment is decided upon, potassium must be given in adequate amounts Since the greater part of the potassium is lost from the cells, the deficiency is much greater than is generally realised ELKINTON and TARAIL estimate that in an adult the lack may be from 228 to 936 m eq , or, in round figures, 8–36 g of potassium If the patient can take food by mouth, the potassium in his food may be reinforced by adding 80–120 m eq (say 3–5 g) to each litre of milk or fruit drinks , a mixture of the two potassium phosphates is more palatable than the chloride Provided there is a reasonable output of urine, potassium therapy by mouth is practically free from danger Alternatively, the potassium can be given subcutaneously, as was done by Dr HAWKINS and his colleagues, or intravenously If given with full understanding and adequate biochemical control either method is safe , but without these, parenteral therapy carries a great danger of potassium intoxication, an example of which was described by HAWKINS et al As a general guide, ELKINTON suggests a maximum infusion-rate of 20 m eq (0 8 g) of potassium an hour, in a solution with a maximum strength of 80 m eq (3 g) of potassium per litre A solution containing 4 5 g of K_2HPO_4, 1 g of KH_2PO_4, and 5 5 g of NaCl per litre, given at a rate of 300 ml per hour, fulfils these conditions

Parenteral potassium therapy is particularly dangerous in patients with a low urinary output Even in conditions such as diabetic coma, where a well-marked potassium deficiency is a constant finding, intravenous potassium should not be given unless there is a free diuresis , in the oliguric stage the outflow of potassium from the cells may exceed the capacity of the kidney to excrete it, and the serum-potassium, already above normal, may be raised to dangerous or even fatal levels by intravenous medication Here again the E C G may be of value in the presence of a raised serum potassium level the T waves become exaggerated, and eventually even P may disappear These findings are an indication for attempting to move potassium from the blood stream, rather than for adding to it Glucose is useful in accelerating the passage of potassium into the tissues, and saline helps not only by correcting dehydration but by producing adequate urinary flow After this flow has been restored is the time to start intravenous potassium therapy, if still needed

Vitamin-A Poisoning

ESKIMOS and arctic explorers have long recognised the toxicity of the liver of the polar bear and arctic fox Ingestion of such liver causes anorexia, nausea, vomiting, irritability, headache, and drowsiness, with scaling of the skin, starting around the mouth Ill effects from excess of vitamin A were observed experimentally by Japanese workers [1] in 1925 , and in 1943 RODAHL and MOORE [2] found that the liver of the polar bear contains about 20,000 I U of vitamin A per gramme RODAHL [3] later established that destruction of the vitamin-A content renders the toxic fraction innocuous MOORE and WANG [4] remarked that in the rapidly growing rat excessive doses of vitamin A predispose to fractures and intramuscular hæmorrhages, while in older animals the skeletal injuries are absent and death comes suddenly from massive visceral hæmorrhages The bleeding tendency was due to hypoprothrombinæmia, which could be corrected by the administration of vitamin K , but this vitamin did not affect the bone changes These findings have been confirmed in dogs [5] , skeletal maturation was accelerated with subperiosteal appositional growth of the cortex

The first account of chronic vitamin A poisoning in an infant was given by JOSEPHS,[6] who observed the condition in a boy, aged 34 months, who had received 240,000 I U of the vitamin since he was 3 months old TOOMEY and MORRISETTE [7] described a similar case, in which they noted cortical thickening of the long bones DICKEY and BRADLEY [8] noticed tender swellings and cortical hyperostoses in a girl, aged 3 years, who had had at least 400,000 I U of vitamin A daily for about 18 months ROTHMAN and LEON's [9] patients —a boy aged 14 months and a girl aged 22 months—had had about 120,000 I U daily for at least a year A further 10 cases have been recorded [10,11,12] In every proved case of such poisoning there has been a latent period of at least 6 months, and usually it is longer than a year When the condition is acute [2,14] the clinical manifestations are transient malaise, headache, giddiness, nausea, and vomiting , but the sequels of chronic poisoning are much more severe and persistent Sometimes pædiatricians have been unaware of the excessive intake until some time afterwards , and meanwhile the disorder has been mistaken for infantile cortical hyperostosis [13] The earliest manifestations are anorexia, pruritus, and irritability —symptoms so common in children that their significance may be overlooked Later signs are yellowish pallor , sparseness or coarseness of the hair , tenderness over the long bones, followed by swellings and limitation of movements , dry, scaly lips with bleeding fissures and angular excoriations , erythematous dry skin , hepatomegaly, rarely with splenomegaly , and a raised level of vitamin A in the blood In diagnosis great significance should be attached to tender swellings of the forearms or legs in an irritable, pale child with anorexia, pruritus, and possibly dry skin or cracked lips The swellings are most common on the forearms (perhaps owing to trauma) , they are never hot or œdematous , they are always firmly attached to deeper structures Radiography shows one single layer of periosteal proliferation, occasionally, irregular in outline, underneath the tender swellings , there is no undue thickening, and no lamellation (which is present with infantile cortical hyperostosis) Hyperostoses of two or more long bones have been identifiable in all cases since TOOMEY and MORRISETTE[7] first described this sign The sites most commonly affected, in decreasing frequency, are ulna, metatarsals (with the exception of the first), clavicle, femur, tibia, fibula, and ribs

---

[1] Takahashi K Nakamiya Z , Kawakami K., Kitasato T *Sci Pap Inst phys chem Res Tokyo* 1925, 3, 81
[2] Rodahl K., Moore T *Biochem J* 1943 37, 166
[3] Rodahl K *Nature, Lond* 1949, 164 530
[4] Moore T , Wang Y L *Biochem J* 1945 39 222
[5] Maddock C L , Wolbach S B Maddock S *J Nutrit* 1949, 39 117
[6] Josephs H W *Amer J Dis Child* 1944 67, 33
[7] Toomey, J H , Morrissette P A *Ibid* 1947 73 473
[8] Dickey, L B Bradley E J *Stanford med Bull* 1948, 6 345
[9] Rothman P E Leon E E *Radiology* 1948 31, 368
[10] Caffey J *Pediatrics* 1950, 3 672
[11] Fried C T , Grand M J H *Amer J Dis Child* 1950 79 475
[12] Wyatt, T C , Caraballo C A Fletcher M. E *J Amer med. Ass* 1950 144 304
[13] Caffey, J *J Pediat* 1946 29 541

According to CAFFEY,[10] vitamin A poisoning has only two features in common with infantile cortical hyperostosis—namely, cortical hyperostoses and tender soft tissue swellings Infantile cortical hyperostosis has always made its appearance during the first 4 months of life (in one case it was present on the first day), whereas the effects of excessive vitamin A intake have never been recognised before the 12th month No examples of either condition arising between the 5th and 11th months have been recorded In every case of infantile cortical hyperostosis yet reported, the face, jaw, and especially the mandible have been thickened, whereas in no reported case of vitamin-A poisoning have these parts been involved Metatarsal hyperostoses have been present in every case of vitamin-A poisoning in which the feet were examined radiologically, but in only one case of infantile cortical hyperostosis The blood vitamin-A level is apparently normal in infantile cortical hyperostosis Fever is the rule in infantile cortical hyperostosis, but it is absent in vitamin A poisoning, apart from transient fever due to intercurrent infection Dramatic recovery—within 7–10 days of the cessation of excessive intake—is characteristic of vitamin-A poisoning, though the disappearance of radiological signs and restoration of normal vitamin A level in the blood may take many months, in contrast, the clinical course of infantile cortical hyperostosis does not change rapidly

The mechanism of vitamin A toxicity is unknown DAVIES and MOORE[14] showed that in animals symptoms depend not on the total amount of vitamin A in the body, but on the ingestion of amounts large enough to outstrip the ability of the liver to remove this substance from the circulation for storage JOSEPHS[6] described the case of an infant, aged 8 months, who received 500,000 I U of vitamin A daily for 4 months without any toxic symptoms or rise of the blood level Possibly impaired absorption of the oily solution of the vitamin during early infancy[15] may partly account for the absence of toxic symptoms in young babies receiving excessive amounts On the other hand, hepatomegaly with increased serum alkaline phosphatase (which is found with impaired liver function) has been present in nearly all cases, and not only absorption of the vitamin from the bowels but also its release from the liver depends on normal hepatic function[16] FRIED and GRAND[11] demonstrated hepatic dysfunction in both their patients The symptoms were not, it seems, due to the vitamin D associated with vitamin A in the fish oil concentrates The symptoms caused by excess of vitamin D are distinctive, and furthermore TOOMEY and MORRISETTE reproduced the clinical picture of vitamin A poisoning by administering the pure vitamin

No case of vitamin A overdosage has so far been reported in this country, but now that we are aware of American experience an occasional case may come to light

Methonium and Hypertension

EARLY reports leave no room for doubt that the methonium compounds are the most powerful hypotensive agents yet developed[1 2 3] Unfortunately, with these as with most other drugs potency is matched by toxicity, the effective dose is often uncomfortably close to that which will do harm, and the right dosage has to be discovered afresh for each case Furthermore, experience is still too short for clinicians confidently to select the patients who will benefit by sustained reduction of blood pressure

Methonium can be given either by mouth or by parenteral injection, but most workers, including Professor SMIRK, who wrote last week (p 346), and Dr FRANKEL, whose letter appears in this issue, now think that oral administration is less satisfactory At least in the early stages of treatment, the patient should preferably be treated in hospital SMIRK[4] gives a trial dose of 15 mg subcutaneously with the patient sitting up in bed, and then records the blood-pressure every ten minutes Thereafter the dose is gradually increased, with injections two or three times a day At first habituation is rapid, but after a few weeks some 200–250 mg will usually produce a constant effect The best method of assessing the result of each dose has to be decided by trial in every case, but normally the effect, which is maximal about forty minutes after the injection, is best judged with the patient sitting up or, if he is ambulant, standing The aim is to secure a fall in blood-pressure to about normal, anyhow at the height of each dose's action, without evoking side-effects These side effects, due to postural hypotension or blocking of autonomic ganglia, include faintness, dizziness or syncope, and dryness of the mouth, anorexia, nausea, abdominal distension, constipation, and mistiness of vision Postural symptoms may be averted if the patient avoids standing still for any length of time—as, for example, in a queue—and if the foot of his bed is raised at night Once present, such symptoms can be countered by the patient contracting his abdominal muscles, walking about, or lying down with the foot of the bed raised, if need be, ephedrine, adrenaline, or noradrenaline may be injected With continuing treatment ill effects tend to become less troublesome, and it is usually possible to arrive at a dosage that is effective without causing more than very slight discomfort Indeed, SMIRK's patients are taught to give themselves regular injections in the same way that diabetics inject insulin The action of these compounds is enhanced by a low salt diet, and so is the risk of bromism[5]

What of the risks of lowering the blood-pressure? These are still not clearly defined, but coronary or cerebral thrombosis may be precipitated in patients with advanced arteriosclerosis, and where renal function is impaired caution is clearly necessary TURNER, who has outlined some of the dangers,[2] suggests in his letter this week indications for using these compounds Until experience is greater, most workers will probably be content to limit their application to

---

14 Davies A W Moore T *Biochem J* 1934 28 288
15 Sobel A E Bessman J Kramer B *Amer J Dis Child* 1949 77 576
16 Popper H Steigman F Meyer K A Zevin S S *Arch intern Med* 1943 72 439

1 Restall P A Smirk F H *N Z med J* 1950 49 206
2 Turner R W D *Lancet* 1950 ii 353
3 Campbell A Robertson E *Brit med J* 1950 ii 804
4 Smirk F H *N Z med J* 1950 49 637
5 Rosenheim M L *Lancet*, Feb 10 1951 p 347 Holt M C Litchfield J W *Ibid*

severe cases (for example, malignant hypertension and hypertension with *left ventricular failure*), to short term disorders (such as toxæmia of pregnancy), to dangerous episodes (hypertensive encephalopathy), and to the relief of troublesome symptoms, such as headache, due to hypertension. Only a long and carefully controlled trial can tell whether methonium may reasonably be given to the youngish patients with benign hypertension, with a view to postponing cardiovascular or renal lesions.

"Prospect of War"

As soon as he steps outside his own field, the expert ceases to speak with professional authority. For this reason CARR SAUNDERS and WILSON,[1] recommend the professions to abstain from pronouncements on the larger moral issues. Lawyers, they say, should remain corporately silent on the ethics of capital punishment, and doctors on the ethics of euthanasia, for, as a body, they are no better qualified than other citizens to distinguish right from wrong. On this view, no occupational group, except perhaps the Church, is entitled to advise the nation on how it should now face the risk of war, for no such group is a recognised authority on the relative morality of aggression, resistance, and submission. Admittedly, expert opinion on matters of expediency may be acceptable and, just as the medical profession could properly explain that euthanasia has its practical inconveniences, it could properly describe the technical difficulties of tending the casualties of a new war. But the expert's function, it is said, is to provide information quite objectively and only when asked to do so. The structure of our specialised society demands that the cobbler shall stick to his last, and if a particular cobbler or doctor becomes convinced that euthanasia, or a large Navy, or friendly letters to the Kremlin, are what is now needed, he should write to his M P about it, as an individual citizen, not as a professional man.

Sound up to a point, this doctrine could easily encourage excessive specialism, and we certainly do not think it should be allowed to narrow the scope of intraprofessional discussions. THE LANCET has always regarded medicine as a very wide subject, and we shall continue to publish articles showing how the work of doctors influences and is influenced by the activities, ideas, and policies of other people. Though we no longer emulate the catholicity of our early issues, we see no reason to pretend that doctors practise in a professional vacuum or are the better for restricting their vision. Thus, at a time when everybody is profoundly affected by preparations for or against a possible war, we have thought it both permissible and right to allow expression of opinion to those of our colleagues who believe that the profession—though it may be no more than a small occupational group in the larger community—can make some special contribution to the attainment of peace. The selection of letters published in the past few weeks under the heading "Prospect of War" reveals three reasons why doctors, as such, might claim a hearing on this subject. The first is that, by tradition and training, they accept a supernational moral code which bids them help enemy and friend alike. As the noblest of hospital mottoes has it, *Nihil humanum a me alienum puto*, and it is in this spirit that a correspondent bids the profession formally declare its neutrality in the internecine strife of men and rededicate itself to the service of all. Secondly, by tradition and training, we are not only humanitarians but also scientists, who should think objectively and take a very long view. As biologists we know that the differences between nations are transient and trivial compared with their common interests, we regard mutual aid as more important to human progress than the struggle for existence, and we recognise that the basic need is to tolerate and cooperate, not to condemn and destroy. Thirdly, through the care of sick minds we have gained at least a little insight into the mental disorders that lead people to hate and fight each other. Have we not learnt enough already to urge our leaders to beware of their emotions? Fear on the one hand, and anger on the other, are evil counsellors.

These are reasons why doctors might think themselves qualified to make some corporate effort to deflect mankind from war. But our correspondents give few signs of the necessary unity among themselves. *In the past decade many kinds of scientists have become anxious about the social implications of their work, and, just as the atomic physicists might decide that, whatever the cost to their own countries,* they would no longer devise instruments of destruction so the medical profession might declare that, in obedience to its higher code, it would take no part in military operations or civil defence. But in fact since most doctors, like most scientists, are citizens first and moralists second, only a tiny minority would feel justified in taking direct action of this kind against the rest of their community. Unless they are prepared to do this, the duty of doctors is plainly to give—and give freely—whatever expert help may be asked of them, for the very natural loathing of modern war felt by all civilised people does not by itself excuse any of us from answering the Government's call to aid in defence. The knowledge that another war might be disastrous to all concerned is now very widely spread, but no response to peril is more futile than to rend one's raiment and utter cries of woe. We can act in one way or we can act in another, but we should try to be clear about what we are doing. Those who feel, with much reason, that what is above all necessary is to refrain from any action that promotes a war mentality should ask themselves whether in the last resort they are not depending on the defence measures taken by other people. It is one thing to base non cooperation on a moral principle that nothing will shake, but quite another to base it on one's personal estimate of a political situation.

Those who hold that the medical profession, as such, can advise its fellow citizens on the prevention of war have yet to explain what acceptable advice we humanitarians, biologists, and psychiatrists could offer without impertinence *to a people* who, though resolved not to submit to force, are almost as slow to wrath as *they have been slow to arm.* If it turns out that, for all the sincerity of their convictions, the advice our colleagues want to give is primarily political, *they* must give it as citizens and not as doctors.

---

[1] Carr Saunders A M, Wilson P A. The Professions. Oxford 1933.

Annotations

PEPTIC ULCER IN OUR TIME

"In the nineteenth century it was commonly believed that cooks and bootmakers were the most frequent sufferers from gastric ulcer, the theory being that cooks injured their stomachs by continually tasting hot and irritating foods while bootmakers pressed their stomachs against the boots on which they were working In the twentieth century opinion has been united in rejecting this belief, if in nothing else "

Having thus cleared the ground, a Medical Research Council report [1] sets out the results of a study—undertaken at the suggestion of Dr F Avery Jones, and sponsored by the council's Industrial Research Board—of occupational factors in the ætiology of gastric and duodenal ulcers

A Peptic Ulcer Coördinating Committee, under the chairmanship of the late Prof J A. Ryle and with Dr Joan Faulkner as secretary included Dr G R M Cordiner Dr C M Fletcher Dr H Gainsborough, Prof A Bradford Hill, Prof R E Lane, Dr W R S Doll, and Dr Avery Jones The last two with the help of Mr M M Buckatzsh, have been responsible for writing the report

Ulcers have been becoming commoner in hospital practice since the first world war, and according to a survey made in 1948 account for 10% of all adult admissions The committee found, from a review of published work on the subject, that it is generally agreed that transport workers are likely to have ulcers, and that rural workers, clerks, and sedentary workers are less prone to them than industrial workers and labourers But—apart from some figures relating to gastric ulcers among the fishermen of northern Norway—the statistical basis of most of these conclusions was "not such as to justify confidence being placed in them", so the committee started on a fresh survey

The types of occupation chosen for study included scientific research, light engineering, glass manufacture, goods transport passenger transport, civil service, hospital service, food marketing, the service and preparation of food, paper manufacture, and agriculture Firms and works' councils proved cooperative, and a list of employees was obtained from each firm or employer Those on the lists were seen first by a social worker, on whose report they were grouped under the headings "no dyspepsia," "minor dyspepsia," and "major dyspepsia ' A doctor then saw all those with major dys sia, and—as controls—10% of those with minor pepsia and no dyspepsia These controls numbered , and only 2 of them proved to have peptic ulcers social worker saw in all 5951 men and women , and 4 of these were referred for interview as cases of major pepsia Ulcer was regarded as proved if a positive gnosis had been made radiographically or at operation, if the patient had had hæmatemesis or melæna The idence of ulcer among 4871 men was 6 5% , and ong 1080 women, 7% The total number of ulcers ong women was so small that most of the rest of the nclusions were drawn only from men

The incidence varies with age, rising to a maximum 9 6% in men aged 45–54 and then decreasing Gastric d duodenal ulcers differ in age of onset, the expectation gastric ulcer being greatest between 35 and 64, while expectation of duodenal ulcer is greatest, and nstant, between 20 and 64 No gastric ulcers were gnosed under the age of 25 The ratio of gastric to odenal ulcers in men was 1 2 2 , but the ratio rose ogressively with increasing age and with descent in e social scale The highest ratio was 1 1 2 over the e of 45 in the Registrar General's social classes IV and V

studying occupational difficulties the committee ssified the men into 20 different groups , and the numbers of ulcers expected in each group was calculated from the figures for the whole survey, age being taken into consideration A significantly high incidence was found among doctors working in hospitals (15%, instead of the expected 6 9%) , but this is believed to be due to more refined standards of diagnosis among doctors If this is so, the committee point out, it must follow that the incidence in the general public is appreciably higher than estimated There was also an unexpectedly high incidence among a group of unskilled workers (11% instead of the expected 4 9%) , but here the committee had reason to think they were dealing with an excess of ulcer subjects who had sought out sheltered employment Apart from these two groups, high incidences were found among foremen and business executives, and low incidences among agricultural workers and—possibly—sedentary workers The theory that transport workers are specially prone to ulcer was not borne out drivers of motor vehicles and bus conductors had the expected incidence So did skilled engineering hands, electrical tradesmen, semi skilled workers in these industries, and heavy manual workers Irregular meals did not seem to have the baneful influence commonly attributed to them, but anxiety over work (not over home affairs) was more often complained of by those with proved duodenal ulcer than those with no dyspepsia, which is consistent with the view that men with the conscientious type of personality are particularly liable to develop duodenal ulcer Gastric ulcers are not found with greater frequency among the anxious, but they are related to social class, being commoner among the poorer than the well to do The committee draw attention to the deficiency of ulcers in agricultural workers, the social gradient of gastric ulcer, and the relation of anxiety to duodenal ulcer, as promising subjects for study

COCA-CHEWING

"I DON'T know whether to take a Benzedrine and go to the party or a Nembutal and go to bed " This is the issue before two young ladies depicted in the *New Yorker* The ingenuity of our new chemical industries, ably assisted by advertising, is creating new habits in drug taking Meanwhile old problems still exist among many peasant peoples accustomed to a regular supply of drugs provided by plants and shrubs growing freely in the countryside There are still large areas of the world in which many of the people have been life long addicts to either opium or hashish or coca These drugs have become part of the local way of life, and neither pharmacologist nor sociologist can assess with accuracy the effects of such addiction on individuals or groups

Coca chewing is practically limited to the Indian population living at high altitudes in the Andes , the habit is widespread among the inhabitants of the Altiplano in both Bolivia and Peru In our "Wider World " series Dr Passmore reported [1]

> Many in the Altiplano chew coca leaves throughout the day and can accurately be designated cocaine addicts It is widely supposed that coca enables a man to carry out hard work at high altitudes with greater efficiency and makes him insensitive to hunger, but that in the long run it leads to serious breakdown in both mental and physical health Yet many experienced observers both lay and medical, doubt the accuracy of these views I heard the opinion that coca chewing was, like tobacco-smoking, a dirty habit but had no serious effect on either health or working efficiency Statements both by individual observers and authoritative international conferences have mostly been adverse to coca "

At the request of the governments of Peru and Bolivia, the Economic and Social Council of the United Nations appointed a commission to inquire into coca-chewing in all its aspects The commission, who spent just under three months in Peru and Bolivia, have now published their findings [2] On the pharmacological side it was found that opinions differed widely both on the usual amount of coca chewed each day and on the amount of cocaine extracted from the leaves Prof Gutiérrez Noriega stated that the daily dose of leaves varied between 10 and 100 g, with 30 g as a mean value The absorption rate from the bolus was found to be 80–90%, and a common daily dose of cocaine was 0 2 g The leaves are usually mixed with some alkaline substance, such as quicklime or ashes obtained from burning grain, this, it is thought, increases the extraction rate While the commission were clearly impressed by Professor Noriega's views, they point out that other pharmacologists do not set the figures so high, thus Prof Asto Salazar estimates the daily absorption of cocaine to be usually no more than 0 005 g The commission collected a bewildering variety of opinion as to the effect of chewing coca leaf, but they boldly conclude that the harmful effects arise primarily from inhibition of the sensation of hunger, which leads to constant malnutrition The habit also induces in some people undesirable intellectual and moral changes which hinder the chewer's chances of improving his social and economic standards, mainly by reducing his capacity for productive work

---

[1] Special Report Series no 276 London H.M Stationery Office 1951 Pp 96 2s 6d

[1] Passmore R *Lancet* 1949 i, 362

The commission were fully convinced that the main cause of the chewing habit was poor nutrition Coca chewing offers escape from the misery of hunger, and where food is good, chewing stops In many parts of the Altiplano present agricultural methods provide the peasants with a diet unsatisfactory in quality and often insufficient in quantity, and "the keynote of the whole action against chewing coca leaf can and must be the bettering of nutrition" At the same time there are other important ætiological factors, such as poor housing, general low levels of hygiene, and lack of education

VOMITING AFTER MORPHINE

THE nausea and vomiting which sometimes follows the administration of morphine is usually ascribed to stimulation of the vomiting centre, and apomorphine, a closely related chemical compound, is the most powerful central emetic known But it has been clearly shown that morphine vomiting largely depends on the position and movements of the body Thus Lee [3] recorded nausea in 3% and vomiting in 2 6% of patients given an injection of morphine when lying in bed, whereas Comroe and Dripps [4] found that in people who were up and about the same injection produced nausea in 40% and vomiting in 16%, a finding that has often been confirmed in normal volunteers It seems likely, therefore, that the vestibular activity accompanying body movement provides a suitable stimulus for a vomiting centre already made hypersensitive by the morphine Rubin and Winston [5] have tested this possibility in normal people by injecting each with 15 mg of morphine sulphate and then stimulating their vestibular apparatus either by spinning them round or by syringing their ear with cold water When the 14 volunteers were given a preliminary injection of saline solution as a control only one complained of nausea and vomited after vestibular stimulation, whereas when the same people were given morphine vestibular stimulation caused nausea in 10 and vomiting in 6—indeed, 3 complained of nausea and 1 vomited before vestibular stimulation

As every seasick traveller knows, excessive vestibular stimulation can cause vomiting in normal people, and the action of morphine seems to be to sensitise the vomiting centre so that it responds to the usually ineffective vestibular stimuli arising from normal body movements One would expect this effect to be counteracted by hyoscine and other seasickness remedies Rubin and Winston found that the anti histamine drug 'Dramamine,' now extensively used in the U S A for the prevention and treatment of all forms of motion sickness, does prevent the nausea and vomiting evoked by vestibular stimulation after morphine, whereas amphetamine has no such action Other anti histamine drugs would be worth trying for this purpose, and there may be some reason for continuing the traditional combination of hyoscine and morphine Above all, however, it should be the rule never to give morphine to an ambulant patient—or hardly ever

THE DOCTOR'S FRIEND

ANY complaint made by a patient against his National Health Service doctor is heard by the medical service committee of the local executive council, and in defending himself before this informal tribunal the doctor may, according to the regulation, have the help of some other person, "provided that no person shall be entitled in the capacity of counsel, solicitor or other paid advocate to conduct the case for any party by addressing the committee or examining or cross examining witnesses"

The London Medical Service Committee have lately had a slight brush with the Ministry of Health over the interpretation of this regulation A solicitor who attended an inquiry with a doctor was observed to be making copious notes of the evidence, and the committee who knew that legal proceedings were pending declined to permit him to remain The solicitor appealed to the Ministry, which held that there is nothing in the regulations to prevent even a paid advocate appearing to assist his client or to take notes if necessary The London committee, however consider themselves a fact finding committee which should not develop into a court "at which possibly counsel or solicitors would be appearing for both sides and would be prompting their clients to ask questions and cross examine witnesses in much the same way as if the lawyers were conducting the examination themselves" They feel that the present regulation does not allow the committee enough discretion as to who may appear to help a doctor (or patient) at a hearing and to what extent counsel, solicitor, or other paid advocate may seek to influence the course of their deliberations To this end they suggest that the offending regulation be amended to read "provided that no person shall be entitled to appear in the capacity of counsel, solicitor or other paid advocate." This would be a return to the wording of the old regulation governing this point of procedure in the old National Health Insurance committee

In Northern Ireland legal representation of the parties before a service committee is not prohibited, and it has been suggested that the same procedure should be adopted in England, Wales, and Scotland But the British Medical Association and the professional protection organisations have agreed that these investigations ought to be friendly and informal and not coloured or possibly frustrated by the introduction of legal advocacy which is appropriate to a court of law Obviously the London Medical Service Committee also agree with this view, but they seem to have misconceived the underlying difficulty The effect of their amendment would be to give the service committee power to forbid the attendance at the hearing of any persons other than (i) the complainant and the respondent doctor with their witnesses (if any), (ii) the secretary or other duly authorised officer or member of the local professional committee concerned (who might incidentally himself be a barrister or solicitor and in any case could take "copious notes"), and (iii) such officers of the council as may be appointed for the purpose (who might also be lawyers) There will be many cases where either the complainant or respondent is nervous, or deaf, or does not speak English fluently, when someone to assist in the presentation of his case would be helpful to the committee. Again both parties have the right to appeal against the findings of the committee and the subsequent decision of the executive council. Such an appeal is in fact a rehearing, but accurate and detailed notes of evidence given at the original hearing may be essential in deciding whether there are grounds for appeal or not.

---

[2] United Nations Report of the Commission of Enquiry on the Coca Leaf May 1950 Economic and Social Council Official Records Fifth Year Twelfth Session Special Supplement no 1 Lake Success Pp 160 Obtainable through H M Stationery Office 15s

[3] Lee L E J Pharmacol 1942 75 161

[4] Comroe J H Dripps R D Surg Gynec Obstet 1948 87 221

[5] Rubin A Winston J J clin Invest 1950 29 1261

Several questions arise. Who can take notes so well as a lawyer—unless it be some other "paid advocate"? Can the chairman of the committee, who is not necessarily a lawyer, decide whether a person assisting in the presentation of the case is a "paid advocate" or not? Does the London Medical Service Committee appreciate that it is the doctor who is the "accused," and that the complainant has nothing to lose whatever the outcome of the inquiry? These and other questions should be answered before the existing regulation, which has apparently worked well, is amended.

FLUORIDE AND CARIES

SINCE the importance of the fluorine caries relationship was first appreciated numerous studies have been undertaken, notably in the U.S.A., to discover whether artificial fluorination of drinking water will reduce the amount of dental caries. It has been shown that, with a fluoride concentration in the drinking-water of 1–1.5 parts per million, the incidence of caries during the formative period of the teeth may be reduced by as much as 65%. In 1945 three investigations into the value of artificially fluorinated drinking-water were started in the U.S.A. and Canada, and the results of one of these studies—at Grand Rapids, Michigan—have now been evaluated.[1]

At Grand Rapids 1 part of fluoride per million was added to the public water supply, which previously had been fluoride free. Analysis of the dental examinations in 1949 showed a considerable reduction in dental caries compared with the rate in 1944 and 1945, and this reduction was most pronounced in the younger age groups, whose dentition was largely calcified after the fluoride was added. It will be of interest to see whether the improvement is maintained. In this country Weaver[2] has shown that the effect of fluoride on the forming teeth, relative to caries resistance, seems to be somewhat evanescent, and that children with a previously low caries-count may in later life acquire more caries and have an average count despite the early and marked effect of fluoride. That fluorination affords more than temporary benefit has still to be proved.

ULTRASONICS IN TREATMENT

SOUND WAVES with frequencies between 16 and 30,000 cycles per second are audible to the human ear, but the frequency can be increased far beyond this range, and then the waves, being no longer audible, are termed ultrasonic. That such ultrasonic waves can be produced by the relatively simple phenomenon of piezo electricity has long been known, and with the impetus of war this knowledge was swiftly extended.

The medical application of ultrasonics has been investigated mainly in Germany and Austria. The energy of ultrasonic waves can largely be converted to heat, and many effects produced by these waves can be attributed to the heat which is generated. They can emulsify immiscible substances, but they can also reverse the process, for cumulative doses can demulsify. Clinically, they are known to cause, in certain circumstances, oxidation and depolymerisation. Their effects on living cells are very varied, extending from the known effects of heat to cavitation and vacuolation. The claims for their effect in treatment, however, seem to reflect enthusiasm for a new-fangled method rather than any encouraging accurate scientific observation. One is reminded of the claims made for short wave diathermy when this was first introduced as a therapeutic agent, before it was recognised as fundamentally a form of heat treatment. The conditions in which good results have been claimed for ultrasonics range from prostatic enlargement to otosclerosis, and much work has been done on the use of these waves in neoplastic conditions, without evidence of benefit. Schliephake[3] claims that the field in which ultrasonics are going to be most useful is that of the "rheumatic" diseases but he does not define their indications or compare the effect of ultrasonics with that of more established procedures.

An objective article by Nelson and his colleagues[4] shows the pitfalls which beset those ardently advocating a new physical agent such as this. There seem to be few, if any, conditions which are not still better treated by other means. In England the Ministry of Health has wisely limited the provision of ultrasonic emittors to certain hospitals, where critical physical and clinical trials are being carried out.

DEPARTMENT OF HEALTH OF EIRE

DURING the union Ireland, unlike Scotland, had no special department of health, but was subject to the same code of laws as England and Wales, except that Ireland was specially excluded from part of it. So on its formation the State of Eire took over a system of State medicine identical in theory with that of England and Wales, which it administered through a department of local government and public health, corresponding roughly to our deceased Local Government Board. In 1947 the government set up a new department of health to deal exclusively with health matters, and passed a comprehensive Health Act which fixed for Eire a form of health legislation somewhat comparable to that of England and Wales before the National Health Service Act of 1946. The Eire code of State medicine follows in the main the English code, but it departs from it in many details which are of great interest to students of the political and social aspects of medicine.

The first report of the department of health of Eire covers the years 1945–49, but some of the statistical tables go back to 1925, and that of tuberculosis and cancer death rates to the beginning of the century. Progress in health has been less than in Great Britain, for the disturbed state of the country between the two wars was a great hindrance to development. Eire is developing a national health service, but this will not be developed along the lines of our National Health Service Act. A notable achievement was the Mental Treatment Act of 1945, which gave to Eire an improvement on our Act of 1930. There is much to be learned from the growth of State medicine in Eire.

THE British Medical Association has decided that it will not after all be able to take part in the joint meeting with the Medical Association of South Africa which was to be held at Johannesburg in July, "as an assurance cannot be given that all members of the British Medical Association will be free to enter South Africa." All will regret that the policy of the South African government has necessitated this decision, but we are glad that the profession in both countries has refused to compromise with the exponents of racial prejudice.

---

[1] Dean H. T. Arnold F. A. Jay P. Knutson J. W. *Publ. Hlth Rep. Wash* 1950 65 1403

[2] Weaver R. *Proc. R. Soc. Med.* 1948 41, 284

[3] Schliephake E. *Brit. J. phys. Med.* 1950 7 152

[4] Nelson P. A. Herrick J. F. Krusen F. H. *Arch. phys. Med.* 1950 1 6

Special Articles

THE MINISTRY OF PENSIONS
ARTIFICIAL LIMB SERVICE
Two years' experience of the National Health Service Act

C Gaulter Magle
F R C P E, D P H
DEPUTY DIRECTOR GENERAL
OF MEDICAL SERVICES

R Langdale Kelham
O B E M R C S
DIRECTOR OF
MEDICAL-SERVICES

T Ritchie
M B Edin
PRINCIPAL MEDICAL OFFICER

D S McKenzie
M B Edin
PRINCIPAL MEDICAL OFFICER

A W J Craft
O B E, M R C S, C I Mech E
PRINCIPAL MEDICAL OFFICER, RESEARCH DEPARTMENT

MINISTRY OF PENSIONS

In the later years of the 1914–18 war, the Ministry of Pensions became responsible for the supply of artificial limbs—and duplicates—to all pensioner amputees, and for maintaining the limbs in good fit and mechanical repair for the remainder of the patient's life

This was a revolutionary step not hitherto attempted in any other country, and it gave a unique opportunity to the group of limb surgeons formed by the Ministry of Pensions They were able to study an immense bulk of clinical material over a long period, from their observations they could decide what was the ideal stump for limb wearing at each site of amputation, and in so doing they could assist limb manufacturers in the evolution of the modern British prosthesis In no other country, until very recently, did doctors concern themselves directly with the art of limb fitting and collate and study the results obtained, and this professional interest may well be a cause of the acknowledged British supremacy in this field

The experience and knowledge gained by the Ministry's medical services in the treatment of war pensioners led to the extension of their work to civilians, and arrangements were made to permit this through the good offices of the governors of Roehampton (Queen Mary's) Hospital In the inter war years the limb service was much in demand by some of the railway companies and by many charitable organisations and local authorities During the 1939 war its work was increased by the schemes initiated by the Ministry of Labour for providing limbs for civilian amputees who needed them for return to work, and by the 1944 Education Act which enabled education departments to use the service for children of school age

From the outbreak of war until 1948, the Ministry of Pensions limb service bore the brunt of the supply, repair, and renewal of all artificial limbs required in this country for war casualties, past and present, working not only for the British Forces, but also for those of some of our Allies During this period 72,308 new limbs were ordered, including duplicates and renewals, and the Ministry's limb surgeons made 206,580 examinations

HOW THE SERVICE WORKS

In 1939 the Ministry's limb service consisted of 19 limb fitting centres situated at selected points throughout the country All were modelled on the centre at Roehampton, which was the hub of the organisation, and besides the medical equipment they included workshops and fitting rooms for the manufacturers of artificial limbs Each centre was a complete unit staffed by medical and technical experts with every facility for the supply and maintenance of the prosthesis The highest standard of workmanship, design, and material was, and still is, secured by a team of technical inspectors

The routine of supplying a patient with a limb is not very different from that of the general hospital outpatient department The amputee is called by letter of appointment, and when he arrives he is taken to the limb surgeon for the prescription of the limb With the prescription he passes on to the contractor After some weeks, like any other patient, he receives his discharge and launches out from the limb centre fully ambulant on his artificial legs, or skilled in the use of an artificial arm He is advised to report by post, on a form, any defect in the limb either from the fitting or mechanical aspect On receipt of the form, the limb centre staff decide whether the patient must attend in person or whether, if only a mechanical repair is needed, the limb can be repaired and returned under a postal system The postal system can be used only by patients who have a duplicate limb, but it has proved its value in saving patient's time and avoiding abstention from work From the beginning of the war till the end of 1945, 79,240 patients attended for repairs, a further 110,095 repairs were dealt with by the postal system

RESEARCH

Every effort has been made over the years to examine and develop the constant flow of ideas from patients, manufacturers, and limb surgeons, and a fully organised research unit, with trained technicians and draughtsmen, under the charge of a limb surgeon who also has engineering qualifications and experience, has been a feature of the Roehampton organisation for some years This unit works in close collaboration with the limb fitting surgeons throughout the country so that interchange of opinion between the clinical and technical side of the service is a recognised procedure Among the many problems now being studied are the benefits of the suction socket limb, which is retained on the stump without supplementary attachment to the body, the cause and treatment of pain in amputation stumps, the effects of amputation on blood pressure, and the choice of disarticulation at the knee for elderly patients

THE LIMB SURGEON

Having thus outlined the main fabric of the service, we can best give an idea of its intricacies by describing the duties of the limb surgeon

This officer is specially trained in the art and practice of limb fitting He first undertakes a course of instruction at Roehampton covering the treatment and preparation of the amputation stump for limb wearing, and the recognition of individual idiosyncrasies in the amputee, the special needs of children, and the æsthetic requirements of women He studies the methods of training in the use of limbs and the supply and use of appropriate additional appliances for the amputee with artificial arms

Methods of training in the use of artificial limbs include stump muscle re education, remedial exercises to improve joint mobility and stump control, the acquirement of balance and the development of confidence in the ability to wear the artificial limb This entails the practising of everyday movements—such as, for a leg amputee, turning, stooping, sitting down, walking up and down stairs, and walking on a cambered surface and over rough ground The arm amputee reaches the goal of occupational efficiency by training in the use of the various appliances

On completion of this course, which lasts from two to three months, the limb surgeon assumes responsibility for the continued rehabilitation of the amputee from the time the operating surgeon considers his work complete. In many cases this transfer of responsibility is decided in consultation between operating surgeon and limb surgeon In the absence of this ideal arrangement, the limb surgeon makes a detailed examination in order to assess (*a*) the functional value of the stump, and (*b*) the patient's general physical and mental capabilities. This first contact is important, for on the proper briefing of the patient will largely depend his sense of confidence and his morale. The limb surgeon then prescribes any treatment still required to render the patient fit to wear a limb. The stage at which limb fitting commences is at his discretion. At the appropriate time he prescribes the prosthesis in detail giving instructions as to the type of limb, whether of metal or wood, the method of suspension, and so on. The choice of prosthesis must depend on the physical condition of the patient, his mental outlook, his probable future occupation, and even the climate and nature of the country in which he is likely to live. In special cases, the limb surgeon supervises the fitting at all stages, and in every case he is responsible for ensuring that the completed limb is satisfactorily fitted.

EFFECT OF THE NATIONAL HEALTH SERVICE ACT

When the National Health Service started in July, 1948, a ready made and nation-wide artificial limb service was already in operation and working smoothly. The limb service had supplied over 200,000 limbs to amputees from the Services, from industry, and from private and other organisations. It had acquired a world wide reputation, and the Roehampton limb centre had become the mecca of all those visiting this country and interested in prostheses. The service was well qualified, therefore, to supply limbs to those needing them in the general population. The machine, already in motion, only had to be geared up to meet the imponderable demands likely to be made. A great variety of clinical problems suddenly streamed into the limb centres; elderly amputees and children with congenital deformities mixed with the war wounded and eventually outnumbered them. Table I gives some idea of the size of the problem set by these new civilian patients.

TABLE I—WORK OF THE LIMB SERVICE FOR THE N H S

Year	New legs ordered	Repairs to legs	New arms ordered	New mutilated hand appliances ordered	Repairs to arms ordered	Surgeons examinations
1948–49	13 670	15 754	2291	245	1028	41 398
1949–50	14 297	21 952	2239	321	1647	61 279

Of the 27,967 new legs ordered for National Health Service cases in the past two years, 77% have been metal ('Duralumin'), 22 99% wood, and 0 01% leather. In the light of these figures it is interesting to recall that Muirhead Little[1] wrote in 1922:

> The battle of the legs is still raging and at the moment aluminium seems to be in the ascendant over wood and leather; it must be remembered however that the two latter have been exposed to a length and severity of proof to which it has not yet been possible to subject the former.

The increase of work after the appointed day was foreseen and appropriate dispositions made. Thirty one additional limb surgeons had been trained and were posted to centres where large populations suggested there might be early and urgent requests for prostheses. The existing limb centres, both at Roehampton and in the provinces, were enlarged where necessary and several new centres were opened or put under construction. At Roehampton and Leeds where the limb centre is at a Ministry of Pensions hospital arrangements were made for the allocation of a number of hospital beds for civilians who were in need of further stump treatment, more advanced rehabilitation, or special study and care in the fitting of a limb.

TABLE II—REVIEW OF 81 PATIENTS OVER 65 YEARS OF AGE ADMITTED TO QUEEN MARY'S HOSPITAL ROEHAMPTON FOR LIMB FITTING OR WALKING TRAINING

Age in years	Result of fitting and training				Total
	Satisfactory	Failure	Death	Incomplete	
65–70	21	9	1	4	35
70–75	10	6	2	2	20
75–80	10	7	0	3	20
over 80	4	1	0	1	6
Total	45	23	3	10	81

Satisfactory = Regular use of prosthesis for at least three months after completion of walking instruction.
Failure = No use made of prosthesis after walking training or attempted training.
Incompleted = Limb fitting or walking training not yet complete or 3 months not yet elapsed after termination of training.
These figures represent only those elderly patients whose admission to hospital was essential.

It is an axiom that the limb surgeons' work is irrevocably linked to the capacity of the manufacturers to produce limbs, and unfortunately the supply of limb fitting technicians, whose training is a lengthy and difficult affair, has not kept pace with the demand for artificial limbs. For this reason some delay in the supply of new limbs has been inevitable, but this is now being steadily overcome.

The new régime has brought no fundamental change of policy. But the consciousness of widening responsibility has sharpened. Greater attention than formerly has been paid to the principle that the greatest benefit to the patient is most likely to accrue from joint consultation. To this end steady and successful efforts have been made, and will continue to be made, to create a firm liaison, founded on mutual respect, between the orthopædic surgeon and the limb surgeon.

EXPERIENCE OF THE PAST TWO YEARS

The Elderly Civilian

To the limb surgeon of the Ministry of Pensions, accustomed to the supervision of the patient from the earliest possible moment—often from the moment the decision to amputate was taken—it has been disquieting to find patients at the limb centres, certified as fit for limb fitting who cannot stand on the sound leg or even use crutches. Again, patients in whom exercise tolerance is so impoverished that their prospects of training are negligible have come with requests for artificial limbs. It cannot be too strongly emphasised that such a patient has no prospect of walking on a prosthesis with safety. The risk of collapse during the severe physical effort and mental strain of learning to walk on an artificial limb is very real in elderly patients, and deaths have occurred (table II).

To convince patients that the prospects of walking are remote and the risks are great is well nigh impossible when operating surgeons have earlier implanted an over sanguine and self sufficient attitude. The need to encourage the prospective amputee to help him overcome his apprehension and revulsion at the thought of amputation is paramount; but when dealing with elderly and enfeebled cases, whose prosthetic success is clearly problematical, encouragement as to future limb wearing should be given with the utmost reserve, with a leaning toward the greater possibility of a wheel chair. If, later, limb fitting is found to be possible without undue risk so much the better for the morale and the contentment of the patient.

Single Amputees

Tables III and IV give the results of a survey of a random sample of 1658 lower limb single amputees and

---

[1] Artificial Limbs and Amputation Stumps. London 1922.

TABLE III—CAUSES OF SINGLE LEG AMPUTATIONS AND AGE INCIDENCE IN 1658 PATIENTS

Age in years	Trauma	Osteomyelitis	Congenital	Tuberculosis	Cardiovascular	Diabetes	Other diseases	Unknown causes	Total cases
Under 11	12	7	13	2	5	0	6	43	88
11–20	38	15	9	12	12	0	20	33	139
21–30	69	34	4	19	21	0	33	75	255
31–40	127	39	9	28	34	4	42	99	382
41–50	99	41	16	23	66	4	48	61	360
51–60	87	16	1	16	70	15	19	38	282
61–70	34	22	0	7	46	7	16	17	149
Over 70	3	1	0	1	5	0	3	0	13

287 upper limb single amputees classified according to age groups and cause of amputation

Double Amputation

The incidence of double amputations of the lower extremity is higher in civilian practice than among war amputees These amputations are largely caused by cardiovascular disease accompanied by varying degrees of debility Limb fitting, when possible, is a longer process calling for patience, stoicism, and determination from the patient The double above knee amputee makes his first steps on short peg legs upon which balance is learned while there is but a short distance to fall In this way confidence is acquired, flexion deformities are reduced, and general physique improved From these pegs, the more promising may graduate in time to full length legs after a further period of training, the whole process may take upwards of a year to complete If patients were told of these prospects from the outset, much of their impatience, which reacts so strongly against their cooperation during the early tedious stages, would be forestalled

Table V shows the age incidence of double leg and double arm amputations

Malignant Disease

Young patients, who have been amputated for malignant disease are in a different category Despite the doubtful prognosis it is considered inadvisable to withhold a prosthesis until the risk of secondary deposits can be excluded To do so would be equivalent to informing the patient of the diagnosis It is the practice to prescribe a limb for these patients at the earliest opportunity and to begin at once the fullest course of training consistent with the patient's general condition The prognosis is so clouded—many survivors living a great number of years—that this policy is considered fully justified despite the disappointment of some early deaths

TABLE IV—CAUSES OF SINGLE ARM AMPUTATIONS AND AGE INCIDENCE IN 287 PATIENTS

Age in years	Trauma	Osteomyelitis	Congenital	Tuberculosis	Cardiovascular	Diabetes	Other diseases	Unknown causes	Total cases
Under 11	5	0	31	1	0	0	0	10	47
11–20	19	0	12	1	2	0	0	5	39
21–30	33	0	8	0	0	0	2	8	51
31–40	41	2	6	0	1	0	2	8	60
41–50	34	0	5	1	0	0	2	14	56
51–60	14	0	2	1	0	1	4	5	27
61–70	2	0	1	1	1	0	0	2	7
Over 70	0	0	0	0	0	0	0	0	0

PSYCHOLOGICAL REHABILITATION

Successful rehabilitation of the limbless depends upon the correct psychological approach from the time of amputation onwards The loss of a limb is a severe psychological trauma followed by anxieties and mental disturbances of varying types depending upon the personality of the patient Some compensation can be offered by explaining to the patient how much he can still hope to do, at the same time indicating activities which must be curtailed He should be impressed with the fact that every amputee can be a useful member of society *and that the loss of a leg or legs does not* foreshadow crippledom

Arm amputees should be encouraged to use their stumps at the earliest moment after amputation and thus develop the idea that the stump will be a useful member All amputees want to be independent and they should not be frustrated by too much unnecessary assistance, which easily tends to convince them that they really are cripples An amputee should be allowed to help in the hospital ward If he has lost a leg he should be encouraged to get about soon on crutches

Suitable stump exercises and correct bandaging should be begun as soon as possible, and the patient should be told that by conscientiously carrying out his treatment he will obtain a limb the sooner

Training in the use of a limb, especially an artificial arm, is most effective when carried out in a limb centre Not that any revolutionary methods are adopted, but rather that the stimulus to the amputee of being trained with others similarly disabled, and by those who have specialised for years in the training of the limbless, has proved so valuable as to be almost indispensable. The instructors moreover, are all trained in artificial limb design and fitting and have long experience of the exertions entailed, and can temper their demands upon patients according to their knowledge Again, during the training period, small adjustments to the fit of a socket are often found necessary, and in the limb centres the contractors' fitters are available to carry out these without retarding the training Full details of training methods have recently been published by the Ministry of Pensions[2]

TABLE V—AGE INCIDENCE IN 128 DOUBLE AMPUTATIONS

Age in years	*Double leg*	*Double arm*
Under 11	12	2
11–20	14	1
21–30	20	3
31–40	16	1
41–50	31	1
51–60	22	2
61–70	3	0
Over 70	0	0

Arm training can only be given in a properly equipped arm training school, whose instructors are themselves arm wearers Unless purely cosmetic function is required, which is rare, the provision of an artificial arm without training is a waste of time and money

CONCLUSION

The most important lesson of the past two years' experience of artificial limb supply is that the closest liaison between the orthopædic surgeon and the limb surgeon is an indispensable prerequisite to complete *rehabilitation of the amputee*

This collaboration should be engaged at all stages, and consultation should, where *possible*, take place before amputation It can be fostered by more frequent requests from the orthopædic surgeon to the limb service for joint discussions and by fuller recognition of the difficulties with which limb fitting and rehabilitation abound

The limb surgeon must recognise that both the amputation and the resultant stump are but one aspect of a major disorder which requires closer supervision In many cases new ideas in rehabilitation and in the maintenance of well being and good function of the stump must be constantly sought

---

[2] Ministry of Pensions Rehabilitation following Amputation M P M 414 1950

A plea is also made for combined operations in research so that all the resources of modern technique be used to improve the structure of the artificial limb and to fortify the patient's capacity to wear it

We are indebted to the Director General of Medical Services for his permission to publish this paper

THE REGISTRAR PROBLEM

N J Logie
M.B Aberd, F.R C S

The future of the many registrars threatened with dismissal by the plan announced last November[1] is still in doubt, but, judging by a statement to which its representatives have agreed,[2] the Ministry of Health is coming to recognise that this plan was too ruthless

Bearing in mind the acknowledged shortage of consultants and the difficult position in which registrars are now placed, several courses are possible

Additional Consultant Posts

The service needs further consultants, though how many will not be clear until the present survey of hospital staffing is completed The ideal number cannot, however, be achieved at once, owing to several factors of which financial stringency and lack of suitable accommodation are perhaps the most important, and it behoves consultants to ask themselves whether they really can justify retaining all their appointments and/or sessions If they cannot, they should surrender some and thus make room for the upgrading of registrars

Creation of a "Specialist" Grade

The formation of a "specialist" grade intermediate between those of registrar and consultant seems desirable on more than one count

1 It would end the uneconomical situation in which the few highly trained handpicked survivors of at least five years competitive training may be flung away (to be replaced by other future victims) at the end of their third or fourth year as senior registrars because no consultant post is immediately available The new grade might be one into which exceptional senior registrars could be fitted should no suitable consultant post be vacant at the time, and if the amount of work was then insufficient, another senior registrar might not be appointed for the time being

2 Not all specialties require that each of their ' permanent officials ' be of full consultant status At present to cover the work registrars are used and abused, or conversely consultants do work which could be done by less experienced and less expensive personnel

3 With a group of specialists on which to draw, there would be less risk of not finding a suitable candidate for a consultant post As things are when no suitable candidate comes forward, either an unsuitable consultant appointment is made or else the work is passed to a senior registrar or to a senior hospital medical officer (S H.M.O)

4 This step would save valuable personnel for the service

5 It would open the way to abolishing the unpopular S.H.M.O grade

6 It would increase the number of posts open to senior registrars

7 It would lead to a reduction in the number of senior registrars, for these specialists would do much of the responsible work now done by senior registrars, who should properly be regarded as trainees

The "specialist" should be given security, suitable status, and an adequate salary (intermediate between that of registrar and of consultant)—none of which a registrar has—while he is furthering his experience or awaiting a consultant post

Two provisos would have to be fulfilled (1) the full consultant needs of the service must be decided on, and (2) the creation of the "specialist" grade must not be used to whittle down the consultant establishment

OTHER OPENINGS

Nowadays opportunities are few for the general practitioner who seeks to specialise, and entry into general practice is especially difficult for ex registrars For those registrars who fail to secure a consultant post these obstacles should be removed

The General practitioner Specialist

There are small hospitals in many townships which are at some distance, or which are not easily reached, from the nearest large centre In these hospitals there is still a place for the man who can deal, for example, with emergency surgery and the simpler surgical problems In such an area the ex registrar should be enabled to learn something of general practice by working as an assistant in a practice for a year before taking it over, while in a partnership practice his initial lack of knowledge would be covered by his partners The scope of his specialised work would be deliberately restricted, and the number of patients on his general practice list would be limited, in order (*a*) to allow him time for his specialised work, and (*b*) to prevent him, or the partnership to which he belonged, from taking advantage of his hospital post by attracting an unfairly large number of patients The local hospital would have the consultant services of a parent hospital behind it

Training for General Practice

The more senior registrars who fail to gain advancement and who wish to enter general practice should be helped to find assistantships or, better still, trainee posts During the period of training any difference between the ex registrar's former salary in hospital and his earnings as an assistant should be paid either by the former employing authority or from a special fund The value of this system would be enhanced if refresher courses were offered to those about to enter general practice

DOMICILIARY CONSULTATIONS

In future the domiciliary consultant service is to be operated entirely by regional hospital boards, boards of governors having no hand in its organisation This is announced in a Ministry of Health circular (R H B [51]11) which also states that consultations should be arranged by the family doctor directly with the consultant and not through the regional board

The circular, reviewing the operation of the service in the past two and a half years, remarks that local health authorities are responsible for securing that mentally ill or mentally defective patients are brought under care

As regards the domiciliary service under the National Health Service Act, the intention is that a consultant (or, where there are not enough consultants, a senior hospital medical officer) shall be available for domiciliary consultation or treatment when the family doctor considers that the patient's condition makes it essential for this to take place at home. Here "home" means the place where the patient is for the time being resident, but it does not ordinarily include a private nursing-home

'The domiciliary service will however, be available to persons who live (i e, are bona fide residents as are some old people) in private nursing homes, and visits by obstetricians or pædiatricians (accompanied by anæsthetists where needed) as part of the domiciliary service should be made available in an emergency for a patient who has been admitted for her confinement to a private maternity home or for her baby during her stay in the maternity home, where medical considerations make it impossible for the patient to be removed to hospital "

---

[1] R.H.B (50) 106 See *Lancet* 1950 ii 537

[2] See *Brit med J* suppl Jan 27 1951 p 24

The decision that regional boards shall administer the service (as some are already doing) means that all contracts for domiciliary consultations should be offered and made by these boards and each consultant should be in contract with only one regional board

Originally it was intended that all requests for a domiciliary consultation should be made through a hospital, "Experience suggests however, that the convenience of all concerned is best promoted by direct application by the family doctor to the practitioner he wishes to call in, and Regional Boards should organise their service accordingly " Furthermore, regional boards should seek the help of executive councils in informing general practitioners of the consultants available for consultation A special record and claim form for consultations is being introduced

Public Health

A HEALTH-SERVICES BUREAU

J A GILLET
M B Lpool, D P H
DEPUTY MEDICAL OFFICER OF HEALTH, ROTHERHAM

EVEN before the National Health Service Act came into operation in July, 1948, the scope of medical and social services was expanding, and this development was greatly hastened by the Act In Rotherham it was felt that the increasing complexity of these various services called for a new section of the health department to deal with inquiries concerning them The scheme envisaged by the medical officer of health and the health committee was for a section which would both meet the needs of people seeking information about such services and would also promote health education

The new section was opened on Sept 6, 1948, in the town hall, but this arrangement proved unsatisfactory because the offices could not be reached directly from the street Accordingly, the section was transferred last year to a building at the centre of the city These premises, which are on a corner site, have three main rooms One large front room, with a shop frontage on two sides, is furnished with chairs, tables, and display cabinets containing posters and pamphlets on health topics issued by the Central Council for Health Education and other agencies Official explanatory pamphlets and application forms for various benefits can also be had Behind this room is an office for private interviews, and also a room in which are stored wheel chairs, crutches, bed rests, bedpans, and other nursing and surgical appliances, which are available on loan in case of need, on return these are cleansed and sterilised Drums containing sterile equipment for domiciliary confinements are issued on request to midwives and general practitioners

The section is staffed by a health services information officer and one female assistant Excellent relations have been established with both the general public and the various agencies providing services locally, such as the hospital management committee, the executive council, and the Ministries of Food and National Insurance The public have come to realise that time can be saved, and frustration and needless journeys avoided, by calling at the bureau when they have problems connected with the health services, and use of the bureau has been encouraged by the willing coöperation of the local press, shopkeepers, business firms, and the transport undertaking in publishing its functions

From the outset the bureau has been busy, since September, 1948, over 11,000 inquiries have been received At first inquiries concerned mainly such simple matters as how to obtain glasses or dentures, or how to change doctors, but now the problems are usually less easy to answer Much time has been spent in explaining the method of completing forms of application for monetary and other benefits, these are often extremely perplexing to members of the public Every effort is made to deal with queries on the spot, giving definite and detailed advice, and avoiding fruitless reference of the inquirer from one office to another

Advantage has been taken of the window space to try to "sell" health to the public There have been displays on "coughs and sneezes," "vaccination and immunisation," "poliomyelitis," "clean food" "child welfare" "accidents in the home," and other topics These displays which are usually changed fortnightly have attracted requests from organisations such as the Women's Co Operative Guild, the Soroptimists, and youth clubs for speakers to talk on medical and medico-social subjects Film shows, talks, and discussions have been arranged by the health services information officer

In Rotherham the welfare services of the borough are not under the direction of the medical officer of health, but one of the large windows and part of the large front room, together with the services of the staff, have been placed at the disposal of the welfare committee These facilities are utilised for the display and sale of goods made by blind people, and there is also a boot repair service. The venture has proved most successful as a means of disposing of goods made by the blind, and one section of the bureau is often able to help the other

That the bureau meets a real need has been proved not only by the number of inquiries but also by the thanks of satisfied "customers" There is the instance of the lady who embarrassed the health services information officer by publicly embracing him in token of her gratitude There is also the case of the middle aged man deaf as the result of the 1914–18 war, who had not realised that for over twenty years he had been entitled to a hearing aid from the Ministry of Pensions His gratitude after being supplied with one only three weeks after calling at the bureau, knew no bounds Finally, there are the repeated statements by callers that before visiting the bureau they had been referred from one office to another without success

Owing to the varied inquiries, the staff has to be fully conversant with the medical and social services, and they have also to be patient and above all sympathetic in their approach to inquirers The bureau, which began two and a half years ago as a tentative experiment, has become a permanent feature of the health department and of Rotherham

Statistics for London in 1950

A preliminary report by Sir Allen Daley, the county medical officer of health, shows that in 1950 the provisional birth rate in London was 15 9 per 1000 population, and the provisional death rate 11 3 The provisional rates for maternal mortality (0 56 per 1000 live and still births) and for infant mortality (25 per 1000 live births) were lower than any previously recorded in London The provisional neonatal mortality rate was 16 5 per 1000 live births

During the year diphtheria cases totalled only just over 100 with 3 deaths, compared with 7500 cases and 250 deaths in a pre-war year Now over 60% of infants under the age of 5 are immunised, and at school ages the percentage reaches 75

In 1950 the number of tuberculosis notifications fell for the first time since the end of the late war, and the provisional death-rate has further declined to a new low record of 0 39 per 1000 population, compared with 0 52 in 1949

Influenza

In England and Wales the prevalence of influenza, judging by figures for the week ended Feb 3, is no longer increasing greatly Influenza deaths in the great towns during each of the six weeks from that ended Dec 30 to that ended Feb 3 numbered 102, 458, 890, 1099, 1239, and 1269 In the week ended Feb 3 the influenza death-rate in the great towns was 61 19 per million population. For the great towns grouped regionally the highest incidence of influenza deaths was in Wales, the incidence of deaths increased materially in the Eastern London and South-eastern and Southern regions and less decidedly in the East and West Ridings and the North Midland areas The death-rates by regions were as follows

Region	*Influenza deaths per million population*
Northern	14 52
East and West Ridings	61 27
North western	79 46
North Midland	81 96
Midland	88 81
Eastern	98 37
London and South-eastern	40 88
Southern	40 20
South western	70 45
Wales	105 52

The proportion of influenza deaths in patients over 55 years of age rose still further to 90 5%.

Weekly claims under the National Insurance Act have fallen substantially, new claims totalled 323,400 in the week ended Jan 30, compared with 370,500 374,400, and 395,600 in the three weeks up to Jan 23[1] Among a group of some 7500 London County Council employees sickness absenteeism of about 15% was recorded in the first half of January but in the latter half of that month it decreased to 12% and finally to 10%

Influenza Abroad —Strains from Turkey and also from Paris have been identified as A-prime Virus A-prime has also been found in Canada

Poliomyelitis

In England and Wales notifications of poliomyelitis during the week ended Feb 3 were as follows paralytic 21 (20), non-paralytic 11 (7), total 32 (27) Figures for the previous week are in parentheses

---

[1] Figures supplied by the Ministry of National Insurance See Registrar-General's Return for the week ended Feb 3 H.M Stationery Office Pp 20 6*d*

Medicine and the Law

Hospital Nationalisation

By an intriguing feat of forensic conclusion the Court of Appeal has decided in the Bland-Sutton case that two different appeals by parties interested are successful but that nevertheless the result remains the same as before

Lady Bland Sutton, who died eight years ago, bequeathed the residue of her estate on trust as an endowment for two objects (1) for a research scholarship, and (2) to pay the income to the Middlesex Hospital for the maintenance and benefit of the Bland-Sutton Institute of Pathology, then carried on in connection with the hospital. In a proviso to her will she directed that, if certain specified contingencies occurred, her trustees (the National Provincial Bank) were to transfer the endowment fund to the Royal College of Surgeons for the general purposes of the college These contingencies included the following events the hospital becoming nationalised or passing by any means into public ownership and the trustees becoming unable lawfully to apply the income to the objects named in the will. When the National Health Service came into operation on July 5, 1948, the bank naturally had to ascertain the effect upon the endowment fund Mr Justice Danckwerts held last July[1] that the contingencies had not happened There was, however, a further legal point for him to consider If the events specified in the proviso ever did happen, it might be at some date in the remote future That being so, the proviso might be invalid because it offended the technical rule of law against perpetuities, if so, the ultimate gift to the college would be void, though, if the college were in the lawyer s sense a charity, then it would escape the consequences of the rule

Mr Justice Danckwerts held that the Royal College of Surgeons was a charitable body and thus would have its chance to receive the fund some day, if and when the specified contingencies occurred But he also held that the contingencies had not happened yet, the Middlesex Hospital had not been nationalised and it had not passed into public ownership His decision did not satisfy two of the interested parties The college appealed against it on the ground that the operation of the National Health Service Act of 1946 did nationalise the hospital did pass it into public ownership and did make the bank unable lawfully to apply the income of the fund to the objects of the will On the other hand, the Middlesex Hospital Medical School, in a cross appeal, maintained that the prospective gift over to the college under the proviso was invalid

Three judges of the Court of Appeal have now unanimously decided that both sets of appellants are right, but that it makes no difference Mr Justice Danckwerts had held that the hospital was not nationalised because it did not wholly pass into public ownership the medical school became an independent corporate body which remained outside nationalisation The Court of Appeal holds that the hospital was nationalised in the sense which Lady Bland-Sutton contemplated Thus the contingency named in the proviso to her will has occurred. But the Court of Appeal also holds that the Royal College of Surgeons is not a charity, the judges finding themselves bound by a decision of 1899 Thus the gift over to the college is declared void There is nevertheless no intestacy Thus, though the Danckwerts judgment is upset and the judge's order of last July is discharged, the result is substantially the same as that which he then reached

The decision in 1899 (*In re the Royal College of Surgeons*) arose over the possible application of section 11 of the Customs and Inland Revenue Act, 1885, to the property of the college The Act exempted property "legally appropriated and applied for the promotion of education, literature science or the fine arts" The charters of the college and the relevant enactments having been exhaustively reviewed, and a judgment to the advantage of the Institution of Civil Engineers having been considered, Lord Justice Romer dwelt upon the dual nature of the objects and purposes of the college It certainly promoted education and science but it also promoted the interests of those practising surgery as a profession No exemption from the 1885 Act, therefore, could be claimed. No fresh material being offered to the Court of Appeal the 1899 decision has been followed Sir Raymond Evershed, Master of the Rolls, observed that the court could not, "without untenable refinements," come to the conclusion that the college's main or only purpose was of a public or charitable character and that any selfish professional purpose was only ancillary or subsidiary thereto

Relative Liability

In Fordyce *v* Doherty the jury has found an anæsthetist guilty of negligence and awarded £400 damages. The patient underwent an operation for duodenal ulcer, curare was injected to obtain muscular relaxation, it was alleged (though this was denied) that the arm was strapped above the head during the operation and that, on recovering consciousness, the patient found that he had lost the use of it. The surgeon who conducted the operation was joined as defendant, but the jury found in his favour on the issue of negligence. Mr Justice Cassels postponed judgment in order to hear legal argument. There will doubtless be discussion of the relative liability of the North West Regional Hospital Board (in whose hospital at Highgate the operation was performed) and the defendant anæsthetist.

---

[1] *Lancet* 1950 ii 155

Meanwhile it may be noted that, in cases arising out of the National Health Service, the Ministry is likely to shift liability, so far as it can, to the shoulders of members of hospital staffs. This, at least, is the view expressed by the legal advisers of the Medical Protection Society in the annual report which that body issued last September. Though the circumstances are not exactly parallel, it was the practice of the Treasury Solicitor, in years before the Crown Proceedings Act had enlarged Government departments' vulnerability to actions for damages, to stand behind the driver of Army lorries or Post Office mail vans when some plaintiff made a successful claim against an individual driver for injuries due to his negligence. The Army Council and the Postmaster General were strictly not liable in law for the actions of their agents or servants, but the Crown paid the damages. As with the nationalised industries, so with the Ministry's hospitals, there are legal problems to be worked out in the coming years. One cannot blame the Ministry of Health (by whatever name it be called) for standing upon its legal rights to the possible detriment of hospital medical staffs, but the ministerial attitude should be noted. In any event the medical practitioner should be aware that his own legal interests and prospective defence may be quite different from those of the hospital or the "employing authority."

Coroners' Rules

The Lord Chancellor and the Home Secretary have appointed a committee to make recommendations on the rules to be made under section 26 of the Coroners (Amendment) Act, 1926, relating to the procedure at coroners' inquests and at post-mortem examinations and as to the forms to be prescribed under section [illegible] of that Act. The chairman of the committee is Mr Justice Austin Jones. The committee is ready to receive written evidence, which should be sent to Mr H W Wollaston, secretary to the committee, Home Office, London, S W 1, before the end of February.

Parliament

Students' Examination of Hospital Patients

In the House of Commons on Feb 6 Mr Fred Longden called attention to the practice in teaching hospitals for patients to be examined intimately by groups of students, often against the natural inclination of the patients. He was sure that the overwhelming number of consultants were all that could be wished, but he quoted a number of cases where he alleged women patients had been subjected to embarrassing and humiliating experiences. That sort of thing, he said, ought to be stopped at the earliest moment. Students should not merely be professionally taught and guided; they should be controlled in their treatment of men and women.

Dr Charles Hill said that in his experience he had never seen or heard of unchaperoned examination such as Mr Longden had described. Everyone must face the fact that if this country was to be happily served by efficient doctors, teaching on the diseased human body was essential. Most patients were only too glad to coöperate, but a minority found it too difficult to bear, and he agreed that where people protested their objections should be respected.

Mr Arthur Blenkinsop, parliamentary secretary to the Ministry of Health, pointed out that there had been no change in the principles of using patients in teaching hospitals to give students the necessary clinical experience. The system had been used ever since our present methods of clinical teaching were evolved. The only difference was that the teaching hospitals had perhaps more students under training than in the past. Unless the principle of clinical examination of patients by students was accepted much of our medical training would be valueless and the public would be endangered. He was convinced that it would be impracticable to get the consent of the patients in advance. But he agreed that where a patient had expressed unwillingness to submit to an examination by students that objection should be dealt with sympathetically and understandingly; no pressure should be used. The Ministry of Health would always be ready to investigate any cases in which it was suggested that any wrongful duress had taken place. During the last year and a half only three or four cases had been reported to the Ministry. He realised that there might be many cases where patients felt unhappy, but the majority appreciated the need for the procedure although they might not like it.

QUESTION TIME

Hospital Registrars

Dr Reginald Bennett asked the Minister of Health what action he was taking to carry out the provisions of his circular about the dismissal of specialists under training from his hospitals; with what professional bodies he was discussing this action; and what results had yet accrued from such discussions.—Mr H A Marquand replied: I have received the proposals of some of the hospital boards and am awaiting others. These will, where necessary, be discussed with representatives of the boards. I am also having discussions, which are not yet complete, with the medical profession's joint committee.

Infectious Diseases

Mr William Teeling asked the Minister if he would give instructions to all medical officers of health that they should release no information about dangerous infectious diseases without his approval.—Mr Marquand replied: No, Sir. I think that the publication of information about local health conditions is very properly a matter for the local authority and not one in which I should normally intervene.

Heroin

Mr A D Dodds-Parker asked the Minister of Health what quantity of heroin was used in the United Kingdom now, compared with 1938; and to what causes he ascribed the difference.—Mr Marquand replied: The quantity in 1938 was 46 kg., and in 1949 it was 136 kg. Diamorphine is widely used in this country as an ingredient for cough linctus. A rise in consumption can therefore be attributed in part to medicinal use under the National Health Service.

Diphtheria Statistics

Mr S P Viant asked the Minister how many of the cases of diphtheria notified in children under 15 were recorded as immunised or not immunised in 1945, 1946, and 1947; and if he would give similar information about the deaths from diphtheria recorded in those years.—Mr Marquand replied:

INCIDENCE OF DIPHTHERIA IN CHILDREN UNDER 15

Year	Notifications	Notifications in which a full course of immunisation had been completed	Notifications not immunised	Deaths	Deaths in which a full course of immunisation had been completed	Deaths not immunised
1945	12 514	4431	8083	593	36	557
1946	7719	2723	4996	325	15	310
1947	3941	1287	2651	198	10	188

Staffing of Health Centres

Mr Somerville Hastings asked the Minister of Health what steps he proposed to take to provide for medical staffing when health centres had been built or acquired by local authorities and local doctors refused to make use of them.—Mr Marquand replied I am afraid I cannot generalise on this subject and the steps to be taken would clearly depend upon the circumstances of the particular case I should hope that agreement would normally be possible

B C G Vaccine

Mr S S Awbery asked the Minister of Health if he would now permit general practitioners to inoculate with B C G vaccine and to give them discretionary powers in closed cases to send an inoculated child away from home—Mr Marquand replied Research into the use of B C G in this country is still continuing and I am advised that any general or indiscriminate distribution of the vaccine would not be prudent at present

Factory Doctors' Charges

Major W W Hicks Beach asked the Minister of Labour whether he was aware that the proper charges of an appointed factory doctor under the Examining Surgeons Order, 1947, were not recoverable through the National Health Service, and if he would take steps to remedy this anomaly—Mr Aneurin Bevan replied These are charges for medical services which the employer is required to obtain under the Factories Acts for the purposes of his general responsibility for health and safety in his employment The National Health Service on the other hand, is provided for members of the community in a personal capacity and not to relieve employers of those obligations It is not anomalous, therefore that these charges are not recoverable from the National Health Service

Colonial Medical Service

Mr John Rankin asked the Secretary of State for the Colonies why the previous local D M.S was asked to retire in view of the fact that the Tanganyika government was recruiting 20 doctors in South Africa owing to the shortage of doctors in the medical service, and what efforts were made to secure Asian doctors from East Africa or unemployed doctors in Malta—Mr James Griffiths replied The shortage of staff in the department at lower levels did not in the Governor's opinion justify retention in the service of the late director after he had qualified for retirement on pension under the relevant Tanganyika legislation No candidates were in fact recruited in South Africa but only 5 vacancies now exist for 2 of which candidates are in sight The Tanganyika government employ a number of Asian doctors A selection committee for recruitment to the Colonial Medical Service was set up in Malta in September 1950, and candidates recommended by it have already been selected for colonial appointments

Makerere College

Mr John Parker asked the Minister the length of the medical course at Makerere College, how many government scholarships were provided and whether leave of absence was granted for medical officers to complete the course to qualify as doctors—Mr Griffiths replied The full diploma course lasts 7 years All of the 28 students at present taking the course receive government grants Selected African assistant medical officers are given leave of absence to acquire special postgraduate qualifications in the United Kingdom to assist them in their duties in East Africa

Mr Parker What provision is made to enable African medical officers employed in Uganda to complete their training to qualify as doctors?—Mr Griffiths Africans holding the Makerere diploma in medicine are already eligible to be licensed as medical practitioners on entering the Uganda government service as assistant medical officers and are accorded the title of doctor in East Africa. It is the aim of the college so to improve and adapt its diploma course that the General Medical Council will admit holders of a diploma to the British Register without further qualification such as is required by them at present

In answer to a further question Mr Griffiths stated that 58 African assistant medical officers are employed by the government of Uganda of whom 9 are in charge of hospital units

In England Now

A Running Commentary by Peripatetic Correspondents

The Registrars were christened, and their training pre-determined
Their duties were important, though too numerous to state,
But like nylons, fully fashioned, through the National Health Service
They achieved a sudden glory This was 1948

They worked, they throve, they studied, they got married and had children
They got Memberships and Fellowships and everything was fine
They examined all the patients who attended all the hospitals
And wrote reports when ordered This was 1949

But the pound's devaluated and the dollar raised on high,
So the Treasury has suddenly turned thrifty
"We do not want to lose you, but we think you ought to go",
And they sacked the Senior Trainees 1950

Still the patients keep on coming with acute and chronic ills
Still the wards and clinics hustle and their work is never done
May it please you, Mr Marquand—won't you set the people free,
Won't you give us back our Registrars in 1951?

* * *

The increasing tendency towards specialisation revealed by medical Lifemen in these columns confirms my view that Medicinemanship (keeping one up on one's patients) is too restricted in scope to satisfy the really progressive Lifeman But in the wider, deeper, and perhaps tougher field of Wardsmanship (keeping one up on one's colleagues), and especially its late development Staffconferencemanship, much fine work is being done It is already clear that the budding consultant must choose between the Damn-Good-Doctor ploy and the Science-is-Movement gambit The latter is new and fashionable but a little too easy A pocketful of graph-paper and no stethoscope are the only essentials The requisite politely blank look to be assumed when asked for an opinion on a murmur or knee-jerk can be acquired in a few weeks if practised daily before a mirror A slide-rule, Fisher's *Design of Experiments*, and an equation or two pencilled on the back of an old kymograph tracing are excellent properties, as are a corked test-tube of soapy water in the waistcoat pocket and a tuft of guineapig fur on the lapel, a man I know got his junior clinical tutorship solely because he used an old piece of cardiac catheter to tie up his coat To establish oneself as a Damn-Good-Doctor is harder, but the rewards are greater A distinguished example is young Hartman-Heerwell, lately appointed to a fat consultantship in the Home Counties because the selection committee liked his statement that he "Didn't believe in all this damned new-fangled biochemistry" His often-repeated feat of inspecting the E C G of a puzzling case in the cardiac department in the basement, running up four flights of stairs and drifting nonchalantly into the ward "to have another look at that heart that's worrying us," just in time to make a confident diagnosis ' by good old-fashioned clinical methods" before the E C G report is telephoned to the ward through the official channels is one of the finest flowers of Wardsmanship Some day we must persuade him to tell us his methods in full

* * *

Before this series ends may I say a few words about the undergraduate branch of medical Lifemanship for the benefit of those who have not yet learnt the trick of carrying a stethoscope through the Metropolis with only the tips of the earpieces emerging from an outer pocket? The art of medical Studentmanship no doubt resembles that of any budding professional man with a position to maintain, but it has some features peculiar to itself For instance, there is the man in the opposite seat on the nine o'clock to Town who suddenly leans forward and asks in a low confidential but generally audible whisper "Why is it that a dose of salts acts at once, but cascara takes twelve hours?" Any attempt at a straight answer would be to admit defeat But for the experienced Studentman there is an infallible counter ploy Don't be snared into leaning across to speak to the man but sit firmly back against the upholstery, express professional concern at the state of his bowels, and follow this up with a few brisk questions of as personal a nature as you can devise A certain winner for the trained man Far more serious situations will arise at home That off-hand question about what one has been doing today is a sinister offensive difficult to ward off because of its persistent though varied repetition Counter ploys are as follows

1 "Oh, nothing much" effective on occasions but leaves the Studentman in an unfavourable position if repeated too often

2 "Working" also occasionally effective but will not always stop your opponent's attack

3 "Attending a post mortem" the most effective ploy, especially if expanded, with full intestinal detail, at supper time

Another form of attack in the home is the Unreasonable Thirst for Information, hidden behind a casual question such as, "Am I right in thinking that there's more than one form of pneumonia?" The ploy here is the Reply of Unlimited Knowledge, in the case mentioned this would take the form of a speedy dismissal of lobar and bronchopneumonia in a few words followed by a learned dissertation on atypical and virus pneumonias If suitably varied, this defensive ploy should last the Studentman until the time comes for him to learn the more complicated art of Doctormanship

A no less important aspect of Studentmanship is that of getting one up on the Chief without actually dropping banana skins in the hospital corridor A fine example of this was played on a certain Registrar (who had certainly better remain anonymous) conducting a teaching round Seeing a student prodding rather disdainfully at a tumour with one hand the Registrar led off with "Are you, perchance, left-handed, Mr Whoosis?" He was at once floored by the triumphant counter ploy "I'm ambidextrous, sir" When the Registrar recounted the tale of his defeat later, the Chief enlightened him on the correct Triplecounter-ploy—obvious when one thinks of it "Then why not use both hands?" But, of course, he is an acknowledged expert in Chiefmanship

* * *

The Ministry of Health Art Club (founded 1924) and Camera Club, the Hygeia (founded 1915), lately held a joint exhibition which should dispose for ever of any doubts hitherto cast on the sensitivity of the staff

Well displayed in the fine conference room were 80 paintings and drawings and 70 photographs There are many architects on the Ministry's staff, and their work was naturally prominent Among Mr Nicholson's several fine water-colours was a simple but effective study of the Undercroft, Westminster, which had quite a Russell Flint atmosphere Mr Deleuse, another architect, had several beautiful water-colour landscapes and a particularly good still life The doctors were not prominent among the exhibitors, but Dr W P Kennedy showed an oil and a water colour of scenes from the Lebanon, and two other landscapes There were some excellent oil paintings, and Miss Eileen Perrett's portrait of an old man was professional in its competence

The photographs were of first-class standard throughout, I have rarely seen a more beautiful collection The dozen shown by Sir Weldon Dalrymple Champneys, the club chairman, were worthy of an exhibition by themselves, and they were run a close second by Dr Harold Davis's pictures Among the rest I was particularly struck by the soft-focus studies by Mr Harrop

It was encouraging (to me) that there was not a single example of the atrocities now labelled "modern" Altogether a highly meritorious show

* * *

Aphorism of the Week

Better half an hour than half a tonsil

Letters to the Editor

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—Professor Smirk's letter in your last issue prompts brief comment lest it should be thought that experience in this country with the penta and hexa methonium compounds differs essentially from that in New Zealand In our experience these drugs will cause a marked fall of blood pressure in nearly all cases of hypertension However, some degree of tolerance tends to develop, and it is not always possible to maintain a satisfactory over all reduction in pressure without undue side effects, at least when the drug is given by mouth Far more clinical experience and detailed studies of the various hæmodynamic effects will be needed before the place of these compounds in the treatment of hypertension can be assessed Meanwhile encouraging results are being obtained in certain groups of patients and a few tentative suggestions may be made

No patient should be submitted to surgical sympathectomy for hypertension until thorough trial with methonium has been made Likewise every patient with malignant hypertension should be so treated

When signs of left ventricular failure are manifest, life is rarely prolonged for more than a year or two Under such circumstances, an attempt to postpone further failure may reasonably be made by adding methonium to the other customary measures

Unless the patient is seen too late, and her condition is so serious as to prevent 48 hours' delay, every pregnant woman with toxæmia or severe hypertension should be given a chance to respond to methonium before pregnancy is terminated In favourable cases improvement will soon be manifest, and it should be possible to decide if it is safe to allow the pregnancy to continue The reward may well be a live child instead of a lost one If the pregnancy can be continued until a live birth is probable, the drug can be stopped a day or two before induction *No ill effects from these drugs on* the fœtus or newborn infant have been observed Finally it will be found that previously intractable symptoms attributable to the hypertension can often be relieved and may not return, at least for some time, after discontinuation of the drug

The time has probably not yet come for the long term treatment of relatively benign cases It is advisable first to obtain further experience in the more serious cases

Potential dangers have been emphasised[1] in order to discourage indiscriminate treatment Untoward events have been reported by a number of workers, and it is strongly recommended that the initial assessment should be made in hospital, where the patient can be under continual observation

RICHARD TURNER

Edinburgh

SIR,—The methonium compounds are now being used in a number of clinics, and growing experience is proving their efficacy in the reduction of hypertension

I have found hexamethonium bromide more effective than the pentamethonium compound My experience is that hexamethonium bromide lowers the blood pressure and relieves the hypertensive symptoms in most cases of essential and malignant hypertension, and in cases of chronic nephritis To observe the blood pressure chart of a hypertensive patient under the influence of hexamethonium bromide is one of the most dramatic experiences in modern clinical medicine The pressure falls precipitately within 24–48 hours, without toxic symptoms—a result that could not be achieved by any other method

---

[1] Turner R W D *Lancet* 1950 ii 353

Patients with chronic nephritis appear to respond equally well. One patient had marked albuminuria and was excreting 8 g of albumin per litre of urine After he had received the drug for eight days, this amount was reduced to 1 g per litre. This may, of course, be fortuitous, but the observation is worth following up in other cases Papillœdema and subjective symptoms such as headache, throbbing, and vertigo were relieved by the drug

One patient, who had undergone bilateral dorsolumbar sympathectomy for malignant hypertension without reduction of her blood pressure, responded promptly to the drug , in fact, she was the only patient in my series who developed toxic symptoms due to hypotension Her blood pressure fell from 260/150 to 110/60 mm Hg , it rose promptly on withdrawal of the drug for twenty four hours, and she ceased to complain of the toxic symptoms of faintness, blurring of vision, and nausea and vomiting caused by the temporary hypotension With this drug at our disposal it seems to me very doubtful whether patients should be advised to undergo sympathectomy for severe hypertension

Two patients with marked hypertension who had suffered minor episodes of cerebral thrombosis were given the drug with beneficial effects They did not develop any further cerebral thromboses although their blood pressures were greatly reduced

I have adopted the following scheme of dosage

Initially 50 mg is given every six hours by intramuscular injection no harmful effects have been seen from this dosage After two days one dose each day is increased to 100 mg reaching a dosage of 100 mg six hourly after a further four days These intramuscular injections usually have the desired hypotensive effect At this point one injection each day is replaced by an oral dose of 1 g this dose is increased by 1 g daily until 4 g a day is being taken by mouth (i e , after a further four days) This dosage is excessive for some patients who may be found to react satisfactorily to 1 g every twelve or eight hours so the daily maintenance dose by mouth may vary from 2 to 4 g

I have found that oral administration has a much less certain hypotensive effect than intramuscular injection The blood pressure fluctuates a good deal , but usually a patient with an initial blood pressure of 260/150 can be maintained at a blood pressure of 170/120 with oral administration

Treatment would certainly be more effective if the patient could give himself injections of the drug at home Many patients with diabetes mellitus are taught to inject insulin , but in the case of the methonium compounds 3–4 injections would be required each day It might be possible to develop a preparation of hexamethonium bromide for injection in a medium from which the drug would be absorbed slowly, giving a continuous effect , one depot injection each day might then suffice

The ten patients who have been treated here by this method are attending as outpatients Such patients must be kept under observation because the ultimate effect of lowering the blood pressure in cases of hypertension is still uncertain It has been reported that after three or four months' treatment the blood pressure has remained at a lower level, even when the drug was withdrawn , but this observation needs confirmation

Wanstead Hospital London E 11   ERIC FRANKEL

ÆTIOLOGY OF CHRONIC GASTRIC ULCER

SIR,—I read with great interest the article of Jan 27 by Mr Doran on the vascular component in the ætiology of chronic gastric ulcer, and his conclusions on the relation between mucosal filling and sympathetic action

It will be recalled that the observation by Barclay and Bentley [1] on the gastric arteriovenous anastomoses included not only the microscopic appearance of injected material but also the macroscopic colour changes of the gastric veins in response to stimulation during operation under general anæsthesia , in one case the saturation of a surface vein rose by 17% in three minutes Under high spinal analgesia the veins did not become pink on handling but retained the normal dark colour associated with unsaturated hæmoglobin

In Mr Doran's series it would be of considerable interest to know, first the height of the epidural block and hence the completeness of the sympathetic block, and secondly what colour changes were observed in the gastric veins during all the laparotomies But even with these data the observed results would not be quite comparable with those of Barclay and Bentley, who used intrathecal instead of epidural block as the method of sympathetic blockade

I have noticed that in some laparotomies under a combination of high epidural and light general anæsthesia the arteriovenous colour contrast is not so consistently marked as under spinal anæsthesia, although a profound vascular hypotension indicated a near total sympathetic block I do not know the explanation of this observation unless it is that the longer time required for complete development of epidural analgesia permits the transmission of a certain number of stimuli at the commencement of operation, and once opened the arteriovenous shunts remain open

Oxygen desaturation changes in gut blood vessels deserve further accurate study, and it is possible that quantitative observations by photo-electric [2] and spectroscopic oxymetry or blood gas analysis under varying conditions of autonomic block will throw more light on the ætiology of chronic peptic ulceration

Southbourne Emsworth Hants   P R BROMAGE

MASS RADIOGRAPHY

SIR,—If Dr Hoffstaedt (Feb 3) believes that the mass radiography method can be a potent force in a programme of tuberculosis control by the earlier diagnosis of active cases than is otherwise possible, then I am happy to declare an identity of view But I must criticise his aptitude for drawing theoretical conclusions from his figures in ignorance of practical considerations If it is really true that a unit in region 1 can only find 25,000 people to examine in a year because of the dispersion of the population, then I can only suggest that the unit should move to areas where the population is denser

The efficiency of a unit must be judged by its absolute results, not by " over all discovery rates " , and I have suggested two targets which should be regarded as minima (*a*) the discovery of 200 new active cases of tuberculosis per year for those who believe that tuberculosis case finding is the only justification for mass radiography , or (*b*) 46,000 examinations per year for those who recognise the benefits of the by products of mass miniature radiography unconnected with tuberculosis. In my opinion, a unit failing to reach either of these targets should carefully examine its methods and approach My own unit during 1950 made 54,965 examinations and discovered 263 active cases of tuberculosis I must maintain that 167 discoveries in a year compares ill with 200 and still more so with 263 I challenged Dr Hoffstaedt's criticism and conclusions about mass miniature radiography because he is apparently unaware of what can be done

Two final points First, $3^1/_2$ million examinations a year is the potential of the full 70 units already planned by the Ministry of Health Second, as every medical director knows, a thousand examinations can easily be made in two days, but not every working day is spent in taking miniature films The expression was used, of course to emphasise the smallness of the contact groups in terms of mass radiography work Dr Hoffstaedt wonders what my unit does during 150 working days for which he is unable to account I can tell him It does almost exactly twice as much work as he believes possible There lay the misconception on which his original paper was based

---

[1] Barclay A E. Bentley F H. *Brit J Radiol* 1949 22 62

[2] Hartman F W Behrmann V G Chapman F W *Amer J clin Path* 1948 18 1

F D BEDDARD
Director
South east London Mass Radiography Unit

Grove Park Hospital,
London, S E 12

REGISTRARS

SIR,—One point which seems to have escaped your correspondents in writing about the registrars threatened with dismissal concerns the retiral age of consultants Some of them in the provinces go on for 2 or 3 years after they have turned 65, and where they happen to be members of regional boards it is difficult to believe that the advantages and disadvantages of this arrangement have been considered entirely on their merits When they were themselves registrars they were not kept kicking their heels by Peter Pans at the top of the queue If these old gentlemen want to work after 65, they should be like the retired admirals in the war who cheerfully became lieutenants, house surgeons are wanted in some places But they have no right to rob these deserving young men of their jobs and of experience I go round the country doing "locums" and see quite a lot of this pilfering by persisting in office It is very hard to protest locally, and almost impossible for a young man

Beckley Rye Sussex. C G LEAROYD

RESPONSE OF MEGALOBLASTIC ANÆMIAS TO PENICILLIN

SIR,—During the past year's work in Kenya on the anæmias of Africans, we were repeatedly struck by the response of some cases of megaloblastic anæmia to crystalline penicillin (sodium salt) G administered for intercurrent infections

On Nov 7, 1950, we examined a negress patient with megaloblastic anæmia The red cell count was 1 700,000 per c mm , hæmoglobin 5 0 g per 100 ml , and hæmatocrit 17%, and the sternal marrow contained megaloblasts and giant stab-cells there was complete histamine fast achlorhydria The patient had had several previous relapses of anæmia, and had been successfully treated with crude or refined liver Although she had no nervous symptoms the findings strongly suggested pernicious anæmia, which so far as we are aware has not been described in the Negro races of Africa

After five days observation, during which her reticulocytes were stable at 1 0-1 4%, she was put on to 400 000 units of crystalline penicillin daily for seven days By the sixth day of this treatment her reticulocytes had risen to 36%, and the red cell count to 2 420 000 per c mm , the hæmoglobin to 5 8 g per 100 ml , and the hæmatocrit to 24% The patient was discharged from hospital with a red cell count of 4,290,000 per c mm , hæmoglobin 12 0 g per 100 ml , and hæmatocrit 38% She visited us as an outpatient on Feb 3, 1951, when she had a red cell count of 4 900,000 per c mm hæmoglobin 13 5 g per 100 ml , and hæmatocrit 43%

The megaloblasts disappeared from the marrow very rapidly after the treatment and the giant stab-cells much more slowly, after treatment was started The only treatment given to this patient during the whole period was 2,800,000 units of penicillin

During the past month we have similarly treated with penicillin the megaloblastic anæmias of pregnancy, with the same striking results The response of both these types of megaloblastic anæmia to penicillin is in every way similar to the responses that we obtain to liver, folic acid, or vitamin B_{12} both in the Kenya cases and the Macedonian anæmias

The mechanism by which penicillin produces these responses is not at present clear , but we suggest that it may act in any or all of the following ways

(1) By changing the flora of the gut, or removing antagonists or competitors or other factors that may be interfering with the synthesis, absorption, or utilisation of hæmopoietic factors

(2) By interfering with bacterial metabolism in ways that may result in the release of hæmopoietic factors for the use of the body itself (i e , glutamic acid metabolism, which is known to be affected by penicillin)

(3) By affecting protein metabolism, and the synthesis of nucleoproteins from basic amino acids

(4) By virtue of its content of hæmopoietic factors such as vitamin B_{12}

A full report of these findings will be published in due course

HENRY FOY
ATHENA KONDI
ANTHONY HARGREAVES

Wellcome Trust Research
Laboratories Nairobi

A THERAPEUTIC EXPERIMENT IN PEPTIC ULCER

SIR,—I have read with interest Dr Stolte's article of Dec 23 Certainly therapeutic studies of placebos are of scientific interest However, Dr Stolte's conclusion that "any treatment for exacerbations of peptic ulcer has a chance of success" seems to me misleading.

In 1947 Gill[1] reported that of 20 patients treated with injections of a physiological saline solution very good results were obtained in 19 (95%) This is considerably better than the results obtained by Stolte yet Gill rightly concluded that ulcer patients should not be treated exclusively with a solution of common salt.

These two investigations prove that the psychical influence of the physician on the ulcer patient is of great importance To conclude from this, however, that any ulcer therapy has a purely psychological effect seems to me very far fetched, especially when we take into consideration such results as those obtained with 'Robaden'[2] in experiments on the rat, ulcers were unaffected by a placebo, whereas with robaden the number of ulcers was reduced

Robapharm Laboratories Ltd ,
Basle W ROSENBERG

DERMATITIS HERPETIFORMIS TREATED WITH CHLORAMPHENICOL

SIR,—This is a record of the first case of dermatitis herpetiformis to be treated in this hospital with chloramphenicol

The patient, a housewife, aged 52, had a spontaneous pneumothorax twenty five years ago, but no tuberculosis was found Five years ago she had an ovarian cyst removed. Her husband and one child, aged 19, are both alive and well.

The patient never had any skin trouble until twenty months ago, when her mouth became ulcerated, and thereafter she had repeated crops of vesicles on the palate, throat, cheeks, and base of the tongue , these readily formed shallow excoriations, causing considerable discomfort Intervals of freedom between attacks were brief

Six months ago, while using a plastic comb, she scratched her scalp, which bled slightly The few small abrasions did not heal, but gradually extended until the whole of the crown of her head was covered by offensive-smelling erosion and scab, against which penicillin and other ointments proved ineffective

Eleven weeks ago three fingers became septic, and one required incision Nine weeks ago a rash developed on the greater part of the body, with associated irritation Eight weeks ago (Oct 25) the patient was admitted to hospital

On admission the area over the vertex was uniformly raw and red, partly devoid of hair, with the surrounding hair matted by ointment and exudate There was pus under the proximal part of the red and thickened nail bed of one finger, paronychia of two other fingers, and pitting of several finger nails Shallow red erosions were found on the mucous membrane of the palate, buccal wall, and sublingual region, while many vesicles and bullæ of varying sizes, with erythematous bases, were present, mainly on the lower abdomen, but also on the rest of the trunk and on the limbs some had already ruptured and a few were secondarily

---

1 Gill A. M. *Lancet* 1947, i 291
2 Grandjean E *Rev méd Suisse rom.* 1948 7 447

infected. Heart, lungs, and other organs were normal; no adenopathy.

Blood-count showed: hæmoglobin 90%, white cells 8800 per c.mm. (polymorphs 68%, lymphocytes 25%, monocytes 5%, and eosinophils 2%). Dermatitis herpetiformis was diagnosed.

For the first six weeks after admission the patient's condition remained unchanged. As vesicles and bullæ ruptured, dried up, and left deeply pigmented areas, so new vesicles and bullæ appeared. Local treatment was extremely painful and necessitated many hours of nursing care each day. Bleeding occurred from the bases of a number of the ruptured bullæ; there was slight axillary adenopathy; and the patient had mild intermittent pyrexia with a temperature up to 100·4°F. A full course of sulphapyridine for three weeks had no effect, and intramuscular injections of 'Anahæmin' 2 ml. on alternate days for two weeks had very little effect.

Blood-counts were as follows:

Nov. 8.—White cells 12 600 per c.mm. (polymorphs 63%, lymphocytes 17%, monocytes 11%, eosinophils 8%, basophils 1%).

Dec. 1.—White cells 15 200 per c.mm. (polymorphs 79%, lymphocytes 16%, monocytes 2%, eosinophils 3%).

Dec. 12.—White cells 10 900 per c.mm. (polymorphs 66%, lymphocytes 30%, eosinophils 4%).

Dec. 15.—Hæmoglobin 80% (11·8 g. per 100 ml.); white cells 10 300 per c.mm. (polymorphs 75%, lymphocytes 21%, monocytes 1%, eosinophils 3%).

Two weeks ago (Dec. 11) treatment was begun with chloramphenicol by mouth, 1 g. five times daily for six days, followed by 0·5 g. five times daily for two days and 0·25 g. five times daily for four days. Since then the patient's progress has steadily continued; old lesions have dried up and only a few very transient small vesicles have appeared in the region of both knees and wrists. Her profound depression was rapidly replaced by a very natural cheerfulness.

Since no report could be found of the effects of chloramphenicol in this condition, it was decided to use a large initial dosage in order to achieve the maximum success as quickly as possible. Although this is only an isolated case, the rapid and dramatic improvement in the patient's general and local condition warrant further trials of chloramphenicol in other cases of this most distressing condition.

I have to thank Dr. W. J. O'Donovan for permission to publish this note.

Whipps Cross Hospital,
Leytonstone,
London.

N. A. THORNE
Senior Registrar,
Dermatological Department.

SCIATICA AND LUMBAR PAIN

SIR,—I may have been lucky in my cases of "sciatica." Of nearly 150 treated in the past few years, only 6 had true sciatica. The remainder, although they had been previously diagnosed as sciatica and had not responded to treatment, were in fact cases of more or less severe gluteal fibrositis, giving rise to sciatic pain.

Obviously, if the gluteal muscles are spastic and painful on pressure, straight-leg movement will be impaired. Forward flexion of the body will put these affected muscles on the stretch, giving rise to sciatic pain. Sciatic pain can be produced in these patients by pressure over the myalgic spots in the gluteal muscles, and it is quite common to find the only spots causing this long-standing pain high up in the origin of the gluteus maximus in the superior curved line of the ilium, or even in the tensor fasciæ latæ.

I do not dispute that prolapse of an intervertebral disc will give rise to sciatica or lumbar pain; but my plea is for more conservative treatment, and in my experience daily treatment with the much-maligned adrenaline cream, massaged into the buttock on the affected side, paying special attention to the true myalgic spots, will usually provide relief. With this treatment it is not unusual for patients to become completely free from pain of long duration within one week.

London, W.1. LOUIS MOSS

VACCINATION AGAINST SMALLPOX

SIR,—In the statements circulated to the press regarding the vaccinal condition of the cases of smallpox at Brighton, I noticed that nothing was said about the revaccination of the first fatal case. I have a letter from Dr. Rutherford Cramb, medical officer of health for Brighton, in which he says that this patient had been vaccinated in infancy and in 1916. Dr. Cramb adds that he does not think it "took." This point does not affect the actual fact that the man had been revaccinated in 1916. This should have been mentioned in any account of the vaccinal condition of the cases.

London, N.W.10. S. P. VIANT

LEUCOCYTE-COUNTS IN THIOURACIL MEDICATION

SIR,—While several criticisms can be made of Dr. Holliday's conclusion (Feb. 3) that leucocyte-counts cannot safely be omitted from the programme of routine supervision in patients undergoing thiouracil medication, one can be stated briefly.

His chief basis for the conclusion appears to be that the mortality-rate in 11 cases of agranulocytosis detected by leucocyte counts was 18% while in 15 cases detected by symptoms it was 46%. The difference in mortality-rates was therefore 28%. Twice the standard error of the difference is, however, about 35%, so the observed difference in mortality-rates is not statistically significant and might readily therefore be due to chance.

Royal Infirmary, Bradford. C. J. YOUNG

RECENT HISTORY OF CORONARY DISEASE

SIR,—It seems possible that the surprising results reported by Dr. Morris in his article of Jan. 6 and 13 might be explained on the hypothesis that arterial calcification is a process in part independent of atheroma (though atheroma provides a setting for it) and much more dependent on physiological ageing.

It is a commonplace that during the last forty years the period of active life has increased greatly. A man in group I or II of the Registrar-General's classification is expected to continue working until he is between 65 and 70 or even older—though of course less actively than when he was younger. It is common to find a solicitor, or executive, interested in gardening or some other physical activity even at 75; and I well remember being walked 27 miles over the Surrey hills by an old friend in his 67th year. Women have also changed; a woman of 70 may still run her home with the minimum of help, and be more independent than was her mother at 50. That is, all ageing processes, calcification among them, are being postponed.

To me this delay of senescence is the most remarkable biological phenomenon of our time. Men and women live to be older in years, but their activity changes little once they have passed the age of 50, and their senescence is correspondingly delayed; when it does arrive, it is shorter. I have been astonished by the number of my father's friends who decided to retire only when overtaken by some localised physical weakness at ages of 70, 75, or even more; they seem to me to be little older than the men of 55 whom I met before 1914.

This may be a local phenomenon. During the late war I met many students from Central Europe; they usually appeared much older than their English contemporaries, and one confided to me that the most surprising thing in England was the youth of the professors. When I told him their real age he was thunderstruck, for they were in fact rather older than the professors in his native country, who appeared far nearer senility.

In England this retardation of senescence appears to hold for groups I, II, and III of the Registrar-General's classification, it is less obvious in group IV, and much less evident in V It seems possible that factors such as nutrition and exposure to the elements may play a part, and it might therefore be worth comparing the incidence of coronary calcification in group V at ages 65–75 with groups I and II at ages of 80 and upwards Alternatively, the hypothesis that the change is due to the reduction in consumption of alcoholic beverages might be considered

Department of Pathology
Central Middlesex Hospital
London, N W 10

GEORGE DISCOMBE

POLIOMYELITIS AND POLIOENCEPHALITIS WITH OPSOCLONIA FOLLOWING APPENDICECTOMY

SIR,—Dr Simpson suggests in his letter last week that the case I reported under the above title (Jan 27) might have been a case of *acute porphyria* He bases this suggestion on five features which he states are most unusual in poliomyelitis but typical of acute porphyria I should like to point out that three of these features (viz, "*considerable* delirium at the onset," "ascending flaccid paralysis," "pyrexia continuing for five to six weeks") were not reported by me A fourth feature (viz, "retention of urine at an early stage"), as I pointed out in my paper, has recently been reported "as being frequently encountered in the poliomyelitis patients both before the onset of paralysis and after"[1] My account of the examination of the cerebrospinal fluid contained only the abnormal features, there were no red cells present

There is, however, further circumstantial evidence to suggest that this was a case of poliomyelitis Two nurses who had come in contact with this case developed typical poliomyelitis within the period of incubation

London W 5

M D WARREN

NURSING INFECTIOUS DISEASES

SIR,—Dr Stanley Banks's letter of Feb 3 must have shocked many readers in its revealing statements on the nursing situation in some of the infectious diseases hospitals Most especially note should be made that "commonly a newly qualified general trained nurse has admitted that she has never had any practice in handling a baby, or in the principles of infant feeding" This becomes a double tragedy when such a nurse, assuming duty as a staff nurse, finds herself trying to cope with 25 infants and children, all under five years of age, acutely ill with whooping cough or measles

How is it that general trained nurses may not obtain any experience in an infants department, and how is it that, where a general hospital nursing school is inadequate in this respect, arrangements are not made with another hospital where an adequate infants department exists? Heads of nurses' training schools have a particular responsibility in this, no doubt arrangements are not always easy, but one feels that in some schools very limited attention may be given to this aspect of a nurse's training If it is true that general trained nurses are having to face unexpected and unacceptable urgent nursing responsibility for infants and young children then the sooner it be universally recognised that a S R C N is a very valuable person the better No field of nursing calls for higher skill or more precise techniques than does the handling of acutely sick infants Most certainly this is not the simple task which, even in high places, is sometimes assumed

Probably every general trained nurse should spend at least six months in a children's hospital or, if it is big enough, in the children's department of the general hospital The very small series of lectures in "children's diseases" now usually given to nurses in general training covers only a few general principles and momentarily lights up the trainee's interest in a fascinating subject

With regard to the dilemma which Dr Stanley Banks describes, of one student nurse and one ward orderly trying to cope with a ward full of ill children, is it not possible (even in an "infectious diseases hospital") for some of the mothers or near relations to go in with the child and look after him or her? In these hospitals, we are told, there are "hundreds" of empty beds why not make some of the empty wards into temporary residential accommodation for the nursing parents, and especially for young mothers? Such an arrangement, as well as helping the hospital, would satisfy all the more enlightened principles of parent child relationship in hospital The experience would be of educational value to the mothers, and it would give them a sense of satisfaction and perhaps enhanced confidence through having *contributed substantially to their child's recovery*

Department of Child Health,
University of Bristol

A V NEALE

MUNCHAUSEN'S SYNDROME

SIR,—Munchausen's syndrome, of which Dr Asher wrote on Feb 10, must be fairly common, since most doctors working in general hospitals have met several cases, even allowing for some distension of the truth in their stories It would not be so important were beds not so short On the contrary, in better times these cases provided interesting exercises in diagnostic ingenuity

The present problem is how to avoid wasting beds on them Regional hospital boards and boards of governors should keep "Munchausen lists" from details supplied by their hospitals (some do this already) Should a doctor have suspicions, he could ring up the board But when should we become suspicious? Being doctors and not detectives, few of us are suspicious at once The main points are, I think, a slightly improbable story in a patient not sent in by a doctor A scarred abdominal wall makes it easier

A recent early case of Munchausen's syndrome walked into the receiving room coughing blood It started, he said, after a lorry crash in the north of Scotland, but he gave the name of the hospital in Scotland as the "Royal George" We thought this sounded more like a "pub," and soon confirmed that no such hospital existed A really difficult case may justify a search of the patient's clothing, in one case of mine this revealed evidence of a recent stay in prison at a time when the patient said he was in hospital

Dr Asher has done a service in providing a concise name for these cases I suggest that, when letting one of them take his own discharge, we tell him that we have found him to be suffering from Munchausen's syndrome Assuming that all casualty officers have read Dr Asher's excellent article, he might then, by announcing his diagnosis cut short his stay at his next place of call In spite of all this we must not forget that those with the Munchausen story, though tricksters, may yet be mentally, and sometimes physically, ill, and that we who are not can, as well as being clever, also be kind

Chase Farm Hospital,
Enfield Middlesex

C ALLAN BIRCH

SIR,—Our thanks are due to Dr Asher for his able description of Munchausen's Syndrome I should however, like to register a protest on behalf of the great Baron von Munchausen, who was far too wise a fool ever to have put himself in peril of having to undergo an abdominal operation, a plausible and likable rogue he would have been more likely to describe a new syndrome he had observed than one suffered by him

It is admittedly hard to improve on Dr Asher's name for the syndrome but, bearing in mind the amount of myth associated with these patients, their constant suffering, their lack of any fixed abode, their multiplicity of names and their apparent immortality, would it not be better known as the Ahasuerus[1] syndrome? The disadvantages are that a wrong ætiology and racial incidence may be inferred, but these objections also apply to the established eponym Œdipus, without having caused any confusion or international misunderstandings

---

[1] Critchley M in the Medical Annual London 1948 p 256

It is surprising that Dr Asher has not discussed the treatment of this condition yet it was a compatriot of von Münchausen, Till Eulenspiegel,[2] who emptied a hospital by explaining to the patients that he would make a universal remedy from the ashes of a sick man to avoid any unnecessary waste, the sickest man would be burnt—the last man out when Eulenspiegel should call for those who had been cured to leave A cure rate of 100% was recorded, but there were unfortunately numerous relapses after the healer had left the district

Cheam Surrey PAUL WINGATE

POTASSIUM DEFICIENCY IN IDIOPATHIC STEATORRHŒA

SIR,—The interesting case report last week by Dr Lubran and Dr McAllen illustrates the importance of potassium deficiency in the steatorrhœa syndrome According to our experience in Birmingham hypokalæmia in varying degrees of severity may be expected at some time in at least 20% of patients with this disorder From the reported case-records it seems likely that hypokalæmia is a common immediate cause of death. Of the 14 fatal cases in our series, at least 7 died in this way, but, with the recognition of the therapeutic importance of potassium, 3 cases have been resuscitated from clinical states previously considered irreversible. More moderate degrees of potassium deficiency may be detected following rapid weight-loss and in association with marked muscle weakness and diminished reflexes It is also probable that the excessive lassitude experienced by many of these patients may result from a general deficiency of electrolytes and of intracellular potassium in particular

Hypokalæmia is not necessarily associated with diarrhœa Some patients have only 1–3 large bulky stools daily, loose but not watery The fæcal excretion of potassium at such times is often 5–7 g daily Even when the stools are normally formed and the patient is apparently well the daily excretion often remains between 2 and 4 g It may well be that one of the beneficial effects of a diet rich in meat is the additional potassium provided

In considering electrolyte excretion in the fæces, there is evidence that sodium and potassium are both reabsorbed and excreted from the intestinal lumen Normally fæcal potassium is negligible and it is excessive only when the body's reserves of sodium are threatened as in diarrhœas of varied ætiology In such states it is probable not only that reabsorption may be diminished but also that potassium is actively excreted The low blood-pressures commonly found in these cases may be an expression of the unstable electrolyte exchanges in steatorrhœa, of 100 cases of idiopathic steatorrhœa, 38 had at some time a systolic pressure of 95 mm Hg or less, irrespective of their clinical condition Clinically the rapid gain in weight that may occur with the administration of potassium by mouth suggests that much of the potassium appearing in the fæces has been derived from the intracellular stores For example one patient, after losing 26 lb in eight months regained this weight in eight weeks with oral potassium therapy

A protest must be made therefore at the assumption by Lubran and McAllen that failure of potassium absorption is the cause of the hypokalæmia in their case Failure of absorption has been the traditional explanation for deficiencies in the steatorrhœa syndrome, and flat tolerance curves have been regarded as proof positive of the theory Evidence is accumulating that this simple hypothesis cannot be the complete explanation for many of the deficiencies encountered

Department of Medicine
University of Birmingham W TREVOR COOKE

RESULTS OF SURGERY IN SCIATICA AND LOW BACK PAIN

SIR,—You have created a most unusual precedent in publishing a scientific contribution four months before it was read, acknowledging the fact quite bluntly in a footnote, and drawing special attention to the article in editorial comment For some reason that is not easy to understand Mr Burns and Mr Young have thought it wise to submit to you material that was to have been presented to the International Society of Orthopædic Surgery and Traumatology next May, which would certainly have been the property of that society thereafter, and is probably their property now It may be, of course, that in the circumstances the paper will not be read at all. Certainly most Colleges, Associations and Societies do not knowingly permit the reading of papers that have already been published long before

London W 1 REGINALD WATSON-JONES

*** The authors of this paper were anxious that their findings should appear as soon as possible When they sent it last October, they frankly stated that one of them was going to read a paper based on the same material at the congress of the International Society in May, but they clearly did not regard this paper as the property of the society, nor did we think we were infringing the society's rights by publishing it In retrospect, however, we agree that we were not entitled, without the society's permission, to give a private contribution the cachet attached to the use of the society's name and we regret that this permission was not asked —ED L

CURRENCY FOR TREATMENT ABROAD

SIR,—Since the war, shortages of foreign exchange have led to restrictions on the number of people going abroad for health reasons Since 1947 applications for currency for patients to undergo medical or surgical treatment overseas have been considered by the Exchange Control Medical Advisory Committee, a panel of experienced consultants set up to advise the Treasury as to cases where currency should be allowed Particulars are submitted through the patient's doctor direct to the committee and each case is considered individually Hitherto currency has been allowed in cases where the treatment offered a reasonable prospect of cure and where the treatment could not be had in the United Kingdom or in another part of the sterling area During the last twelve months 93% of those who applied have been granted currency

The committee is now pleased to be able to announce that it will be possible to relax the hitherto rigid rules under which applications for certain European countries have been dealt with. The Treasury have decided that as the result of the establishment of the European Payments Union, of which this country is a member and of Britain's present favourable balance of payments position with the other members of the Union it will be possible to release more currency for travel for health reasons in certain countries In future, therefore currency will be available for treatment in any of the countries listed below in cases of genuine illness, irrespective of whether treatment can be obtained in the sterling area Chronic ill health will be considered on climatic or other reasonable grounds

The countries are Austria, Belgium France Greece, Italy, Liechtenstein, Luxemburg the Netherlands Portugal (including Madeira and the Azores), Spain

---

[1] Ahasuerus = Cartaphilus = Buttadeus = Lakedæmus = The Wandering Jew

[2] Ein kurzweilig Lesen von Dyl Ulenspiegel Strassburg 1515

(including the Canary Islands), Switzerland, Turkey, and the Western Zones of Germany

The procedure for obtaining a permit enabling the patient to purchase currency remains the same the patient's doctor is asked to send a statement of the medical condition together with his recommendation for treatment abroad to the Medical Secretary, Exchange Control Medical Advisory Committee, Tavistock House North, Tavistock Square, London, W C 1

The rules for applications for currency for treatment in countries not listed above remain unchanged, except that where treatment is available in countries on the above list currency will not be provided for a country not on the list In the case of Norway, Sweden, and Denmark, in view of special arrangements with these countries, currency for travel is freely available and it is no longer necessary to apply to the committee, applications should be submitted direct to a bank, who will advise on the details required

The members of the committee are grateful for the help they have received from doctors The need for currency restrictions of this kind is *not* relished by anyone, but we believe the system is working fairly and that it enables those who genuinely require to use currency for overseas treatment to receive permission with the minimum of formality

Exchange Control Medical Advisory Committee Tavistock House North, Tavistock Square London W C 1

HARLEY WILLIAMS
Secretary

PROSPECT OF WAR

SIR,—In this correspondence, the psychologists make great play with the concept that fear and provocation are in full swing in both international camps and dub these emotions as psychopathic There is mental confusion here, due to the two different meanings of the word "fear" There is nothing psychopathic in fear, as denoting the realisation of danger It is, in fact, an essential factor in survival Nor is it psychopathic to take precautions against an envisaged danger It would be better to use the word "panic" for irrational or disproportionate fear Similarly it would be well to drop the use of the words provocation and paranoia to describe rational precautions against a clearly perceived danger I see no panic fear in my countrymen in general, but it is plainly to be seen in some of our Professors

Bridlington

P D H CHAPMAN

SIR,—I wonder whether your readers experience the same feeling of helplessness, tinged with exasperation, that I do when I read of the comings and goings of the politicians and diplomats? At the present time we have the sorry spectacle of the members of the United Nations acting as judges and counsel on their own disputes instead of submitting them to a *real* International Court of Justice, which men of good will throughout the world would honour and whose decisions they would be prepared to back up Whilst there are good arguments against an International Police Force, I do not think it would be difficult to recruit the judges for the above court

I am inclined to think that Dr Alex Comfort is right when he condemns these power addicted men who are moved more by considerations of prestige than the desire for peace I can see no hope for peace, unless the non powerseekers combine all over the world (and I include the U S A and the U S S R) to insist that the politicians shall cooperate or compromise or else clear the way for others Such an organisation could be called the Society for the Prevention of Cruelty to People Alternatively, politicians should be debarred from holding office for longer than one year, and I can even foresee that conscription of reliable citizens as M P s, backed by a neutral civil service, may be found necessary

There is no logical reason why the world's resources should not be assessed and exploited for the human race by an organisation parallel to the aforementioned international court It has always amazed me that as a profession we struggle to save the lives of a few, whilst the politicians can direct the destruction of many

Hull

L I HARDY

SIR,—Dr Lindsey Batten (Feb 10) gives a moving and sincere analysis of the terrible predicament which is looming up Yet I would wish to enlarge and modify his picture

I believe he is correct when he points out that there have been occasions in the past when men of good will simply *had* to fight a war But the world situation today is unprecedented in the degree to which, for purposes of war and peace, this is "one world" No longer can any country's problems be *solved by war*, because of the wholesale destruction of man's productive powers which atomic war inevitably entails The certain result of a world war in this atomic era would be the devastation of enormous areas those who imagine that on the whole their particular areas and creeds would emerge the stronger would do well to reflect that the highly industrial west is far more vulnerable than the predominantly agrarian east, and that the breakdown of western civilisation would result in the appearance of Communism in *all* the devastated countries These are cogent reasons for insisting on the abandonment of war as an instrument of policy—*and they are reasons which have never before existed*

Kindliness, humanitarianism, ordinary productive work, and the fundamental satisfactions of freely expressing our individual talents in our social life—these are the values which we feel we must fight to preserve But how to fight for them? Are they to be preserved by war which multiplies a thousandfold the situation in Nagasaki, where women are *still* aborting and giving birth to monsters five years after the explosion of one atomic bomb? By war which will place those doctors (who do not think hard and courageously here and now) in the company of the builders of the gas chambers, the war criminals, the released armament kings—which is already using our military personnel to teach the Germans how to fight under their former Nazi generals!

Are those the weapons which will enable our values to triumph? Some will answer "No, but we must seek what allies we can" To say this is simply to state that "the end justifies the means"—forgetting that the end is destruction, and that the whole spirit of that remark is exactly what is held to be the menace of totalitarianism Can we prevent murder by wholesale murdering?

No the fight is on another level—that of all of us as reasonable individuals We have to understand the insidious drift to war as well as the pathology of the open war seekers We have to appreciate the limbo of dulled apathetic negativity into which our organs of written and spoken opinion have unwittingly led us A month or two ago a well known magazine featured coloured photographs taken from the aeroplanes which showered jellied petrol *and other* bombs upon Korean villages, and remarked upon the strange beauty of the scene . . So far have we gone along the road to megalomania, paranoia, and perversion Instances could be multiplied

Politicians, caught in the complicated mesh of party politics, cannot think straightly

Only ordinary decent people who are prepared to think, to face their consciences, and then to act—only these can catalyse our recovery from this drifting nightmare There are already thousands of such people (some of them already active in the various peace movements). There must be hundreds of thousands as quickly as possible, once that order of magnitude is attained, there will be millions, and the first essential step to sanity will be taken with the repudiation of despair and destruction. *Peace will break out.* People's heads will lift, and the men of little stature in our governments will suddenly realise what a healthy democracy means.

Action of this kind will not be easy for each of us (how could it be in our present situation?)! We shall be attacked by those fearful that we favour unilateral disarmament in our present plight. To them it must be patiently explained that we do not propose any such thing, but rather the public and national repudiation of war as suicidal, and the careful examination of schemes for multilateral disarmament which are already in being.

As individual doctors, we can do a great deal to wake people up out of this nightmare—but there isn't much time. If we do not do our utmost, we shall (even though dead) bear a heavy responsibility as citizens of a country which could have turned the scales in favour of sanity at a most critical moment in the history of mankind.

I firmly believe that, as a matter of plain fact, this country *can* do it. I seek your help in the publication of this appeal.

London N.W.3 A. F. MOHUN

SIR,—We have been gratified to find, from private correspondence as well as from that published in THE LANCET, that so many colleagues share our point of view. Disagreement would appear to be based upon three premises: (1) that problems of peace and war are political and are not suitable subjects for a medical journal; (2) that the appeal was addressed to doctors in the wrong countries; and (3) that the danger of war derives solely from Russian aggression. In summary, our answers to these points are:

1. Doctors have a social responsibility as well as a personal one to their patients; they have an ethical tradition and an international allegiance. War is a symptom of mental ill health. Its results include wounds and disease. Doctors are, therefore, properly concerned in preventing it. An "epidemic of trauma" requires prophylactic treatment as much as any other epidemic.

2. We accept the suggestion that an appeal to doctors should be international in its scope. If citizens in other countries do not possess the same type of personal liberty which we have here, this does not absolve us from our own duty. The government and press of each country attribute the blame to others, but dare we assume that none of the responsibility is on our side? A war may start because either one of two parties wishes it or because both sides are stampeded into it by imaginary bogies. Each country should avoid decisions which can be misconstrued and should ensure that actions taken are determined only by real dangers.

3. It is not, in our opinion, true that the sole danger of war rests with Russian aggressiveness. Clearly it would not be possible to reach agreement here on what constitute real threats from the East; but the nature of propaganda makes it inherently likely that some, at least, of the publicised threats are exaggerated. Moreover, we believe, that some recent actions of the Western powers may not unreasonably be interpreted by others as being aggressive (whatever have been the intentions behind them). To specify, there is the advance beyond the 38th parallel in Korea, the occupation of Formosa, the decision to build a new German army, and the release of Krupp and other Nazi supporters.

Some, we recognise, will not accept these arguments; but supposing they are valid, what should we, as doctors do? Why, for instance, could we not take seriously Dr. Lambert's suggestion of a health race instead of an arms race? Much thought is needed before we are entitled to answer these questions. We therefore propose that a forum should be created on which a policy acceptable to a large proportion of the profession can be determined. We ask all who are interested to write to us so that they can be invited to take part in an exploratory meeting.

RICHARD DOLL
ALFRED ESTERMAN
IAN GILLILAND
HORACE JOULES
DUNCAN LEYS
LIONEL PENROSE
MARTIN POLLOCK

24, Lansdowne Road
London W.11

Obituary

CLARE OSWALD STALLYBRASS

M.D. Lond., M.D. Lpool, D.P.H.

DR. C. O. Stallybrass was a member of the medical staff of the public-health department of the city and port of Liverpool for over thirty years. But he never allowed administration to take first place or to make him anything less than Locke's "whole, sound, round-about man." First and foremost he was a good doctor, and he was never cribbed and confined in his chosen field of public health. He loved medicine, and his work was done in the fertile atmosphere of that tradition.

[Liverpool Daily Post

He was born in 1881, son of the late Rev. W. O. Stallybrass, of Wallasey. From Birkenhead School he entered the University of Liverpool in 1898 and he took the Conjoint qualification in 1905, graduating M.B. Lond. with honours two years later. During his house-appointments at Liverpool Royal Infirmary and the Maternity Hospital he had already become interested in preventive medicine, and after a year as R.M.O. at Parkhill Fever Hospital he took his D.P.H. In 1909 he became assistant medical officer in the Liverpool port medical service. He started a campaign of rat-searching and rat-proofing of ships, and his methods have since been copied throughout the world. In 1900 he took his M.D. Lond. in State medicine.

During the 1914–18 war Stallybrass's career at Liverpool was interrupted by his service abroad as a sanitary officer in Macedonia and later as a specialist with the Serbian Army. For his work during an epidemic of typhus he was awarded the Order of St. Sava. On his return to Liverpool he was appointed an assistant medical officer to the city, and he became the epidemiologist of the strong team headed by E. W. Hope, which did so much to develop Liverpool's health service. Stallybrass's *Principles of Epidemiology,* which first appeared in 1931, revealed a mind of high quality. It was a departure from tradition, at least in this country, for it was an attempt by a doctor engaged in the day-to-day work of a health department to bring within one compass the sum of contemporary epidemiological knowledge. With Hope, and, later with Prof. W. M. Frazer, he collaborated in the well-known *Textbook of Public Health* and with Hope and Hanna he wrote *Industrial Hygiene and Medicine.* He was also lecturer in public health to the University of Liverpool for many years.

His medicine was warmed by humanity, and it must have been a delight as well as a challenge to him when, on the transfer of the poor-law hospitals to the local authorities in 1929, he was entrusted with their improvement and development. The task occupied him for years, continuing after his appointment as deputy M.O.H. in 1933. He carried out the work with sympathy and understanding, and his sense of medical tradition and his integrity dissolved many difficulties. During the war years the hospitals of the city withstood the strain magnificently, and looking back it is clear that the hospitals and the community are deeply in Stallybrass's debt

After he retired in 1948 he at last found time to revise his book on epidemiology He continued to take a lively interest in the learned societies of the city, over most of which, including the Medical Institution, he had presided His social conscience, whetted perhaps by his medical work, remained keen and he was an active member of the Personal Service Society and the Merseyside Marriage Guidance Council, and chairman of Liverpool Children's Hospitals management committee He also became a crusader for a bold and intensive attack on tuberculosis, which he urged in his popular lecture when the British Medical Association went to Liverpool last year for its annual meeting On this occasion Liverpool University gave him the honorary degree of M D He died at Clatterbridge Hospital on Jan 28

A colleague writes "Stallybrass had an engaging inability to say no to requests which touched the things in which his heart and mind were employed Lectures, articles, papers, letters—he found time and energy for all, without stint or loss of quality Immersed in his job, he was 'always busy about things belonging to his craft' My most abiding impression of him is perhaps his eagerness He was a tallish, thin man who strode along with a slight stoop forwards as though he wanted to see everything, and who—like an intense but not unwelcome Ancient Mariner—held you while he extracted your views on some problem, or your reaction to some idea or thesis of his When he was president of the Liverpool Medical Institution, there seemed to be no subject on which he could not say something to the point Outside medicine he had the same breadth and depth the Twenty Club found that he was equally at home in stamp collecting, archæology, music, literature, and mountaineering He maintained his eager alertness of mind and heart to the end A man of real quality, erudite, gentle, shrewd, kindly, humble, and unaggressive, he had the affectionate and admiring regard of his colleagues and many friends"

Dr Stallybrass married Irene, daughter of the late Canon Wetherhead, and they had two sons

Births, Marriages, and Deaths

BIRTHS

BINNS—On Feb 3 at Redruth the wife of Surgeon Lieut Commander G A Binns R N—a son
DAVENPORT—On Feb 4 at St Albans the wife of Surgeon Commander J E Davenport R N—a daughter
DICKSON—On Feb 6 the wife of Dr J W Dickson—a daughter
MATHESON—On Jan 28 at Bearsted, Kent the wife of Dr Kenneth Matheson—a son
NAGLEY—On Feb 9 at Farnborough, the wife of Dr M M. Nagley—a daughter
RING—On Feb 2 in London the wife of Mr Peter Ring, F R C.S—a son
SLATER—On Feb 9, the wife of Dr H B Slater—a son
TROTTER—On Feb 2 in London the wife of Dr J K Trotter—a son

MARRIAGES

ARKLE—BUXTON—On Feb 3 at High Beech Essex Clive Ernest Arkle M R C S to Morna Annabel Buxton
COCHRANE—MARGETTS—On Feb 3 in London Alexander Auld Cochrane M B to Nancy Margetts
DOWLING—HOWORTH—On Feb 6 at Preston Edmund John Dowling M B to Elizabeth Howorth M.B

DEATHS

BENNETT—On Feb 3 Henry Ward Bennett, M B Manc
CROSSKEY—On Feb 8 John Henry Crosskey M C M B Birm aged 58
HARVEY—On Feb 2 Percival George Harvey M D Lond
HENDRY—On Feb 8 James Robertson Hendry M B Glasg
MOUAT—On Feb 6 at Sidmouth Janet Ainslie Shiells Mouat M B Edin D P H
POIGNAND—On Feb 1 Ralph Newman Poignand B A M B Camb aged 72
POPHAM—On Feb 4, in London Robert Brooks Popham F R C.P F aged 88
RADFORD—On Feb 6 William John Radford M R C S
SMITH—On Feb 8 at St Albans James Smith M B Edin D.P H
TURNER—On Feb 5 in London Harry Morton Stanley Turner M B F M.D Durh D T M & H F R.S E
WOODROFFE—On Feb 10 Anthony James Warren Woodroffe B A M B Camb

Notes and News

DOCTOR AND PATIENT IN NORTHERN IRELAND

THE Prime Minister's announcement, in October, 1949, of the British Government's intention to impose a charge of up to 1s for prescriptions was followed in Northern Ireland by reports from a number of urban practices that attendances in surgeries fell off sharply for several weeks apparently due to the belief that the charge would apply in Northern Ireland with immediate effect ' This comment is made in the annual report[1] of the Northern Ireland General Health Services Board, which adds "Allowing for people deterred by genuine financial need, this fall in attendances may well indicate that a number of persons attend surgeries unnecessarily or for trivial reasons ' The report says that unreasonable behaviour by patients seems to be increasing, and it cites the following examples threats to change to another doctor if a desired preparation is not prescribed, or if a certificate of incapacity for work is not supplied, irresponsible or thoughtless transfers to other doctors who are thought to be more generous in supplying prescriptions or certificates, failure in non urgent cases to adhere to the proper surgery hours, unnecessary and inconsiderate requests for visits made late in the day or at night, attempts to obtain emergency treatment at inconvenient hours from doctors other than the patient s own doctor when no real emergency exists in order to save the patient trouble, refusal to follow a doctor s instructions, and failure by patients who have complained against their doctor to appear at service committee investigations

TERMINATION OF PREGNANCY

WOMEN who feel they have reasonable medical grounds for seeking the termination of pregnancy are often at a loss to know how to proceed The Abortion Law Reform Association wish to inform them of the proper course to pursue, and of the wider interpretation of the law for which recent decisions in the courts give precedence The proper course, they can now say is for the woman to consult her general practitioner and put before him the physical and mental grounds for her request If he regards the request as reasonable he should take a second opinion, and if this opinion is also in favour of terminating the pregnancy he should arrange for a competent surgeon to perform the operation. Judgments in the *Bourne* and *Bergmann Ferguson cases* give legal precedents to show that it is legal for a patient to ask her doctor for a termination of pregnancy, legal for the doctor to consider the request, and if he endorses it to get a second opinion, and legal for a surgeon to act on such opinions and to operate if these opinions are based on the preservation of the life or the health of the woman and are given in good faith

EMPLOYMENT FOR THE BLIND

"AN employer has to make his business pay and no plan for placing blind people in industrial employment can hope to succeed on any other basis than that the blind worker can and should do a full week s work in return for a full week's wage

These words are the keynote of the report[2] of the *Working Party* set up by the Ministry of Labour who have been considering the facilities for employing blind people The report recognises blindness as a handicap, but as a handicap which can be, and often is, overcome There are about 87 000 registered blind persons in Great Britain, of whom 36 400 are within the normal working age range of 16 to 65 Of these about 11,000 are employed or training for employment. Among the remaining 25,000 of working age it is estimated that about 3000 would be capable of doing a job To give them their chance, the Working Party recommend the expansion of facilities for training and of services for finding suitable jobs Another way to help is they suggest, by breaking down prejudices against the employment of blind people in open industry, as distinct from sheltered workshops In the last 10 years at least 3000 blind people have been placed in normal jobs Light engineering shorthand and typing, telephone switchboards, and physiotherapy are all jobs at which they have proved their worth ' The care of the blind, the Working Party hold, offers scope to both public and voluntary bodies, and the best results will probably be achieved by joint endeavour

---

[1] Northern Ireland General Health Services Board Second Annual Report for the Year 1949–50 Issued by the Board 9, Upper Queen Street, Belfast Pp 38 1s

[2] H M Stationery Office 1951 Pp 72 1s 9*d*

BEHIND THE SCENES WITH SHAW

SECRETARIES of great men seldom remind us we may make our lives sublime Those who see the prophet off duty, knit us mittens, endure his wilfulness, and smile to themselves at his foibles are inevitably more aware of the moss and stonecrop on the colossus than of the noble proportions best seen from a distance Miss Blanche Patch[1] knew Shaw only as an ageing man, his wilfulness and foibles gaining on him as they must on even great ancients, and her stories of him, though kindly and well told, are mainly trivial. All the same they give some idea of the last quiet years, when, as she says, "he was bored with us all and eager to be gone," when the brilliant talker wished to stop talking, and the only passion left to him was work. Some things she tells us which no-one else could, or perhaps would There is a charming section on his postbag, and a good deal, of rather specialised interest, about his diet His relations with his doctors were more reasonable than we have been led to suppose She admits he was attracted by osteopaths, faith healers, and any form of yoga but, on the other hand, when a doctor succeeded in convincing him that extract of pig's liver would cure his pernicious anæmia he placed himself in the doctor's hands and was entirely obedient On the whole, he listened equably to what his doctors had to say and then used his own judgment —which after all is what most doctors do themselves when they are ill.

A VERONESE FOR WESTMINSTER HOSPITAL?

FOR some months Paolo Veronese's *Resurrection* has been hanging over the altar in the Westminster Hospital chapel on loan from its present owners The governors of the hospital now have the opportunity to buy the picture for use in perpetuity in the chapel They will give up to half the cost from their discretionary funds if the remainder is subscribed. Donations should be sent to the Rev C Hildyard, 2, The Cloisters, Westminster Abbey, S W 1

University of Oxford

In a congregation held on Feb 6, the title of clinical lecturer in the university was conferred on the following

D A. Abernethy surgery, R. W Armstrong psychiatry A. D Carleton diseases of the skin A M. Cooke medicine D C Corry surgery, A Elliot Smith, surgery F G Hobson medicine F H Kemp radiology Sir William MacArthur tropical medicine, R G Macbeth diseases of the ear nose and throat P C Mallam medicine W Ritchie Russell neurology J C Scott surgery V Smallpeice diseases of children J A. Stallworthy obstetrics and gynæcology W Stobie, diseases of the chest (till Sept. 30 1954) W B Foley orthopædic surgery till Sept 30 1955)

University of Liverpool

At recent examinations for the diploma in tropical medicine and hygiene the following were successful

G G Bisley S-C Cheng J Devota Z Galis R T Kakade M. Postiglione S K. Rana P H E. Smith, B Teelock P A. Varasoonthrosoth.

Dr S K. Rana and Dr P H E Smith have been recommended for the Milne medal in tropical medicine and Dr P H. E Smith for the Warrington Yorke medal in tropical hygiene

Royal College of Surgeons of England

At a meeting of the council on Feb 8 with Sir Cecil Wakeley, the president in the chair, the Hallett prize for 1951 was awarded to Dr M W Reece

Diplomas of membership and diplomas in public health were awarded to those named in our report of the council of the Royal College of Physicians (*Lancet*, Feb. 3, 1951, p 297)

University of Malaya

Dr B H. Sheares has been appointed to the chair of midwifery and gynæcology

Born in 1907 in Singapore Dr Sheares qualified from King Edward VII College of Medicine Singapore He came to this country in 1947 on a Queen's fellowship for a year's postgraduate study during which he took the membership of the Royal College of Obstetricians and Gynæcologists Since his return to Singapore he has acted as head of the department of midwifery and gynæcology

Ross Institute of Tropical Hygiene

The annual course for laymen will be held at the institute, Keppel Street, London, W C 1, this year from Monday, July 23 to Friday, July 27 inclusive

Noah Morris Memorial Lecture

The first Noah Morris lecture will be given by Dr H. P Himsworth in the chemistry department of the University of Glasgow at 4.30 P.M on Wednesday, Feb 28 He will speak on Nutritional Factors in Liver Disease

General Medical Council Elections

Nominations for 2 Scottish medical representatives, 1 Irish representative, and 8 English representatives (including 1 living in Wales) should be sent to the council on or before Feb 28 Further particulars were given in our advertisement columns last week

British Association of Forensic Pathologists

This association has lately been formed with a membership, covering both England and Scotland, of people teaching forensic medicine and engaged in the practice of the subject The president is Sir Sydney Smith and the secretary is Dr Francis Camps, 79, Harley Street, London, W 1

Swiss Society of Internal Medicine

This society is holding its 19th annual meeting at Chur from June 1 to 3 The programme includes discussions on the pathology and treatment of nephritis and on the treatment of hypertension. Further particulars may be had from Prof Eric Martin, Policlinique Médicale Universitaire, Avenue du Mail 2, Geneva

Congress on Tuberculosis and Diseases of the Chest

A conference on this subject has been called during the Festival to show the work of men and women from Great Britain and to stimulate discussion It will be held in Oxford from July 16 to 21 and is sponsored by the Faculty of Radiologists, the Society of Thoracic Surgeons the Tuberculosis Society of Scotland the Society of Medical Officers of Health, the British Pædiatric Association, and the British Tuberculosis Association. The speakers will include Dr Marc Daniels and Dr Margaret Macpherson (Tuberculin Surveys), Dr A. Q Wells and Dr J Young (Vaccination with the Vole Bacillus), Dr Honor Smith and Prof R S Illingworth (Treatment of Tuberculous Meningitis), Dr J W Crofton Dr L E Houghton, and Dr Christopher Clayson (Present Position of Chemotherapy in Tuberculosis), Mr A. L d'Abreu and Dr J H. Hutchison (Bronchiectasis in Children) Dr J E Geddes (Rehabilitation and Resettlement), Mr R C Brock, Mr Price Thomas, Mr Oswald Tubbs, and Mr Holmes Sellors (Cardiac Surgery) Dr C M Fletcher (Pneumoconiosis) Dr F H. Young, Mr Ronald Edwards, and Mr V C Thompson (Pulmonary Resection for Tuberculosis) Further particulars may be had from the hon. secretary Dr Stephen Hall, 16 Grosvenor Place, London S W 1

Meeting of W.H O Executive Board

The meeting of this board, which opened at Geneva on Jan. 22 (see *Lancet*, Feb 3, 1951, p 297, *Ibid* Feb 10, p 357) ended on Feb 5 On Feb 1 the board agreed to recommend to the fourth World Health Assembly (to be held at Geneva in May) a budget for $7,677,000 in 1952 This is a compromise between the original proposal for a $8 380 000 budget put forward by Dr Brock Chisholm, the director-general, and the recommendations of the standing committee on administration and finance The board unanimously decided to allocate $50,000 worth of medical supplies to Turkey, to prevent epidemics among Turkish refugees from Bulgaria The Turkish government had declared that Turkey had been asked to admit within ten to twelve months 250,000 members of the Turkish minority living in Bulgaria About 60 000 immigrants had already arrived, and about 1000 refugees were crossing the frontier every day The board also agreed to recommend for approval by the World Health Assembly a four year plan for world health. This plan, which covers the period 1952–55, will provide a framework in which the detailed annual programmes of W.H O will be developed Major headings are strengthening of public health administrations expansion and improvement of training resources for health personnel of all categories and development of permanent world wide services and projects in coöperation with other agencies

The Darling foundation prize has been awarded to Prof H. E Shortt F.R.S, and Dr P C C Garnham for their joint work on the life-cycle of the malaria parasite in man and the monkey Prof Rene Sand, of Belgium, has been nominated for the Leon Bernard foundation prize.

---

[1] 30 Years with G.B.S London Gollancz 1951 Pp 256 12s 6d

Sickness Records

The Institute of Actuaries is holding a meeting in the hall of the Chartered Insurance Institute, 20, Aldermanbury, London, E C 2, on Monday, Feb 26, at 5 P M, when Mr F H Spratling, F I A, and Mr F J Lloyd, F I A, will speak on Personnel Statistics and Sickness absence Statistics

Horse Shoe Club

A meeting of this club, which was formed in 1932 to foster friendship and the exchange of medical research and clinical workers between America and Great Britain, will be held on Thursday, Feb 22, at 5 P M at 11, Chandos Street, London, W 1, Dr Geoffrey Bourne will be in the chair

Use of the Film in Medical Teaching

The Royal Society of Medicine and the Scientific Film Association are holding a demonstration and discussion on this subject on Monday, Feb 19, at 5 P M, at 1, Wimpole Street, London, W 1 The openers are Prof K J Franklin, Prof Robert Cruickshank, Dr P Cardew, Dr G Loxton, and Dr Brian Stanford

The Medical War Relief Fund

From September, 1949, to August, 1950, the distribution subcommittee of the fund made 26 awards, of which 23 were gifts and 3 were loans, amounting in all to over £3000 Most of the awards were for the education of children whose fathers had been killed in the war Help was also given to doctors who had suffered financial hardship as a direct result of the war and had found difficulty in re establishing themselves in practice Since the fund was started £19,000 has been voted in loans The fund has a balance of £15,000, and while it is expected that some of the beneficiaries, especially the younger children, will need continued help, the committee thinks it unnecessary for the time being to invite further contributions Mr F A Juler has succeeded Dr C L Batteson as honorary treasurer, and Dr A V Kelynack succeeds Dr A Macrae as honorary secretary

Courses for Health Workers from Overseas

The first of the British Council's courses for visitors from overseas this year will be on industrial medicine It is being planned with the help of Dr R E Lane, Nuffield professor in the department of occupational health in the University of Manchester, and will be held in Manchester and Birmingham from March 1 to 20 Another course, on port health and sanitary control, will be held from April 23 to May 4 under the direction of Dr M T Morgan in London and of Prof W M Frazer and Dr Edward Peirce in Liverpool There will also be a course on rehabilitation and resettlement of the disabled in London from Oct 15 to Nov 7 under the direction of Dr Harold Balme There are also to be courses on public health (London and Leeds, Sept 9–23) and water pollution (London and Birmingham, May 21–June 2) Medical publishing will be included in a course on book production and publishing (Edinburgh and London, April 5–20)

Travelling Fellowships

The Medical Research Council invite applications for the following travelling fellowships for 1951–52

Rockefeller Travelling Fellowships in Medicine —These fellowships are intended for graduates resident in this country who have had some training in research work in clinical medicine or surgery, or in some other branch of medical science and who are likely to profit by a period of work at a centre in the United States or elsewhere abroad before taking up positions for higher teaching or research in the United Kingdom The stipend of fellowships tenable in the United States will be $2600 per annum for a single fellow, and $3000 for a married Fellow

Dorothy Temple Cross Research Fellowships in Tuberculosis —The object of the fellowships is to give opportunities for study or research to qualified British subjects of either sex intending to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis in all or any of its forms The fellowships will as a rule be awarded to candidates who wish to work outside the United Kingdom The stipend of fellowships will be £650 per annum for a single fellow and £900 for a married fellow

Alexander Pigott Wernher Travelling Fellowships and Grants —These awards are intended for qualified medical graduates with some experience of research in ophthalmology or otology In general fellowships will be offered for periods of up to a year for specific research purposes but grants may also be given for short term visits abroad to study methods of investigation and treatment Fellowships will provide for maintenance allowance and travelling expenses whereas grants will ordinarily cover travelling expenses only

Forms of application may be had from the secretary of the Council, 38, Old Queen Street, London, S W 1, and must be returned not later than May 1

Laboratory Animals Bureau

The annual congress of the bureau will be held at the University of Liverpool on Monday and Tuesday, April 9 and 10 Sir Henry Cohen, F R C P, will open the congress, and Prof R E Glover will be in the chair The speakers will include Dr J W Howie Requests for invitations to the congress should be addressed to the Director, Laboratory Animals Bureau, Medical Research Council Laboratories Holly Hill, London, N W 3

Lord Haden Guest has been appointed a Lord in waiting to the King

Prof Leslie Banks is making a lecture tour of Middle East countries, arranged by the British Council He is to visit Iraq Persia, Syria, and the Lebanon

Prof Henry Barcroft is visiting Pakistan, under British Council arrangements to study the development of preclinical medical training facilities

CORRIGENDUM —Lady Wood informs us that Dr George Cathcart, whose obituary we published on Jan 20 (p 17 took no formal part in the Queen's Hall Promenade Concerts beyond finding the cost of instituting the low French pitch

Appointments

MCCOLLUM D H M B Belf appointed factory doctor Penkridge district Staffs

MANUWA, S L A O B E M D Edin, F R C S E D T M & H director of medical services Nigeria

Diary of the Week

FEB 18 TO 24

Monday 19th

UNIVERSITY COLLEGE Physiology Theatre Gower Street W C 1
5 45 P M Mr C J O R Morris PH D Separation Methods in Biochemistry (First of three lectures)

INSTITUTE OF NEUROLOGY National Hospital Queen Square W C 1
5 P M Dr A Subirana (Barcelona) Temporal Lobe and Cerebral Dominance

INSTITUTE OF PSYCHIATRY, Maudsley Hospital Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture demonstration

MEDICAL SOCIETY OF LONDON, 11 Chandos Street W 1
8 30 P M Dr S Cochrane Shanks Influence of Radiology on the Diagnosis of Abdominal Disease (First Lettsomian lecture)

Tuesday, 20th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene Keppel Street W C 1) Dr G W Harris Neural Control of the Pituitary Gland

INSTITUTE OF DERMATOLOGY St John's Hospital Lisle Street, W C 2
5 P M Dr R T Brain The New St. John's Hospital Pharmacopœia

CHADWICK LECTURE
2 30 P M (26, Portland Place W 1) Brigadier A E Richmond History of Poliomyelitis in England and Wales

Wednesday, 21st

INSTITUTE OF DERMATOLOGY
5 P M Dr R W Riddell Medical Mycology

INSTITUTE OF OPHTHALMOLOGY Judd Street, W C 1
5 30 P M Mr Geoffrey Knight Diagnosis of Parasellar Syndromes

NORTH WEST METROPOLITAN REGION MENTAL DEFICIENCY SOCIETY
8 P M (Harperbury Hospital Harper Lane Shenley near St Albans Herts) Mr H Phillipson M A Clinical Applications of Modern Projection Tests

Thursday 22nd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields W C 2
5 P M Mr F G Hollands Malignant Disease of the Urinary Bladder (Hunterian lecture)

ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Dr Frank Howitt Rehabilitation

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Prof E C Dodds F R S Sex Hormones

MEDICO LEGAL SOCIETY
8 15 P M (26 Portland Place W 1) Sir Sydney Smith The Medico Legal Institute and the Problem of Crime

LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant Liverpool, 3
8 P M Dr Robert Hughes Dr W S Holden Percutaneous Cerebral Angiography

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd Dundee) Dr J Sturrock F R C O G Modern Trends in Gynæcology

Friday, 23rd

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mr A Lister Treatment of Congenital Glaucoma

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES 11 Chandos Street, W 1
8 P M Dr Pierre Durel Current Treatment of Venereal Diseases in France

INFECTION AND IMMUNITY IN SMALLPOX*

A. W. DOWNIE
M.D., D Sc Aberd
PROFESSOR OF BACTERIOLOGY IN THE UNIVERSITY OF LIVERPOOL

THE recent outbreak of smallpox at Brighton is another reminder of the continuing hazard of the introduction of virulent smallpox into this country from parts of the world where it is endemic. In this lecture, however, I shall not, except incidentally, be concerned with the spread of infection in the community. I propose to consider the course of infection and development of immunity in the person who becomes ill as a result of infection with variola virus—i.e., the pathogenesis of smallpox. Any addition to our knowledge of this subject is likely to help in our understanding of the spread of infection in the community and its control.

The sequence of events which follow penetration of the tissues by micro-organisms, and the response of the host, have excited the interest of clinicians and pathologists for many years. Nevertheless, in many diseases, especially in virus infections, our knowledge is still very incomplete. In certain of the milder virus infections, such as measles, german measles and mumps, a good deal of information has recently been obtained by the study of experimentally induced infections in human volunteers. In smallpox this method of investigation obviously cannot be followed. But some information on the pathogenesis of smallpox may be obtained from the experimental pox diseases of animals and by the use of laboratory methods to supplement the clinical study of patients. In re-examining the matter a good deal of what I have to say will be speculative, and I shall in many places be posing old questions without providing fresh answers.

In earlier studies of smallpox the methods used for the detection of virus were (*a*) the microscopic examination of stained smears from the skin or mucous surfaces—a method extensively used by Paschen, and (*b*) the inoculation of animals—the cornea in the rabbit or the skin or mucous membranes of monkeys. These methods are not very sensitive. Inoculation on the chorio-allantois of the developing chick embryo serves to demonstrate the presence of variola virus and may be used to estimate its concentrations in tissues and fluids from smallpox patients. A few drops of smallpox vesicle fluid which has been diluted many thousand times with saline will still produce characteristic lesions on the membrane of the chick embryo.

THE INCUBATION PERIOD

The smallpox patient becomes ill from 9 to 15 days, commonly 12 days, after exposure to infection. What is happening in the body during this period? This question may be asked in many other infectious diseases and receive an equally unsatisfactory answer. Any hypothesis concerning the course of events in the incubation period of smallpox must take account of the accepted opinion among epidemiologists that at any rate most patients are not infective during the greater part of this period. Acting on this belief Friedemann (quoted by Kaiser 1949) in the Berlin epidemic of 1916–17 allowed several hundred smallpox contacts complete freedom to mix with other patients until the lapse of the normal incubation period. This procedure did not apparently promote the spread of the disease. Dixon (1948) during the smallpox outbreak in Tripolitania allowed contacts to carry on business activities between the 3rd and 9th day after exposure and never observed secondary cases arising from such contacts incubating the disease.

It is generally believed that the virus enters the body via the upper respiratory passages. It has been suggested that the virus first invades and grows in the mucosa of the respiratory tract and that there is great multiplication of virus in this tissue. From this focus virus enters the blood stream and infects the skin and other tissues at or just before the onset of illness. A primary lesion in the respiratory tract has not, however, been demonstrated. Councilman et al. (1904) in their study of post-mortem material from 54 cases found no evidence of such a primary lesion. The value of such negative findings is perhaps not great; pathological processes occurring during the clinical illness might obscure evidence of earlier changes, and many of Councilman's cases had been complicated by secondary bacterial invasion of the lungs. However, if a primary lesion occurs in the respiratory tract during the incubation period it is apparently not such as to render the patient infective by discharge of virus from the air-passages to the environment.

There are two forms of smallpox where the portal of entry of the virus is not the respiratory tract—namely, variola inoculata and congenitally acquired infections.

Variola Inoculata

As far as the available records show, the incubation period in variola inoculata was two or three days shorter than that of smallpox as ordinarily acquired. This difference might be due either to the greater size of the infecting dose of virus, to the more rapid entry of virus to the lymphatics or blood through the trauma of the inoculation, or to the more rapid growth of virus in the skin than in the respiratory mucosa, or to a combination of these factors. Involvement of the local lymphatic glands seems to have been a regular feature of variolation, but it seems unlikely that in this inoculated smallpox proliferation of virus in the mucous membrane of the upper respiratory passages was an essential feature of the incubation period.

Transmission of Smallpox Virus through the Placenta

In congenitally acquired infection the incubation period is often shorter than in the disease as naturally contracted. Marsden and Greenfield (1934), who have published the most complete data on this subject, found that in many of their cases the interval from the time of onset of illness in the mother to the time of appearance of the eruption in babies soon after birth was 9–12 days; if the babies were infected at the time of onset of the mothers' illness, the incubation period of the disease in these babies was 2 or 3 days less than in smallpox as usually acquired. As they observed, this congenitally acquired infection resembles variola inoculata in this respect. In a few of their cases and in those recorded by Dixon (1948), however, the incubation period was about that seen in the naturally acquired disease. Here, again, there is no question of infection by the respiratory route. The virus enters the fœtal circulation in the placenta, perhaps after infection of the cells separating maternal and fœtal blood, and in the incubation period it must multiply in the internal tissues of the fœtus. As some of the fœtal blood passes directly from the umbilical vein to the liver, Kupffer cells might well take up virus from the beginning of the incubation period.

In naturally acquired smallpox, then, the incubation period is 2 or 3 days longer than in variola inoculata and in the congenitally acquired infection. These 2 or 3 days might represent the interval which occurs, in the common form of the disease, between the implantation of virus on the mucosa of the respiratory tract and its spread by the blood stream to those other tissues where multiplication is to continue.

---

* University of London lecture given on Jan. 26, 1951.

Sickness Records

The Institute of Actuaries is holding a meeting in the hall of the Chartered Insurance Institute, 20, Aldermanbury, London, E C 2, on Monday, Feb 26, at 5 P M, when Mr F H Spratling, F I A, and Mr F J Lloyd, F I A, will speak on Personnel Statistics and Sickness absence Statistics

Horse Shoe Club

A meeting of this club, which was formed in 1932 to foster friendship and the exchange of medical research and clinical workers between America and Great Britain, will be held on Thursday, Feb 22, at 5 P M, at 11, Chandos Street, London, W 1, Dr Geoffrey Bourne will be in the chair

Use of the Film in Medical Teaching

The Royal Society of Medicine and the Scientific Film Association are holding a demonstration and discussion on this subject on Monday, Feb 19, at 5 P M, at 1, Wimpole Street, London, W 1 The openers are Prof K J Franklin, Prof Robert Cruickshank, Dr P Cardew, Dr G Loxton, and Dr Brian Stanford

The Medical War Relief Fund

From September, 1949, to August, 1950, the distribution subcommittee of the fund made 26 awards, of which 23 were gifts and 3 were loans, amounting in all to over £3000 Most of the awards were for the education of children whose fathers had been killed in the war Help was also given to doctors who had suffered financial hardship as a direct result of the war and had found difficulty in re-establishing themselves in practice Since the fund was started £19,000 has been voted in loans The fund has a balance of £15,000, and while it is expected that some of the beneficiaries especially the younger children, will need continued help, the committee thinks it unnecessary for the time being to invite further contributions Mr F A Juler has succeeded Dr C L Batteson as honorary treasurer, and Dr A V Kelynack succeeds Dr A Macrae as honorary secretary

Courses for Health Workers from Overseas

The first of the British Council s courses for visitors from overseas this year will be on industrial medicine It is being planned with the help of Dr R E Lane, Nuffield professor in the department of occupational health in the University of Manchester, and will be held in Manchester and Birmingham from March 1 to 20 Another course, on port health and sanitary control, will be held from April 23 to May 4 under the direction of Dr M T Morgan in London and of Prof W M Frazer and Dr Edward Peirce in Liverpool There will also be a course on rehabilitation and resettlement of the disabled in London from Oct 15 to Nov 7 under the direction of Dr Harold Balme There are also to be courses on public health (London and Leeds, Sept 9–23) and water pollution (London and Birmingham, May 21–June 2) Medical publishing will be included in a course on book production and publishing (Edinburgh and London, April 5–20)

Travelling Fellowships

The Medical Research Council invite applications for the following travelling fellowships for 1951–52

Rockefeller Travelling Fellowships in Medicine —These fellowships are intended for graduates resident in this country who have had some training in research work in clinical medicine or surgery, or in some other branch of medical science and who are likely to profit by a period of work at a centre in the United States or elsewhere abroad before taking up positions for higher teaching or research in the United Kingdom The stipend of fellowships tenable in the United States will be $2600 per annum for a single fellow, and $3600 for a married Fellow

Dorothy Temple Cross Research Fellowships in Tuberculosis —The object of the fellowships is to give opportunities for study or research to qualified British subjects of either sex intending to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis in all or any of its forms The fellowships will, as a rule be awarded to candidates who wish to work outside the United Kingdom The stipend of fellowships will be £650 per annum for a single fellow and £900 for a married fellow

Alexander Pigott Wernher Travelling Fellowships and Grants —These awards are intended for qualified medical graduates with some experience of research in ophthalmology or otology In general fellowships will be offered for periods of up to a year for specific research purposes but grants may also be given for short-term visits abroad to study methods of investigation and treatment Fellowships will provide for maintenance allowance and travelling expenses whereas grants will ordinarily cover travelling expenses only

Forms of application may be had from the secretary of the Council 38, Old Queen Street, London, S W 1, and must be returned not later than May 1

Laboratory Animals Bureau

The annual congress of the bureau will be held at the University of Liverpool on Monday and Tuesday, April 9 and 10 Sir Henry Cohen, F R C P, will open the congress and Prof R E Glover will be in the chair The speakers will include Dr J W Howie Requests for invitations to the congress should be addressed to the Director, Laboratory Animals Bureau, Medical Research Council Laboratories, Holly Hill, London, N W 3

Lord Haden Guest has been appointed a Lord in waiting to the King

Prof Leslie Banks is making a lecture tour of Middle East countries, arranged by the British Council He is to visit Iraq Persia, Syria, and the Lebanon

Prof Henry Barcroft is visiting Pakistan, under British Council arrangements to study the development of preclinical medical training facilities

CORRIGENDUM —Lady Wood informs us that Dr George Cathcart, whose obituary we published on Jan 20 (p. 171), took no formal part in the Queen's Hall Promenade Concerts beyond finding the cost of instituting the low French pitch

Appointments

McCOLLUM D H M B Belf appointed factory doctor Penkridge district, Staffs

MANUWA S L A O B E, M D Edin, F R.C.S.E. D T.M.& H director of medical services Nigeria

Diary of the Week

FEB 18 TO 24

Monday 19th

UNIVERSITY COLLEGE Physiology Theatre Gower Street W C 1
4 45 P M Mr C J O R Morris PH D Separation Methods in Biochemistry (First of three lectures)

INSTITUTE OF NEUROLOGY National Hospital Queen Square W.C.1
5 P M Dr A Subirana (Barcelona) Temporal Lobe and Cerebral Dominance

INSTITUTE OF PSYCHIATRY, Maudsley Hospital Denmark Hill S E 5
5 30 P M Dr E Stengel Lecture demonstration

MEDICAL SOCIETY OF LONDON 11, Chandos Street, W 1
8 30 P M Dr S Cochrane Shanks Influence of Radiology on the Diagnosis of Abdominal Disease (First Lettsomian lecture)

Tuesday, 20th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene Keppel Street W C.1) Dr G W Harris Neural Control of the Pituitary Gland.

INSTITUTE OF DERMATOLOGY St John s Hospital Lisle Street W C 2
5 P M Dr R T Brain The New St John's Hospital Pharmacopœia

CHADWICK LECTURE
2 30 P M (26, Portland Place W 1) Brigadier A E Richmond History of Poliomyelitis in England and Wales

Wednesday, 21st

INSTITUTE OF DERMATOLOGY
5 P M Dr R W Riddell Medical Mycology

INSTITUTE OF OPHTHALMOLOGY Judd Street, W C 1
5 30 P M Mr Geoffrey Knight Diagnosis of Parasellar Syndromes

NORTH WEST METROPOLITAN REGION MENTAL DEFICIENCY SOCIETY
8 P M (Harperbury Hospital, Harper Lane Shenley near St Albans Herts) Mr H Phillipson, M.A Clinical *Applications of Modern Projection Tests*

Thursday 22nd

ROYAL COLLEGE OF SURGEONS Lincoln s Inn Fields W C.2
5 P M Mr F G Hollands Malignant Disease of the Urinary Bladder (Hunterian lecture)

ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Dr Frank Howitt Rehabilitation

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M *Prof E C Dodds* F R.S Sex Hormones.

MEDICO LEGAL SOCIETY
8 15 P M (26 Portland Place W 1) Sir Sydney Smith The Medico Legal Institute and the Problem of Crime

LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant, Liverpool 3
8 P M Dr Robert Hughes Dr W S Holden Percutaneous Cerebral Angiography

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small s Wynd Dundee) Dr J Sturrock F R C O G Modern Trends in Gynæcology

Friday, 23rd

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mr A Lister Treatment of Congenital Glaucoma

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES 11 Chandos Street W 1
8 P M Dr Pierre Durel Current Treatment of Veneral Disease in France

That viræmia occurs in all cases early in the disease there can be no doubt

GROWTH OF VIRUS IN THE SKIN AND DEVELOPMENT OF THE FOCAL ERUPTION

Although focal lesions are clinically obvious only on the skin and mucous membranes, post mortem studies have shown that specific lesions, less numerous than on the skin, may occur in internal organs The virus shows a special preference for skin epithelium, although there is histological evidence of infection of endothelial cells of capillaries in the dermis and this presumably precedes the infection of the malpighian layer of the epidermis By the time macules appear in the skin on the 3rd or 4th day of the disease there has been extensive multiplication of virus in the epithelial cells, and stained smears from scrapings of the papular lesions show very numerous virus particles Histological examination of the skin from patients who die early confirms the impression obtained from examination of smears There must be at this stage a tremendous amount of virus in the skin of the patient who is to develop a confluent rash

In the average case virus is not present on the surface of the skin at this stage owing to the impervious nature of its superficial layers In the mucous membrane of the mouth and pharynx, however, there is no such covering, and, at the time macules are appearing in the skin, lesions in these mucous membranes are breaking down and discharging virus on the surface It is from the expulsion of droplets containing this virus that the patient becomes infective about the 3rd day The few attempts made to isolate virus from the throat before the 3rd day of illness by egg inoculation have been unsuccessful Ricketts and Byles (1908, p 59) state that "the disease is seldom infectious before the outcrop of the focal rash" an opinion with which most clinicians and epidemiologists with experience of smallpox agree If smallpox were, like influenza, always highly infectious from the onset, when clinical diagnosis is impossible, control of outbreaks by the isolation of cases and vaccination of contacts would be very difficult.

DEVELOPMENT OF IMMUNITY

The fall in temperature and improvement in the patient's condition, which becomes evident as the skin eruption appears, suggest that immunity to the virus or its products develops about the 4th to 6th day of illness This is supported by observations to be mentioned presently But antibody formation—an essential part of the immune response—which often occurs at this time does not, in most cases, prevent the progressive evolution of the skin eruptions through vesiculation and pustulation By the time the vesicular stage is reached, or even earlier, probably all the epithelial cells of the skin which are to be infected already harbour virus, and within the cells the virus is protected from the action of antibody The subsequent development of pustulation is part of the inflammatory reaction to the necrosis of epithelial cells previously infected by virus The secondary fever, when it occurs, is probably caused, as Ricketts suggests, by the absorption of toxic products of tissue breakdown, and is related to the extent of skin involved

I mentioned that there is other evidence of the development of immunity about the 5th day of disease It was shown by Ricketts and Byles (1908), and subsequently confirmed by Marsden (1948), that a decreasing number of patients may be successfully vaccinated in the early days of illness and very few after the 1st or 2nd day of the focal eruption Fig 2 has been prepared from their data It might be suggested that the failure of vaccination was due to an interference effect—to a refractory state of the skin in consequence of previous infection of this tissue with variola virus It seems more likely to be due to the presence of specific antibody, which can be demonstrated in the blood after the first few days of illness It must be kept in mind that an immunity response by the antibody forming tissues may take place a short time before excess antibody is demonstrable in the blood by laboratory methods

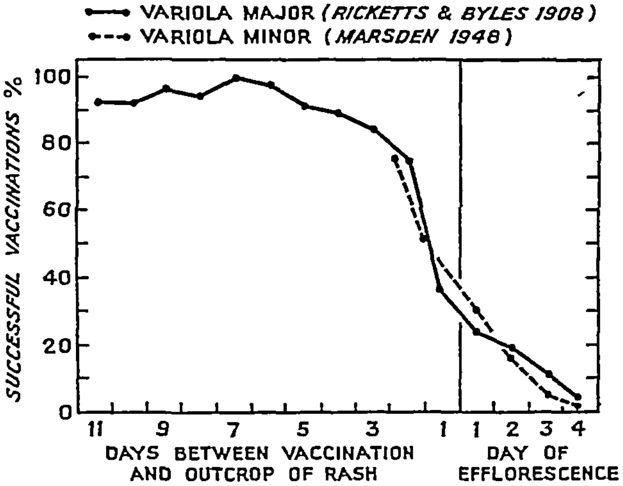


Fig 2.

Antibody in serum may be estimated by various techniques—by complement fixation, by tests for inhibition of virus hæmagglutinin, or by various types of neutralisation tests against variola or vaccinia virus. Only the third kind of test measures the power of serum to inhibit the infectivity of the virus, but the first two serve to indicate an antibody response to virus antigen

Collier et al (1950) tested sera from 800 smallpox patients in Java for vaccinial antihæmagglutinin Their findings showed that this antibody was present in significant amount between the 2nd and 5th day of illness, increased up to the 9th day, and remained at a high level thereafter Our own observations on a much smaller number of sera gave similar results (McCarthy and Downie, to be published) Estimation of antibody by complement fixation gave results which paralleled those obtained by the test for antihæmagglutinins Estimation of neutralising antibody in our series was made by inoculating mixtures of sera and variola virus on the chorio allantois The extent of the reduction of the pock-count gave an estimate of the neutralising potency of the sera Many of the patients whose sera we have examined had been previously vaccinated, most of them years before In order to assess the significance of our results in smallpox cases, therefore, we have to take account of the duration of antibody response following vaccination This is discussed later, but in considering the possible pre-existing antibody in the smallpox cases who had been vaccinated, we can say that complement fixing antibody, if present at all after vaccination, disappears within a few months and that antihæmagglutinin is usually not to be found after one or two years Neutralising antibody may be detectable for many years

In the sera from smallpox cases complement fixing antibody and antihæmagglutinin were present in high titre toward the end of the first week from the onset of illness Neutralising antibody had also appeared or increased in amount at this time We have made few observations on sera from toxic cases, but Collier et al (1950) note that patients who die in the early eruptive stage show a poor antibody response as estimated by antihæmagglutinin titrations Some of their patients who died towards the end of the 2nd week or later showed a high antihæmagglutinin titre Such an occurrence is not unknown in other diseases where death may result

Evidence from Infection in Animals

In the absence of direct evidence from observations in smallpox, as to the site of multiplication of the virus in the incubation period, we may turn to Fenner's work on mousepox which provides useful suggestions (Fenner 1948a and b) This work was summarised by Professor Burnet not many months ago (Burnet 1950) In mouse pox, infection takes place through the skin After an incubation period of 7–8 days a local lesion appears, followed after 2 more days, in mice which do not die of the acute disease, by a generalised skin rash which in its evolution has some resemblance to the eruption of small pox Fenner infected batches of mice by intradermal inoculation and followed the spread of virus by titrating the virus content of various organs of animals killed at daily intervals afterwards He concluded that virus from the skin passed within a few hours to the local lymphatic glands, where it proceeded to proliferate Within a day or two, small amounts of virus passed into the blood stream, from which it was removed by phagocytic cells lining sinusoids in the spleen, liver, and presumably other tissues such as bone marrow In these organs there was further multiplication followed by an overflow of virus into the blood, at this time the skin was infected and the rash appeared 2 or 3 days later As Fenner noted, the sequence of events in the incubation period was similar to that observed in mouse typhoid by Ørskov and his colleagues (1928, 1930)

In Fenner's papers I have found no mention of systematic examination of the lungs for virus during the incubation period We know that intravenously injected bacteria and inanimate particulate material is partly removed from the circulation in the alveolar walls of the lung In Fenner's mice it seems possible that virus was removed in a similar manner during the initial viræmia, as well as during subsequent passage of the blood through liver and spleen In rabbitpox, which is clearly more akin to smallpox, the virus localises and produces lesions in the lungs with great regularity (Greene 1934) And after intradermal injection of some strains of vaccinia virus into rabbits, pulmonary lesions are commonly seen (Douglas et al 1929, Pearce et al 1936) These observations seem to suggest that if there is an initial viræmia early in the incubation period in smallpox, virus might be removed from the blood by phagocytic cells in the pulmonary capillaries and multiply there as well as in phagocytic cells in liver, spleen, and other tissues during the incubation period

Where then is the initial site of penetration and multiplication of virus in smallpox naturally acquired? We simply do not know It seems most unlikely that the virus multiplies sufficiently in the epithelial layers of the mucous membrane at the site of initial lodgement to give rise directly to the viræmia which ushers in the clinical illness It is difficult to believe that such local proliferation of virus could go on for so long and the patient not be infective for others Might the initial infection of the tissues be lower down in the respiratory tract—for example, in the smaller bronchi or bronchioles, from which dissemination to the environment might less readily occur? Another possibility is that the virus might pass through the mucous membrane without infecting the epithelial cells and be carried to the lymphatic glands to multiply there There is no evidence in favour of this idea, and later, at the onset of illness, the virus distributed by the blood stream infects the epithelial cells in the upper respiratory tract readily enough.

In any event, whether some degree of proliferation of virus takes place in epithelial cells at the site of entry or not, it seems likely that, during the incubation period, infection progresses in the manner suggested by Fenner's work The lymphatic glands draining the site of entry become infected early, and after a day or two virus is liberated from or within infected cells in these glands and passes to the blood stream to give a primary and *possibly transient viræmia* The virus is quickly removed from the circulation by phagocytic cells lining the sinusoids of the liver and sinuses in the spleen and bone marrow, and perhaps by phagocytic cells in the lung capillaries Only after a further period of multiplication and progressive infection of these cells does overflow of virus take place, giving the secondary and more intense viræmia at or just before the onset of illness. The complete disappearance of the capillary walls in the liver, which Councilman and his colleagues noted in rapidly fatal cases, may well have been the result of the extensive infection of the Kupffer cells during the incubation period

There is no generally accepted explanation for the localisation of virus in the skin during the secondary viræmia The liability to intermittent slowing of the circulation in the skin capillaries, and the probability that virus is within cells or associated with cell fragments may be important factors The concentration of the eruption at pressure points is compatible with the idea that capillary stasis may determine skin localisation (Ricketts and Byles 1908)

THE ONSET OF ILLNESS

The overflow of virus into the blood stream to give the secondary viræmia is believed to coincide with the onset of illness This viræmia leads to widespread infection of the skin, mucous membranes, and other tissues, although lesions do not become apparent in the skin for a further 2 or 3 days There may be viræmia shortly before the onset of illness, but on this point we have no direct evidence If the time of appearance and development of skin lesions in monkeys and rabbits after intravenous injection of variola virus and vaccinia virus respectively, are any guide as to what happens in the skin of the smallpox patient, the viræmia occur just about the onset of illness and not before Th observations of Dixon on infection contracted in uter are compatible with this It seems likely that, excep in severe cases, the period of viræmia may be limited t a day or two or even to a few hours Kyrle and Morawet (1915) claimed to have demonstrated the infectivity o blood, by intravenous inoculation of monkeys, throughou the clinical illness until the skin lesions were drying up These findings have not been confirmed by our ow observations (Downie et al 1950), or by those o MacCallum et al (1950), using the chorio allantoic metho to detect virus Fig 1 summarises the combined fin ings of the two laboratories up to the end of Decemb 1950 It will be noted that, with one exception, positi results were obtained only in patients who ultimate died of their disease and in whom the viræmia mig be expected to be greater in degree and more prolonge The method permits of the examination of only sm samples of blood, and more positive results might ha been obtained if larger volumes of blood had be examined or if specimens had been obtained earlier the illness In a few instances concentration of spe mens by high speed centrifugation of lysed blood-ce was tried, but such specimens gave negative resu

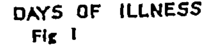


Fig 1

That viræmia occurs in all cases early in the disease here can be no doubt

GROWTH OF VIRUS IN THE SKIN AND DEVELOPMENT OF THE FOCAL ERUPTION

Although focal lesions are clinically obvious only on the skin and mucous membranes, post-mortem studies have shown that specific lesions, less numerous than on the skin, may occur in internal organs The virus shows a special preference for skin epithelium, although there is histological evidence of infection of endothelial cells of capillaries in the dermis and this presumably precedes the infection of the malpighian layer of the epidermis By the time macules appear in the skin on the 3rd or 4th day of the disease there has been extensive multiplication of virus in the epithelial cells, and stained smears from scrapings of the papular lesions show very numerous virus particles Histological examination of the skin from patients who die early confirms the impression obtained from examination of smears There must be at this stage a tremendous amount of virus in the skin of the patient who is to develop a confluent rash

In the average case virus is not present on the surface of the skin at this stage owing to the impervious nature of its superficial layers In the mucous membrane of the mouth and pharynx, however, there is no such covering, and, at the time macules are appearing in the skin, lesions in these mucous membranes are breaking down and discharging virus on the surface It is from the expulsion of droplets containing this virus that the patient becomes infective about the 3rd day The few attempts made to isolate virus from the throat before the 3rd day of illness by egg inoculation have been unsuccessful Ricketts and Byles (1908, p 59) state that "the disease is seldom infectious before the outcrop of the focal rash" an opinion with which most clinicians and epidemiologists with experience of smallpox agree If smallpox were, like influenza, always highly infectious from the onset, when clinical diagnosis is impossible, control of outbreaks by the isolation of cases and vaccination of contacts would be very difficult.

DEVELOPMENT OF IMMUNITY

The fall in temperature and improvement in the patient's condition, which becomes evident as the skin eruption appears, suggest that immunity to the virus or its products develops about the 4th to 6th day of illness This is supported by observations to be mentioned presently But antibody formation—an essential part of the immune response—which often occurs at this time does not, in most cases, prevent the progressive evolution of the skin eruptions through vesiculation and pustulation By the time the vesicular stage is reached, or even earlier, probably all the epithelial cells of the skin which are to be infected already harbour virus, and within the cells the virus is protected from the action of antibody The subsequent development of pustulation is part of the inflammatory reaction to the necrosis of epithelial cells previously infected by virus The secondary fever, when it occurs is probably caused, as Ricketts suggests, by the absorption of toxic products of tissue breakdown, and is related to the extent of skin involved

I mentioned that there is other evidence of the development of immunity about the 5th day of disease It was shown by Ricketts and Byles (1908), and subsequently confirmed by Marsden (1948), that a decreasing number of patients may be successfully vaccinated in the early days of illness and very few after the 1st or 2nd day of the focal eruption Fig 2 has been prepared from their data It might be suggested that the failure of vaccination was due to an interference effect—to a refractory state of the skin in consequence of previous infection of this tissue with variola virus It seems more likely to be due to the presence of specific antibody, which can be demonstrated in the blood after the first few days of illness It must be kept in mind that an immunity response by the antibody-forming tissues may take place a short time before excess antibody is demonstrable in the blood by laboratory methods

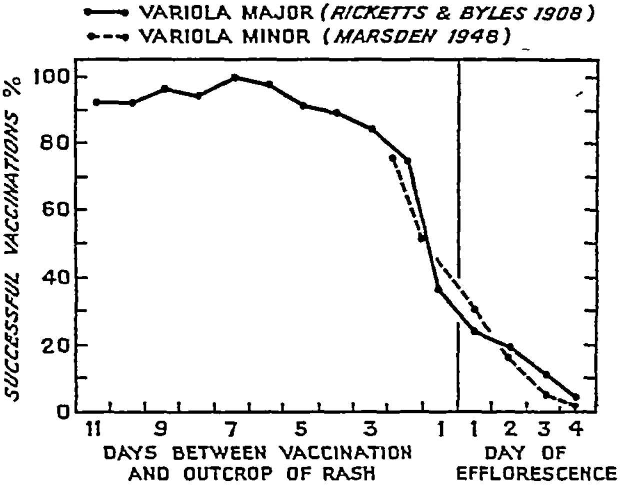


Fig 2

Antibody in serum may be estimated by various techniques—by complement fixation, by tests for inhibition of virus hæmagglutinin, or by various types of neutralisation tests against variola or vaccinia virus. Only the third kind of test measures the power of serum to inhibit the infectivity of the virus, but the first two serve to indicate an antibody response to virus antigen

Collier et al (1950) tested sera from 800 smallpox patients in Java for vaccinial antihæmagglutinin Their findings showed that this antibody was present in significant amount between the 2nd and 5th day of illness, increased up to the 9th day, and remained at a high level thereafter Our own observations on a much smaller number of sera gave similar results (McCarthy and Downie, to be published) Estimation of antibody by complement fixation gave results which paralleled those obtained by the test for antihæmagglutinins Estimation of *neutralising antibody* in our series was made by inoculating mixtures of sera and variola virus on the chorio allantois The extent of the reduction of the pock-count gave an estimate of the neutralising potency of the sera Many of the patients whose sera we have examined had been previously vaccinated, most of them years before In order to assess the significance of our results in smallpox cases, therefore, we have to take account of the duration of antibody response following vaccination This is discussed later, but in considering the possible pre-existing antibody in the smallpox cases who had been vaccinated, we can say that complement fixing antibody, if present at all after vaccination, disappears within a few months and that antihæmagglutinin is usually not to be found after one or two years Neutralising antibody may be detectable for many years

In the sera from smallpox cases complement fixing antibody and antihæmagglutinin were present in high titre toward the end of the first week from the onset of illness Neutralising antibody had also appeared or increased in amount at this time We have made few observations on sera from toxic cases, but Collier et al (1950) note that patients who die in the early eruptive stage show a poor antibody response as estimated by antihæmagglutinin titrations Some of their patients who died towards the end of the 2nd week or later showed a high antihæmagglutinin titre Such an occurrence is not unknown in other diseases where death may result from the late effects of earlier damage to vital tissues or from secondary infection

The application of laboratory methods for the measurement of the immune response has served to confirm the views, based on clinical experience, of such authorities as Ricketts and Byles It seems that the speed of the immune response determines the severity of the disease and that the outcome will be decided by what happens in the body in the first few days of illness In persons (usually well protected by vaccination) who suffer from *variola sine eruptione* the rapid formation of antibody engendered by the stimulus of infection does not prevent the liberation of virus from cells where it has been multiplying during the incubation period That viræmia occurs in such cases is supported by the observation of Bancroft (1904) He mentions, without giving details, a pregnant woman who, after contact, had only a vague illness with some headache but later gave birth to a baby who developed a typical smallpox eruption 2 days after birth In these *sine eruptione* cases antibody probably combines with the liberated virus and prevents infection of the skin epithelium If the response is less effective some of the virus exposed to antibody in the blood stream early in the disease may be neutralised, thus diminishing the number of focal lesions, or the antibody may prevent progressive infection of skin epithelium before the eruption becomes clinically apparent, thus preventing the full development of the skin lesions and so leading to modification of the rash

PERSISTENCE OF ANTIBODY

As second attacks of smallpox are uncommon it seems likely that antibody might be demonstrable years after recovery as in certain other diseases We have made observations on sera from a number of persons who had suffered from smallpox 1–8 years previously, most of them during the 1946 outbreak on Merseyside In these sera complement fixing antibody was no longer detectable and the titre of antihæmagglutinins was low, but all the sera showed a high level of neutralising antibody It is apparent therefore that while the two in vitro tests reveal the early antibody response during the clinical illness in persons not recently vaccinated, the antibody demonstrated is not that which is most likely to be associated with specific resistance to infection The power of a serum to prevent infection of susceptible tissue by variola virus is probably a more useful indication of an individual's resistance to the disease

Using the same techniques we have examined the sera from persons at different periods after vaccination or revaccination Antibody was not found before the 10th day after primary vaccination, but by the 13th day it was demonstrable by all three methods In smallpox, antibodies are not usually detectable before the 3rd day of illness—i e, about 15 days from the time of infection It has always been believed that the immunity response following vaccination was more rapid than that following infection in smallpox patients, and that the protection, usually though not invariably, afforded by vaccination at the time of contact could thus be explained The results of serological tests are in keeping with this belief The maximum titre was reached 3–4 weeks after primary vaccination but did not usually attain the levels reached by the smallpox convalescent sera A year after vaccination complement fixing antibody and antihæmagglutinin were not usually to be found, but in some subjects, vaccinated many years before, neutralising antibody to variola virus was still present As might be expected, the amount and persistence of antibody varied in different individuals It is well known that smallpox often attacks persons who have been successfully vaccinated years before, although the disease is frequently mild In such persons antibody may be absent from the blood or present only in low concentration, but we had details supplied by Dr W H Bradley of a nurse vaccinated 2 years before who suffered from a very mild attack of smallpox and in whose serum, taken immediately before she was infected, we found a considerable titre of neutralising antibody for variola virus It is possible that antibody in the blood deteriorates in quality as well as in quantity with the passage of time

As variola virus may be exposed to the action of antibody for only short periods between release from one cell and entry into another, it may be that only antibody of high avidity can effectively protect a person from infection of a degree that would become clinically apparent We have recently tried modifications of our technique in an attempt to measure avidity of sera—i e, speed of combination with virus So far our results have not been very conclusive

SUMMARY

It is still not possible to give a factual account of the course of events which follows human infection with the virus of smallpox Nevertheless the outline of the story seems fairly clear, and, if much detail has to be filled in by speculation, this is inevitable in our present state of knowledge As I see it, the following summary seems reasonable, although in parts it lacks supporting evidence

The site of entry of the virus to the tissues is in the *upper respiratory tract* At most only a minimal or closed lesion occurs in the mucous membrane and the virus quickly passes to lymphatic glands and by blood stream to internal organs Progressive infection of cells in these organs, with increase in virus, takes place during the incubation period Towards the end of this period, or at the onset of illness, there is an overflow of virus into the blood stream, and liberation of the products of cell breakdown The skin and other tissues are infected with virus at this time, and in most cases the immune response with the formation of antibody follows a few days later The speed and extent of the antibody formation determines the extent of the rash and the severity of the disease The maturation of the eruption proceeds after the antibody has appeared and is secondary to the destruction of cells infected in the first few days of illness Patients who die in the later pustular stage of the eruption may have a high titre of antibody in their sera, in such patients death is due to the late effects of earlier virus activity or to some complicating disability or infection Antibody persist at a high level for some years after smallpox After vaccination neutralising antibody may be detectable for many years, but is not usually present in as high a concentration as after smallpox and it varies considerably in different individuals The quality as well as the quantity of antibody in the blood may be of importance in determining relative immunity to smallpox infection

REFERENCES

Bancroft I R (1904) *J med Res* 11, 322
Burnet, F M (1950) *Lancet* i 1059
Collier W A Smith A M Heerde A F (1950) *Z Hyg InfektKr* 131 555
Councilman W T Magrath G B, Brinckerhoff W R (1904) *J med Res* 11 12
Dixon C W (1948) *J Hyg Camb* 46 351
Douglas S R, Smith W Price L R W (1920) *J Path Bact* 32 99
Downie A W McCarthy K Macdonald, A (1950) *Lancet* ii 513
Fenner, F (1948a) *J Path Bact* 60, 529
— (1948b) *Lancet* ii 915
Greene H S N (1934) *J exp Med* 60, 441
Kaiser M (1949) Pocken und Pockenschutzimpfung Vienna
Kyrle J Morawetz G (1915) *Wien klin Wschr* 28 697
MacCallum, F O, McPherson C A Johnstone D F (1950) *Lancet* ii 514
Marsden J P (1948) *Bull Hyg, Lond* 23, 735
— Greenfield C R M (1934) *Arch Dis Childh* 9 309
Ørskov, J Moltke O (1928) *Ztschr f ImmunForsch* 59 357
— Lassen H C A (1930) *Ibid* 67, 137
Pearce, Louise Rosahn, P D Hu C K (1936) *J Immunol* 31 73
Ricketts T F Byles J B (1908) Diagnosis of Smallpox London

VITAMIN K IN THE PREVENTION OF HÆMORRHAGIC DISEASE OF THE NEWBORN

J D HAY
M.A Camb, M.D Lpool, M R C P, D C H
ÆDIATRICIAN, MILL ROAD MATERNITY UNIT, ASSISTANT PÆDIATRICIAN, LIVERPOOL MATERNITY HOSPITAL

F P HUDSON
M.R C P.E, D C H.
PÆDIATRICIAN, WALTON HOSPITAL, LIVERPOOL

T S RODGERS
M.D Lond., M.R C.P, D.P.H., D C H
ORMERLY PÆDIATRICIAN, BROADGREEN AND SEFTON GENERAL HOSPITALS LIVERPOOL

From the Department of Child Health, University of Liverpool

THE level of prothrombin in the blood of healthy nfants is low from about twelve hours after birth to he end of the fifth day of life, and the blood coagulation ime is relatively prolonged during this period (Waddell nd Guerry 1939, Dam et al 1939, Nygaard 1939, Quick and Grossman 1940) Unusually low prothrombin evels are often, but not invariably found in infants with hæmorrhagic disease of the newborn Equally low levels however, may occur without any bleeding

The discovery by Dam (1934) of vitamin K in alfalfa and certain liver fats and his demonstration that it is essential to the formation of plasma prothrombin (Dam 1934, Dam et al 1936), were followed in 1939 by Waddell and Guerry's work which suggested that the administration of vitamin K to the newborn infant immediately after birth prevents the development of the usual hypoprothrombinæmia and prolongation of clotting time, or, if given later, when these changes have already taken place, ensures a rapid return to normal

Vitamin K has therefore been widely used during the past ten years in the treatment of neonatal bleeding but the results obtained to date suggest that its value in controlling bleeding is limited, and that blood transfusion is still essential in severe cases The efficiency of the vitamin in preventing hæmorrhagic disease when it is given to the infant immediately after birth is also doubtful Lehmann (1944) reported on 13 250 babies to whom vitamin K had been given within an hour of birth, and compared the incidence of hæmorrhage in them and in 17,740 babies who had not received vitamin K His results, in the opinion of THE LANCET (1944), did "not show conclusive evidence of the prophylactic value of vitamin K"

Several workers have given vitamin K to pregnant mothers shortly before delivery, and have observed the effect on the prothrombin level and blood coagulation-time of the infants during the first week of life Some also noted the incidence of bleeding in these infants

MacPherson et al (1940) gave vitamin K by mouth to 31 mothers before delivery, and reported an effect on the infants' prothrombin level similar to that obtained by giving vitamin K to the infant after birth.

Bohlender et al (1941) obtained the same result in the infants of 50 mothers to whom they gave intravenous vitamin K before delivery

Beck et al (1941) found that the administration of vitamin K to 1022 mothers in labour eliminated the neonatal fall in prothrombin level in their infants they also noted that the blood clotting time approached that of normal adults In addition they remarked that only 5 out of the 1022 infants of mothers who had received vitamin K ante partum showed hæmorrhage,' whereas in 21 of 1037 controls hæmorrhage of some sort took place

A series of 1693 infants of mothers to whom vitamin K had been given before delivery was reported by Sanford et al (1942) They too observed the raised prothrombin levels in the infants but concluded that the frequency of hæmorrhagic manifestations in their series was unaffected by vitamin K Since the incidence of hæmorrhagic disease of the newborn probably varies from 1 in 200 to 1 in 1000 infants, such a conclusion from only 1693 cases was probably unjustified

The dose of vitamin K differed in each of these series MacPherson et al (1940) concluding that 50 mg was the best dose by mouth, and Bohlender et al (1941) injecting 1 mg intravenously The time of administration before delivery also varied, MacPherson et al (1940) considering 4–12 hours to be the best time, Bohlender et al (1941) finding that all their injections from 5 minutes to 23 hours 15 minutes before delivery were successful in raising the infants' blood-prothrombin level

Poncher, in 1942, expressed his views as follows

> "So far as the effect on the prothrombin time is concerned, it can be definitely stated that if oral preparations are given to a normal pregnant woman twenty four to twelve hours before she goes into labor, or if vitamin K is administered daily before delivery, the prothrombin time of the infant will be normal and there will be no untoward effect on the mother Water soluble preparations given parenterally will be effective in prophylaxis when given as late as one hour before delivery although it is desirable to have a longer interval to obtain the maximum effect The dosage recommended is 2 mg daily of the oral preparations and a single dose of 2 mg of the water soluble parenteral preparations at least from six to four hours before delivery There would seem to be little advantage in giving oral prophylactic therapy more than a week before labor as there is no evidence for a cumulative effect In fact, a single oral dose of 5 mg at the start of the first labor pain may be practical in most cases If a woman goes into labor without adequate prophylaxis a single dose of a parenteral preparation can usually be given in a sufficient time to be effective before she delivers"

In 1944, THE LANCET published a leading article reviewing the information available at that time which summed up by saying It is probably advisable to give menaphthone either to every mother at or just before the beginning of labour or to every newborn child as a prophylactic against hæmorrhagic disease"

INVESTIGATION

The clinical experiment reported here was planned to assess the practicability of giving vitamin K to mothers in large busy maternity units and its efficacy in preventing hæmorrhagic disease of the newborn The units participating were the five largest maternity units in Liverpool the Liverpool Maternity Hospital the Mill Road Maternity Unit and the maternity units of the Broadgreen, Sefton General, and Walton Hospitals comprising 544 maternity beds and about 12,550 deliveries a year

Our intention was to administer a vitamin K analogue during labour to some 10,000 mothers and to set aside 10,000 controls during this period to whom no vitamin was given the general care and treatment of the two groups being otherwise identical The dose decided on was 50 mg given by intramuscular injection We aimed at giving vitamin K between four and twelve hours before delivery The mothers were placed in the experimental or control series by the simplest practical method of allocating the deliveries in alternate weeks to the experimental series The numbers involved and the limited laboratory facilities available precluded the estimation of blood prothrombin levels or coagulation time

As the experiment proceeded, it became clear that many mothers in the ' experimental" weeks were not receiving vitamin K before delivery, such causes as precipitate labour before or soon after admission being mainly responsible In addition many mothers' labours were shorter or longer than had been anticipated, with the result that vitamin K was administered less than four or more than twelve hours before delivery The findings at the end of two years' experiment have therefore been reviewed, and our report concerns 4602 mothers who received vitamin K under the conditions specified, and 12,136 "controls" to whom no vitamin K was administered

RESULTS

Hæmatemesis and/or melæna occurred in 34 infants Of these, 11 were born to mothers who had received vitamin K before delivery The clinical details of the 34 cases are summarised in tables I and II The difficulty of confirming the diagnosis of hæmorrhagic disease is well known Infants not infrequently vomit blood which has been swallowed at birth, and this is especially likely to happen when the mother has had an antepartum hæmorrhage In all our cases the pædiatrician seeing the case at the time bleeding occurred formed the opinion that hæmorrhagic disease was the most likely diagnosis The occurrence of bleeding other than from the stomach or the bowel has not been recorded in this analysis, owing to the difficulty of excluding other causes of such hæmorrhages, nor has intracranial hæmorrhage been considered, for the experimental and control series are not strictly comparable

Hæmorrhagic disease of the newborn occurred therefore in 11 out of 4602 infants whose mothers had received vitamin K before delivery—i e , in 1 in every 418 cases —and in 23 of 12,136 infants whose mothers had not been given vitamin K—i e , in 1 in every 527 cases

TABLE I—HÆMORRHAGIC DISEASE IN INFANTS WHOSE MOTHERS HAD NOT RECEIVED VITAMIN K

Case no	Month and year of birth	Birth weight lb	Birth weight oz	Delivery	Clinical details
1	10/49	6	12	Vertex	Bright red blood in stool on 3rd day
2	3/49	8	0	Vertex	Severe melæna 53 hr after birth
3	5/49	6	8	Concealed APH, vertex forceps	Melæna on 1st and 2nd days
4	2/50	7	4	Vertex	Small hæmatemesis on 3rd day
5	9/48	5	14	Cæsarean section for eclampsia	Recurrent severe hæmatemesis starting 53 hr after birth
6	11/48	6	13	Vertex	Hæmatemesis on 2nd day
7	4/49	7	0	Vertex	Melæna on 3rd and 4th days
8	12/48	5	9	Vertex	Fairly severe melæna on 1st 2nd 3rd and 4th days
9	9/48	7	7	Vertex and forceps	Melæna and hæmatemesis on 7th day
10	2/49	8	11	Vertex	Melæna on 2nd and 3rd days
11	10/48	6	12	Vertex retroplacental clot	Hæmatemesis and melæna on 4th day
12	6/48	7	2	Cæsarean section	Melæna on 5th and 6th days
13	12/48	7	9	Cæsarean section	Melæna on 1st 2nd and 3rd days and hæmatemesis on 2nd day
14	1/48	6	9	Vertex and forceps	Hæmatemesis on 4th day
15	12/49	4	6	Cæsarean section	Hæmatemesis and melæna for 24 hr starting on 2nd day
16	1/50	6	14	Cæsarean section	Melæna and epistaxis on 2nd day
17	5/50	6	2	Vertex	Hæmatemesis on 3rd day melæna on 2nd 3rd 4th and 5th days vaginal bleeding on 6th day
18	7/49	7	10	Breech with forceps to head	Hæmaturia at 12 hr hæmatemesis on 2nd day died on 3rd day necropsy confirmed diagnosis
19	9/48	7	4	Vertex and forceps	Melæna on 2nd and 3rd days
20	1/49	6	13	Vertex	Hæmatemesis on 2nd day
21	6/49	6	0	Twin breech	Melæna on 3rd 4th and 5th days
22	5/49	4	10	Vertex	Hæmatemesis on 2nd day melæna on 3rd day
23	7/48	7	6	Mid forceps for disproportion	Melæna on 2nd day

TABLE II—HÆMORRHAGIC DISEASE IN INFANTS WHOSE MOTHERS HAD RECEIVED VITAMIN K

Case no	Month and year of birth	Birth weight lb	Birth weight oz	Delivery	Time of vitamin K before delivery	Clinical details
1	10/49	5	10	Vertex accidental APH	8 hr 20 min	Melæna on 1st day
2	12/48	6	12	Vertex	4 hr 5 min	Bright red blood seen in two stools on 2nd day
3	4/50	4	7	Vertex and forceps	8 hr	Melæna from 3rd to 7th day, concurrent umbilical sepsis, and septicæmia
4	7/48	5	13	Vertex	1 hr 10 min	10 melæna stools starting 9 hr after birth
5	9/48	8	13	Vertex	2½ hr	Melæna on 1st and 2nd days
6	9/48	5	13	Vertex	4½ hr	Hæmatemesis and melæna on 1st day
7	9/48	3	3	Vertex	2 hr	Hæmatemesis and melæna on 3rd day
8	8/48	8	1	Vertex	48 hr	Melæna on 2nd day
9	11/48	4	9	Vertex APH	15 min	Melæna from 1st to 3rd day
10	8/49	5	1	Vertex APH	48 hr	Melæna on 5th day
11	5/49	6	1	Vertex	30 min	Two small vomits o altered blood 24 h after birth

DISCUSSION

In view of the great variability of the incidence of hæmorrhagic disease in previous reports this difference is not considered to be significant, but it is quite clear that in this series the administration of vitamin K to mothers in labour did not prevent hæmorrhagic disease

Poncher (1942) wrote "Vitamin K and its analogues are effective in prevention and treatment of all hypoprothrombinemic states encountered in the newborn period which are not due to extensive liver damage restoration of prothrombin levels to normal invariably follows administration of adequate doses of vitamin K (if it is given by routes which will facilitate absorption), and cessation of bleeding follows if deficiency of prothrombin is the causative factor in the hæmorrhage'" If his opinion is accepted, it seems either that the administration of vitamin K did not prevent the fall of blood prothrombin level in the infants in this series, or that the bleeding was due to some cause other than prothrombin deficiency

CONCLUSIONS

Vitamin K given to pregnant women before deliver does not always prevent hæmorrhagic disease of th newborn Its administration involves additional expense and increases the demands on the already over taxed nurses of maternity units It should therefore not becom part of routine treatment during labour in these units Opinions will vary about the advisability of its administration to mothers in labour, or to their infants soon afte birth, when there is an increased risk of neonatal bleedin —i e , in maternal toxæmia, premature labour, difficu or instrumental delivery, injury, asphyxia, and rhes incompatibility

SUMMARY

Vitamin K was administered to 4602 pregnant wom before delivery There were 12,131 controls Hæm rhagic disease was observed in 11 of the newborn infa of the vitamin K group (1 in 418) and in 23 of t controls (1 in 527)

It is concluded that vitamin K had no effect on t incidence of hæmorrhagic disease in this series

We wish to thank Prof N B Capon for his guidance planning this investigation, the obstetricians for th coöperation in allowing us to treat their patients, pædiatric registrars for the detailed supervision and record of the experiment and the nurses for cheerfully undertak

e additional duties involved. Messrs. Roche Products Ltd ecially prepared the 50 mg ampoules of 'Synkavit' and pplied them at reduced cost

REFERENCES

ck. A C. Taylor E S Colburn R. F (1941) *Amer J Obstet Gynec.* 41 765 Abstract in *J Amer med Ass* (1941) 117 558
ohlender G P Rosenbaum W M., Sage E C (1941) *J Amer med Ass* 116 1763
am H (1934) *Nature Lond* 133 909
— Schenkeyder F Tage-Henson E (1936) *Biochem J* 30 1075
— Tage-Henson E Plum P (1939) *Lancet* ii 1157
ncet (1944) i 506
ehmann J (1944) *Lancet* i 483
acpherson A I S., McCallum E Haultain W F T (1940) *Brit med J* i 839
ygaard, K. K. (1939) *Acta obstet gynec. scand* 19 361
oncher H. G (1942) *J Pediat* 20 637
tick, A. J., Grossman A. M. (1940) *Amer J med Sci* 199 1
anford H N., Shmigelsky I Chapin J M. (1942) *J Amer med Ass* 118 697
Waddell W W Jun., Guerry D (1939) *Ibid* 112 2259

THE TREATMENT OF GENERALISED STAPHYLOCOCCAL INFECTIONS

A. MELVIN RAMSAY
M.A., M.D Aberd
ASSISTANT PHYSICIAN

J VAHRMAN
M.B Lond.
SENIOR REGISTRAR

NFECTIOUS DISEASES UNIT ROYAL FREE HOSPITAL, LONDON

EXPERIENCE in a puerperal sepsis unit has shown hat while hæmolytic streptococcal infections have ecome mild and yield readily to penicillin therapy, eneralised staphylococcal infections still present many f the same problems as in the pre-penicillin period Ve review here our experience of these infections in hree periods—(1) pre-penicillin, (2) early penicillin, nd (3) late penicillin—in the hope of throwing light n the value of penicillin therapy, the best conditions or its use, and the limitations which may necessitate the mal of other antibiotics

PRE-PENICILLIN PERIOD

Between January, 1937, and December, 1943, 23 oatients with generalised infection due to *Staphylococcus pyogenes* were treated in the unit Of these, 18 followed abortion and 5 full-term delivery The 18 cases in the post abortum group constituted 36 8% of all cases in that group in which *Staph pyogenes* was isolated on cervical culture Thus the organism exhibits an invasive power far exceeding that of any other organism in puerperal infection, the corresponding figure for the hæmolytic streptococcus over the same period was 11% Of the 23 cases 10 proved fatal, a rate of 43 4%, which is lower than that of blood-stream infections due to the hæmolytic or anaerobic streptococcus in that period Chronic invalidity associated with infective foci on heart valves, in lung, and in joints was common Treatment with sulphonamides and staphylococcal antitoxin seemed to have little effect on the course of the disease

Clinically, although all cases gave repeatedly positive blood-cultures, the type of infection varied from the acutely fulminant to the subacute or chronic form which often subsided after the formation and evacuation of a single abscess Intermediate between these two extremes were the patients with widespread lesions, some of whom died after thirty to seventy days, while others recovered after a protracted course, often with residual lesions such as damaged heart valves healed lung abscesses, and chronic arthritic changes

EARLY PENICILLIN PERIOD

Between December, 1943, and April, 1946 8 cases were treated with small dosage of penicillin (i.e, about 15 000 units three hourly or four hourly), 2 were fulminant and proved fatal Of the 6 patients who recovered, only 2 showed good response to this dosage of penicillin Our early experience of penicillin in these generalised staphylococcal infections showed that (1) small dosage of penicillin, though sufficient to sterilise the blood stream even in the heaviest infections did not necessarily arrest the disease and (2) early cessation of penicillin therapy favoured relapse

The first point is illustrated by the following case

Case 23 (see table II and fig 1) was admitted on the twelfth day of disease and had bacterial counts of 3600 and 4820 organisms per ml. in the cultures made from blood taken on the first two days in hospital A course of penicillin 705,000 units in twelve days was followed by sterile cultures on the

TABLE I—PRE-PENICILLIN PERIOD

Case no	Post abortum or post partum	Grade of severity*	Duration of illness (days)	Cervical culture	No of positive blood cultures	Highest bacterial count (per ml)	Result	Notes
1	P.A	F	5	—	1		Died	*P.M* pancarditis pulmonary and renal abscesses
2	P.A.	P	33	—	1		Died	*P.M* peritonitis pulmonary and muscle abscesses
3	P.A	P	28	—	3	194	Died	*P.M* pulmonary embolism, pulmonary renal and splenic abscesses
4	P.A.	P	86—70	—	1		Recovered	Skin muscle, and breast abscesses left empyema, purulent arthritis of rt. knee Transferred to general hospital, developed infection of a vertebra
5	P.A.	M	33	—	1		Recovered	
6	P.A	M	27	—	1	8	Recovered	Inflammatory mass rt. pelvis
7	P.P	P	45	—	2		Recovered	Multiple abscesses both breasts treated by incision
8	P.A.	F	4	—	1		Died	*P M* pulmonary renal, and cerebellar abscesses
9	P.P	P	83	—	1		Recovered	Renal abscesses
10	P.P	P	59	—	1		Recovered	Pelvic peritonitis bilateral femoral thrombosis long stay in hospital
11	P.A.	M	33	—	1		Recovered	
12	P.P	P	27	—	2		Died	*P.M* muscle pulmonary and renal abscesses
13	P.A.	F	11	+	1	28	Died	*P.M* cardiac renal, and splenic abscesses
14	P.A.	P	45	+	1		Died	*P.M* pulmonary abscesses parametritis
15	P.A.	P	67—24	—	1	75	Died	Skin breast and cerebral abscesses. Transferred to general hospital for investigation of suspected spinal compression. died 1 month later no necropsy report available
16	P.P	F	9	—	1	95	Died	*P.M* left empyema and pulmonary and pelvic abscesses
17	P.A.	F	11	+	1	66	Died	*P.M* pulmonary and pelvic abscesses
18	P.A.	P	169	—	1		Recovered	Skin and renal abscesses suppurative arthritis of knee joint, and empyema thoracis
19	P.A.	M	39	—	1		Recovered	
20	P.A.	P	44	—	3	20	Recovered	Abscess rt arm
21	P.A.	P	135	—	1		Recovered	Muscle abscesses
22	P.P	P	47	—	1	230	Recovered	Skin abscess
23	P.A.	P	105	+	1	40	Recovered	Pulmonary and renal abscesses

* F, fulminant P, pyæmic M mild

who received vitamin K under the conditions specified, and 12,136 "controls" to whom no vitamin K was administered

RESULTS

Hæmatemesis and/or melæna occurred in 34 infants Of these, 11 were born to mothers who had received vitamin K before delivery The clinical details of the 34 cases are summarised in tables I and II The difficulty of confirming the diagnosis of hæmorrhagic disease is well known Infants not infrequently vomit blood which has been swallowed at birth, and this is especially likely to happen when the mother has had an antepartum hæmorrhage In all our cases the pædiatrician seeing the case at the time bleeding occurred formed the opinion that hæmorrhagic disease was the most likely diagnosis The occurrence of bleeding other than from the stomach or the bowel has not been recorded in this analysis, owing to the difficulty of excluding other causes of such hæmorrhages, nor has intracranial hæmorrhage been considered, for the experimental and control series are not strictly comparable

Hæmorrhagic disease of the newborn occurred therefore in 11 out of 4602 infants whose mothers had received vitamin K before delivery—i e, in 1 in every 418 cases—and in 23 of 12,136 infants whose mothers had not been given vitamin K—i e, in 1 in every 527 cases

TABLE I—HÆMORRHAGIC DISEASE IN INFANTS WHOSE MOTHERS HAD NOT RECEIVED VITAMIN K

Case no	Month and year of birth	Birth weight lb	Birth weight oz	Delivery	Clinical details
1	10/49	6	12	Vertex	Bright red blood in stool on 3rd day
2	3/49	8	0	Vertex	Severe melæna 53 hr after birth
3	5/49	6	8	Concealed A P H vertex forceps	Melæna on 1st and 2nd days
4	2/50	7	4	Vertex	Small hæmatemesis on 3rd day
5	9/48	5	14	Cæsarean section for eclampsia	Recurrent severe hæmatemesis starting 53 hr after birth
6	11/48	6	13	Vertex	Hæmatemesis on 2nd day
7	4/49	7	0	Vertex	Melæna on 3rd and 4th days
8	12/48	5	9	Vertex	Fairly severe melæna on 1st 2nd 3rd, and 4th days
9	9/48	7	7	Vertex and forceps	Melæna and hæmatemesis on 7th day
10	2/49	8	11	Vertex	Melæna on 2nd and 3rd days
11	10/48	6	12	Vertex retroplacental clot	Hæmatemesis and melæna on 4th day
12	6/48	7	2	Cæsarean section	Melæna on 5th and 6th days
13	12/48	7	9	Cæsarean section	Melæna on 1st 2nd and 3rd days and hæmatemesis on 2nd day
14	1/48	6	9	Vertex and forceps	Hæmatemesis on 4th day
15	12/49	4	6	Cæsarean section	Hæmatemesis and melæna for 24 hr, starting on 2nd day
16	1/50	6	14	Cæsarean section	Melæna and epistaxis on 2nd day
17	5/50	6	2	Vertex	Hæmatemesis on 3rd day melæna on 2nd 3rd 4th and 5th days vaginal bleeding on 6th day
18	7/49	7	10	Breech with forceps to head	Hæmaturia at 12 hr hæmatemesis on 2nd day died on 3rd day necropsy confirmed diagnosis
19	9/48	7	4	Vertex and forceps	Melæna on 2nd and 3rd days
20	1/49	6	13	Vertex	Hæmatemesis on 2nd day
21	6/49	6	0	Twin breech	Melæna on 3rd 4th and 5th days
22	5/49	4	10	Vertex	Hæmatemesis on 2nd day melæna on 3rd day
23	7/48	7	6	Mid forceps for disproportion	Melæna on 2nd day

TABLE II—HÆMORRHAGIC DISEASE IN INFANTS WHOSE MOTHERS HAD RECEIVED VITAMIN K

Case no	Month and year of birth	Birth weight lb	Birth weight oz	Delivery	Time of vitamin K before delivery	Clinical details
1	10/49	5	10	Vertex accidental A P H	8 hr 20 min	Melæna on 1st day
2	12/48	6	12	Vertex	4 hr 5 min	Bright red blood seen in two stools on 2nd day
3	4/50	4	7	Vertex and forceps	8 hr	Melæna from 3rd to 7th day concurrent umbilical sepsis, and septicæmia
4	7/48	5	11	Vertex	1 hr 10 min	10 melæna stools starting 9 hr after birth
5	9/48	8	13	Vertex	2½ hr	Melæna on 1st and 2nd days
6	9/48	5	13	Vertex	4½ hr	Hæmatemesis and melæna on 1st day
7	9/48	3	3	Vertex	2 hr	Hæmatemesis and melæna on 3rd day
8	8/48	8	1	Vertex	48 hr	Melæna on 2nd day
9	11/48	4	9	Vertex, A P H	15 min	Melæna from 1st to 3rd day
10	8/49	5	1	Vertex A P H	48 hr	Melæna on 5th day
11	5/49	6	1	Vertex	30 min	Two small vomits of altered blood 24 hr after birth

DISCUSSION

In view of the great variability of the incidence of hæmorrhagic disease in previous reports this difference is not considered to be significant, but it is quite clear that in this series the administration of vitamin K to mothers in labour did not prevent hæmorrhagic disease

Poncher (1942) wrote "Vitamin K and its analogues are effective in prevention and treatment of all hypoprothrombinemic states encountered in the newborn period which are not due to extensive liver damage invariable restoration of prothrombin levels to normal follows administration of adequate doses of vitamin K (if it is given by routes which will facilitate absorption), and cessation of bleeding follows if deficiency of prothrombin is the causative factor in the hæmorrhage" If his opinion is accepted, it seems either that the administration of vitamin K did not prevent the fall of blood prothrombin level in the infants in this series, or that the bleeding was due to some cause other than prothrombin deficiency

CONCLUSIONS

Vitamin K given to pregnant women before delivery does not always prevent hæmorrhagic disease of the newborn Its administration involves additional expense and increases the demands on the already overtaxed nurses of maternity units It should therefore not become part of routine treatment during labour in these units Opinions will vary about the advisability of its administration to mothers in labour, or to their infants soon after birth, when there is an increased risk of neonatal bleeding—i e, in maternal toxæmia, premature labour, difficult or instrumental delivery, injury, asphyxia, and rhesus incompatibility

SUMMARY

Vitamin K was administered to 4602 pregnant women before delivery There were 12,131 controls Hæmorrhagic disease was observed in 11 of the newborn infants of the vitamin K group (1 in 418) and in 23 of the controls (1 in 527)

It is concluded that vitamin K had no effect on the incidence of hæmorrhagic disease in this series

We wish to thank Prof N B Capon for his guidance in planning this investigation, the obstetricians for their coöperation in allowing us to treat their patients, our pædiatric registrars for the detailed supervision and recording of the experiment and the nurses for cheerfully undertaking

additional duties involved Messrs Roche Products Ltd cially prepared the 50 mg ampoules of 'Synkavit' and plied them at reduced cost

REFERENCES

, A C, Taylor, E S, Colburn, R F (1941) *Amer J Obstet Gynec* 41 765 Abstract in *J Amer med Ass* (1941) 117 558
ender, G P, Rosenbaum, W M., Sage E C (1941) *J Amer med Ass* 116 1763
H (1934) *Nature Lond.* 133 909
Schonheyder F Tage Henson E (1936) *Biochem J* 30, 1075
Tage Henson E Plum P (1939) *Lancet,* ii 1157
cet (1944) i 506
mann J (1944) *Lancet,* i 493
pherson, A I S McCallum E Haultain W F T (1940) *Brit med J* 1, 839
aard K K (1939) *Acta obstet gynæc scand* 19, 361
cher, H G (1942) *J Pediat* 20 637
ck A J Grossman A M. (1940) *Amer J med Sci* 199, 1
ford H N Shmigelsky, I Chapin, J M. (1942) *J Amer med Ass* 118 697
ddell W W jun, Guerry D (1939) *Ibid* 112 2259

THE TREATMENT OF GENERALISED STAPHYLOCOCCAL INFECTIONS

A. MELVIN RAMSAY
M.A, M.D Aberd
ASSISTANT PHYSICIAN

J VAHRMAN
M.B Lond
SENIOR REGISTRAR

FECTIOUS DISEASES UNIT, ROYAL FREE HOSPITAL, LONDON

EXPERIENCE in a puerperal sepsis unit has shown at, while hæmolytic streptococcal infections have come mild and yield readily to penicillin therapy, neralised staphylococcal infections still present many the same problems as in the pre penicillin period e review here our experience of these infections in ree periods—(1) pre penicillin, (2) early penicillin, d (3) late penicillin—in the hope of throwing light the value of penicillin therapy, the best conditions r its use, and the limitations which may necessitate the al of other antibiotics

PRE PENICILLIN PERIOD

Between January, 1937, and December, 1943, 23 atients with generalised infection due to *Staphylococcus yogenes* were treated in the unit Of these, 18 followed bortion and 5 full term delivery The 18 cases in the post abortum group constituted 36 8% of all cases in that group in which *Staph pyogenes* was isolated on cervical culture Thus the organism exhibits an invasive power far exceeding that of any other organism in puerperal infection, the corresponding figure for the hæmolytic streptococcus over the same period was 11% Of the 23 cases 10 proved fatal, a rate of 43 4%, which is lower than that of blood-stream infections due to the hæmolytic or anaerobic streptococcus in that period Chronic invalidity associated with infective foci on heart valves, in lung, and in joints was common Treatment with sulphonamides and staphylococcal antitoxin seemed to have little effect on the course of the disease

Clinically, although all cases gave repeatedly positive blood cultures, the type of infection varied from the acutely fulminant to the subacute or chronic form which often subsided after the formation and evacuation of a single abscess Intermediate between these two extremes were the patients with widespread lesions, some of whom died after thirty to seventy days, while others recovered after a protracted course, often with residual lesions such as damaged heart valves, healed lung abscesses, and chronic arthritic changes

EARLY PENICILLIN PERIOD

Between December, 1943, and April, 1946, 8 cases were treated with small dosage of penicillin (i e, about 15,000 units three hourly or four hourly), 2 were fulminant and proved fatal Of the 6 patients who recovered, only 2 showed good response to this dosage of penicillin Our early experience of penicillin in these generalised staphylococcal infections showed that (1) small dosage of penicillin, though sufficient to sterilise the blood stream even in the heaviest infections, did not necessarily arrest the disease, and (2) early cessation of penicillin therapy favoured relapse

The first point is illustrated by the following case

Case 23 (see table II and fig 1) was admitted on the twelfth day of disease and had bacterial counts of 3600 and 4820 organisms per ml in the cultures made from blood taken on the first two days in hospital A course of penicillin 705,000 units in twelve days was followed by sterile cultures on the

TABLE I—PRE PENICILLIN PERIOD

Case no	Post abortum or post partum	Grade of severity*	Duration of illness (days)	Cervical culture	No of positive blood cultures	Highest bacterial count (per ml)	Result	Notes
1	P.A	F	5	+	1		Died	*P M* pancarditis pulmonary and renal abscesses
2	P A	P	33	+	1		Died	*P M* peritonitis pulmonary and muscle abscesses
3	P.A	P	28	—	3	104	Died	*P M* pulmonary embolism pulmonary renal and splenic abscesses
4	P.A.	P	86 +70	+	1		Recovered	Skin, muscle and breast abscesses left empyema purulent arthritis of rt. knee Transferred to general hospital developed infection of a vertebra
5	P.A	M	33	+	1		Recovered	
6	P.A	M	27	+	1	8	Recovered	Inflammatory mass rt. pelvis
7	P.P	P	45	—	2		Recovered	Multiple abscesses both breasts treated by incision
8	P.A.	F	4	+	1		Died	*P M* pulmonary renal, and cerebellar abscesses
9	P.P	P	83	+	1		Recovered	Renal abscesses
10	P P	P	59	+	1		Recovered	Pelvic peritonitis bilateral femoral thrombosis long stay in hospital
11	P A	M	33	+	1		Recovered	
12	P.P	P	27	—	2		Died	*P M* muscle pulmonary and renal abscesses
13	P A.	F	11	+	1	28	Died	*P M* cardiac renal and splenic abscesses
14	P A	P	45	+	1		Died	*P M* pulmonary abscesses, parametritis
15	P.A	P	67 +24	+	7	75	Died	Skin breast and cerebral abscesses. Transferred to general hospital for investigation of suspected spinal compression, died 1 month later no necropsy report available
16	P.P	F	9	+	1	95	Died	*P M* left empyema and pulmonary and pelvic abscesses
17	P.A	F	11	+	1	66	Died	*P M* pulmonary and pelvic abscesses
18	P.A	P	169	—	1		Recovered	Skin and renal abscesses suppurative arthritis of knee joint and empyema thoracis
19	P A.	M	39	+	1		Recovered	
20	P.A	P	44	+	3	20	Recovered	Abscess rt arm
22	P.A	P	135	+	1		Recovered	Muscle abscesses
24	P.P	P	47	+	1	230	Recovered	Skin abscess
27	P.A	P	105	+	1	40	Recovered	Pulmonary and renal abscesses

* F fulminant P pyæmic M mild

first, second, fourth, and eighth days of its administration, but the patient died after fourteen days, and necropsy showed vegetations on the heart valves, and cerebral hæmorrhages from embolic lesions in the pons and medulla

The second point is illustrated by cases 21 and 28

Case 21 (see table II and fig 2), aged 29, was admitted two days after a three month abortion, having been pyrexial for twenty four hours The day after admission the uterus was evacuated because of hæmorrhage Ten days later the patient developed staphylococcal septicæmia The blood culture was positive on six occasions, and, despite treatment with 100 g of sulphapyridine and sulphathiazole, the bacterial count rose from 75 to 703 organisms per ml By this time a systolic bruit had developed in the pulmonary area The patient was next given a course of 790,000 units of penicillin in seven days, pyrexia subsided and two consecutive blood cultures were sterile Three days after penicillin had been stopped the pyrexia recurred and blood culture produced *Staph aureus* 167 organisms per ml After a course of 870,000 units of penicillin pyrexia again subsided and three consecutive blood cultures proved sterile After two weeks a second relapse occurred with two positive blood cultures and a count of 187 organisms per ml A third course of 375,000 units of penicillin was given and this finally controlled the septicæmia, seven consecutive sterile blood cultures being obtained Owing to the development of endocarditis convalescence was protracted and the patient was finally discharged from hospital after a stay of one hundred and ninety one days

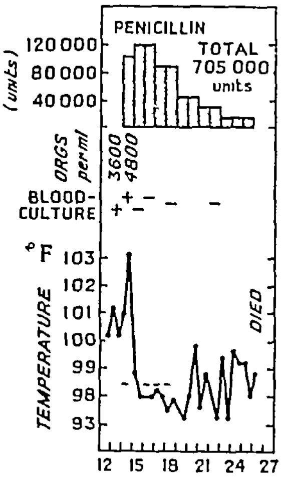


Fig 1—*Staph aureus* septicæmia with mitral stenosis with recent vegetations subdural hæmorrhage septic splenic infarcts and chronic nephritis (case 23, table II)

Case 28 (see table II), aged 23, became pyrexial eight days after an abortion and was admitted to a general hospital *Staph aureus* was grown both from the vaginal swab and on blood culture Arthritis of the right wrist and knee developed, and radiography of the chest showed patchy consolidation of the right middle and lower zones The patient was treated with penicillin 700,000 units and sulphathiazole 28 g in five days and transferred to the unit twelve days after the commencement of her illness As in the previous case, a succession of small courses of penicillin did not arrest the disease, and successive blood cultures gave bacterial counts of 580, 1200, and 2800 organisms per ml Improvement finally took place after a course of penicillin 1,875,000 units in fourteen days This was maintained for two weeks, when a further relapse necessitated a course of penicillin 1,540,000 units in seventeen days *Staph aureus* was isolated from the sputum on 47 occasions in sixty nine days and was penicillin sensitive throughout Septicæmia in this case resulted from the constant reinfection of the blood from multiple lung foci The patient was finally discharged from hospital after a stay of one hundred and ninety-eight days

As a result of these and similar cases in this period it was felt that more intensive and prolonged dosage of penicillin was required from the outset in this type of case

LATE PENICILLIN PERIOD

At the beginning of this period 5 cases were treated with penicillin 500,000 units three hourly from the time the diagnosis was made This had the effect of immediately arresting embolic spread and shortened considerably the stay in hospital Cases 34 and 36 had penicillin resistant strains of organism

Case 34 (table III), aged 35, was admitted on the thirty-fifth day of illness with low grade septicæmia and much enlarged liver and spleen A highly resistant strain of *Staph aureus* sensitive to 6 25 units of penicillin per ml was isolated from the blood on seven consecutive days, the highest bacterial count was 10 organisms per ml Clinical improvement did not take place until the dose of penicillin was raised to 500,000 units three hourly

Case 36 (table III), aged 18, became infected after cæsarean section performed at the twenty eighth week of pregnancy because of toxæmia The patient became pyrexial from the day of operation She was given a course of penicillin in gradually increasing doses over eleven days Within twenty four hours of the end of the course an embolic mid tarsal arthritis developed The patient was next transferred to the unit, and penicillin therapy was started again in doses of 500,000 units three hourly for four days and thereafter in reduced dosage for nine days A total of 29 mega units was given Pyrexia subsided within twenty four hours of the commencement of treatment, and the affected joint did not suppurate

Case 32 (table III), aged 33, comparable to case 28 above had bilateral purulent pleural effusions, and 35 colonies of penicillin sensitive *Staph aureus* per ml were found in the blood There were multiple skin emboli and red cells in the urine The patient was given 4 mega units of penicillin daily for eleven days and thereafter 2 mega units daily for fourteen days She was discharged after sixty one days in hospital

Case 33 (table III and fig 3), aged 30, with peritonitis and pulmonary abscesses, responded satisfactorily to penicillin 500,000 units three hourly for nine days The dose was then reduced too rapidly, and the patient developed an infection in the right sternoclavicular joint Penicillin 500,000 units six hourly was given for nineteen days before activity in

TABLE II—EARLY PENICILLIN PERIOD

Case no	Post abortum or post partum	Grade of severity	Duration of illness (days)	Cervical culture	No of positive blood cultures	Highest bacterial count (per ml)	Resistance of organism to penicillin	Amount of penicillin (units)	Result	Notes
21	P A	P	191	+	9	703		2,035 000	Recovered	Endocarditis and muscle abscesses
23	P A	P	21	+	2	4820		705 000	Died	*P M* endocarditis renal and splenic abscesses, and cerebral hæmorrhages
25	P A	F	6	+	2	2000		45 000	Died	*P M* endocarditis pulmonary renal and splenic abscesses
26	P A	P	103	+	4		Sensitive	1 005 000	Recovered	Bilateral empyema thoracic pulmonary renal and skin abscesses
28	P A	P	210	+	12	2800	Sensitive	5 475 000	Recovered	Pulmonary abscesses suppurative arthritis knee joint
29	P P	P	40	–	2	16		930 000	Recovered	Pulmonary abscesses aseptic arthritis rt. wrist and lt. knee
30	P A	P	38 +	+	3	280		2 560 000	Recovered	Osteomyelitis rt. femur and multiple skin emboli Transferred to general hospital (period unknown)
31	P A	P	24	–	1			1,000 000	Recovered	Pulmonary abscesses

TABLE III—LATE PENICILLIN PERIOD

Case no	Post abortum or post partum	Grade of severity	Duration of illness (days)	Cervical culture	No of positive blood cultures	Highest bacterial count (per ml.)	Resistance of organism to penicillin	Amount of penicillin (units)	Result	Notes
32	P.A	P	62	+	2	35	Sensitive	85,900 000	Recovered	Bilateral empyema thoracis, pulmonary renal and skin abscesses
33	P.A	P	76	+	1	500	Sensitive	83 350,000	Recovered	Peritonitis pulmonary abscesses Generalised tenderness of muscles on admission, rt sternoclavicular arthritis but no abscess formation followed
34	P A	M	47	+	7	10	Sensitive to 6 25 units/ml	36 850 000	Recovered	
35	P.A	P	59	+				24 920 000	Recovered	Peritonitis, pulmonary abscesses Long illness, treated with penicillin in general hospital before transfer
36	P.P	P	70 +61	+	1		Resistant strain	39 600 000	Recovered	Cæsarean section wound infected mid tarsal arthritis and renal infection
37	P.A	F	8	+	5	21	Sensitive to 0 6 units/ml on admission 3 days later sensitive to 20 units/ml.	14 000 000	Died	*P M* pulmonary, renal and cerebral abscesses
38	P A.	P	27	+	2		Sensitive	25,250 000	Died	*P M* endocarditis, cerebra abscesses renal necrosis

the joint completely subsided. The organism was penicillin sensitive

It was felt that massive dosage of penicillin from the earliest possible moment, and avoidance of the temptation to withhold penicillin merely because pyrexia had subsided, might provide the key to treatment of both the resistant strain of organism and the latent and inaccessible focus of infection Recent experience, however, suggests that penicillin may not be the final answer to the problem of generalised staphylococcal infection Two cases illustrate well the difficulties still encountered.

Case 37 (table III) aged 28, was admitted eleven days after an abortion A year previously the patient had had a nephrectomy for hydronephrosis, this was complicated by empyema, for which penicillin was administered before the empyema was drained There had been intermittent discharge from the nephrectomy wound since the operation

On admission the patient was shocked and pale The hæmoglobin was 30% Two pints of blood was given, and under general anæsthesia a large mass of putrefying placenta was removed

Progress—Next day the patient was still pyrexial the hæmoglobin had risen to 42% the venous pressure was raised and the liver was palpable 3 in below the costal margin The blood pressure was 95/40 Next day a systolic murmur was heard at the pulmonary base The patient had neck rigidity and a positive Kernig sign The cerebrospinal fluid (C S.F) contained 1660 cells per c.mm (polymorphs 98%) and total protein 60 mg per 100 ml The nephrectomy sinus was discharging

Treatment was begun with penicillin 500 000 units three hourly After a loading dose of 4 g, Sulphatriad was given in doses of 1 g three hourly The treatment was continued until death but did not sterilise the blood stream A further transfusion was given Next day the patient became comatose and died in six hours

Blood-cultures were positive on five occasions in five days, and the bacterial count did not exceed 21 organisms per ml The organism obtained from the blood and the nephrectomy wound were of the same phage type When first obtained from the blood the organism was sensitive to penicillin 0 6 unit per ml The organism obtained from the blood the day before the patient died was sensitive to penicillin 20 units per ml

Necropsy showed purulent fluid in the lateral ventricles and an area of softening in the pons The left lung was adherent to the chest wall, there were two septic infarcts one in the upper and the other in the lower lobe of the left lung The heart valves were healthy but the muscle showed toxic changes There was a small amount of renal tissue left associated with chronic inflammation A sinus extended

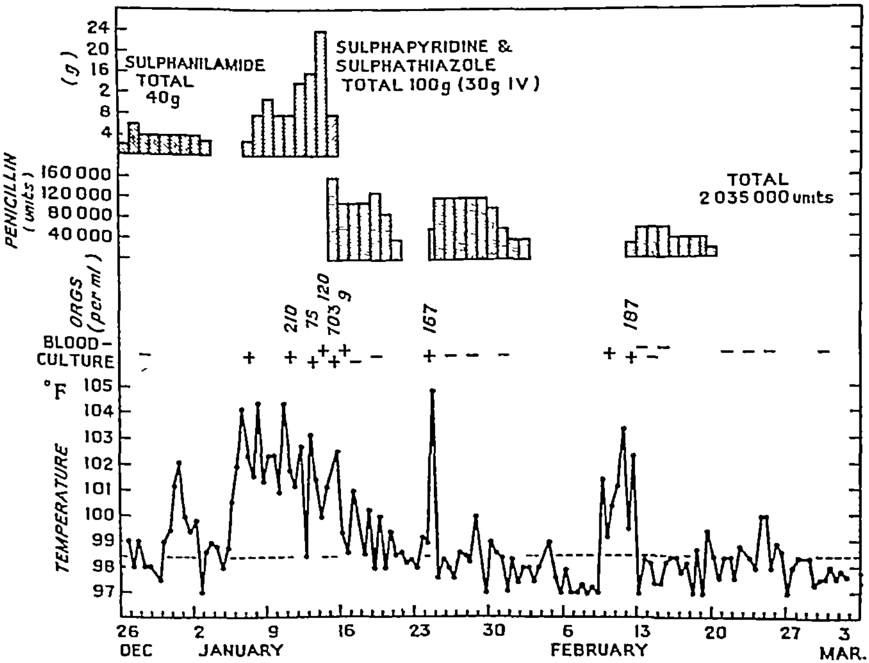


Fig 2.—*Staph aureus* septicæmia with infective endocarditis (case 21, table II)

TABLE I—RESULTS OF TREATMENT AND TOXIC EFFECTS WITH LYSIVANE

Type and no of cases treated	Improvement			No change	Worse	Developed toxic effects *
	Grt	Mod	Slt			
Postencephalitic 24						13(6)
Severe 13	1	4	4	4		
Moderate, 8		3	1	2	2	
Mild 3			2	1		
Idiopathic 17						11(3)
Severe 1					1	
Moderate, 12	1	7	4			
Mild, 4	1	1		2		
Arteriosclerotic 2						
Severe 1			1			
Moderate 1		1				
Total, 43	3	16	12	9	3	24(9)

* Numbers of cases in which treatment had to be suspended are shown in parentheses

Toxic Symptoms

Drowsiness	7	Pressure on head or head ache	4
Ataxia	7	Flushing of face	3
Muzziness or confusion	6	Slurred speech	3
Blurred vision	6	Nausea and vomiting	2
Lightheadedness or giddiness	6	Dryness of mouth	2
Derealisation or depersonalisation	4	Stiffness worse	2
" Funny feelings "	4	Tremor worse	1
		Oculogyric crises worse	2

When examined on Dec 9, 1948, his face was immobile and there was a moderate increase of tone in the right arm and leg, but there was no tremor He held his right hand flexed and did not swing it when walking His gait was shuffling, and he dragged the right leg

Treatment —Initially he was given 'Rabellon' tab 1 t d s without any improvement He began taking parpanit on Jan 20, 1949, and when he was taking 75 mg six times a day there was considerable improvement but he complained of nausea and occasional vomiting He remained free from toxic symptoms on 50 mg six times a day On Sept 29, lysivane was gradually substituted for the parpanit, the initial dosage of 50 mg t d s being increased later to 50 mg ten times a day This dose caused some retching and was therefore reduced to 50 mg eight times a day

Progress —The patient noted much more improvement than with parpanit He said he could pick coins out of his pocket with his right hand much more easily and could sit down and rise to his feet more quickly , his writing improved , and the dragging of his right leg disappeared On later visits he said " There is no further improvement because there is nothing to improve on " The immobility of his facies was still obvious though improved, and tone in the right arm and leg was now normal In March, and again in April, 1950, he was given artane in addition to the lysivane, but on each occasion it was discontinued because of nausea and vomiting No added effect was noticed Artane was not tried alone

This was a mild case which improved considerably on lysivane

Case 2 —*Severe postencephalitic* A man, aged 37, had had encephalitis lethargica in 1925 Rigidity and tremor began in the left arm in 1930 and slowly progressed to involve the left leg He developed a festinant gait with dragging of the left foot and a mask like facies and was having oculogyric crises about once a week, each lasting up to three hours

Treatment —He had been taking tincture of hyoscyamus min. 70 t d s this was stopped, and lysivane 50 mg t d s was started on Jan 25, 1950 and increased by 50 mg daily At first the dosage was halted at 600 mg daily, by which time the duration of the oculogyric crises had been reduced to 20 minutes and there was slightly less rigidity Next the dosage was increased by daily increments of 50 mg to 750 mg daily, with marked subjective improvement , his posture noticeably improved, and he was free from oculogyric crises for seven days Then the dosage was slowly increased in the next three weeks to 1500 mg daily His gait improved, the oculogyric crises were still infrequent, he was cheerful, and for the first time for years he became useful in the ward He still receives 1500 mg of lysivane daily and has not had any unpleasant side effects

This case was assessed as moderately improved

Case 3 —*Severe postencephalitic* A man, aged 39 It was not possible to obtain any accurate history of the onset of his condition, he had a mask like facies and was having three or four oculogyric crises every week, each lasting up to nine hours Well marked tremor was present in the tongue, jaw, and right arm and leg, with typical cog wheel rigidity, a flexed posture, and a tendency to propulsion and retropulsion He could not dress, do his hair, or feed himself Dysarthria was severe, and he had frequent severe attacks of hyperkinesia accompanied by behaviour disorders.

Treatment —He had been receiving tinct hyoscyami min. 75 daily He was now given lysivane 50 mg t d.s. and the hyoscyamus was gradually withdrawn in the next seven days, while the lysivane was increased by 50 mg daily to 300 mg a day In a fortnight he could feed himself for the first time in years The dose was gradually increased to 500 mg daily He began to feel and look better, his face became more animated, his speech was slightly easier to understand, his behaviour disorders were less frequent, the duration of the oculogyric crises was reduced to 20 minutes, and he could dress himself Little further improvement occurred over the next four weeks, though the dosage was raised to 1500 mg daily for three weeks He then complained that the tablets made him dopey and confused With difficulty he was persuaded to persevere with them, and he was also given 10 mg of amphetamine sulphate daily, with no improvement. He still complained of feeling queer on the tablets and refused to take any more A change was made to artane starting with 5 mg t d s and increasing to 30 mg daily with no ill effects The greatest improvement that had been reached with lysivane was maintained by artane in this dose Oculogyric crises became rare and less severe For the first time in many years the patient was fit to be entrusted with ward work

This case was assessed as moderately improved with lysivane, though the patient could not tolerate a long course of this drug His improvement was then maintained with artane

TOXIC EFFECTS OF LYSIVANE

Of the 43 patients who received lysivane, 24 complained of unpleasant side effects, and in 9 cases these were sufficiently troublesome to necessitate discontinuing the drug The symptoms were never alarming and always subsided rapidly on the withdrawal of lysivane In only one case was there any untoward result a patient with idiopathic parkinsonism became ataxic, fell, and sustained a crush fracture of D12 and L1 vertebræ Most of the patients who experienced side effects complained of several symptoms The details are given in table II

Four patients developed mild depersonalisation, and 4 others complained of " funny feelings " which seemed to be in the same category Only one had to stop the treatment , in the others the sensation was transient, mild, and either subsided spontaneously or as a result of reduction in the dosage of lysivane

Accentuation of symptoms was observed in 5 patients —rigidity in 2, oculogyric crises in 2, tremor in 1—and in 3 cases this necessitated the discontinuance of lysivane , it proved transient in the other 2 (1 with increased rigidity and 1 with increased tremor)

As a result of a warning from the manufacturers of lysivane about the possibility of agranulocytosis, frequent white cell counts were made in all the cases No leucopenia was observed

RESULTS WITH ARTANE

Artane was given to 51 patients with results which are summarised in table II Of the 31 postencephalitics, 24 were improved, 5 unaffected, and 2 became worse, of the 16 idiopathic cases, 11 were improved and 5 unchanged , one arteriosclerotic was greatly improved whereas the other was unaltered , and 2 patients with extrapyramidal disorders of obscure ætiology were symptomatically improved Altogether, 38 of the 51 cases derived some benefit, 11 were unchanged, and 2 became worse

TABLE II—RESULTS OF TREATMENT AND TOXIC EFFECTS WITH ARTANE

Type and no of cases treated	Improvement			No change	Worse	Developed toxic effects*
	Grt	Mod	Slt			
Postencephalitic 31						9 (1)
Severe 19	1	10	4	2	2	
Moderate 11	2	2	4	3		
Mild 1	1					
Idiopathic 16						9 (2)
Severe 1				1		
Moderate 11	1	6	1	3		
Mild 4	1	1	1	1		
Arteriosclerotic 2						1 (0)
Severe 1				1		
Mild 1	1					
Others 2						
Moderate 2	1	1				
Total 51	8	20	10	11	2	19(3)

*Number of cases in which treatment had to be suspended are shown in parentheses.

Toxic Symptoms

Giddiness	5	Epigastric pain	1
Dry mouth	4	Drowsiness	1
Depersonalisation	4	Increased tremor	1
Nausea and vomiting	3	Slurred speech	1
Blurred vision	2	Ataxia	1
Increased rigidity	2	Flushing of face	1
Weakness of legs	2		

Illustrative Cases

Case 4 —*Moderate idiopathic* A man, aged 57 When examined on Jan. 25, 1950, he had a mask like facies and tremor with moderate rigidity of both arms His gait was little affected but he did not swing his arms

Treatment and Progress—Artane was started with 2 mg t d.s and increased to 5 mg t d s At first there was little improvement except that the face was more animated, but in the fourth week his tremor ceased, and at the end of a month his rigidity had also improved Some side-effects were now noted, particularly transient diplopia on upward deviation of the eyes Troublesome flushing and sweating also occurred after taking the tablets and, on the chance that these symptoms might be due to liberation of histamine, he was given phenergan 25 mg at night, with considerable benefit

This case is assessed as moderately improved

Case 5 —*Moderate postencephalitic* A man, aged 47, had noted increasing weakness and tremor of his right arm since 1944 A year after the onset the right leg became similarly affected His only previous treatment had been physiotherapy and benadryl When he was examined on Jan 25 1950, his facial expression seemed normal but tremor and cog wheel rigidity of moderate severity were present in the right arm and leg He did not swing either arm on walking, and his gait was slow

Treatment and Progress —He was started on artane 2 mg t.d.s which was rapidly increased to 5 mg t d s Within seven days he felt much more alert but there was little alteration in his physical signs, and the dose was therefore increased to 17 5 mg daily

Here the patient thought his condition was vastly improved, but the improvement was assessed as only moderate

Case 6 —*Severe postencephalitic* A woman, aged 34, an example of the completely helpless cases Her history is unknown She had a mask like facies, was having oculogyric crises lasting three hours two or three times a week, there was intense cog wheel rigidity of all her limbs, and severe contractures had formed in all her major joints, so she was incapable of attending to her bodily needs

Treatment had been with tincture of stramonium in high dosage Artane 2 mg t d.s was started on Jan. 9 1950 and a slight reduction in rigidity soon became apparent Amphetamine sulphate 10 mg daily was then given in addition. In the next fortnight she improved further and for the first time for many years she printed her name Artane and amphetamine sulphate were gradually increased until Feb 27 she was receiving 35 mg of artane daily in seven doses and one morning dose of 20 mg of amphetamine sulphate Movement was now possible at most joints to an extent limited by the contractures Oculogyric crises now occurred once or twice a week and usually lasted only one or two hours Improvement continued In March she could adjust her hair slide and soon afterwards she wrote her first letter for many years Artane has been slowly increased to 80 mg daily in six divided doses, and amphetamine sulphate to 25 mg b d

The parkinsonism in this case has been materially improved, but contractures prevent the patient taking full advantage of the reduction in rigidity, and she remains almost completely helpless She was assessed as slightly improved

TOXIC EFFECTS OF ARTANE COMPARISON WITH LYSIVANE

Though 19 patients complained of side effects (table II), in only 3 was it necessary to discontinue treatment Up to now, changes in the blood picture have not been noted in any of the patients

The difference in the toxic effects of lysivane and artane is not fully brought out in the tables On the whole the symptoms produced by artane were trivial and certainly less severe than those seen with lysivane The difference is seen best in the numbers of cases where the drugs had to be discontinued—with lysivane 9 patients out of 43, and with artane only 3 out of 51 It should be noted too that patients who developed multiple side effects on one drug were likely to develop similar symptoms on the other, and such patients often developed toxic symptoms with the other drugs used in the treatment of parkinsonism, particularly parpanit and diparcol Rapid withdrawal of either artane or lysivane seemed to be quite safe In 4 cases in which the parkinsonian symptoms had improved, a change to dummy tablets caused a dramatic return of their former severity, but in no case could any symptoms be ascribed to the actual withdrawal.

DISCUSSION

In lysivane and artane we have two potent substances for the relief of some of the symptoms and signs of parkinsonism There seems to be no sure method of forecasting whether a particular case will respond satisfactorily to either compound, except that cases which have not responded to other substances in adequate doses seem likely to resist the beneficial effects of artane or lysivane, whereas if there has been some response to other remedies better results are likely to follow a change to one of these two substances

The few published reports of cases treated with artane agree to a remarkable extent in the percentage of cases responding favourably Thus Doshay and Constable (1949), report 117 cases, with 76 1% improved , Corbin (1949) 80 cases with 76 9% improved , Ellenbogen (1950) 12 cases with 66% improved , and Phillips et al (1950) 35 cases with 80% improved In the present series the improvement rate was similar—74 5% improved out of the 51 cases treated with artane Like most of the other observers cited, we found that postencephalitic cases required, and tolerated, higher doses than the other varieties. We have given our patients much larger doses than those reported by other workers A few of our cases are now receiving 60–100 mg of artane daily with a striking absence of side effects, though the average is about 50 mg daily Artane often gives patients a feeling of well being over and above that which might reasonably be expected to follow the relief of symptoms

Ellenbogen (1950) and Phillips et al (1950) state that doses higher than 35–45 mg daily cause no additional improvement in the postencephalitic In the present series, on the contrary, it was found necessary in most cases to exceed 50 mg before the full benefit was obtained. In many postencephalitic cases amphetamine has a potentiating effect on artane, this is a firm clinical impression though difficult to assess quantitatively.

Hitherto no series of cases treated with lysivane has been published. In the present series 72% of the patients who received lysivane showed some degree of improvement, compared with 74.5% with artane. In general, however, the improvement obtained with artane is somewhat greater than with lysivane. 8 out of 51 cases (16%) showed "great improvement" with artane, compared with only 3 out of 43 (7%) with lysivane. Artane is decidedly less toxic than lysivane, and of the 9 patients who were intolerant to lysivane in the present series, all but 2 were able to take artane later, though some had slight toxic symptoms. Moreover, the side effects that occurred were in general less severe with artane than with lysivane. Either lysivane or artane can be rapidly withdrawn with no other ill effect than a sudden return of symptoms in their previous severity.

Most of the 24 patients treated with both lysivane and artane preferred the artane. This was related to its greater efficiency, its lower toxicity, and the sense of well being that artane produces. Nevertheless, some patients derived equal benefit from the two drugs, and a few were decidedly better on lysivane.

Most of the severe postencephalitic cases treated with artane and amphetamine sulphate were in a distressing state of almost complete immobility. None were capable of ward duties. Since the introduction of artane and amphetamine sulphate treatment there has been a striking change in the atmosphere of the ward. Most patients can now feed themselves, and many can dress and attend to their own toilet. A few can get about, though with difficulty, and some have taken on simple ward duties. Apart from the benefit to the patients themselves this has considerably lightened the nurses' tasks.

Both artane and lysivane seem to reduce the rigidity more than the tremor, but occasionally the tremor becomes more marked as an extreme degree of rigidity (which had previously masked it) becomes less. In many instances tremor also was remarkably reduced. This was particularly striking in a patient with severe tremor of the right arm following a vascular lesion (Benedikt's syndrome), in which artane 5 mg four times a day produced a dramatic improvement, which has been maintained up to date.

Artane has some effect in reducing the number and duration of oculogyric crises. In one woman who had previously been having an attack lasting four hours once a week, since treatment with artane, the attacks have occurred every 10–14 days and have lasted only one or two hours. Lysivane seemed equally effective in this respect. Thus a man who previously had two oculogyric crises lasting about three hours every week, when taking a daily dose of 1250 mg of lysivane had more than a week between attacks, and the attacks lasted only an hour. Neither of these cases received any amphetamine sulphate.

SUMMARY AND CONCLUSION

Artane and lysivane have been used in the treatment of 70 cases of parkinsonism. 51 patients receiving artane, 43 lysivane, and 24 both drugs at different times. Improvement was noted in 74.5% with artane, and in 72% with lysivane.

Both artane and lysivane control the rigidity better than the tremor. Both reduce the number and duration of oculogyric crises in postencephalitic parkinsonism.

Higher dosage of artane than that reported by other workers has been used with good effect and minimal side effects.

The action of artane is often enhanced by amphetamine sulphate in postencephalitics.

Artane is less likely to produce unpleasant side-effects than lysivane, and for this reason is likely to prove the drug of choice for most cases of parkinsonism.

I am indebted to Dr Macdonald Critchley, of King's College Hospital, and Dr W A Caldwell, physician superintendent, West Park Hospital, Epsom, who allowed access to their cases and encouraged this present investigation, Dr W R Thrower for his help, and Messrs May and Baker Ltd for supplies of lysivane.

REFERENCES

Corbin, K B (1949) *J Amer med Ass* 141 377
Cunningham R W, Harned B K, Clark M C, Cosgrove R R, Daugherty N S, Hine, C H, Vessey, R E, Yuda N N (1949) *J Pharmacol* 96 151
Doshay L J, Constable, K (1949) *J Amer med Ass* 140 1317
Ellenbogen B K (1950) *Lancet* i, 1034
Phillips J, Montuschi I, Sharkey, J (1950) *Ibid* p 1131
Sigwald J (1949) *Pr méd* 57, 819

THE DUST CELLS IN THE LUNGS OF THE ALBINO MOUSE*

THEIR STRUCTURE, RELATIONS, AND MODE OF ACTION

Charles Clifford Macklin
M D, Ph D Toronto, F R S C
RESEARCH PROFESSOR OF HISTOLOGY, UNIVERSITY OF WESTERN ONTARIO, LONDON, CANADA

Dust cells are phagocytes which have developed in the pulmonary alveoli of man and other mammals and ingest particles of carbon and other material entering the lung with the inspired air. In man the dust cells are seen under unfavourable conditions in ordinary sections, because the available lungs are often diseased, putrefied, and imperfectly fixed. The lungs of the albino mouse, however, offer excellent opportunity to study the dust cells both in their normal forms and relations and under experimental conditions. The results of such study may aid in the understanding of alveolar phagocytes in man.

SUMMARY OF OBSERVATIONS

Dust cells are fundamentally mural phagocytes

When normal lungs of albino mice and other mammals are quickly fixed without previous collapse, the alveolar phagocytes (dust cells) are found almost exclusively attached to the alveolar walls rather than free (figs. 1 and 2). This means that under normal conditions they are sessile. Counts made on thin stained sections of such material show as many as 99% or more of the dust cells morphologically affixed to the alveolar walls.

Free dust cells in uncollapsed normal alveoli are few

In normal lung tissue fixed without previous collapse a few alveolar phagocytes are found free in the alveoli; these are usually round or ovoid. Counts show as few as 1% or less in this untethered condition; these are regarded as cells whose phagocytic potencies have been expended. They have been loosened from their moorings in the alveolar walls, and would probably have found their way to the ciliary escalator of the bronchial tree.

Methods of fixation without collapse

For the demonstration of dust cells in their normal habitat on the alveolar walls in the mouse, the method of immersion of the fresh flayed unopened thorax in fixing solutions such as Regaud's or Bouin's at room temperature was found satisfactory. For larger animals, as well as the mouse, the method of perfusion of fixing solution through the pulmonary vasculature of the unopened thorax gave good results.

Freeing of mural phagocytes by collapsing the lungs and refilling with fixative

In fresh normal mouse lungs which were collapsed and promptly filled via the trachea with fixing solution most of the alveolar phagocytes were free in the alveoli and only 5% (by actual count) remained definitely fixed in the alveolar walls This is taken to mean that the operation of collapse and refilling dislodges the alveolar phagocytes from the walls The free cells were usually irregular in outline Lungs of the dog and other mammals also showed a much larger number of free alveolar phagocytes after the collapse refill technique than after the vascular perfusion method This finding may help to explain the common view of alveolar phagocytes as free cells rather than as tethered cells

---

* Given at the International Anatomical Congress, Oxford, July 27, 1950

Freeing of mural phagocytes by collapse alone

In mouse lungs which had been collapsed, cut up, and fixed by immersion of the pieces, free dust cells were found in the alveoli which remained partially open, and in larger numbers than in the lungs fixed without previous collapse This is taken to mean that collapse alone dislodges many of the phagocytes formerly affixed in the alveolar walls In dog lungs fixed by vascular perfusion of the unopened thorax, free alveolar phagocytes were fairly abundant in local areas of partial collapse, whereas in the surrounding normally distended parts they were scarce

Free dust cells in alveolar exudate

In certain mammalian lungs fixed by vascular perfusion of the unopened thorax, some of the alveoli contained serofibrinous exudate, and in these the number of free dust cells was much greater than in the normal alveoli of the same lungs This suggests that the presence of fluid in the alveoli favours a shedding of mural phagocytes from their walls The possibility of ingress of phagocytes from other sources later on in this condition is admitted

No observed apparent entering of connective tissue by alveolar phagocytes

No unequivocal evidence was found of alveolar phagocytes apparently in the act of entering the interstitium of the lung from the alveoli, either in this series of animals or in thousands of sections of lung tissue examined during several decades If the dust cells were in the habit of making their way into the connective tissue spaces of the lung they should often be arrested en route, and would then be seen in process of leaving the alveoli and possibly the respiratory bronchioli also, but the testimony of the sections does not support this hypothesis Apparently neither the alveolar nor the bronchial walls are penetrated by the spent alveolar phagocytes The mode of insertion of the phagocytes into the alveolar walls may have erroneously led to the assumption that they were entering the connective tissue

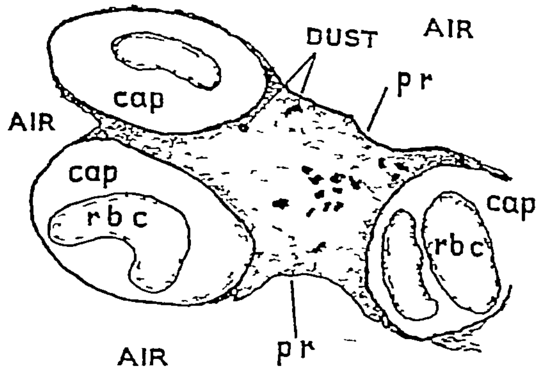


Fig 1—Mural phagocyte mouse lung It shows three air surfaces There are two fairly broad particle receptors (p.r) Note the closeness of association with the capillaries (cap) containing red cells (r.b c.) The larger black grains are dust particles some of which overlie the nucleus which is lightly outlined (Wright's stain × 4500)

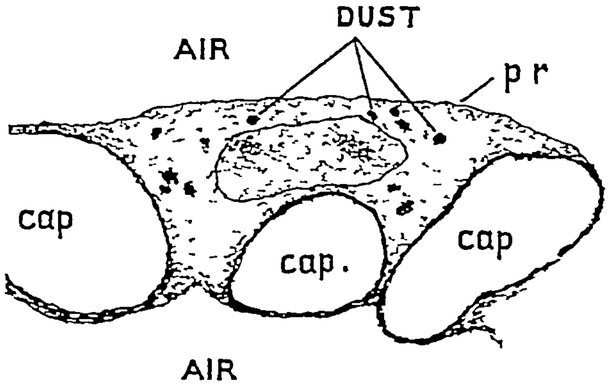


Fig 2—A mouse mural phagocyte with a broad particle receptor (p r) above and two processes directed downward separated by a capillary (Harris hæmatoxylin Fast green, × 4500)

Evacuation of spent alveolar phagocytes via the bronchial tree

In mice and all other mammals studied there is abundant evidence of dust cells in the mucous film of the bronchioli and bronchi, these are probably spent phagocytes being wafted to the region of the glottis by ciliary action They are recoverable from sputum, as Hayek (1950) and others have noted When so found they are termed "heart failure cells"—a designation of dubious value This route of elimination is regarded as the only one available for these used dust cells (Macklin 1950)

Tissue phagocytes of the lung (histocytes, histiocytes)

The dust-laden cells in the connective tissues of the lungs of man and other mammals which often appear in groups around arteries, veins, and parts of the bronchial tree, and in and around the lymphatic channels and nodes, are regarded as histocytes which have obtained their loads from stray dust particles which have eluded the alveolar phagocytic guards and have worked their way into the connective tissue Superficially these cells resemble the alveolar phagocytes in some ways, and particularly because of their content of dust particles They remain in situ for long periods and tend to gather in clumps In this view there are two kinds of dust cells (1) alveolar phagocytes of endodermal origin which take in dust particles *only from air surfaces*, and (2) histocytes of mesodermal origin, which take in dust particles *only from the connective tissue spaces* The latter type is here referred to only incidentally The view, still current, that spent alveolar dust cells are disposed of by way of the lymphatic system of the lung is regarded as unsupported by evidence Hayek has also noted these two different kinds of dust containing phagocytes in the lung

Seating of alveolar dust cells

Most alveolar wall phagocytes are in alveolar angles with processes inserted into tunnels through the alveolar walls which are encircled by capillary loops, others, resting on connective tissue, are placed in sockets, similarly environed These receptacula apparently anchor the phagocytes and provide them with means of obtaining nutriment, and their surfaces may be looked on as basement membranes, in the sense that this term is used by Ham (1950), permitting interchange of materials between the blood and the phagocyte Originally an epithelial cell, the alveolar dust cell continues to be a surface cell, but it secures itself more firmly and enlarges its area of contact with blood capillaries by sinking and branching A demonstration of the often branched nature of the mural phagocytes and their insertion into alveolar pores has been provided by fresh lungs washed with an ammoniacal silver solution and cut into sections (Macklin 1949) obtained In many postencephalitic cases amphetamine has a potentiating effect on artane, this is a firm clinical impression though difficult to assess quantitatively

Hitherto no series of cases treated with lysivane has been published In the present series 72% of the patients who received lysivane showed some degree of improvement, compared with 74 5% with artane In general, however, the improvement obtained with artane is somewhat greater than with lysivane 8 out of 51 cases (16%) showed "great improvement" with artane, compared with only 3 out of 43 (7%) with lysivane Artane is decidedly less toxic than lysivane, and of the 9 patients who were intolerant to lysivane in the present series, all but 2 were able to take artane later, though some had slight toxic symptoms Moreover, the side effects that occurred were in general less severe with artane than with lysivane Either lysivane or artane can be rapidly withdrawn with no other ill effect than a sudden return of symptoms in their previous severity

Most of the 24 patients treated with both lysivane and artane preferred the artane This was related to its greater efficiency, its lower toxicity, and the sense of well being that artane produces Nevertheless, some patients derived equal benefit from the two drugs, and a few were decidedly better on lysivane

Most of the severe postencephalitic cases treated with artane and amphetamine sulphate were in a distressing state of almost complete immobility None were capable of ward duties Since the introduction of artane and amphetamine sulphate treatment there has been a striking change in the atmosphere of the ward Most patients can now feed themselves, and many can dress and attend to their own toilet A few can get about, though with difficulty, and some have taken on simple ward duties Apart from the benefit to the patients themselves this has considerably lightened the nurses' tasks

Both artane and lysivane seem to reduce the rigidity more than the tremor, but occasionally the tremor becomes more marked as an extreme degree of rigidity (which had previously masked it) becomes less In many instances tremor also was remarkably reduced This was particularly striking in a patient with severe tremor of the right arm following a vascular lesion (Benedikt's syndrome), in which artane 5 mg four times a day produced a dramatic improvement, which has been maintained up to date

Artane has some effect in reducing the number and duration of oculogyric crises In one woman who had previously been having an attack lasting four hours once a week, since treatment with artane, the attacks have occurred every 10–14 days and have lasted only one or two hours Lysivane seemed equally effective in this respect Thus a man who previously had two oculogyric crises lasting about three hours every week, when taking a daily dose of 1250 mg of lysivane had more than a week between attacks, and the attacks lasted only an hour Neither of these cases received any amphetamine sulphate

SUMMARY AND CONCLUSION

Artane and lysivane have been used in the treatment of 70 cases of parkinsonism 51 patients receiving artane, 43 lysivane, and 24 both drugs at different times Improvement was noted in 74 5% with artane, and in 72% with lysivane

Both artane and lysivane control the rigidity better than the tremor Both reduce the number and duration of oculogyric crises in postencephalitic parkinsonism

Higher dosage of artane than that reported by other workers has been used with good effect and minimal side effects

The action of artane is often enhanced by amphetamine sulphate in postencephalitics

Artane is less likely to produce unpleasant side-effects than lysivane, and for this reason is likely to prove the drug of choice for most cases of parkinsonism

I am indebted to Dr Macdonald Critchley, of King's College Hospital, and Dr W A Caldwell, physician-superintendent, West Park Hospital, Epsom, who allowed access to their cases and encouraged this present investigation, Dr W R Thrower for his help, and Messrs May and Baker Ltd for supplies of lysivane

REFERENCES

Corbin, K B (1949) *J Amer med Ass* 141 377
Cunningham R W Harned B K, Clark, M. C, Cosgrove, R. R, Daugherty N S Hine, C H, Vessey, R E, Yuda N N (1949) *J Pharmacol* 96 151
Doshay L J Constable K (1949) *J Amer med Ass* 140 1317
Ellenbogen B K (1950) *Lancet* i 1034
Phillips J Montuschi F Sharkey J (1950) *Ibid* p 1131
Sigwald J (1949) *Pr méd* 57, 819

THE DUST CELLS IN THE LUNGS OF THE ALBINO MOUSE*

THEIR STRUCTURE, RELATIONS, AND MODE OF ACTION

Charles Clifford Macklin
M D, Ph D Toronto, F R S C
RESEARCH PROFESSOR OF HISTOLOGY, UNIVERSITY OF WESTERN ONTARIO, LONDON, CANADA

DUST cells are phagocytes which have developed in the pulmonary alveoli of man and other mammals and ingest particles of carbon and other material entering the lung with the inspired air In man the dust cells are seen under unfavourable conditions in ordinary sections, because the available lungs are often diseased, putrefied, and imperfectly fixed The lungs of the albino mouse, however, offer excellent opportunity to study the dust cells both in their normal forms and relations and under experimental conditions The results of such study may aid in the understanding of alveolar phagocytes in man

SUMMARY OF OBSERVATIONS

Dust cells are fundamentally mural phagocytes

When normal lungs of albino mice and other mammals are quickly fixed without previous collapse, the alveolar phagocytes (dust cells) are found almost exclusively attached to the alveolar walls rather than free (figs 1 and 2) This means that under normal conditions they are sessile Counts made on thin stained sections of such material show as many as 99% or more of the dust cells morphologically affixed to the alveolar walls

Free dust cells in uncollapsed normal alveoli are few

In normal lung tissue fixed without previous collapse a few alveolar phagocytes are found free in the alveoli these are usually round or ovoid Counts show as few as 1% or less in this untethered condition, these are regarded as cells whose phagocytic potencies have been expended They have been loosened from their moorings in the alveolar walls, and would probably have found their way to the ciliary escalator of the bronchial tree.

Methods of fixation without collapse

For the demonstration of dust cells in their normal habitat on the alveolar walls in the mouse, the method of immersion of the fresh flayed unopened thorax in fixing solutions such as Regaud's or Bouin's at room temperature was found satisfactory For larger animals, as well as the mouse, the method of perfusion of fixing solution through the pulmonary vasculature of the unopened thorax gave good results

Freeing of mural phagocytes by collapsing the lungs and refilling with fixative

In fresh normal mouse lungs which were collapsed and promptly filled via the trachea with fixing solution

---

* Given at the International Anatomical Congress, Oxford, July 27, 1950

umb bell shaped alveolar phagocytes

After exposure to much dust a phagocyte occupying single pore may appear with both ends swollen and the uddle constricted Such cells cannot be released from ıe pore They represent a special type of pore affixation, nd are not necessarily to be considered as in act of assing from one alveolus to another

CONCLUSIONS

Alveolar dust cells under normal conditions are ttached to the alveolar walls by insertion into pores ır sockets From the environing capillaries of these ımplacements they derive their nutriment When spent ey become free and are disposed of via the bronchial tree

They never enter the connective tissue of the lung, d hence are never found in the lymphatic system ıey are of endodermal origin and thus are epithelial type They are not to be confused with the histocytes the connective tissue of the lung, which often take dust particles which have adventitiously penetrated e alveolar walls

Alveolar dust cells are readily dislodged from the veolar walls by collapsing the lung Their vacated tes of attachment in partitional alveolar walls are ıown as pores They also become free in the presence fluid in the alveoli, and gradually after experimental posure to dust such as that of carmine granules

They may have as many as four air faces or particle ceptors, and these may extend as thin flanges over ıighbouring capillaries.

To display them in normal relation to the alveolar all an adequate fixation technique is imperative, such prompt immersion of the fresh skinned unopened ıorax in Bouin's or Regaud's fluid

I wish to thank the National Research Council of Canada r aiding this research project with a grant for technical sistance, and Mr Charles E Jarvis for his excellent work in e preparation of the material and photomicrographs

REFERENCES

ırgmann W (1936) in von Möllendorff W Handbuch der mikroskopischen Anatomie des Menschen Berlin vol v p 799
ırleton H M (1934) *Proc roy Soc* sect B 114 513
am A W (1950) Histology London p 142
ayek H von (1950) Communication to Internationa Anatomical Congress Oxford
acklin C C (1947) *Anat Rec* 97 397
— (1949) *Proc int Cong exp Cytology Stockholm* 1947 p 383
— (1950) *Proc Inst Med Chicago*, 18 78

INCIDENCE OF PENICILLIN-RESISTANT AND STREPTOMYCIN-RESISTANT STAPHYLOCOCCI IN A HOSPITAL

PHYLLIS M ROUNTREE
D Sc Melb , Dip Bact

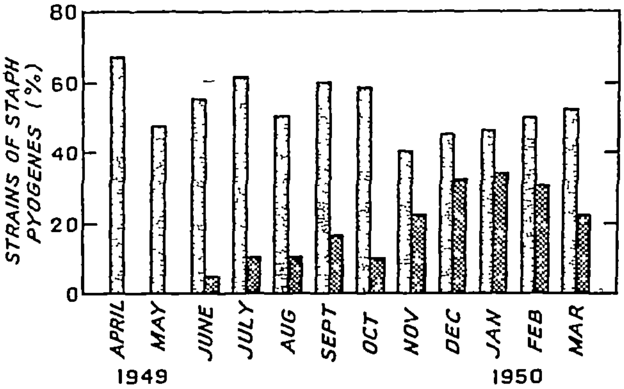
R G H BARBOUR
B Sc Agr Sydney

EDGAR F THOMSON
M.B N Z , F.R A C P

rom the Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Sydney, Australia

IN a previous communication (Rountree and Thomson 949) it was reported that 92 (47%) of 196 patients ıelded penicillin resistant strains of *Staph pyogenes*, ıd 7 (3 5%) yielded streptomycin resistant strains We ıve continued our examination of all strains of *Staph yogenes* isolated in this hospital, and we now record ır findings during the twelve months from the beginning April, 1949, to the end of March, 1950

In calculating the incidence of resistant strains we ave used in the present series the numbers of patients ıther than the numbers of cultures examined No more ıan one culture from each patient has been included ıless there was a change in phage type during the atient's stay in hospital We have also distinguished between inpatients and outpatients The laboratory methods have remained the same as those previously described



Monthly incidence of penicillin resistant (stippled) and streptomycin resistant (hatched) strains of *Staph pyogenes*

RESISTANCE TO PENICILLIN AND TO STREPTOMYCIN

603 strains of *Staph pyogenes* obtained from 513 inpatients and 90 outpatients were examined for sensitivity to penicillin and streptomycin with the following results

Antibiotic resistance	*No of patients and % of total* *Inpatients*	 *Outpatients*
Penicillin sensitive	239 (*46 6%*)	68 (*75 4%*)
Penicillin resistant	274 (*53 4%*)	22 (*24 6%*)
Streptomycin-sensitive	441 (*86 0%*)	89 (*98 9%*)
Streptomycin resistant	72 (*14 9%*)	1 (*1 1%*)

Penicillin

Some of the 22 (24 6%) outpatients penicillin resistant strains were isolated from patients who had been treated with penicillin, and we do not consider that the incidence of penicillin resistant strains in the general population is 24 6% The incidence of 53 4% inpatients penicillin resistant strains cannot be directly compared with the incidence obtained by Rountree and Thomson (1949) in both inpatients and outpatients If, however, the figures for both types of patients in the present series are combined, the incidence becomes 49%, which does not significantly differ from 47% found in the previous series We therefore conclude that there has been no increase in the incidence of penicillin resistant strains in this hospital during the period under review

Streptomycin

All the streptomycin resistant strains examined were also penicillin resistant From only one outpatient was a streptomycin resistant strain isolated , this was obtained after local streptomycin therapy of a varicose ulcer and was of the same phage type as the previously isolated sensitive strain

From 72 (14%) of the 513 inpatients streptomycin resistant strains were isolated The *accompanying figure* shows the monthly incidence of penicillin resistant and streptomycin resistant strains expressed as percentages of the total number of strains of *Staph pyogenes* examined each month The figure shows clearly the increase month by month in the incidence of strains resistant to streptomycin There were no such strains isolated in April and May, 1949, but thereafter the figures rose from 2 strains out of 52 examined in June until 13 of 33 strains examined in January were streptomycin resistant

The streptomycin resistant strains were obtained from various sources, including sputum, urine, blood, and pleural fluids, but most of them came from clean surgical wounds cross infected in hospital In some of these patients streptomycin resistance developed after streptomycin therapy given when the infecting organism was found to be penicillin resistant, but there were many cases in which the organism was streptomycin resistant on first isolation

Dust collecting air surfaces of alveolar phagocytes

The alveolar phagocyte may have one, two, three, or even four functional air faces or particle receptors (figs 1 and 2) These vary in area Often one is quite extensive, the others being relatively small Under routine conditions of life these are usually flat or concave, conforming to the contour of the alveolar wall They are often spread like thin omenta over adjoining capillaries (Bargmann 1936) They arrest dust particles, which are engulfed and segregated in clumps in the underlying cytoplasm This mechanism is the normal one for dealing with particulate matter which gains entry to the alveolar air spaces So far as can be learnt from ordinary sections, these plaques cover a relatively small part of the alveolar wall Particles falling on other regions (the bare areas and the air surfaces of the alveolar granulocytes) normally find their way quickly to the plaques by a mechanism that is not understood The thin edges of the plaques have been mistaken for respiratory "squames" by some workers

Origin

The alveolar dust cell is regarded as of endodermal origin (Carleton 1934) and as being a sister of the granular cell of the alveolar wall A dust containing mural phagocyte and an alveolar granular cell may be found side by side in a relation like that of adjoining epithelial cells, and separated by what seems to be a single cell membrane Under a form of biodynamics, certain cells are differentiated in the normal course of life as mural phagocytes, while other residual epithelial cells of the alveolar wall, which are regarded as more primitive, remain as granular cells These latter cells are notable for their content of special granules (Macklin 1947) In usual conditions in mice one finds mainly well differentiated cells of these two types in the alveolar wall, and but few cells which could be regarded as intermediate in type

Mitochondria

The mitochondria are scarce or absent in mural phagocytes and diminish with the densification of the cytoplasm, which apparently is a concomitant of ageing Large spheroids were noted, suggesting a fusion of smaller ones

Gash irrigation results

When fresh collapsed mouse lung is slashed through a drop of physiological salt solution and the part drained on to a slide, liberated dust cells are recovered, together with cells of intermediate type, having granules as well as dust grains A few elements, called pure foam cells, are also seen, and these are regarded as released alveolar granular cells (Macklin 1949)

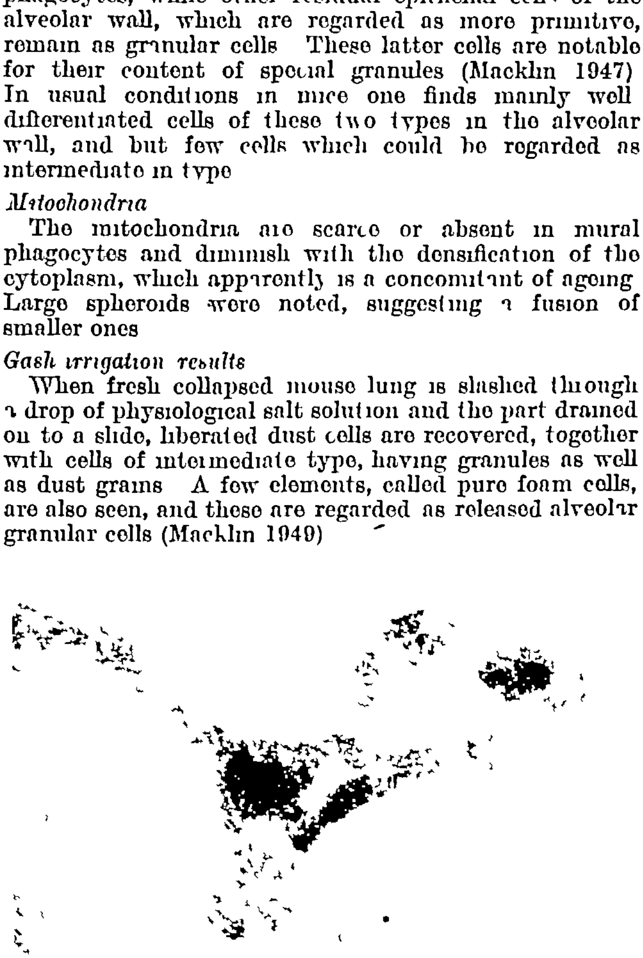


Fig 3—Photomicrograph of a mouse mural phagocyte which was exposed to an hour's vital dusting with carmine powder and fixed by block immersion of the unopened thorax an hour after the end of dusting Two air surfaces are visible The cytoplasm is crowded with carmine grains No carmine grains are seen on the alveolar air surfaces elsewhere. (Harris hæmatoxylin, Orange G ; × 1700)

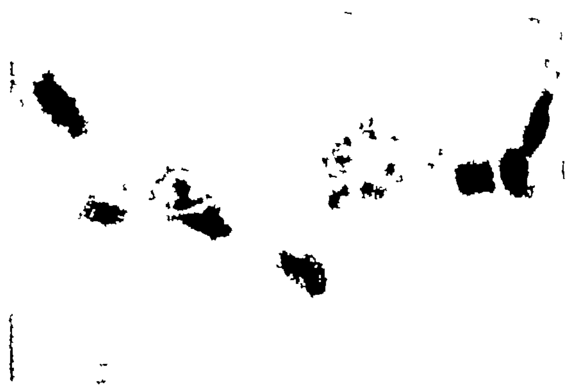


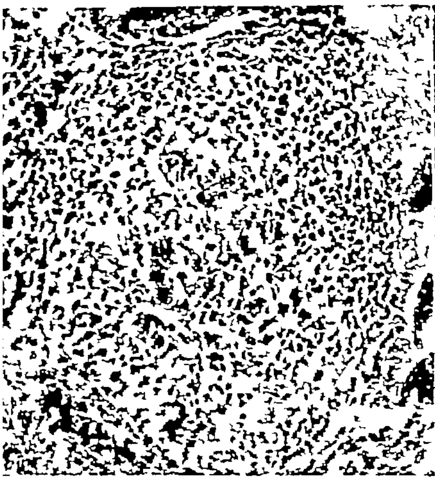
Fig 4—Photomicrograph of one of the rare instances in this mouse lung of a phagocyte which has become free from the alveolar wall (Harris hæmatoxylin, Orange G ; × 1700)

Carmine dusting experiments

One hour after the cessation of exposure of the atropinised mouse to an hour's dusting with carmine powder, the lungs, fixed by immersion of the flayed unopened thorax in Regaud's fluid, show almost all the carmine grains within the wall phagocytes (fig 3) The almost complete clearing of the relatively large areas of alveolar wall, in which no extensions of the mural phagocyte appear, is remarkable What few grains remain are almost all in small clumps Almost 100% of the phagocytes, by actual count, are inserted into the alveolar walls These varied greatly in carmine content, some (called carminophages) were packed with red granules and were very conspicuous, while others, which seemed to contain more black particles of ordinary dust, had taken in lesser numbers of red particles It was rare to find a free carmine containing cell at this stage (fig 4) If however, a week is allowed to elapse after an hour's dusting of the atropinised mouse with carmine powder, the picture is very different Now, by actual count, 65% of the alveolar phagocytes are free, and only 35% are fixed in the wall, and these bulge prominently into the alveolar space and do not show the flattened and extended plaques characteristic of the usual, unstimulated, condition This evidence suggests that the phagocyte may carry on its functions under these conditions while free It may even return to a pore, using it as a "filling station" (a term used in Canada for a source of gasoline for automobiles needing refuelling) because of the accessibility of the capillaries It may be that such a cell may move about the wall and insert a process or processes into one or more pores from time to time as the emergency demands, for food is available nowhere else This evidence, too, shows that the alveolar phagocytes may remain a week or more apparently at work, without being evacuated At this stage there were fewer phagocytes, made conspicuous by close packing of the granules, than in the one hour stage, and this suggests that the well laden phagocytes have departed Stimulation such as this causes the phagocytes to swell and become more compact, the flanges being drawn in and merged with the general cytoplasm

Replacement

The source of alveolar phagocytes has been well debated for many years In the usual course of life the spent and dislodged mural phagocytes must be replaced It is assumed that the loss is made good from sister cells remaining in the walls Perhaps recruits can find their way to vacated emplacements (pores or sockets) in the walls from other loci, and therein establish themselves In the healthy lung there seems to be no diminution in number of alveolar phagocytes with age The replenishment of the supply of alveolar phagocytes after conditions of special stimulation, as in the pneumonias, cannot be here considered



1—A single tuberculous focus in the endometrium (× 160)

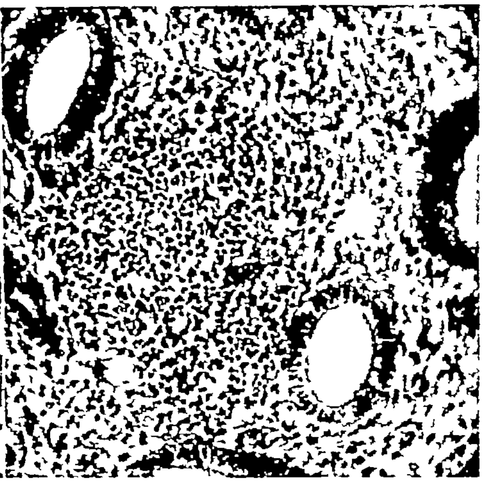


Fig 2—Lymphoid aggregate in the stroma of normal endometrium (× 160)

itions , but these normal structures differ from the)ercles in the uniformity of their cells and the regularity their grouping It is presumed that the tubercle cilli lodge in the lymphoid areas of the stroma as they in other organs Thus the lesion is often seen close a gland, and as it enlarges it pushes into and finally rsts into the gland lumen Essentially the endometrial)ercle comprises a central zone of endotheloid cells, th prominent eosinophil cytoplasm, surrounded by a riable zone of lymphocytes and plasma cells When lesion bursts into the lumen, lymphocytes and other lammatory cells will be found within the lumen me of the epitheloid cells may attempt to form int cells , but giant-cells do not constitute tuberculosis, d tuberculosis is frequently diagnosed without them ie periodic shedding of the endometrium cuts short e *formation of mature tubercles*

Most often these circumscribed lesions are the only normal feature in the endometrium , but there may infiltrations of inflammatory cells in the stroma, th or without the focal lesions Where a section ows these infiltrations, and there is no other demon rable cause for the inflammatory response (e g , retained oducts of conception), it is probably wise to suspect berculosis Unlike normal lymphoid aggregates, such flammatory cells appear diffusely in the stroma

There are other granulomas—though more particularly the fallopian tube—which can be confused with berculosis These include actinomycosis and those ie to helminth infestation, and to oily substances, iabsorbed sutures, talc, and other foreign bodies hese may be distinguished either on clinical evidence, by appropriate staining methods, or by studying eir appearance under polarised light Where bacterio gical confirmation is possible, the exclusion of these ternatives is less important

The aim of the bacteriological investigation is to olate *Mycobacterium tuberculosis* by culture or animal oculation or both, and to submit for typing each strain)tained Identification of the organism establishes the agnosis, and it can be tested for drug sensitivity revious work on the typing of strains obtained from ynæcological cases has been scanty and difficult to raluate

Cultivation is possible on a variety of media

First the pieces of endometrium must be converted into a rm suitable for inoculation and this may be done by inding with sterilised quartz sand in a sterile pestle and iortar A loopful (or several) of the ground up material planted on one or more slopes of Dorset egg and Löwenstein ensen media A fluid medium is also used Cultures are xamined at ten days and weekly up to two months

Guineapig inoculation is usually performed using treated material The treatment may be as given above, or one of the many chemical methods may be used Chemically treated material is often regarded as more suitable for culture and inoculation To cover up risks of bacterial contamination, both forms of treated material may be used for culture and for animal inoculation In our experience a simpler method is giving reliable results

Through a small incision in the thigh of the guineapig, the untreated material is placed in the muscles, and the skin is closed with one or two sutures The operation requires a short anæsthetic, but the time taken from the *curettage to its completion* need be only a few minutes Provided the material is placed deeply, the wound heals perfectly in five or six days The stitch either falls out or is removed by the guineapig Smears are taken from the regional and lumbar lymph nodes and the spleen, and stained for tubercle bacilli The organism is further inoculated on to culture media as described above

There are other methods for the detection of tubercle bacilli in the endometrium, but we have not used them The Ziehl Neelsen technique, which entails much tedious bench work, gives inferior results, and probably (though we have no experience of it) this is also true of fluorescence microscopy of the endometrium (Clegg and Foster Carter 1946, Browning and Mackie 1949) The vaginal discharges, particularly during menstruation, may be searched for organisms (Halbrecht 1947), but this method is not universally applicable

RESULTS

The main object of this paper is to emphasise the value of adequate investigation when judging the results of chemotherapy None of our treated cases can be included in this report, for only preliminary tests have been completed The results of pre treatment investigations of 24 patients can, however, be described

In 18 cases endometrial tuberculosis was diagnosed both histologically and by the method of guineapig inoculation described above In 4 cases diagnosed histologically, animal inoculation gave negative results In 2 of these tuberculous endometritis was present but the material examined was from the tubes only In the other 2 the disease was seen in the tube or ovary, but not in the endometrium, and only one animal test was performed in each case—on material obtained at operation Perhaps a repetition of the test would have given bacteriological confirmation , this has been our experience in 3 of the 18 cases already mentioned Finally there are 2 patients whose investigation has so far given discordant results

In certain cases positive findings (histological and bacteriological) have been followed by double negative findings though the patient had not had any treatment In another case a test after a course of streptomycin gave a positive guineapig result with negative histology (One sample of endometrium, divided, was used for the test)

A few patients with pulmonary tuberculosis have been investigated but with consistently negative findings Negative results have also been returned on a number of occasions in which endometrial tuberculosis has been suggested on clinical grounds These two negative groups comprise about 30 cases

PHAGE TYPES OF STREPTOMYCIN RESISTANT STRAINS

It is apparent that we are observing with the streptomycin resistant strains the same type of increase in incidence as has already taken place with penicillin resistant strains, and it becomes of interest to consider what phage types are involved in this development of streptomycin resistance The phage types differentiated among 70 streptomycin resistant strains were as follows

Phage type	*No of strains*
31B	21
47	17
47/31B	11
7	4
7 other types	14
Not typable	3

In contrast to the scheme of classification adopted by Barber and Whitehead (1949) we have preferred to differentiate between types that are fairly closely related —e g , 7, 31B, 47, and 47/31B—rather than to include all these strains in one group, 6/7/47 Though there is no doubt that there is a close genetic relationship between these strains (Smith 1948), the differences observed in their "pattern reactions" with the series of phages used have remained constant during the period under consideration Further, successive cultures from the same patient have yielded strains with identical "pattern reactions" , any change in the phage reactions has been regarded as evidence of cross infection with another strain and has usually been correlated with other observable changes in colony appearance This differentiation of closely related types has allowed us to follow the rising incidence of types 47 and 47/31B, which were infrequently found in the hospital during the previous period from October, 1948, to March, 1949

The three types 31B, 47, and 47/31B account for 49 (70%) of the streptomycin resistant strains typed 4 strains of type 7 were recognised , of the remaining 17 strains 3 were not typable and the other 14 belonged to 7 other phage types These 14 strains, however, with 2 exceptions, belonged to types which can be included in the 6/7/47 group

The increased incidence in this hospital of strains of *Staph pyogenes* insensitive to both penicillin and streptomycin is therefore due to the propagation in the hospital environment of strains belonging to only a few phage types

One fact of obvious interest is that the strains of type 7 and 31B are those which were predominant in the hospital as penicillin resistant streptomycin sensitive strains before the introduction of extensive streptomycin therapy The emergence of streptomycin resistant variants during streptomycin therapy of patients cross infected with these strains and with strains of type 47 has been previously observed (Barbour 1950) After these streptomycin resistant strains had appeared in patients they were subsequently isolated from the noses of nurses and from the dust and air of the wards Examination of 90 colonies of *Staph pyogenes* obtained on blood agar plates used for taking a series of air samples in surgical wards during February, 1950, showed that 75 colonies were penicillin resistant and 58 resistant to both penicillin and streptomycin All the doubly resistant colonies belonged to types 31B, 47, or 47/31B

It might be concluded from this evidence that antibiotic resistant staphylococci of group 6/7/47 predominate in hospitals because, as antibiotic sensitive strains, they were already well established in the hospital environment when penicillin and streptomycin were introduced On the other hand, it has been suggested (Barber and Whitehead 1949) that strains of this group are genetically less stable than those of other phage groups and so give rise to resistant mutants more rapidly In our opinion the data presented here do not allow us to distinguish between these two hypotheses, and it seems possible that both mechanisms may be operating

SUMMARY

Of the 603 strains of *Staph pyogenes* isolated from inpatients and outpatients between April, 1949, and April, 1950, and examined for sensitivity to penicillin and streptomycin and for phage type, 274 (53 4%) from 513 inpatients yielded penicillin resistant strains, compared with 22 (24 6%) from 90 outpatients

Strains resistant to both penicillin and streptomycin were obtained from 72 (14%) of 513 inpatients compared with 1 of 90 outpatients This incidence of 14% was significantly higher than the 3 5% obtained with 1% patients examined in the preceding six months (Rountree and Thomson 1949)

At least 65 of these doubly resistant strains belonged to phage types of the genetically related group 6/7/47

This work was supported in part by a grant from the Australian National Health and Medical Research Council We wish to thank Mr G Barr and Miss V Sife for their excellent technical assistance

REFERENCES

Barber, M , Whitehead J E M (1949) *Brit med J* ii 565
Barbour, R G H (1950) *Aust J exp Biol med Sci* 28, 411
Rountree, P M , Thomson, E F (1949) *Lancet* ii 501
Smith, H W (1948) *J Hyg , Camb* 46, 82

TUBERCULOSIS OF THE ENDOMETRIUM

INVESTIGATION AND TREATMENT

MAGNUS HAINES
M D Lond

DIRECTOR OF PATHOLOGY, CHELSEA HOSPITAL FOR WOMEN, LONDON

With the technical assistance of J W LAW, A I M L T

IN the earlier literature references to unsuspected uterine tuberculosis are few Comyns Berkeley (1935) found unsuspected genital tuberculosis in 62 of 795 (7 7%) females dying of pulmonary tuberculosis, the body of the uterus being affected in 18 (2 3%)

Over the past ten years several authors (Schockaert and Ferin 1939, Sutherland 1943, Halbrecht 1946, O'Brien and Lawlor 1947) have reported finding tuberculosis in the endometrium of women who were symptomless The incidence has been unexpectedly high 5·3% (Sharman 1947) and 6% (Schockaert and Ferin 1945). These reports, however, refer to women seeking advice at fertility clinics—a selected group In the general population of women under hospital care the incidence is estimated at about 1% (Sutherland 1943) The subject in general has been reviewed by Sutherland (1943, 1950) and Bamforth (1950)

Since 1946 we have been investigating a small group of similar cases, and recently we have undertaken controlled treatment by chemotherapy

INVESTIGATION

Whenever tuberculous infection is found in a specimen of endometrium, obtained either for examination or during full curettage, the patient is asked to return for a repeat biopsy This should be within the seven days preceding an expected period, at which time the volume of the specimen should be greatest On this second examination the material is divided into two portions —one for histology and one for bacteriology

Histologically tuberculosis in the endometrium resembles tuberculosis in other tissues , but the more advanced stages (caseation, fibrosis, and calcification) are rarely seen The lesion (fig 1) is typically a focal one, situated about midway in the endometrium It is in the stroma but adjacent to glands The normal endometrium has lymphoid aggregates (fig 2) in corresponding sympathetic fibres from the 2nd, 3rd, and 4th sympathetic ganglia are inextricably mixed up with the plexus, and one cannot be certain of having removed them unless the whole plexus is dissected out; not only is this a time-consuming and sanguinary operation, but also it is impossible to be sure when the task is completed because the plexus and the areolar tissue appear so much alike.

CASE RECORDS

Case 1.—A man, aged 44, had enjoyed excellent health up to the age of 40. At that time he married, but the union was a failure, and he started to have mild attacks of asthma, which disappeared when he obtained a divorce. Good health followed until 6 weeks after his second marriage, nearly 2 years ago. The asthma then began in earnest although his second wife was a paragon. Time after time he relapsed with severe attacks always necessitating hospital treatment and completely incapacitating him for work.

Investigations into possible allergy made him worse. He was found to be sensitive to moulds but desensitisation did not help, and he developed a mould mania: he pulled up the boards of his house in his obsessional witch hunt, and when in hospital, much to the matron's annoyance, he found some penicillium growing in his bed locker. He was examined psychiatrically and it was thought that the uncertainty of the reaction of his children to their new mother might explain his trouble. It may have been so, but the knowledge of it did not make the slightest difference to the patient. Between attacks he was perfectly well, and there was no evidence of any permanent damage to his lungs.

He was considered suitable for operation, and vagal resection was done when he was asthma free in March, 1950, nineteen days separating the operations on the two sides.

The response was dramatic. He put on weight, lost his asthma, and left hospital a new man. He went back to work for 4 happy months, after which he returned to hospital with a relapse. His attacks before and after operation seemed to me to be exactly the same, but he is again at work and he regards the operation as miraculous. He still thinks of his 15 weeks' freedom, says that his present relapses have not been nearly so severe as his previous attacks, and continually advises fellow sufferers to seek operation.

Case 2.—A married woman, aged 62, had begun to have asthma about 12 years ago; at that time her husband won some money and immediately took to drink and became unmanageable. Her daughter, now married, started attacks at the same time, and it is alleged that the wheeziness in one precipitated it in the other. Attacks in the patient appeared to coincide with her husband's bouts of drinking. No allergic factors were discovered, but she stated that she sometimes had dermatitis with the asthma. This latterly had been complicated by bronchitis, purulent and occasionally bloodstained sputum being coughed up. Her spasms were of appalling severity, and in them she was often unconscious and always incontinent. Heart-failure had been a complication early this year. In between the severe attacks she was always giving herself injections of adrenaline. Vagal resection was advised in view of the failure of all the usual measures, and the left side was done on July 27, 1950. The right side was done on Aug. 22.

The result to date has been remarkable. She has been entirely free from asthma since the first operation and denies having had the slightest trace of a wheeze. She has thrown away her inhaler and all her drugs, is living an entirely normal life, and says she has never been so well for 12 years. Her domestic troubles, though still present, no longer appear to worry her now that she is free from asthma.

Case 3.—A girl, aged 21, had had eczema and asthma from the age of 4 years. Since "the bombing" the asthma had been progressively worse, and from the time that I came to know her 2 years ago she had been in and out of hospital a dozen times or more. Why she relapsed nobody knew. She was a flat inhibited dull sort of girl, unlike the usual asthmatic type, and we all rather felt that she did not make much effort to get better, though her attacks were so very violent. She was found by skin tests to be sensitive to house-dust, horsehair, feathers, moulds, and fish, but specific desensitisation, and later 'Lertigon,' made no improvement. Yet she, too, was well in between the attacks with no evidence of chronic infection or emphysema. For this reason I advised vagal resection, which was done in June, 1950. For four months she improved and had no attacks, but she remained somewhat wheezy and was taking half a tablet of 'Neo Epinine' daily. She also complained of cough and shortness of breath. She relapsed in November with a typical attack, but she too insisted that it was not nearly so severe as those before operation.

Case 4.—A single woman, aged 31, had had chest trouble of one kind and another since infancy. She had pneumonia at the age of 4, pleurisy at the age of 7, and multiple attacks of bronchitis during adolescence. True asthma started about the age of 21 and continued from that time with increasing severity. In January, 1950, associated with a bad attack, she had a right-sided spontaneous pneumothorax. A second pneumothorax (also right-sided) developed in March with a further attack of asthma. Physical examination at the end of April showed her to have severe emphysema and chronic bronchitis, and at that time she was also dyspnoeic and wheezy.

Vagal resection was performed on May 6 and 20, 1950, and in addition it was considered that the bilateral thoracotomy would fix the lungs by pleural adhesions to prevent any further pneumothoraces. The immediate postoperative course was good; her asthma disappeared and she went home much improved. This improvement was maintained for 2½ months, but she was never strong enough to get back to her work as a secretary. She relapsed in mid-August with a severe attack of asthma complicated by bronchitis. With heavy sedation she gradually improved sufficiently to go to the South of England. There she relapsed again and has required a further period in hospital since coming home. Her doctor tells me that, although her attacks have been severe, she has never been so acutely ill as before the operation.

Case 5.—A boy, aged 15, had had asthma prurigo syndrome since the age of 3 years, the eczema and asthma often alternating. Precipitating factors known to the patient were certain fruits, fish, grass in May and June, and house-dust. During the past few years the asthmatic attacks had been getting progressively severe in spite of desensitising injections to the appropriate allergens. In between the attacks he was reasonably well and played games at school. He was alert and bright mentally, with a very good visual and auditory memory. Because of the increasing severity and progressive lessening of free intervals vagal resection was advised, and the operations were performed in January, 1950. He stood them well and remained free from asthma while in hospital. He relapsed on the doorstep the moment he arrived home. For the first 3 months after operation the asthma was less severe, attacks lasting ½–1 day and occurring at intervals of 7–10 days. Between June and August they became slightly more infrequent, occurring at intervals of 12–14 days. In August, while free from attacks, the patient began to have precordial pain and tachycardia on exertion. These symptoms persist. His asthma has relapsed badly. He is now getting attacks every day. He is losing weight, not growing, and his condition is no better and perhaps worse than before operation.

Case 6.—A girl, aged 18. She had had attacks of asthma, worse in the summer, since the age of 7, and in the past year the attacks had been extremely severe and very frequent. She had been found to be sensitive to pollens, mixed moulds, and house-dust, but desensitisation to these had not materially affected her. On the psychological side it was thought that there might be some instability of background, since her father and mother were separated and she was looked after by her grandmother. Vagal resection was decided on, and the right side was done on Aug. 29, 1950. The patient stood the operation well but developed a cold a fortnight later; it was therefore decided that she should convalesce before the other side was done. I saw her again a fortnight later, when she had been admitted to hospital as an emergency. Her asthma had returned and her condition was exactly the same as before operation. None of us could detect the slightest difference in the spasm of the operated and non-operated sides. The condition cleared quickly and the second side has now been done, but insufficient time has elapsed for assessment.

COMMENT

If one had to hazard a guess at the outcome of any new form of treatment in asthma, one could safely predict that the immediate result would be good but that

TREATMENT

Until recent times no clear views on treatment have been expressed, except for cases in which symptoms and signs have indicated removal of the uterus and/or tubes and ovaries Modern chemotherapy, however, has offered new hopes of cure

The drugs available are streptomycin and *p* amino salicylic acid, and though the lesions are small and often few in number, we think it necessary to give a heavy treatment—i e, daily doses for three months of 1 0 g streptomycin and not less than gr 10 *p* aminosalicylic acid Apparent cures should not be accepted as definite until there is presumptive evidence that the patient's disease has been arrested over two or three years

The small size of the endometrial lesion does not mean that the infection can be eradicated easily Though endometrium and fallopian tubes may be involved at the same time, the infection is blood borne and comes from a distant focus The chemotherapeutic attack is on the distant focus as well as on the uterus In the cases reported by others, and those encountered by us, there has often been a history of tuberculous disease for ten or fifteen years or more

Accordingly, frequent biopsies of the endometrium are inadvisable, and after a course of treatment it seems best to wait for three months, repeating the examination two or three times per annum subsequently The material should always be examined both histologically and bacteriologically A negative histological result while waiting (two months) for the bacteriological finding can raise false hopes

DISCUSSION

The silent tuberculous lesion of the endometrium is not as rare as has been supposed and it can be recognised by methods which are easy to follow In 22 of our cases the diagnosis was unequivocal and absolute bacteriological confirmation was obtained in 18 We have not yet proceeded with the typing of strains of *Myco tuberculosis* isolated, but this is clearly desirable We attach great importance to reducing the number of post chemotherapy biopsies and curettages and increasing the intervals between them (Haines 1950) Cure cannot reasonably be presumed because the endometrium has not developed a new tuberculous focus in the month —or even the three months—following treatment, for pelvic tuberculosis is a blood borne disease and the focal point must often be outside the gynæcological field Caution in judging the effects of streptomycin treatment is as necessary here as in other forms of tuberculosis

SUMMARY

Of 24 cases of tuberculous endometritis, recognised histologically, the diagnosis was confirmed bacteriologically in 18 and 2 are still under review Examination of 30 other patients gave negative results

The need for care in judging the effects of treatment is emphasised Repeated biopsies are necessary, but should not be frequent

We wish to express our thanks to the clinical staff of Chelsea Hospital for Women for their help in following these cases, and to Mr H J Turner for the photography

REFERENCES

Bamforth J (1950) Modern Trends in Obstetrics and Gynæcology Edited by K Bowes London
Berkeley C (1935) quoted in J H Teacher s Manual of Obstetrical and Gynæcological Pathology London p 49
Browning, C H Mackie, T J (1949) Textbook of Bacteriology London, p 245
Clegg J W Foster Carter A F (1946) *Brit J Tuberc* 40 98
Haines M (1950) *Lancet* ii 377
Halbrecht, I (1946) *Schweiz med Wschr* 76 708
— (1947) *Lancet*, ii 947
O Brien J R Lawlor M K (1947) *J Obstet Gynæc* 54 636
Schockaert J A Ferin J (1939) *Bull Soc belg Gynéc Obstét* 15 407
— — (1945) *Verh Akad Geneesk belg* 4, 5 quoted by Bamforth
Sutherland A M (1943) *J Obstet Gynæc* 50 161
— (1950) *Glasg med J* 31 279
Sharman, A (1947) *Brit med J* ii 83

BRONCHIAL ASTHMA TREATED BY BILATERAL RESECTION OF THE VAGUS*

A REPORT OF SIX CASES

C A CLARKE
M D Camb, F R C P
ASSISTANT PHYSICIAN, ROYAL LIVERPOOL UNITED HOSPITAL
(DAVID LEWIS NORTHERN BRANCH)

BRONCHIAL asthma, as every honest man knows, is incurable Children may grow out of it, and adults have long periods of freedom, but the fact remains that an asthmatic is always a potential wheezer, and no particular drug or method of treatment is a specific against relapse You have only to look at the case records of any asthma clinic to see the natural history of the disease—relapse and remission—unfolding itself

The worst cases are a challenge to medical science, and where all else has failed, operations have been performed on the autonomic nervous system with a view to isolating the lungs from external influences

Miscall and Rovenstine (1943) and Carr and Chandler (1948) reported success from bilateral injection or excision of sympathetic ganglia Klassen et al (1950) obtained equivocal results in three patients treated by vagus resection and showed by bronchography that bronchospasm was still present Blades et al (1950) reported "cure" or improvement in twenty two out of thirty eight patients treated by vagus resection, the operation in some cases being confined to one side only Earlier, Rienhoff and Gay (1938) had attempted complete denervation by bilateral resection of the posterior pulmonary plexus, and they reviewed twenty one cases between 4 and 8 years after operation (Gay and Rienhoff 1942) There had been nine deaths, seven in the immediate postoperative period Four cases were entirely unimproved The successes numbered eight—three "100%," one "75%," and four "50%"—but one of the last died from heart failure 7 months after operation There was no correlation between the ages of the patients and the success, or otherwise, of the operation The operators were impressed by the fact that they were quite unable to forecast which cases were likely to do well and which badly, their only criterion for operation was failure of medical treatment, and they suggest that the best cases may be those in which one has no clue to the exciting cause They would exclude all cases palpably associated with any known cause—be it psychoneurotic, infective, or allergic They make two points of interest about their operation (1) where asthma occurred between the two operations it tended to be unilateral and confined to the unoperated side, and (2) it often took several months for the asthma to clear, the attacks gradually becoming less and less severe

The present series was selected for very much the same reasons as Rienhoff and Gay's, but the patients had been, on the whole, less continuously ill.

The operations were done by Mr Ronald Edwards and Mr H V Wingfield, at the Liverpool Chest Surgical Unit, Broadgreen Hospital, the technique being as follows

The chest was opened up via the bed of the displaced 6th or 7th rib The vagus nerve was identified posterior to the lung root, and all branches going to the posterior pulmonary plexus were divided, segments being excised from them The main branch to the anterior plexus was also divided About 3 weeks separated the operations on the two sides.

The procedure resembles that of Rienhoff and Gay, but they would criticise us for leaving the sympathetic connections Mr Edwards states, however, that the

---

* Abridged from a paper read to the British Association of Allergists at York on Oct. 7, 1950

Necropsy Findings—The liver was grossly enlarged and diffusely and densely studded with tumour nodules from a few millimetres to a few inches in diameter Secondary deposits were found in the right fourth and fifth ribs and in the body of the sternum. The lungs were congested and œdematous, the kidneys swollen and deeply congested. The pancreas was somewhat adherent to the liver, it appeared normal in all respects and in all parts except in the substance of the mid body, where fleshy nodules could be felt No extrahepatic primary growth was found, and a primary intrahepatic carcinoma was diagnosed

Histology—Sections of the liver showed a hepatoma of multifocal origin. In the kidneys epithelial damage to both sets of convoluted tubules was severe, and the lumina contained much eosinophilic granular debris and some detached cells Congestion was well marked, and most glomeruli showed a similar debris, with hæmorrhage in the capsular spaces of some The cytological findings in the pancreas are presented below with the account of the effects of alloxan Here suffice it to say that numerous sections of the nodules in the body of the pancreas showed these to consist of simple hæmolymph glands

Biochemistry—The results of relevant tests were as follows

Date	*Investigation*	*Results and comments*
Dec 5 1949	Urea level of ascitic fluid	12·6 mg per 100 ml
10 1949	Blood urea	61 mg per 100 ml (36 hours after intravenous alloxan 20 g)
Nov 14 1949	Blood lipoids	Cholesterol 173 mg per 100 ml total lipoids (Mata) 1160 mg per 100 ml (normal = 450–550 mg) blood fatty acids = 987 mg per 100 ml (normal = 310–360 mg)
17, 1949	Serum-citric acid	53 3 mg per 100 ml (5 controls = 1 66 2 15 3·6 2 9 and 2 4 mg)
17 1949	Blood pyruvic acid	3 72 mg per 100 ml (normal about 1 mg)
17 1949	Urinary citric acid	133 mg per 100 ml. ≡ 1 86 g per 24 hr (6 male controls = 30 27 5 35 75 44 22 5 and 19 2 mg)
17 1949	Urinary pyruvic acid	10 0 mg per 100 ml ≡ 0 14 g per 24 hr (control = 1 24 mg per 100 ml.)
20 1949	Urinary citric acid	71 4 mg per 100 ml ≡ 1 16 g per 24 hr
20 1949	Urinary pyruvic acid	6 56 mg per 100 ml ≡ 0 11 g per 24 hr
Dec 1 1949	Urinary citric acid	77 5 mg per 100 ml ≡ 1·04 g per 24 hr
1 1949	Urinary pyruvic acid	3 8 mg per 100 ml ≡ 51 1 mg per 24 hr
8, 1949	Plasma citric acid	19 8 mg per 100 ml
8 1949	Blood pyruvic acid	2 3 mg per 100 ml

At no time were any ketone bodies found in the urine on repeated routine tests Citric acid was determined by the method of Pucher et al (1936), and pyruvic acid by that of Friedemann and Haugen (1943)

DISCUSSION

It is considered that the condition was one of organic hyperinsulinism due primarily to hypertrophy and hyperplasia of the islets of Langerhans, and later complicated and exacerbated by the development of a primary liver-cell carcinoma

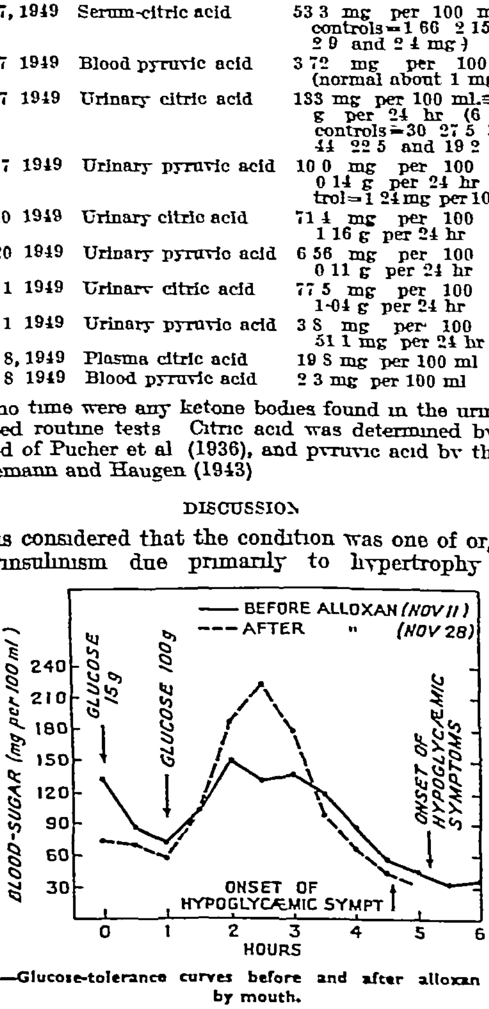


Fig 2—Glucose-tolerance curves before and after alloxan 8 3 g by mouth.

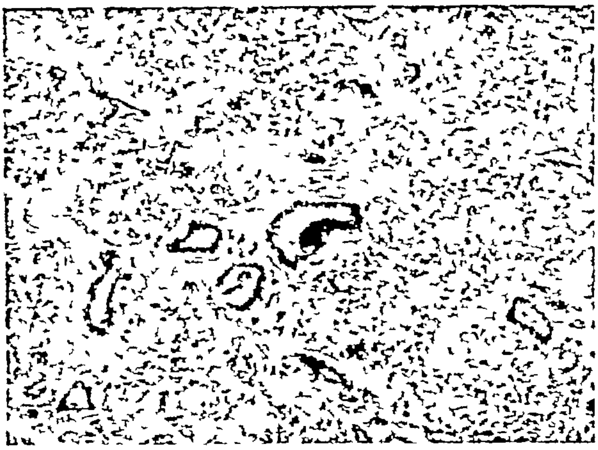


Fig 3—Pancreas showing abundant islet tissue in places associated with small ducts (Hæmatoxylin and eosin, × 95)

Clinical Evidence

In the present instance Whipple's three criteria (Graham and Oakley 1950) of organic hyperinsulinism are satisfied (1) the attacks occurred when the patient was fasting, (2) the attacks were relieved by glucose given without the patient's knowledge—i e, when he was in coma—and (3) the blood sugar level was below 50 mg per 100 ml. during the attacks (fig 2) Conn's (1947) criterion that severe hypoglycæmia is always precipitated by a short fast was also satisfied.

Owing to the rapidly increasing severity and frequency of the attacks Conn's (1940) standard dietary preparation for the glucose tolerance tests could not be used, and the tests had to be modified Glucose (100 g) had to be given at least once during the night preceding the test At 7 A.M 50 g of glucose was given, this was followed by a light breakfast at 8 A.M The tests were begun at 9 A.M with 15 g of glucose followed by 100 g at 10 A M The two curves (fig 2) require little comment Other workers—e g, Kane (1947)—have described also attacks of acute abdominal pain associated with hyperinsulinism

Although we have no definite clinical evidence of the effect of alloxan on the hypoglycæmia, the attacks decreased in frequency and severity during the twenty-four hours after the patient's discharge from hospital The nature and significance of his terminal coma are uncertain After 8 g of alloxan by mouth, the second glucose tolerance test showed a suggestive peak at $2^1/_2$ hours Lukens (1948) records the experimental production of diabetes by oral alloxan, though it is generally agreed that oral administration is ineffective

The toxic effects of alloxan (which have been noted by others) include thrombophlebitis, rigors, vomiting, and tetany (Graham and Oakley 1950) Brunschwig et al. (1944) observed restlessness, cyanosis, perspiration, dyspnœa, vomiting, and severe hæmolytic anæmia with jaundice Conn and Hinerman (1948) remark on the light red colour of the urine after alloxan and independent of hæmaturia, and attribute it to a reduction product This was also seen by us Conn and Hinerman (1948) and Brunschwig et al (1944) state that the blood-urea level did not rise after the administration of alloxan, though the transitory occurrence of casts, red cells, and a trace of albumin in the urine were seen In the present case, thirty six hours after the intravenous injection of 20 g of alloxan the blood urea level rose to 61 mg per 100 ml., and hæmaturia and oliguria were followed by anuria a relapse would follow That this has generally happened in the present small series is clear, though whether the remissions have been due to psychological causes or to some non specific effect of the operation is not known The results up to now must be regarded as poor, and it is clear that it is possible to have typical bronchial asthma after resection of the vagus nerves to the lungs We feel, however, that at any rate no harm has been done, and the procedure seems to be reasonably safe in Mr Edwards's hands It is just possible, too, that in some of the cases we are witnessing the gradual post operative improvement noted by Rienhoff and Gay This, and the striking result in case 2, leads us to think that there is just enough evidence to warrant the operation in intractable cases We agree, however, with Rienhoff and Gay that there is no indication that any particular type of patient will benefit, the only criterion being "failure of medical treatment"

SUMMARY

Six patients with intractable bronchial asthma underwent bilateral resection of the vagus The results on the whole were disappointing, but it is felt that there is a case for further observations

My thanks are due to Dr R Coope, Dr L Findlay, and Dr W S Sutton for permission to report their cases

ADDENDUM

Four months after this article was written a follow up showed

Case 1 —Several relapses Condition similar to that before operation

Case 2 —Remained entirely well

Case 3 —No further relapses, occasional wheeziness Distinct general improvement

Case 4 —No further relapses Slow improvement and back at work Wheezy bouts occasionally, relieved by aminophylline or inhaler

Case 5 —Marked improvement since tonsillectomy in October, 1950

Case 6 —No relapse since second operation Married

REFFRENCES

Abbott O A Hopkins, W A, Guilfoil, P H (1950) *J thorac Surg* 20 571

Blades B Beattie E J Elias W S (1950) *Ibid* p 584

Carr D Chandler H (1948) *Ibid* 17 1

Gay, L N Rienhoff W M (1942) *Bull Johns Hopk Hosp* 70 386

Klassen K P Morton D R Curtis G M (1950) *J thorac Surg* 20 552

Miscall L Rovenstine E A (1943) *Surgery* 13 495

Rienhoff W M Gay, L N (1938) *Arch Surg* 37, 456

ORGANIC HYPERINSULINISM TREATED WITH ALLOXAN

W S L Gilchrist
M D Belf, M R C P
CONSULTANT PHYSICIAN

M J G Lynch
M B N U I, M R C P
PATHOLOGIST

FARNBOROUGH HOSPITAL, FARNBOROUGH, KENT

THIS case is considered worthy of publication because of the two factors in the ætiology and the results of treatment with alloxan

CASE RECORD

The patient, first seen in 1949, was a man aged 36 working as overseer at the General Post Office His illness had begun in childhood, for in 1918 he had griping pains in both sides of the lower abdomen, radiating into the left side of the chest At first the pains would come on after every meal on two successive days, with no further pain for about a year Early in 1949, however, the attacks grew more frequent and severe, lasting for two hours (The appetite remained good) He took to his bed on Sept 6, 1949, because of increasing prostration and night sweats, which wakened him at night The attacks, from being intermittent, became regular, occurring each midnight, occasionally he had a further attack at 6 A M At this stage his wife sought the advice of a pharmacist, who suggested the use of glucose Taken at bedtime this prevented most of the midnight attacks, but he continued to have occasional attacks at 6 A M Attacks were promptly relieved by glucose He had lost half a stone in weight in the year preceding his admission to hospital on Oct 13, 1949 A feature of note in his past history was that about 1937 he had an attack of infective hepatitis

On examination he was thin but not emaciated The liver edge was palpable in the right midclavicular line at the level of the umbilicus, it was round, firm, and not tender Two moderate sized nodules were palpable on the edge of the right lobe

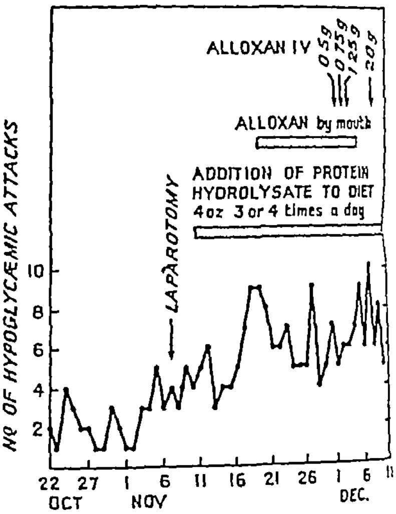


Fig 1—Frequency of hypoglycæmic attacks.

Progress —At 6 A M on Oct 15 he woke and asked for water He then became restless and excited, and struggled violently His recovery was spontaneous At 5 15 A M on Oct 24 he came out in a cold sweat and became irrational, recovered a little, and then suddenly lapsed into coma at 6 30 A.M Two hours later, when seen by the house physician, he was in a deep coma, breathing stertorously, and sweating profusely His pulse was rapid and irregular and his blood pressure 160/70 mm Hg The plantar responses were extensor On being given 15 ml of 50% glucose intravenously he recovered rapidly At this time he was having two or three (hypoglycæmic) attacks each day (fig 1) Usually he would begin to sweat profusely, lapsing rapidly into coma unless given glucose by mouth On other occasions the attacks were more gradual and showed all the features typical of hypoglycæmia.

Diet —On Oct 22 he was put on a 2000-calorie diet, equivalent to 210 g of carbohydrate and 75 g of protein a day Unfortunately his appetite became very capricious and it proved impossible to proceed with proposed observations on a high protein diet He was given 100 g of glucose orally at the beginning of each attack

Operation —On Nov 7, a laparotomy was performed by Mr Cyril Cookson The liver was found to be much enlarged and congested, with large firm whitish nodules on its surface The tail of the pancreas appeared normal, but its head was fused with the liver No evidence of peptic ulceration was found A small piece of liver was taken for histological examination This specimen was unrepresentative and was wrongly taken to be a metastasising islet-cell tumour

Postoperative Course —Shortly afterwards the patient deteriorated steadily and developed ascites The hypoglycæmic attacks increased in frequency and severity The addition of casein hydrolysate to his scanty diet did not affect their occurrence His condition continued to deteriorate steadily and a secondary deposit appeared on the right side of his chest

Alloxan Therapy —From Nov 19 to Dec 5 he had 17 3 g of alloxan (14 8 g by mouth and 2 5 g intravenously (fig 1)) However, the frequency of hypoglycæmic attacks increased On Dec 8 alloxan 20 g was administered in 250 ml of physiological saline solution, together with intravenous penicillin 500,000 units in 45 minutes On Dec 9 there were oliguria, albuminuria, and hæmaturia, followed next day by anuria and a slight icteric tinge in the skin Two very severe hypoglycæmic attacks occurred that afternoon At 7 P M his wife took him home against medical advice His doctor informs us that he had a mild hypoglycæmic attack at midnight on Dec 10 1949, and a more severe attack at 3 next morning At 8 A M he complained of pain in the lumber region Thereafter he lapsed into coma and he died at 4 30 P M on Dec 11, 1949

TUBERCULOSIS OF THE NASOLACRIMAL DUCT

P. G. KONSTAM
F.R.C.S.E.
LATE ACTING DIRECTOR, CASUALTY SERVICE

M. J. MEYNELL
M.D., B.Sc. Sheff., M.R.C.P., D.P.H.
CLINICAL PATHOLOGIST

THE GENERAL HOSPITAL, BIRMINGHAM

TUBERCULOSIS of the nasolacrimal duct is sufficiently ncommon to be worth recording, particularly if, as we believe, the condition arises primarily in the duct without evidence of disease of either the eye or the nose, nd when there is no evidence of tuberculosis elsewhere—e., it is a primary complex. The condition can be best described as a primary tuberculous "chancre" of the nasolacrimal duct.

The only English reference found is that of McKenzie 1939), who describes a case secondary to tuberculosis of the turbinate bones, and summarises previous reports.

Seifert (1899) stated that tuberculosis of the nasoacrimal duct was always secondary to tuberculosis of the bony walls (very rare and possibly associated with upus), the nose, or the conjunctiva. He held that the commonest route of infection was from the nose. So long as the mucous membrane of the lacrimal sac was healthy and the lumen of the duct was patent, infection was unlikely owing to the free flow of secretion. As soon as the lower opening was closed, infection might enter from above in the tears, or more likely from below—i.e., the nose. Seifert mentioned three cases of tuberculous nasolacrimal duct due to primary nasal infection.

Work has been done experimentally in rabbits. Gourfein (1899) showed that a primary infection of the nasolacrimal duct could be produced two to four months after the introduction of tubercle bacilli into the conjunctival sac. He concluded that the lacrimal ducts were not protected by natural secretions.

Aurand (1900) described a case in a man, aged 24, who presented with an infection of the lacrimal sac which was followed three years later by tuberculosis of the nose and conjunctiva.

CASE RECORD

A boy, aged 14 months, was first seen in the casualty department on Oct. 6, 1949. Examination revealed a small indurated nodule with superficial ulceration, the whole the size of a small pea, just beside the right inferior lacrimal canaliculus. There was another ulcer about $^1/_4$ in. in diameter, flat and dry, on the cheek in the region of the superficial parotid (preauricular) glands. The right submandibular glands were visibly enlarged and palpable. There was a decided right hemifacial œdema. No other abnormalities were detected. The child's general condition appeared good.

Previous History.—In June, 1949, his mother noticed a swelling of his right eye which discharged a small quantity of purulent material. Shortly after this she noticed a small swelling over the parotid gland. He was taken to a doctor, who treated him with sulphonamides. In September the doctor incised the swelling over the parotid. Apparently a small quantity of purulent material was obtained and the resultant ulcer never healed properly. Three weeks before the boy was brought to the hospital his doctor noticed further swellings in the submandibular region.

Family History.—He is an only child. His mother, when first seen, denied any family history of tuberculosis. All we could do by way of investigating her was to radiograph her chest and estimate her erythrocyte sedimentation rate (E.S.R.). Radiography showed some consolidation below the apex of the left lung which could very well be tuberculous. The E.S.R. was normal. There were no physical signs of tuberculosis of the chest, and the mother refused to have her sputum examined. After a good deal of persuasion we managed to obtain a radiograph of the father's chest which showed calcified spots on the right side—evidence of old fibroid phthisis. The father reluctantly admitted having been in a sanatorium for some time with an artificial pneumothorax. He refused to indicate when his sputum had last been positive, but hinted that it was not long ago. He would not coöperate, and nothing beyond a radiograph could be got from him.

Investigation of Patient.—The submandibular swelling was aspirated. The specimen consisted of mucopus. Stained films showed debris with occasional pus cells. A few acid-fast and alcohol fast bacilli were present. No other organisms were seen. Cultures showed no growth after seventy two hours. Cultures on Sabouraud's medium remained sterile after fourteen days' incubation at 20–22°C. A blood-count showed Hb 76% and white cells 9600 per c.mm. (differential count not significantly altered). Radiography showed no obvious abnormality of chest or sinuses. Sinus puncture was not attempted. Examination of nose, pharynx, and eyes was negative. A Mantoux test was strongly positive in a dilution of 1 in 100 000. A biopsy specimen from the edge of the ulcerated area over the parotid lymph gland proved to be skin and subcutaneous tissue. The dermis was densely infiltrated by acute and chronic inflammatory cells and many typical tuberculous giant cells, strongly suggesting tuberculosis.

Treatment and Progress.—A course of streptomycin 0.25 g. six hourly was begun on Oct. 21, 1949. The child's general condition remained good and at no time did he have pyrexia. However, on Nov. 7 the fluctuant swelling over the submandibular region was aspirated and more mucopus was removed. The child was thenceforth given 'Calciferol' 50,000 units daily in addition to the streptomycin. Despite this therapy the swelling increased, so it was excised on Nov. 19, 1949. The entire mass of superficial and upper deep cervical glands was removed. They had broken down and were in different stages of destruction. Histologically the lymph nodes were almost entirely replaced by large numbers of typically tuberculous follicles. Caseation was present. All the lymph nodes showed a well defined fibrous tissue reaction. Cultures on Lowenstein-Jensen medium and animal inoculation test proved positive for tubercle bacilli. The streptomycin sensitivity tests showed a fully sensitive strain of tubercle bacilli. No section was made of the original lesion in the nasolacrimal duct, because it was considered unjustifiable. Swabs of the nasolacrimal ulcer and of the conjunctiva showed no tubercle bacilli on either microscopy or culture. The boy received 31.5 g. of streptomycin in four weeks and two days and 800 000 units of calciferol in sixteen days. The lesions dried and began to heal with some scarring. The hemifacial œdema completely disappeared. He was discharged, and it was arranged for him to attend hospital as an outpatient.

DISCUSSION

The lesion in the present case is believed to be a primary tuberculous complex because (1) no tuberculosis was found elsewhere, (2) the age was only 14 months, and (3) the regional lymph glands were severely affected, the process going on to caseation.

Admittedly there is no history of a negative Mantoux reaction before the onset of this condition, but the evidence on the whole is in favour of such a presumption. In addition, we consider this case to be one of primary involvement of an apparently healthy nasolacrimal duct in view of the negative findings in either the nose or the eye.

Presumably the original source of infection is the father, who had a history of phthisis and whose sputum had contained tubercle bacilli. He seems to have infected both mother and child. It is also presumed that the organisms were introduced into the patient's conjunctival sac. A heavy infection in a child of this age might produce a condition not unlike that produced in rabbits by Gourfein (1899).

Thanks are due to Dr. C. Parsons for permission to publish, Miss P. M. Weight for secretarial assistance, and Mr. A. C. Allsop for the bacteriological examinations.

ADDENDUM

After this paper was written the child had a further flare up of the lesion over the nasolacrimal duct, and, despite the original reluctance to remove this, partial dacryocystectomy was done. This lesion showed a characteristic tuberculous infiltration, so we ultimately

Biochemical Evidence

The relevant findings are listed above Significantly high values were obtained for blood fatty acids, serum citric acid, and blood pyruvic acid The urinary excretion of citric and pyruvic acids was excessive Although the former represent only three stages in the long chain of energy changes involved in oxidising glucose, the uniformly high values obtained indicate an accumulation of the products of the C_6 tricarboxylic acid cycle (Breusch 1948) The raised pyruvic acid level may be due to the excessive secretion of insulin (Bueding et al 1942) Derangement of the metabolism of protein and fat due to liver disease may also have contributed to the raised values obtained

Dr H Weil Malherbe informs us that he has found a slight decrease in the serum citrate level in artificial hypoglycæmia This suggests that in the present case the liver did not break down citrate

Histological Evidence

The photomicrograph of a section chosen at random (fig 3) shows that the pancreas contained an abnormal number of islets Many of these islets were abnormally large (fig 4) Although K C Richardson (cited by Graham and Oakley 1950) believes that the variation in size of the normal islets is so great that one cannot diagnose hyperplasia, we are of the opinion that the island here depicted is pathological

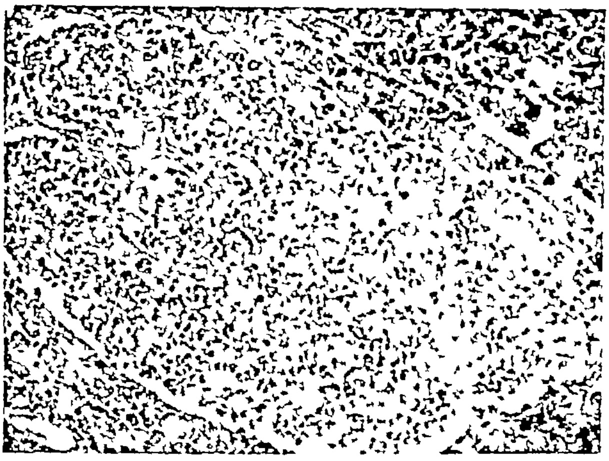


Fig 4—Pancreas showing giant islet measuring 660 µ × 360 µ (1089 cells counted) (Gomori's stain ; × 120)

Effect of Alloxan

The necrotising effect of alloxan on the islet cells, especially the α cells, was observed in all sections In all sections which were examined no undamaged islet was seen Changes took the form of cellular loosening and detachment, with loss of constituent cells in varying degree, some islets consisted of almost empty spaces with a few tattered cells and amorphous granular cytoplasmic debris Many cells appeared swollen, and most presented a matt eosinophilic appearance when stained with hæmatoxylin and eosin, the nuclei appearing small and pyknotic These changes agree with those observed in rabbits by Dunn et al (1943a and b, 1944) In addition, interstitial hæmorrhage was found in some islets (fig 5)

A good account of the cytological effects of alloxan in man is given by Conn and Hinerman (1948), who found similar changes in a portion of normal pancreas removed from a patient who had had 60 g of intravenous alloxan in nine days

Brunschwig et al (1944), however, found only "questionable evidence of injury to a number of cells in some of the islets" Two explanations, of practical importance, have been put forward to account for this discrepancy The first is the fact that alloxan, known to be rapidly eliminated, was administered too slowly, and the second that the preparation of alloxan used may have been ineffective

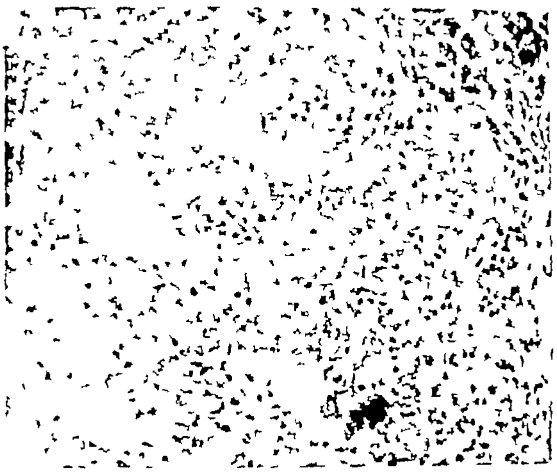


Fig 5—Pancreas showing interstitial hæmorrhage and necrosis of constituent cells in islet of Langerhans (Hæmatoxylin and eosin × 165)

SUMMARY AND CONCLUSIONS

A case of organic hyperinsulinism treated with alloxan is described The toxic effects of alloxan are listed as a warning against its indiscriminate use, and it is suggested that therapeutic results are more likely to be obtained with intravenous injections of 100–200 mg per kg of body weight given rapidly (10–30 minutes) as a 5% solution

Our thanks are due to Dr G Brownlee for much helpful criticism and advice We are also indebted to Dr George Graham, to Dr D Haler, to Mr E A Jones of the Wellcome Research Laboratories, and to Mr E Scott, Mr E A Checksfield, and Mr E Poynter of the Farnborough Hospital. The alloxan was supplied by Messrs L Light and Co, Ltd, Wraysbury, Middlesex

REFERENCES

Breusch F L (1948) *Advances Enzymology* 8, 343
Brunschwig A Allen J G Owens F M jun, Thornton T F jun (1944) *J Amer med Ass* 124, 212
Bueding, E Fazekas J F Herrlich, H Himwich, H E (1942) *Science* 95, 282
Conn J W (1940) *Amer J med Sci* 199 555
— (1947) *J Amer med Ass* 134 130
— Hinerman J W (1948) *Amer J Path* 24 429
Dunn J S Kirkpatrick J, McLetchie N G B, Telfer S V (1943a) *J Path Bact* 55 245
— McLetchie, N G B Sheehan, H L (1943b) *Lancet*, i, 484
— Duffy E Gilmour M K, Kirkpatrick J McLetchie N G B (1944) *J Physiol* 103 233
Friedemann, T E Haugen G E (1943) *J biol Chem* 147, 415.
Graham G Oakley, W G (1950) *Quart J Med* 19, 21
Kane W (1947) *Amer J digest Dis* 14, 195
Lukens F D W (1948) *Physiol Rev* 28 304
Pucher G W Sherman, C C Vickery H B (1936) *J biol Chem.* 113 235

"The development of the concept of general practice from health centers will require three steps, the first of which is the grouping of family practitioners to practice from health centers This is much more difficult in the democratic than in the totalitarian countries The necessary change of medical mores in democratic countries will require a long and slow educational process, apart from the magnitude of the physical problem of providing the necessary number of centers The second and third steps to extend the practice of clinical medicine to include the diagnosis and prevention of social pathology and to integrate the personal health services into general practice, which are now provided through 'ad hoc' public health agencies for separate population groups, will require in the United Kingdom at least a quarter of a century, for two reasons The general practitioner will have to receive his clerkship training in an environment much different from that which is limited to teaching institutions dealing primarily with cases of illness mostly referred for consultation Satisfactory clerking in turn, will not be possible until students can practice in health centers with physicians as captains of medical teams taking the family as the unit "
—Dr John B Grant, *Tijdschr soc Geneesk* June, 1950

TABLE III—ERYTHROCYTE SEDIMENTATION RATES

Case no	Initial period (days)	Actual E.S.R. values (mm in 1 hr)				E.S.R. change (mm)		
		Initial	Start of treatment	After 48 hr	End of treatment	Initial period	First 48 hr	Remainder
1	9	55	30	20	48	−25	−10	+28
2	8	25	34	34	44	+9	0	+10
3	5	42	34	28	30	−8	−6	+2
4	6	80	84	74	78	+4	−10	+4
5	5	50	50	50	56	0	0	+6
6	10	80	66	68	72	−14	+2	+4
7	10	70	44	38	44	−26	−6	+6
8	6	52	46	46	42	−6	0	−4

fallen in the observation period, so the change cannot be ascribed to the treatment In case 4 there was a fall of 10 mm following a slight rise before treatment began, no corresponding improvement was noted in her joints, but she developed well marked euphoria after the first injection (see below)

In the last few days of the course all but one of the patients had a slight or moderate rise in E.S.R. In case 8, where there was a slight fall, the patient's general condition became definitely worse with a great increase in pain, and the fall of 4 mm in E.S.R. certainly did not indicate improvement in the arthritis

HÆMOGLOBIN

Hæmoglobin was estimated three times a week in the initial and treatment periods No significant changes were noted Excluding the patient who had melæna, there was an average gain of 2% in the initial period and a loss of 1% during treatment

EOSINOPHIL COUNTS

If deoxycortone acetate and ascorbic acid exerted a cortisone like effect, one would expect the average eosinophil count to be lower during treatment than in the initial period Table IV shows that this was not so The counts were done three times a week at about the same time of day A dry differential count on 2000 cells was made and the total white cells were counted at the same time This method has been strongly criticised by Rud (1947), and the findings are presented with considerable hesitation

Cases 1, 6, and 7, who had the greatest falls in E.S.R. in the initial period, also had the lowest eosinophil counts In case 8 there was a marked clinical deterioration during treatment and yet the eosinophil count appeared to have fallen, but only two counts were done during treatment, which was limited to five injections so this result is of little significance

TABLE IV—EOSINOPHIL-COUNTS

Case no	Average number of eosinophils per c.mm	
	In initial period	During treatment
1	106 (*3*)	177 (*3*)
2	208 (*1*)	172 (*4*)
3	172 (*3*)	199 (*3*)
4	228 (*3*)	346 (*3*)
5	322 (*4*)	302 (*3*)
6	74 (*5*)	85 (*4*)
7	88 (*6*)	187 (*3*)
8	152 (*3*)	82 (*2*)

Figures in parentheses show number of counts done

MENTAL REACTIONS

In cases 4 and 6 a striking euphoria was noted some minutes after the first injection of deoxycortone acetate and ascorbic acid This lasted for about three hours and was not repeated after subsequent injections In both patients there was some evidence of improvement in the next forty eight hours—case 6 in clinical condition and case 4 in E.S.R.

DISCUSSION

Patients admitted for treatment with deoxycortone acetate and ascorbic acid seemed to progress on a standard plan Before treatment started there was immediate clinical improvement with a fall in E.S.R. This continued for the first two days of treatment, but then nearly every case went downhill This illustrates the great importance of an adequate period of observation in hospital before treatment is begun In the present cases the results would have been much more favourable if the injections had been started on the day of admission

The well established tendency of these patients to improve if admitted to hospital is not easy to explain The most important factor is probably restoration of morale The present patients had read about cortisone in the press and had high hopes that they were to receive an effective substitute The improvement seemed to last 7–14 days and was nearly always followed by deterioration In 5 of our 8 patients the turning-point came in the later days of treatment Whether disappointment at the failure of the initial injections was a factor in the exacerbation must remain an open question

It is certain that deoxycortone acetate and ascorbic acid are no substitute for cortisone The observers who have reported favourably on this combination (Lewin and Wassén 1949, Le Vay and Loxton 1949, Douthwaite 1949, Fox 1949, Robertson 1950, Nashat 1950) agree that the relief is obvious within a few minutes of the injection and is accompanied by exhilaration, it may last hours or days and may be repeated after subsequent injections Some of these patients have been treated as outpatients, and there is no record of any long preliminary observation period in hospital, this point was emphasised by Fox (1949) If the good results are due to the moral effect of cortisone's reputation, reinforced by the euphoria which is sometimes a direct effect of the injections, it would be worth while investigating the value in rheumatoid arthritis of other drugs which produce euphoria, as has been done in pulmonary tuberculosis

SUMMARY

The results of intramuscular deoxycortone acetate and intravenous ascorbic acid in 8 patients with active rheumatoid arthritis are reported

No significant improvement was obtained

Several patients improved between their admission to hospital and the start of treatment, illustrating the importance of an initial period of observation when assessing any new treatment

Euphoria followed the injections in 2 cases and this effect may be partly responsible for the improvement noted by other workers

I wish to thank Dr A. H Douthwaite and Dr E R Boland under whose care the patients were admitted for their invaluable help and advice during the preparation of this paper

REFERENCES

Bywaters E G L Dixon A St J Wild J B (1950) *Lancet* i 951
Copeman W S C et al (1950) *Ibid* p 830
Douthwaite A H (1949) *Ibid* p 1244
Fox W W (1949) *Ibid* p 1156
Kellgren J H (1949) *Ibid* p 1108
Le Vay D Loxton G E (1949) *Ibid* p 1134
Lewin E Wassén E (1949) *Ibid* p 993
Nashat F (1950) *Ibid* i 135
Robertson J A (1950) *Ibid* p 134
Rud F (1947) cited *Ibid* p 1042

proved that the three lesions with which he originally presented were tuberculous—that is, the nasolacrimal duct and preauricular and submandibular glands were the sites of tuberculosis The patient has remained well up to the present

REFERENCES

Aurand L L (1900) *Int Congr Med*, Paris (sect. ophthal), p 388
Gourfein D (1899) *Rev méd Suisse rom* 19, 380
McKenzie W S (1939) *J Laryng* 54, 33
Seifert, O (1899) *Münch med W schr* 46 1766

DEOXYCORTONE ACETATE AND ASCORBIC ACID IN RHEUMATOID ARTHRITIS

K S MacLean

M A, M D Camb, M R C P

ASSISTANT TO DIRECTOR, DEPARTMENT OF MEDICINE, GUY'S HOSPITAL

The results obtained with deoxycortone acetate and ascorbic acid in a small series of cases of rheumatoid arthritis at Guy's Hospital support the views of Kellgren (1949), Bywaters et al (1950), Copeman et al (1950), and others that, as a substitute for 'Cortisone,' this treatment is completely ineffective Observations were made which emphasise the difficulties of assessing results in rheumatoid arthritis and may partly explain the wide differences of opinion on this treatment

The 8 patients, all women, were observed for at least five days before being given deoxycortone acetate and ascorbic acid During this period they received full passive movements of all affected joints once daily and analgesics in about the amounts they had been taking before admission All of them were seen within two or three days of admission

The course of treatment consisted of 8 daily injections of deoxycortone acetate 5 mg intramuscularly, followed immediately by ascorbic acid 1 g intravenously, except in case 8, where only 5 injections were given because the patient's arthritis was obviously becoming worse and the intramuscular injections were followed by severe pain

Table I gives brief details of the 8 patients on admission

Case 1 had psoriasis, which had been present for two years, this flared up in the latter part of her treatment, new patches appearing on her hands

Case 2 had melæna on the fifth and sixth days of treatment, which was never satisfactorily explained, she had had unexplained hæmoptyses in 1931 and 1944 and hæmatemesis nine months before admission. Her clotting time and prothrombin time were now normal

Several patients had had symptoms of arthritis for many years, but they had been deteriorating before admission, and in all cases the rheumatoid arthritis was considered active

TABLE I—CONDITION ON ADMISSION

Case no	Age (yr)	General condition	Muscle wasting	Joints affected	Pain on admission	Duration of symptoms (yr)	E.S R. (mm in 1st hr)	Hb (%)
1	57	Bedridden	Sev	Multiple	Mod	7	80	78
2	60	Almost bedridden	Mod	Multiple	Sev	37	25	86
3	47	Immobile through ankylosis of knees otherwise active	Slt	Multiple	Slt	18	42	80
4	63	Bedridden	Sev	Multiple	Sev	24	80	74
5	57	Mobile	Slt	Multiple	Mod	1½	50	70
6	42	Bedridden	Sev	Multiple	Mod	11	80	60
7	46	Mobile	Nil	Hands ankles rt wrist	Slt	3½	70	78
8	16	Mobile	Nil, obese	Hands wrists elbows knees rt sacro iliac	Mod	10/12	50	90

CLINICAL CONDITION

The day to day changes in rheumatoid arthritis are not easily assessed In these patients the range of passive movement in the affected joints varied so much from hour to hour that conclusions drawn from such changes would be misleading Assessment was therefore based on clinical findings, particularly what amount of movement the patient could perform This amount no doubt depends largely on how the patient is feeling when examined, but, as Bywaters et al (1950) point out, subjective feelings are a valuable indication of progress in this disease, and it would be impossible to divorce them from the clinical state of the disease Table II summarises the patients' clinical progress in (1) the initial observation period, (2) the first 48 hours of treatment, and (3) the remaining days of treatment

TABLE II—CLINICAL PROGRESS BEFORE AND DURING TREATMENT

Case no	Duration of initial observation (days)	Progress during		
		Initial period	First 48 hr of treatment	Remaining days of treatment
1	9	Great improvement	No change	Mod deterioration (spread of psoriasis)
2	8	Mod improvement	No change	Mod. deterioration (melæna)
3	5	Mod improvement	No change	No change
4	5	Slight improvement	No change	Mod deterioration
5	5	Slight improvement	Slight improvement	Slight deterioration
6	10	Slight improvement	Mod improvement	Slight deterioration
7	10	Great improvement	No change	No change
8	5	No change	Slight deterioration	Mod deterioration

It is clear that improvement was greatest before treatment began The 2 patients who improved in the first 48 hours of treatment had been improving previously During the remainder of the course no patient improved and 6 deteriorated

Case 1 deteriorated considerably and developed a new manifestation in the cervical spine Clinical deterioration was not obvious until the third day of treatment, but she had slight pain in the neck the day before treatment started, so it is unjustifiable to ascribe the exacerbation to the drugs

BLOOD FINDINGS

The erythrocyte sedimentation rate (E S.R., Westergren), hæmoglobin, and eosinophil count were done every 2 or 3 days In some cases capillary blood was used for E S R because deformity of the joints made venepuncture difficult

These results (table III) accord well with the patients' clinical condition In the initial period cases 1 and 7, who showed great clinical improvement, showed a corresponding fall of over 20 mm in E S.R, cases 3, 6, and 8 had a slighter fall In case 2 a moderate clinical improvement was accompanied by a slight rise in E S R., this patient did badly later, and the initial response may have been largely subjective

In the first forty eight hours' treatment 4 patients showed falls in E S R, but in 3 of them the rate had ntricle The fibrosis extended irregularly through the vocardium, and there was some unevenly distributed thicken g of the endocardium The valves appeared normal An te mortem thrombus was attached to the wall of the left entricle at the apex. There was no evidence of coronary sease The left kidney showed a well-demarcated area of ecrosis about 4 × 2 × 0 3 c cm. with a surrounding red zone he liver spleen, and lungs showed only congestion. The eritoneum contained some faintly turbid fluid which on ulture yielded only contaminants Nothing else abnormal as found.

Histology —The sections were all stained with hæmatoxylin nd eosin and Levaditi s stain for spirochætes No organisms ere seen. The myocardium was infiltrated diffusely with brous tissue, some of which was considered to be weeks old, hile in other places it was still being laid down, and patches f myocardial degeneration were present There was only a ery scanty cellular infiltration by an occasional polymorph r lymphocyte No Aschoff bodies were seen. In the left idney (fig 3) the outer half of the cortex was necrotic, apart rom a small subcapsular area There was a surrounding one of hyperæmia A few polymorphs, lymphocytes and ibroblasts were present and some collagen had been laid own. The necrotic area was considered to be not more han a week old. Elsewhere the kidneys appeared normal he liver showed some centrilobular congestion. The lungs howed alveoli full of red blood-cells and pigment-laden hagocytes but no bronchial necrosis or evidence of pulmonary nfection was seen. No *Trichina spiralis* embryos were seen n the heart or in the diaphragm.

DISCUSSION

Since Fiedler s (1900) original description of interstitial myocarditis over 44 cases have been published with an acute, subacute, or chronic course Covey (1942) notes that this disorder occurs mainly in young persons aged 20–30 Sudden death is very common, and the condition is more often recognised post mortem than clinically The usual clinical picture is that of rapidly progressive heart-failure in a previously healthy young person

There is often a history of infection of the upper respiratory tract, as in the present case Finland et al. (1945) have suggested that influenza-A virus may be concerned, they publish two cases of influenza with interstitial myocarditis, and influenza-A virus was recovered from the lungs post mortem in these two cases Schmidt (1948) isolated a virus from a chimpanzee dying of interstitial myocarditis The evidence, however, of the occurrence of myocarditis in human influenza epidemics is so far inconclusive The present case came to necropsy during an influenza-A outbreak, but similar lesions were not found post mortem in two patients who died of influenza in the epidemic and in whom the virus was found.

Other ætiological agents mentioned are *Treponema pallidum, Staphylococcus citreus,* bacterial toxins, and *Trichina spiralis* In the present case no organisms were seen in the heart with Gram s stain, and post mortem culture of the peritoneal fluid yielded contaminants only The appearances were not those of eosinophilic myocarditis caused by sulphonamides as described by French and Weller (1942) A deficiency of vitamin B_1 was considered by Toreson (1944) to be a possible cause, but there was no history of dietary deficiency in the present case and the blood pyruvic-acid level was within normal limits

A zone of unilateral cortical necrosis of the kidney was a feature of the present case and has not previously been reported. Despite the presence of ante mortem thrombus in the left ventricle, the appearances of the renal lesion, by reason of its site and extent, were considered to be those of cortical necrosis and not infarction Either vascular spasm or renal anoxia may have been the cause of the cortical necrosis

We are indebted to Dr C Gray Imrie for permission to publish this case and for his helpful advice

REFERENCES

Covey G W (1942) *Amer J clin Path* 12 160
Fiedler (1900) *Zbl inn Med* 21 212
Finland M. Parker F jun. Barnes M. W Jolliffe L S (1945) *Amer J med Sci* 209 455
French A. J , Weller C V (1942) *Amer J Path* 18 109
Schmidt E C H (1948) *Ibid* 24 97
Toreson W E (1944) *Arch intern Med* 73 375

LATE INFECTIVITY IN HEPATITIS

Patrick N Meenan
M.D N U I. D C.P
ASSISTANT PATHOLOGIST ST VINCENT S HOSPITAL,
PATHOLOGIST, NATIONAL CHILDREN S HOSPITAL, DUBLIN

In controlling the spread of infective hepatitis it is important to know how long the patients are infectious The period of infectivity is probably short, but it is uncertain at what stage in the illness it occurs Cases have been shown to be infectious eight days before and seven days after the onset of symptoms (McFarlan 1945), but it is generally accepted that fourteen days' isolation from the onset provides a safe margin (Pickles 1939) The case described here, however, suggests that this period is sometimes barely sufficient

There is general agreement on the incubation period Booth (1928) set the limits at 20–40 days, and they were subsequently narrowed down by Pickles (1939) to 26–30 days The latter limits seem rather too narrow, for Naughten et al. (1950) in an outbreak involving 114 people found that the shortest incubation period was 18 and the longest 43 days, and the present case also supports this view

CASE-RECORD

A probationer nurse aged 20 was taken ill with " influenza " on Jan. 14, 1949 and went to bed She improved in the next few days and resumed duty on Jan 21 Next day she was jaundiced Another nurse had an attack of jaundice, diagnosed as infective hepatitis about a month previously but she was much senior to the patient and no history of more than the most casual contact could be elicited Many other nurses had been at considerably greater risk without contracting the infection.

The patient was at no time very ill and from the onset of jaundice she was allowed up daily though she was confined to the ward which contained three other beds her bed being screened off

On Jan. 26 the patient s parents visited her when she was sitting up in bed Both of them sat beside the bed and on the same side the mother being nearer about a yard from the patient They chatted for about three quarters of an hour, when the mother left and the father moved into her chair and remained another fifteen or twenty minutes Both parents kissed the patient on their arrival and departure Neither had anything to eat while in the ward They had travelled about 100 miles by rail for the visit and left for home immediately afterwards

None of the physicians or nurses attending the patient developed jaundice at any time subsequently, and the patient recovered uneventfully

Thirty two days later on Feb 27 the patient s mother, aged 63 complained of influenza ' and on March 7 she developed jaundice The attack was severe requiring hospital treatment but she ultimately recovered completely In hospital she was fully investigated and infective hepatitis was diagnosed The father, aged 70 showed no sign of infection at any stage Neither of the parents gave any history of a previous attack of jaundice One other case of jaundice occurred locally about the end of February, but there was no contact between the two cases and no other case had occurred in the area for more than six months

"ISOLATED" MYOCARDITIS ASSOCIATED WITH UNILATERAL CORTICAL NECROSIS OF THE KIDNEY

I McLean Baird
M B St And, M R C P
MEDICAL REGISTRAR

J C Burne
M A, M B Camb
ASSISTANT PATHOLOGIST

ROYAL HOSPITAL, SHEFFIELD

"Isolated" myocarditis is relatively rare It is characterised by congestive cardiac failure in a previously healthy young person, and often ends in sudden death At necropsy an enlarged heart is found, but usually no other abnormal findings Histologically, there is degeneration of the myocardium, which is often grossly fibrotic throughout Fiedler (1900) first described this condition as "interstitial myocarditis" Covey (1942) collected 44 published cases and reported an additional one The association of unilateral cortical necrosis of the kidney with isolated myocarditis has not been previously recorded

CASE RECORD

A girl, aged 3 years, had been quite well until January 1949, when she developed a cough and pyrexia Her doctor treated her with a week's course of sulphonamides, and her condition improved On March 8 her symptoms had become worse, and subsequently her condition deteriorated so much that her doctor suspected "whooping cough and pneumonia" and arranged for her admission to an isolation hospital on March 14 On admission there were no physical signs except a few fine crepitations at both lung bases On March 19 the child complained of abdominal pain and developed generalised œdema, ascites, enlargement of the liver, and breathlessness On March 21 partial suppression of urine began, 4–8 oz being passed daily On March 23 she was transferred to Sheffield Royal Hospital for further investigation

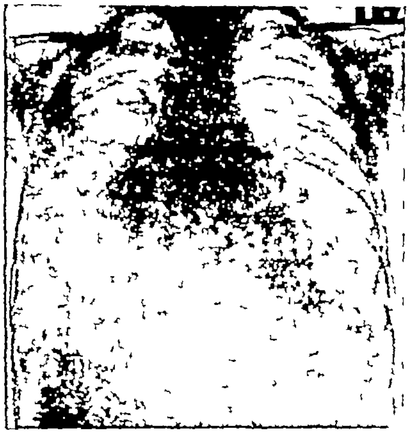


Fig 1—Radiogram of chest on admission showing right half of diaphragm obscured by fluid and heart dilated to right and left

On examination she had a temperature of 100 8°F, pulse rate 132, respirations 48 a minute, there was generalised œdema, with slight cyanosis but no venous congestion, the chest moved well, the trachea was central and the percussion note was resonant throughout, there were occasional crepitations at both bases The heart was enlarged to the left, with a rate of 130, the rhythm was regular, and the heart sounds were muffled The liver was enlarged to 3 finger breadths below the costal margin, and shifting dullness was present in the flanks The spleen was not palpable

Radiography of the chest (fig 1) showed that the right half of the diaphragm was obscured by fluid, the heart was dilated to the right and to the left, but there did not seem to be any pericardial effusion, and there was a small effusion on the right side, extending into the horizontal fissure and over the right diaphragm

Electrocardiography (fig 2) showed low potential Q R S complexes in all three leads, with a tendency to right axis deviation The P waves were large and bifid in lead III and inverted in lead I There was also a ventricular extrasystole The electrocardiogram was compatible with severe myocardial damage and was closely similar to other recorded electrocardiograms in Fiedler's disease The common findings are low potential of all complexes with inversion of T waves, slurring and spreading of Q R S complexes, and ventricular extrasystoles of heart block (Finland 1945)

Examination of the blood showed white cells 9800 per c mm. (neutrophils 61%, lymphocytes 35%), erythrocyte sedimentation rate 3 mm in 1 hr (Westergren), Serum proteins 5 5 g per 100 ml (albumin 3 5 g per 100 ml, globulin 2 0 g per 100 ml), serum non protein nitrogen 47 mg per 100 ml and blood pyruvic acid 0 44 mg per 100 ml (within normal limits)

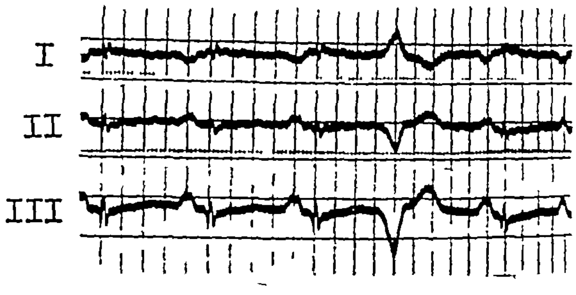


Fig 2—Electrocardiograms showing low-potential Q R S complexes in all three leads, with tendency to right axis deviation; P waves large and bifid in lead III and inverted in lead I, and ventricular extrasystole

A catheter specimen of urine showed a trace of albumin and no casts, and was sterile on culture

Progress—On April 6 the child developed some dullness and diminished breath sounds at the right base, suggesting a small effusion The 7-day course of sulphadimidine was stopped on April 7 On April 7 radiography showed that the heart remained much enlarged and had probably increased in size The contours were less clearly defined, and pericardial effusion was seen The effusion in the right pleura had increased and was obscuring the right upper lobe The left lung was clear On April 8 the child's temperature had risen to 99 5°F and her pulse rate to 150, with much deterioration in her general condition and cyanosis A paracentesis thoracis on April 8 produced only 15 ml of an opalescent fluid containing a few lymphocytes The deterioration in condition continued, with distressed rapid respirations An oxygen tent did not help, and the child died later that night

Necropsy—The body was that of a well nourished little girl with distended abdomen and œdema of the ankles There was 50 ml of clear fluid in the pericardium The heart weighed 190 g (normal for age 60 g) There was a patchy fibrosis on the epicardial surface, especially over the right

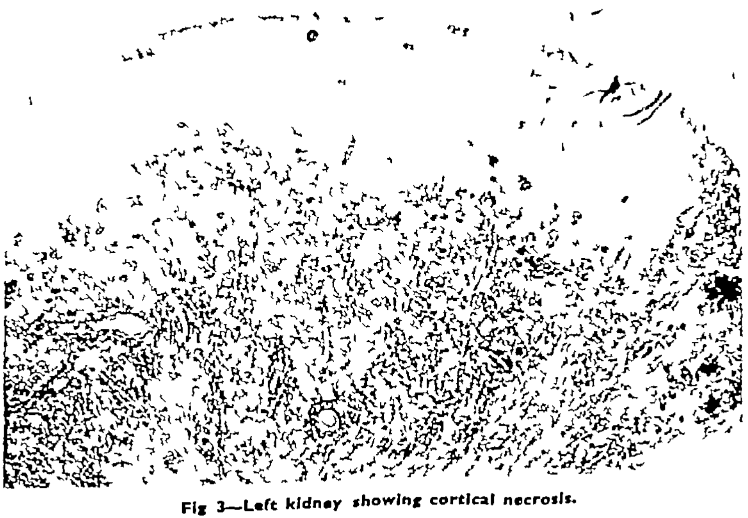


Fig 3—Left kidney showing cortical necrosis.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Treatment of Burns in Large Numbers

THE United Services section met on Feb 9, with SIR GORDON GORDON-TAYLOR, the president, in the chair, to discuss the treatment of burns in large numbers

Colonel E J PULASKI presented the results of treatment by the exposure method, reintroduced by A B Wallace, of Edinburgh His cases consisted of two groups—one treated within 24 hours after injury, and the other some $4^{1}/_{2}$ days after injury Like Wallace, he had at first hesitated to expose burns which had taken place more than 24 hours before, but he now felt that this method was applicable to treatment of burns up to a week old Of 60 cases in the first group, 30 were full-thickness burns and 20 partial-thickness burns Grafting was carried out, on average, on the 24th day, but now grafting would be carried out earlier

Describing the procedure on admission, Colonel Pulaski said that debridement and cleansing should be as complete and as gentle as possible With recent burns this could be done under intravenous morphine, but with older burns light general anæsthesia was used Cleansing should be carried out under operating-room conditions He did not give antibiotics locally, but, for large burns, penicillin, 300,000 units daily, was given intramuscularly After the burned areas were cleansed the patients were put in a warm room and the affected areas exposed, with the extremities elevated In 24–48 hours a dry crust formed, which gave no pain to touch, and thereafter patients were allowed up as their condition permitted General therapy now took precedence over local therapy Patients with burns of less than 15% of body surface were given fluids by mouth, others were given saline and plasma or plasma-substitute on the formula, 1 ml of fluid per kg body weight multiplied by percentage of body-surface burned In patients with burns of more than 25% of the body surface, automatic feeding by catheter was adopted Additional fluids were given, where necessary, to maintain a urinary output of 60 ml per hour

The advantages of the exposure method were the absence of cross-infection, of "burn odour," and of the so called toxic or septic phase, reduction of physiological complications, small morphine requirements, less acute need for blood and protein intake, improved mental outlook, little weight-loss, and briefer hospitalisation The problems of this method were that patients complained of discomfort or of feeling cold, and might in fact have chills during the first 24 hours, and some patients might be very distressed at the sight of their wounds (curiosity was a problem when the crust separated, but this could be overcome with proper education)

Colonel Pulaski was not convinced that exposure was the best technique for all types of burns under all conditions, but it did seem satisfactory for burns confined to one side of the body and for burns of the head, neck, and perineum It had proved suitable in extremes of climate It was essentially a hospital treatment—good nursing care was still needed

Surgeon Commander W V BEACH, in a paper read for him by Surgeon Commander D F WALSH, said that blast injuries and flash burns due to high explosives had long been a serious factor in war at sea, and in field warfare the tendency had been to replace the high explosive bomb by the phosphorus and petroleum types, thereby increasing the proportion of casualties due to thermal effects After an atomic explosion, outside the lethal 1000-yard radius blast and flash would not be synchronous, since blast settled down quickly to travel with the speed of sound, and so there was every reason to hope that, by educating the public, the majority of flash burns might not be complicated by blast injuries

It was found at Hiroshima—and this had since been verified experimentally—that the clinical course and prognosis of all burns were adversely affected by even low doses of radiation The casualties from an atomic air-burst over a large city were now expected to number from 10,000 to 50,000, not 250,000 as formerly forecast, but this estimate did not allow for bombs of a more powerful type than that used at Hiroshima, or for multiple simultaneous explosions Almost all cases of flash burns would suffer from radiation effects as well, for γ-radiation continued to be emitted for 60–90 seconds after the explosion, the range of neutron radiation was about 700 yards, and survival within that radius could be expected only for those in deep shelters

While the majority of flash burns would be complicated by radiation, with training of the population to seek shelter even after the explosion, exposure to the full intensity of the irradiation hazard could be greatly reduced Broadly speaking, among the surviving victims, the more severe the flash burn, the greater was the dose of irradiation received, and thus the poorer the prognosis The effects of radiation varied, however, and certain phenomena *observed after ionising radiation* were inconsistent with known physics In Japan many with marked epilation had recovered White clothing did not protect against γ-radiation but was a factor in protection against flash With regard to civilians, much could be done by educating them now to realise the war dangers of bare arms, hands, legs, and faces

Flash burns would probably be confined to one aspect of the body Because of the numbers, modification of the optimum treatment would be necessary For first-degree burns exposure was the treatment of choice, and for mild second-degree burns with vesication this method was equally satisfactory Blisters should not be excised, but pricked with a sterile needle, or else the fluid might be aspirated via normal skin to prevent infection. Commander Beach thought that under ideal conditions more rapid return to full duty of the patient with deep second-degree burns could be secured by the closed pressure dressing, which also involved less strain on the nursing staff than did the exposure method In the tropics, however, he treated burns of all depths by exposure Both there and in fighting ships, battened down for long periods in warm or even temperate waters, it was better than the occlusive dressing, which caused sweating and overheating

In war an important factor would be the enormous numbers of flash burns that would have to be treated Burns by flash from atomic explosion would be particularly easy to treat by exposure, since the patients would probably have one sound surface to lie on Furthermore it might be beyond the capacity of industry and of nursing resources to produce and apply satisfactorily pressure dressings to all for whom they might be indicated under peace-time conditions Nevertheless, every effort must be made to supply the best, as opposed to the easiest and most convenient, treatment, and he did not think that exposure was best for deep burns, since with this method final healing was delayed The treatment of shock would probably necessitate the widespread use of plasma substitutes

Cleaning the burn, except when it was obviously contaminated, was better avoided, when carried out, it must be done very gently Antibiotic therapy was at present limited to penicillin, streptomycin, and chloramphenicol, in due course 'Terramycin would doubtless be available The relative value of topical penicillin was still disputed In England penicillin was administered both parenterally and topically, in America against established infections reliance was placed on parenteral administration of the appropriate antibiotic Surgeon Commander Beach was convinced of the value of topical penicillin applied as a powder or in a cream, he used 10,000 units per g in a base of 'Lanette wax SX,' and trouble with untoward sensitivity was negligible

With regard to nutrition, Stare, of Boston, administered fat emulsions as a rapid and simple method of supplying adequate calories and at the same time affording efficient utilisation of other elements in the diet.

Although many flash burns would eventually be treated by the open method training should begin now in the proper application of pressure dressings by doctors and first-aid workers

Mr WILLIAM GISSANE said that in Birmingham they saw no reason why the easiest and most efficient treatment for a given patient should not be the treatment of choice for that patient They used the open method for all burns of the face and for most burns of the buttock

DISCUSSION

It seems clear that the mother was infected by her daughter, who was therefore infectious on the thirteenth day of her illness This is a later stage than has previously been noted The epidemiological implication is that the fourteen days' isolation commonly enforced (where any isolation is enforced) may be too short in some cases It is easy to make too much of one isolated incident in the face of the excellent results obtained with the fourteen day period, more particularly as it is obviously necessary to fix some reasonable time Past experience shows that a fortnight from the onset of symptoms will cover the vast majority of cases, but one is accustomed to think of a patient as infectious early in this period rather than, as in this case, towards the end of it It is not known whether the patient continued to be infectious after the thirteenth day or whether, if isolation had been enforced for another day, the infection might not have been transmitted Fourteen days should apparently be regarded as a minimum rather than a maximum, even though it is almost certainly uncommon for a patient to be infectious thirteen days after the onset of symptoms

The incubation period of the second case—thirty two days—fits in well with an infection derived during the visit to the patient, and may be considered as supporting evidence Why the father was not infected at the same time it is difficult to say, but in view of the parents' ages it is more remarkable that one was infected than that the other escaped The incidence of infective hepatitis drops sharply after the age of 30, and it is unusual in a woman of 63

It is interesting to speculate on whether the infection was contracted by kissing the patient, or by droplet spread during conversation, although, as is usual in these cases, there were no respiratory signs or symptoms The former seems more likely, since it would bring the victim into contact with a higher concentration of virus

SUMMARY

A nurse transmitted infective hepatitis on the thirteenth day of illness to her mother, aged 63

The incubation period in the second case was thirty two days

It is suggested that the usual fourteen days' isolation should be regarded as a minimum rather than a maximum period

REFERENCES

Booth W G (1928) *Publ Hlth, Lond* **41**, 237
McFarlan A M (1945) *Quart J Med* **14** 125
Naughten M Russell, J J , Mecann, P N (1950) *Irish J med Sci* **292**, 184
Pickles, W N (1939) Epidemiology in Country Practice Bristol

New Inventions

FINGER-NAIL KNIFE FOR COMMISSUROTOMY IN MITRAL STENOSIS

THE operation of dividing or splitting the commissures of the damaged valves in mitral stenosis gives considerable relief in selected cases The present tendency at operation is to avoid interference with the leaves of the valves themselves and to enlarge the narrowed opening by dividing along the line of the commissures If the fused tissue is split outwards to the margins of the ring, the two valve leaves are separated and will regain some of their normal function

The fused commissures in these cases are thickened and sclerosed at the stenotic opening but at the periphery they consist of thinner fibrous tissue which splits easily It is usually possible to divide the commissures by digital pressure, the finger being introduced through the auricular appendage, but in some instances where the edge of the opening is unduly firm or even calcified there is a risk of tearing across or into one leaf of the valve The anterior leaf is more liable to damage than the posterior, and rendering it incompetent leads to dangerous regurgitation

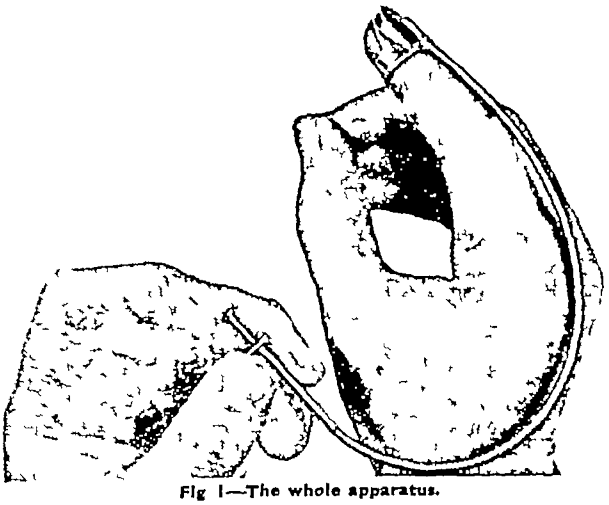


Fig 1—The whole apparatus.

The advantage of a cutting instrument in mitral valvulotomy is obvious if such an instrument can be readily introduced and guided by the finger into the mitral opening Various forms of valvulotome have been described and used, but many of them are difficult to manipulate

The instrument here illustrated is designed to fit on the index finger and resembles a retractable steel finger-nail The appliance has been made by Mr L G Wray, instrument curator at the Middlesex Hospital, on the basis of a cut away thimble The knife, which is about the size of the normal index finger nail lies in a hood attached to the dorsum of the thimble ring It can be advanced or retracted by a cable of the camera shutter type The palmar aspect and sides of the finger are left free for palpation of the mitral opening When the lines of the commissures have been orientated the knife blade is advanced, and a few millimetres of the rolled or nodular margin are nicked The blade is then retracted, and steady pressure with the side of the finger is used to split the membrane out to the edges of the mitral ring

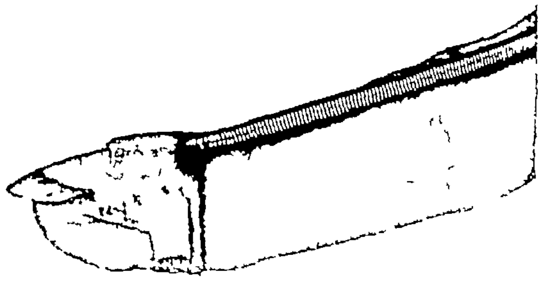


Fig 2—Knife with blade advanced

The apparatus is covered with a smooth finger-cot to eliminate rough surfaces, and when the blade is advanced it punches a small hole through the tip of the cot

The value of this instrument was particularly well illustrated in one case where the valve edges were calcified and visible radiologically With the aid of the finger-nail knife valvulotomy was done in one manœuvre and with a minimum of disturbance

T HOLMES SELLORS
F R C S

London

Mr **DAVID MATTHEWS** said there was no doubt that with exposure treatment extensive burns healed quickly and the patients were seen to be in good general condition within a few days If necessary, patients could be put in a chair within a week, skilful nursing care was needed but in no great numbers He thought that this method had a large place in the treatment of burns, but doubted whether it was applicable in Britain in winter-time Nor was it applicable if the patient had to make a journey of any distance In these circumstances the absorptive method would be used In the event of large numbers of burns occurring in war-time much of the treatment would have to be undertaken by civilians because there would not be enough medical personnel He thought it advisable that steps should be taken to train the public now without frightening them. He thought that the doctors would have to deal with the fluid-replacement side of the problem and should be trained for this It would probably be impossible under such circumstances for them to be anything but advisory with regard to local treatment He visualised the necessity of mobile medical teams

Sir **CLAUDE FRANKAU** said the committee on flash burns, of which he was chairman had decided, broadly, that when transporting patients to "cushion" hospitals closed treatment would be necessary They had evolved certain methods for treating burns of the hands and face They had also concluded that if the population was caught unawares casualties would probably be very numerous, the populace of this country never had been "shelter-minded" There would be a chart on treatment He disagreed with sending medical teams into a city which had been atom-bombed, to treat patients in unaffected hospitals, there was nothing to show that there would not be another atom bomb or other bombing the next day

Mr **D H PATEY** thought that the present neglect of antisera was unwise

Surgeon Captain **S G RAINSFORD** remarked that the exposure method seemed easy, but he scarcely thought it would be practicable in the English, let alone the Scottish, climate The principle of the absorptive dressing was to keep the burn dry He recommended using a hygroscopic paste, a powder of zinc oxide made up in 3% glycerin was admirable for this purpose, for it prevented the part becoming waterlogged and sodden

Reviews of Books

Recent Advances in Physical Medicine

FRANCIS BACH D M, D.PHYS MED, physician Rheumatic Unit St Stephen's Hospital, Chelsea physician in charge Physical Medicine Department, Mount Vernon Hospital London J & A. Churchill 1950 Pp 490 27s 6d

IN collecting his team Dr Bach has cast his net wide no fewer than 38 authorities, both medical and lay, have written articles on a great variety of subjects He has included chapters on physiology, organisation, the school-child, resettlement of the disabled and the training of the doctor and physiotherapist, as well as chapters on physical methods of treatment and the practice of physical medicine in various medical and surgical conditions Dr P Bauwens writes well on electro-diagnosis, with special reference to electromyography, and in a long section on the application of physical medicine to various conditions the editor contributes a detailed article on the rheumatic diseases He discusses especially the ætiology in which the patient's emotional state plays an important part, and briefly but critically analyses what the discovery of the effect of 'Cortisone' and A C T H. on rheumatoid arthritis may imply An illuminating article by Dr J W T Patterson on physical medicine in the Army shows what real advances were made during the war in training and assessment of physical capability Rehabilitation and resettlement are well described by such authorities as Dr T M Ling and Dr A R Thompson

Atlas of Human Anatomy

Vol II M W WOERDEMAN, M D, professor of anatomy and embryology, University of Amsterdam Amsterdam Wetenschappelijke Uitgeverij N V London Butterworth 1950 642 plates £3 3s

VOL I of this atlas dealt with the bones, joints, and muscles, and vol II, published two years later, is devoted to the viscera (281 figures), the blood-vessels (102 figures), the nervous system (184 figures), and the special senses (75 figures) As in the first volume, the drawings reach a high standard of accuracy and clarity The labelling is generally clear and unequivocal, but both the leaders and their terminal crosses are perhaps slightly too small, and in some cases they are confusingly numerous The B N A terminology is employed, with occasional English equivalents in brackets, the general effect falls strangely on English ears, and might militate against the book in this country in times when the medical student has no leisure to master two terminologies

The section on splanchnology includes 49 plates dealing with the teeth so that the atlas shall be suitable for use in dental schools Several bronchograms have been included to illustrate the subdivisions of the lungs Some of the pictures of the peritoneum are difficult for the student to interpret, and here colour would probably help Some 20 of the book's plates are wholly or partly in colour, but the best use has not always been made of it For example, two colour plates are expended on cross sections of the liver and spleen, while two very complex plates (472 and 473), showing pathways in the central nervous system, are in black and white

A few plates depict the development of the brain but there are no other embryological figures The peripheral nervous system is illustrated by half tone diagrams of individual nerves the cutaneous distribution being shown separately, with autonomous zones shaded In many of these diagrams, however there are several unexplained degrees of shading, which may mystify the student As is customary in anatomy books, the dermatomes are lent a spurious air of reproducibility by being drawn with great precision

The blood vessels are also dealt with on a diagrammatic plan with "ghost" backgrounds of bones and occasional muscles This scheme renders the book a systematic rather than a regional atlas, and to this extent reduces its value to the student Professor Woerdeman refers to "a special volume dedicated to regional anatomy" but it seems that this is not to appear in this country If so, this is a great pity, since the main function of an atlas is surely to act as a two-dimensional dissection when a three-dimensional one is not available One would learn almost nothing of the relationships of nerves and arteries from the two existing volumes It is to be hoped that a third will after all be forthcoming

Surgeons Twoe and a Barber

Being some Account of the Life and Work of the Indian Medical Service (1600–1947) DONALD MCDONALD London Heinemann Medical Books 1950 Pp 295 42s

"THE history of the Indian Medical Service was written once for all by Dixon Grey Crawford and published by him in 1914" Thus opens the preface of the present work, which brings the story up to the dissolution of the service in 1947 For completeness' sake Lieut-Colonel McDonald follows Crawford in dealing first with the prominent men and events in India from 1600, after first recording the discovery of India in 1498 by Vasco da Gama The founding of the East India Company in 1600 was followed by the dispatch to India of four ships each of which carried "Surgeons twoe and a barber" hence the title of this work In the account of the next century and a half McDonald closely follows Crawford in dealing with the most prominent men and events, but in a more popular form and in chronological order, some additional information based on studies of early records is included It was not until 1764–79 that the presidency medical services of Madras and Bengal were constituted from the medical men then serving in India, in 1896 they were combined into one general service for the whole of India The mutiny in 1857 resulted in the Crown taking over the government of India, numerous administrative changes resulted in the

When an atom bomb dropped, all the burn casualties would happen in a few moments For these the most practicable and easiest method was desirable Injuries might be complicated by radiation effects and the effects of blast, so preparation must be made for burns associated with other injuries With open wounds including burns the aim should be to delay infection until definitive measures could be planned With all these injuries there was much to be said for the early cover of open wounds by a closed dressing He believed that at casualty-receiving hospitals the simplest mass-method was to cover burns by dressings and to give antibiotics locally and systemically at the earliest possible moment

In Birmingham they advocated closed dressings for all serious burns of the body and limbs By this method the depth of burns could be accurately assessed about the 14th day, when skin grafts for full thickness burns could be started The optimum time was the 14th–17th day, and where a burn was really extensive, needing perhaps repeated use of the same donor site, surgical skill was especially important Split skin grafting was an art acquired only after long practice

Treatment of shock, Mr Gissane continued, was the first priority A burn with partial skin loss might result in considerable plasma loss, and partial skin-loss areas should be included in estimating the total area of the burn Shock from plasma loss could be expected in burns of 15% or more of the body-area in an adult, and of 10% or more in a child, and the aim should be to replenish the plasma before clinical shock manifested itself Generally speaking, the smaller the area of the burn, the longer the plasma loss took to reach a dangerous level

Mr A B **WALLACE** said that no one method was suitable for all burns, but there must be a simple procedure for mass treatment The two problems in mass burn casualties were (1) to save life where possible, and (2) to limit infection In general, civilians with minor burns would have to be treated as outpatients, but from the point of view of the medical officer in the Services, concerned to restore the man to fighting fitness, a minor burn was just as important as a major burn A simple classification of superficial or deep burn was all that was necessary

The method of local treatment adopted must give a dry surface in the shortest possible period, and the surface must be kept dry

The "rule of nine" (modified Berkow's table) could be adopted in regard to transfusions, fluid requirements, and urinary output In the treatment of shock, burns of 9% surface-area in children and 18% of surface area in adults could be controlled by oral therapy Burns beyond these extents required intravenous fluids An adult should be given plasma and saline at the rate of one bottle of each for each 9% of total body area that was burned, children should receive half this amount The urinary output per hour ought to be 54 ml for adults and 27 ml for children, and the daily fluid intake, again on the "rule of nine," should be 9 times 9 ml per kg body-weight in children, and 9 times 6 ml per kg in adults For a superficial burn the proportional intravenous fluid requirement was two bottles of plasma to two of saline, and for a deep burn one of plasma to two of blood and one of saline

Mr Wallace preferred the term "absorptive dressing" to "pressure-dressing", on no account should pressure be applied to the tissues This method was interchangeable with exposure He did not agree that with deep burns exposure delayed healing Burned areas should be grafted as soon as possible Exposure gave immediate control of infection, even with penicillin resistant organisms

Major H L **WOLFE** said that in the event of an atomic explosion burns would be due to people being trapped in burning buildings, &c, or to flash burns At Hiroshima 70,000 people were killed and 70,000 injured, about 20–30% of deaths were due to flash burns (some might have died later of X-radiation) It was estimated that if people were caught in the open, as in Japan, 65% would have burns, perhaps associated with other injuries, and of all burns 85% would be due to flash burns and 15% to fires

Leader-Williams and Smith[1] had estimated that in an urban area with a density of 43 persons per acre, as in London, the total number of casualties would be about 27,000, about 2500 of these would be due to burns. Flash burns would occur on exposed parts, and elsewhere if the clothing caught fire, which dark clothing was especially liable to do In a clear atmosphere flash could cause burns up to 2½ miles away Among the civilian population, who would be mostly in houses or shelters, there would be a smaller number of flash burns, but the number of burns due to fires in buildings would be greater In a well organised city with adequate warning and proper shelters, the number of casualties should approach nil Obviously one could not get this result, and the average figure for burns would be 2000. In the Services the numbers would depend on the conditions in which the personnel found themselves.

Group Captain G H **MORLEY** discussed methods of limiting casualties, especially from irradiation Light coloured clothing and any kind of covering to the skin gave some protection, and he advised slacks for women and light-coloured uniforms for civil defence workers. People on essential services should be issued with gauntlets, preferably of 'Nylon,' on the lines of a Bunyan bag In considering the warfare of the future, saturation bombing should not be forgotten, and many people might be unable to get immediate medical treatment There ought to be some 'self help", and Group Captain Morley suggested that every person should carry a 1 oz pack of an approved application for burns, with appropriate instructions on it Simple treatment methods would be required There would be a place for skin banks, and surgeons skilled at skin grafting eyelids would be needed to prevent blindness in certain cases of burns of the face The right approach to the problem of treating mass burn casualties was best summed up in the Scout motto "Be prepared"

Surgeon Commander J J **KEEVIL** said that his experience in the late war convinced him that sorting teams would be essential In this respect some discipline would have to be recognised, and there would have to be a wider application of the ideas of first aid which Sir James Cantlie had in 1910 Efforts must be directed towards finding methods of treatment which made transport easy and which could be applied by the relatively unskilled

Surgeon Lieut -Commander (D) **JOHN BUNYAN**, R N V R, pointed out the advantages of the envelope method of treatment, which provided for mobility and prevented secondary infection Moreover, when there were mass casualties, it enabled patients to be looked after by friends and relatives He urged the importance of positive first-aid, to relieve pain and reduce the secondary effects of the burns When thousands of casualties had to be attended to, asepsis might have to give way to antisepsis He illustrated his remarks with a colour film showing the good results obtained with the envelope technique

Mr **PATRICK CLARKSON** confirmed the value and practicability of the exposure method He found this slower than others—even in superficial burns the crusts took 3 weeks to separate completely—but this would be offset in the case of mass casualties by other advantages It was always a hospital procedure, it was not suitable for circumferential trunk burns, but might become so if adrenocorticotropic hormone (A C T H) was found, in fact, to allow patients with even extensive burns to be ambulatory throughout He favoured replacing fluid, electrolytes, and colloid empirically rather than by a formula Altemeier's collagenases for slough removal were promising The outstanding training need at the moment was diffusion of the established healing techniques of plastic surgery among general surgical trainees He had been told by those who had treated β particle burns that in future they would not treat these conservatively but would remove the affected band skin early and replace it by planned pedicle abdominal flaps

---

[1] Leader Williams E Smith J *Practitioner* 1950 165 594

Annotations

THE COXSACKIE VIRUSES

HE name of Coxsackie, the small town near New York re the prototype was isolated, is now applied to a sized and still expanding group of viruses which ickling mice produce myositis, loss of muscle power, death Members of the group are widely distri d in the United States, and they have been isolated i patients suffering from paralytic and non-paralytic omyelitis, aseptic meningitis, "summer grippe," and rodynia or epidemic myalgia, as well as from healthy ple In size (10–12 mμ), physical properties, and aviour they resemble the laboratory strains of polio litis virus According to their pathogenic properties suckling mice Dalldorf divided them into A and B ins, A causing myositis only, whereas B also produce ere neurological lesions including cystic degeneration large areas of the brain There is no type specific erentiation within group B, but at least 7 immuno ically distinct types have already been differentiated group A. Extending the work of Sickles and Dalldorf,[1] lnik and Ledinko[2] at Yale have recently confirmed reliability of the neutralisation test for following the munological reactions in infections with the Coxsackie uses They have also shown that different types of us can be distinguished by complement fixation, and at the time of appearance of complement fixing anti dies in patients is quite distinct in infections with two pes of the virus Coxsackie viruses have usually been olated during outbreaks of infectious disease or from tients known to have certain diseases, and in many ses there has been an associated rise in neutralising id complement fixing antibodies Infections in labora ry workers who have developed an acute febrile illness ith thoracic or abdominal pain after working with the rus have also been followed by a similar serological sponse Experienced workers with these viruses are owever still troubled by the thought that association ith a disease does not necessarily imply a causal relation-ip, and, as Dalldorf remarked, we are still in the nomalous position of having discovered the cause of a isease before discovering the disease

In 1949 Finn and colleagues[3] described an outbreak of pidemic pleurodynia, one of the clinical conditions hought to be caused by a Coxsackie group-A virus, in Boston, and they have recently[4] isolated from stored hroat washings of these patients a virus antigenically imilar to the "Connecticut 5" virus isolated by Melnick rom a case of non paralytic poliomyelitis Stored sera ollected from these patients during the first 4 days of llness contained no demonstrable antibodies, whereas amples collected 10 days later completely neutralised the virus It was also shown that this strain bore no antigenic relationship to certain other members of the Coxsackie group, and this raises the important point that different immunological types may be responsible for different clinical conditions In another recent investigation Huebner and his colleagues[5] studied a small outbreak of acute febrile illness and isolated Coxsackie virus group A type 2, from the fæces of all those affected No clinical diagnosis could be made from the patients' symptoms, which included headache, muscle pains and stiffness, nausea and vomiting Epidemiological associations of virus isolation with illness under such conditions are unjustifiable, so Huebner and his colleagues extended their observations to the rest of the small community in which their patients lived Five other strains of the type 2 virus were found in normal people scattered in various parts of the area, and 77% of 158 inhabitants possessed neutralising antibodies Three additional types of Coxsackie virus were also isolated during the survey, and not a single case of poliomyelitis or meningitis was diagnosed in the area throughout the summer and autumn when the investigations were in progress These isolations of virus from healthy people show that the organism may be widely prevalent in a community and that the danger of spurious associations with different types of illness is very real On the other hand, a similar situation exists with poliomyelitis virus, and excessive caution may be as dangerous as jumping to rash conclusions Laboratory evidence shows conclusively that the Coxsackie viruses do invade the human body, and it seems unlikely that such invasion cannot on occasion be recognised clinically Huebner and his colleagues are trying to solve the Coxsackie puzzle by intense epidemiological investigations in a small community, Melnik and the Yale University workers are tackling it from the laboratory angle They have already extended our knowledge, but the challenge remains—find the diseases

EPIDEMIOLOGY AND THE WORLD HEALTH ORGANISATION

In his address to the epidemiological section of the Royal Society of Medicine on Feb 16, Dr Yves Biraud, the French director of the Epidemiological Services Division of W H O, was able to give an encouraging account of international efforts now being made against communicable diseases After tracing the origins of W H O's work in quarantine and epidemic intelligence, and paying tribute to the earlier activities of the Office International d'Hygiène Publique, the Pan American Sanitary Bureau, the Health Organisation of the League of Nations, and UNRRA, he described the world-wide intelligence system developed by W H O since it took over in December, 1946 Based on the epidemic-intelligence stations at Geneva, Singapore, Alexandria, and Washington, this is now primarily a wireless system, with confirmation by telegraphic and other communications Geneva alone received 6500 separate reports last year, and the world is substantially covered, with the exception that the U S S R has not collaborated since 1937 On the quarantine side, the unsatisfactory state of adhesions to the various conventions makes the promulgation of the new international regulations, to be considered by a special meeting at Geneva in April before the World Health Assembly, an urgent as well as an important matter. Dr Biraud emphasised the advantages of the new procedure by which if a country is unwilling to adopt a regulation, it must positively contract out of it—instead of negatively refraining from ratification

The coördination of research on communicable diseases is, he said, effected mainly by expert committees, and the new system of large panels of experts, from which members are chosen according to the agenda of the particular meeting, allows for adequate geographical representation and for flexibility The influence of these committees lies primarily in making technical advances widely known and diminishing the delays in their application Though direct research is not undertaken by W H O., grants are made to stimulate and coördinate investigations on subjects in which W H O is interested, examples being the World Influenza Centre at Mill Hill and the Brucellosis Centre at Copenhagen, and the Tuberculosis Research Unit at Copenhagen which is investigating both B C G vaccines and the statistical results of the many millions of B C G inoculations Field research is also undertaken or stimulated thus studies are being made of fæcal vibrios in Madras, of the delimitation of endemic yellow-fever areas by the mouse protection test, and of vaccination of dogs against rabies zenith of the service being attained by the end of the 19th century All this is told in detail in the present volume

---

[1] Sickles G M, Dalldorf G *Proc soc. exp Biol med* 1949 72 30
[2] Melnick J L Ledinko N *J exp Med* 1950 92 463
[3] Finn J J Weller T H Morgan H R *Arch int Med* 1949 83 305
[4] Weller T H Enders J F Buckingham M Finn J J *J immunol* 1950 65 337
[5] Huebner R J Armstrong C Beeman E. A. Cole R M *J Amer med Ass* 1950 144 609

Of greater interest is the history of the decline of the service during the first half of the 20th century, for the outstanding events took place after the publication of Crawford's work The first crucial blow was struck at the service by Lord Morley's order of 1907 that "no further increase of the civil side of the service can be allowed" The lengthy previous recruitment of highly qualified men through keen competition at once slumped to such an alarming extent that the order was not enforced, but recruitment never recovered The Montagu-Chelmsford report of 1918 and the later Indian Round Table Conference led to loss of all confidence in the future of the service and the final cessation of competitive examinations for officers The story of the long series of committees on the medical services in India, with no resulting action, is fully recorded The simple fact is that the good work of the Indian Medical Service professors of the medical colleges of India in educating many thousands of able Indian doctors during a century or more inevitably led to service appointments on the civil side being handed over steadily to increasing numbers of well-qualified Indian practitioners The second world war, with very numerous Indian volunteers, led to a manyfold increase of Indian army medical officers, to the formation of the present Indian Army Medical Corps, and to the dissolution of the Indian Medical Service in 1947 when political events (which are excluded as far as possible from this work) resulted in the government being handed over to Indians

Colonel McDonald's comprehensive work brings out the versatility of I M S officers over a long period in administrative, scientific, clinical, and research branches Many besides the surviving members of the service and their friends will be interested in reading this illuminating record of a medical service which has probably never been surpassed

Pathology in General Surgery

Paul W Schafer, M D Chicago University of Chicago Press, London Cambridge University Press 1950 Pp 581 £6 11s 6d

In this book the author keeps well to the fore the clinical aspects of general surgical diseases and correlates them with the macroscopic and histological appearances The greatest value of the work lies in its 495 illustrations, almost all in colour A surgeon familiar with the appearances shown is in the best of positions to devise rational methods of treatment, and for this reason by itself the book would be a useful possession In addition Dr Schafer discusses succinctly but clearly the views that are held as to the inner meaning of the pictures revealed by the microscope, and at the end of each section he supplies a useful list of references He does not confine himself absolutely to pathology but reviews current practice in therapeutics The book will certainly appeal to those engaged in the teaching of clinical surgery

Researches in Binocular Vision

Kenneth N Ogle, Ph D, research consultant in the Section of Ophthalmology, Mayo Foundation and Mayo Clinic, Rochester, Minnesota Philadelphia and London W B Saunders 1950 Pp 345 37s 6d

Most of this book is devoted to the problems of dissimilar images on the two retinæ, but the text also contains a full discussion of the fusional processes in normal binocular vision As an exposition of the physiology of normal and abnormal binocular vision the book is unique, both in its scope and its thoroughness Its inspiration has come from the work of Ames and his associates at the Dartmouth Eye Institute, and the theoretical and clinical aspects of aniseikonia therefore loom large The substantial contributions made by Dr Ogle himself to the problems of binocular vision take their due place in this well balanced exposition of a difficult subject The account of studies on the longitudinal empirical horopter is particularly good

This book is a record of intensive and inspiring work but also an obituary notice That after 18 years the Dartmouth Eye Institute was closed down because of personal difficulties is a sad reflection on human wisdom

Textbook of Bacteriology (2nd ed London H Kimpton 1950 Pp 491 40s)—J M Dougherty and A J Lamberti have thoroughly revised their book. It is written for the science student or for those taking bacteriology in the premedical course, and for such students, and possibly also for senior nurses, it gives a clear and reliable account of the subject

A History of Biology (2nd ed London H. K Lewis. 1950 Pp 579 35s)—That the teaching of science should be given a historical approach has long been thought desirable, but the difficulty of avoiding a mere miscellany of biographical titbits has deterred many teachers from making the attempt. Prof Charles Singer's *History of Biology*, first published in 1931, has shown how the subject can be presented satisfactorily After a review of ancient science, its later decline, and its revival in the 14–16th centuries, he discusses the nature and origin of modern scientific method and thought and then provides what is virtually a series of histories of the great problems in biology The result is both readable and intellectually satisfying to the student of biology, and well deserves its subtitle of "*A general introduction to the study of living things*" It could also be read with profit by the non scientist wishing to learn something of the basic problems with which biologists are faced

Food Poisoning (3rd ed London Leonard Hill 1950 Pp 318 17s 6d)—Mr Elliot B Dewberry's compilation (the word is his own) describes the causes, signs, symptoms, and methods of prevention of the more or less acute diseases attributable either to articles of diet harmful per se or to food containing pathogenic bacteria or bacterial toxins. The plan of the book is queer part I is devoted to the history of food poisoning and to salmonella infections, part II to staphylococcal food poisoning, to poisoning by metals, fungi, plants, and shellfish and to food allergies, and part III to botulism and the laboratory investigation of food poisoning Parts I and III and the chapter on staphylococcal intoxication are excellent, but the chapters on the more esoteric forms of poisoning might be enlarged with advantage If an account of poisonous plants be included it is not of great value unless the reader is enabled to identify the plant responsible, and some mention might be made of the dangers of fruit and vegetables sprayed with one of the persistent organic phosphates With these reservations the book can be recommended If we have a doubt it is on the audience addressed for the sanitary inspector, the physician, the bacteriologist, and the food manufacturer all see food poisoning from different aspects But each will learn something from this book, and for further information on detail an imposing list of references and an adequate bibliography are provided. An admirable luxury in such a book is the gallery of portraits of those who have contributed to the subject To be useful the plates of fungi should be in colour, and those of bacteria, motor vans, and other people's laboratories tell us nothing at all

Symposia on Quantitative Biology Vol XIV *Amino Acids and Proteins* (Cold Spring Harbor, L.I, New York Long Island Biological Association 1950 Pp 217 $7)—The first of these symposia was held at Cold Spring Harbor in 1933 and there has been one each year since that time except for a break of three years from 1943 to 1945 The subject selected has varied from year to year Protein chemistry was the topic in 1938 but the advances made in the eleven years justified devoting another symposium to this subject in 1949 Nucleic acids and nucleoproteins were discussed in 1947 As was natural, the participants at the symposium were mostly American, but papers were contributed by Fromageot (France), Pedersen (Sweden) Linderstrom Lang (Denmark), and several by British scientists (Synge, Danielli, and Sanger) The 22 papers included in this volume deal with many aspects of protein chemistry Most of them were highly specialised, but Murray Luck's article on the liver proteins is more general, and the paper by Kaufmann and others on the localisation of cellular proteins by enzymatic hydrolysis is accompanied by beautiful and instructive photographs Dorothy Hodgkin's paper on X ray analysis and protein structure is also freely illustrated by diagrams and photographs Much of the work reported at this symposium has been published in the specialised journals, but volumes of this high standard have a real place in international scientific literature

THE LANCET

LONDON SATURDAY, FEB 24, 1951

ACTH and Cortisone in Hæmatology

It is now well known that 'Cortisone' and the pituitary adrenocorticotropic hormone (ACTH) produce profound metabolic changes in normal people and have considerable, if temporary, effects in the 'collagen" diseases These substances are also being widely tested in certain hæmatological disorders After the observation, originally reported by **Dougherty** and **White**, that the adrenal cortex hormones reduced lymphoid tissue and caused dissolution of lymphocytes, it was natural to see whether ACTH and cortisone would reduce the hyperplastic tissue in such conditions as lymphatic leukæmia and lymphosarcoma The early results were encouraging, and so physicians have gone on to test these substances in other forms of leukæmia and in Hodgkin s disease

Dameshek and his co-workers[1] found that neither of 2 cases of myelocytic anæmia responded to ACTH., but of 6 cases of acute or subacute lymphatic leukæmia all except 1 (which was in an adult) had remissions The 5 cases which responded were all in children, in 4 the bone-marrow and peripheral-blood picture became normal or almost normal during the remissions, and there was an increase of hæmoglobin, reticulocytes, and platelets, suggesting that the ACTH actually stimulated the remaining normal marrow, swollen lymph glands, spleen, and liver also returned to normal size This result was obtained with a dose corresponding to about 80 mg of Armour standard daily for fourteen days, after which the dose was gradually reduced to 40 mg twice weekly The remissions were being maintained at the time of the report, but when in 1 case the ACTH was stopped the leukæmia relapsed. Further experience has shown that in acute leukæmias relapse takes place sooner or later, and an unfortunate feature of these relapses is that the patients no longer respond to ACTH or cortisone **Stickney** et al[2] used larger doses, they gave 200 mg of ACTH, or 200–300 mg of cortisone, daily for twenty to thirty days in adults, and 50–75% less for children Of 12 patients with acute leukæmia who received cortisone, 2 had complete remissions—i e, the patient was clinically well, and blood and bone marrow were no longer leukæmic Of these 2 patients 1, aged eighteen, relapsed five weeks after treatment was stopped and did not respond to further ACTH or cortisone, and the other, aged ten, was still well after three weeks ACTH was given to 6 patients with acute leukæmia, 1 had a complete remission after receiving a total dose of 1 g, and the remission had been maintained for sixteen weeks **Spies** et al,[3] however, reported different experiences Of 5 cases of acute leukæmia treated with ACTH 3 responded satisfactorily One patient remitted after fourteen days' treatment with 100 mg ACTH daily and the remission was maintained for five months, then a second similar course of ACTH again produced a remission, which lasted six months Another patient, a boy of seven with acute lymphatic leukæmia, responded quickly to ACTH, but within twenty-four hours of stopping treatment there was clinical and hæmatological evidence of impending relapse, so treatment was resumed and was maintained for forty-three days, when he had had 1750 mg after twenty-nine days he again relapsed, but responded once more after nine days' treatment Results like those of **Spies** seem to be exceptional, most reports indicate failure to respond to second courses of ACTH. or cortisone **Farber** and his colleagues[4] believe that in acute leukæmia the results with ACTH and cortisone are inferior to those obtained with folic-acid antagonists (aminopterin and amethopterin), the remissions being shorter and failure with second courses more common Of 17 children treated with ACTH, 5 had complete remissions which lasted up to ten weeks, cortisone 100 mg daily was given to 3 affected children, with remissions in 1 They noted that ACTH or cortisone would produce a remission in patients who had become resistant to folic acid antagonists, and vice versa, and they suggested that results might be better if the two forms of treatment were combined

Since ACTH. acts specifically on lymphoid tissue it might be expected that the chances of remission would be greater in lymphatic than in myeloid or monocytic leukæmia but so far the evidence is conflicting Some reports do not state the type of leukæmia, and when primitive cell forms predominate in the blood and bone marrow it is often very difficult to decide whether an acute leukæmia is lymphoblastic or myeloblastic All seem agreed however, that monocytic leukæmia does not respond at all **Pearson** and **Eliel**[5] have stated that in children and adults with acute granulocytic or acute lymphatic leukæmia "temporary remissions can be induced with considerable regularity," but monocytic leukæmia was unaffected They gave ACTH or cortisone to 10 adults and 80 children with acute leukæmia, and good remissions followed in 4 adults and 9 children Unfortunately they confirm earlier reports that remissions are short—3–8 weeks in their cases—and refractoriness soon develops They also confirm the observation by **Farber** that patients who have become refractory to folic acid antagonists will respond to ACTH or cortisone ACTH and cortisone might also be expected to affect chronic lymphatic leukæmia, but the results have been curious, the enlarged lymph glands, spleen, and liver shrink rapidly, but the blood and bone marrow pictures remain unchanged[2 5] Results in lymphosarcoma have been conflicting, **Spies** et al[3] reported a good response to cortisone in 2 patients, **Pearson** and **Eliel**[5] found moderate benefit in 2 cases, 1 of which after relapse, responded to a second course These drugs have no effect in Hodgkin s disease or chronic myeloid leukæmia[5] **Pearson** and **Eliel** treated 2 patients with myeloma, in

---

[1] Dameshek W Saunders R H Zannos L *Bull New Engl med Center* 1950 12 11

[2] Stickney J M Heck F J Watkins C H *Proc Mayo Clin* 1950 25 488

[3] Spies T D Stone R E Lopez G C Milanes F Toca R L Reboredo A *Lancet* 1950 ii 241

[4] Farber S Downing V Kennedy B H Shwachman H Toch R *Blood* 1950 5 787

[5] Pearson O H Eliel L P *J Amer med Ass* 1950 144 1349

Assistance to countries in campaigns against particular diseases sometimes involves aid in emergencies, as in the cholera epidemic in Egypt in 1947 and the more recent typhus epidemic in Afghanistan, but chiefly consists in providing specialised technical staff to help a large number of countries in starting or intensifying campaigns against an even larger number of communicable diseases the foreign experts in the teams are "matched" with local experts, with obvious advantages W H O has also assumed technical leadership in the health aspects of other bodies' programmes, some of them very large, such as the $4 million allocated to health work in the United Nations Programme for Technical Assistance

The impression left on Dr Biraud's hearers, enhanced by his unique experience of 25 years as an international medical civil servant in this field, was that W H O is not only worthily carrying on the work of the older organisations but is making a new and remarkable contribution to the reduction of communicable disease throughout the world

PREVENTION OF HÆMORRHAGIC DISEASE OF THE NEWBORN

WHEN it was found that the level of prothrombin in the blood of infants is normally low from about twelve hours after birth till the end of the fifth day, this period was recognised as that in which hæmorrhagic disease of the newborn occurred The discovery of vitamin K and of its action in raising the level of prothrombin in the blood suggested a means of treating this condition, and possibly of preventing it Treatment of infants with hæmorrhagic disease with vitamin K or its analogues has, however, never been really satisfactory, and all authorities recommend blood transfusion as well A possible way of preventing the disease was to give vitamin K to an infant immediately after delivery , or giving vitamin K to the mother some days before the labour would raise the infant's prothrombin concentration above danger point Before hæmorrhage is likely, the prothrombin concentration in the blood must be grossly reduced—to about 15% or below

It is now twelve years since these facts became known, but obstetricians and pædiatricians are still doubtful of the value of the prophylactic administration of vitamin K, because the reported results have been conflicting In 1944[1] we concluded that, despite differing reports, a case had been made out for the prophylactic use of vitamin K and its analogues, especially since the vitamin is non toxic in the doses recommended , and it seemed to be an advantage to have the infant's prothrombin concentration above danger levels throughout the first five days of life Since then other reports have indicated that hæmorrhages take place in infants even though the prothrombin concentration is normal For instance, Falls and Jurow,[2] who observed the incidence of retinal hæmorrhages in infants whose mothers had received prophylactic vitamin K, confirmed once again that this treatment does raise the infant's prothrombin level, the figures being higher than those for infants of untreated mothers Nevertheless, of 33 infants 8 had retinal hæmorrhages, and they therefore concluded that there must be other causes of hæmorrhage This lack of complete correlation between hæmorrhagic incidents in the first five days of life and the prothrombin level in the blood is now sufficiently well known to have reached the textbooks, but the other causes of hæmorrhage have not been clearly defined

In this issue Dr Hay and his colleagues in Liverpool record the results of a large scale effort to answer this question of the prophylactic value of vitamin K The report deals with no less than 4602 infants whose mothers had received prophylactic vitamin K, and a control group of 12,136 infants whose mothers had had no treatment In the first group 11 infants had hæmorrhagic disease of the newborn, while in the second the affected infants numbered 23 , the incidences were therefore 1 in 418 in the prophylactically treated group, and 1 in 527 in the control group From these figures they conclude that prophylactic vitamin K has no effect on the incidence of hæmorrhagic disease In the absence of blood studies, however, we do not know whether the prothrombin concentration in the 34 affected infants was below danger level, and therefore whether prophylactic vitamin K had raised the prothrombin of the 11 infants of the first group , or whether vitamin K could have been expected to have had any effect on the actual hæmorrhages in these cases The Liverpool workers admit the difficulty of excluding other causes of hæmorrhage, and the nature of their investigation obliged them to depend on the opinion of the pædiatrician who saw the patient at the time of the bleeding that hæmorrhagic disease was "the most likely diagnosis " The result is that though the negative evidence is impressive it is not yet conclusive and so long as it seems possible that vitamin K may prevent some cases of hæmorrhagic disease we shall stick to our former opinion that it should be given

PSYCHOLOGICAL PROBLEMS OF MOTHERS AND CHILDREN

FOR each of its round table conferences the Josiah Macy Jr Foundation, New York, brings together a team of authorities on some matter of topical interest The Third Conference on Problems of Infancy and Childhood[1] dealt with three topics (1) the anxieties of mothers as expressed to physicians , (2) the psychological situation of mother and child on return from the hospital , and (3) the emotional reactions of children to tonsillectomy and adenoidectomy

It was agreed that mothers who are given anticipatory guidance and opportunities for discussion at the maternity hospital, before returning home, experience much less anxiety about their infants than do mothers who are not prepared in this way Among mothers who received no such guidance the chief anxieties were found by several observers to concern crying, hunger, feeding problems, vomiting, failure to gain weight, constipation, noisy breathing, and a rash on the face Complaints by mothers regarding illness in their infants were of three types (1) connected with a real disorder, (2) determined by contemporary outlook on matters affecting babies, and (3) prompted by maternal psychopathology The conference agreed that the mother should know in advance the doctor who is to look after her baby , and the relative discontinuity of medical care in urban communities was deprecated

Dr Sibylle Escalona emphasised that the period immediately after returning home is crucial for the subsequent development of the mother-child relationship In this period the mother and the whole family are especially open to suggestion , and so this is a good time for trying to influence the new family situation created by the arrival of another member The hospital practice of denying mother and baby the chance of becoming intimately acquainted, from the day of birth, is inimical to secure mother child relationship The present trend however, is towards "rooming in", and this also enables the mother to return home with greater knowledge of baby management, and thus with greater confidence

Dr Lucie Jessner and Dr Samuel Kaplan described their observations on the emotional response of an unselected group of children to tonsillectomy In children und on the other hand, has always insisted on professional privilege which is independent of the wishes of the patient. French doctors do not accept the view that the latter's consent removes the main objection to publication in court of medical information obtained in private consultation. They have pointed out that a practitioner's special training and knowledge enables him to draw conclusions from what he has been told, or to gather from indications facts which the patient did not wish to communicate or which were even unknown to them. Where the doctor has discovered a mental or physical illness of which the patient was unaware, and has for medical reasons found it advisable to hide this knowledge, he will naturally be unwilling to divulge the information in open court. To do so, French doctors maintain, would not only be contrary to the Hippocratic Oath and the professional code but would be objectionable from the scientific standpoint. This attitude has been accepted by the French courts, which have held that the duty of secrecy is binding on French medical practitioners "as a duty inseparable from their calling." It is a general and absolute duty from which doctors cannot be freed, either by express order of the court or by the consent of the patient.

---

[1] *Lancet*, 1944 i 506

[2] Falls H F, Jurow, H N *J Amer med Ass* 1946 131 203

[1] Problems of Infancy and Childhood Transactions of the T Conference March 7–8 1949 Josiah Macy Jr Foundation New York.

Whether medical privilege of such wide scope is altogether desirable is a question on which French lawyers and medical men are still at issue. It is hard to avoid the conclusion that professional privilege so widely extended must give rise to difficulties in practice, not least to litigant patients themselves. But in this country, whose courts do not recognise medical privilege at all, it is certainly worth pondering over the reasons for, and implications of, French practice on medical secrecy. In at least one part of the Commonwealth, the State of Victoria (Australia), the medical profession already enjoys the same professional privilege as lawyers possess under the common law.

Electrical Stimulation of the Brain

THE discovery by FRITSCH and HITZIG[1] in 1870 that parts of the brain are electrically excitable raised a host of possibilities which neurophysiologists have been exploring ever since. Perhaps the most valuable studies are those of Prof. WILDER PENFIELD, F.R.S., and his successive colleagues at the Montreal Neurological Institute, because they were made on the unanæsthetised human brain. The observations now summarised in book form by Professor PENFIELD and Dr RASMUSSEN[2] were made over a period of 20 years during brain operations under local anæsthesia, with their patients' intelligent coöperation. In patients with focal epilepsy they have often reproduced an epileptic aura from an area of brain which is not usually susceptible to electrical stimulation. They have also been remarkably successful in reproducing complex sensations by stimulating the temporal lobes, and they give many instances of psychical seizures, including complex visual or auditory hallucinations, produced in this way.

Most of their work, however, has inevitably been concerned with the sensorimotor cortex, and they have many records of the local sensations resulting from stimulation of the postcentral gyrus, which cannot be studied in animals. They have revised the "homunculus" published by PENFIELD and BOLDREY[3] in 1937 to show at a glance how the parts of the body are represented in the precentral and postcentral gyri. In their two diagrams of the sensory and motor homunculi we see a nightmare hemi mannikin sprawling head downwards, with his foot dangling out of sight into the longitudinal fissure and the successive parts of his body varying in size according to the extent of their representation. The sensory diagram brings home to one how large a share of the postcentral gyrus is taken by the hand and lips; the little finger is drawn as large as the index, and PENFIELD reminds us of the importance of sensation in the ulnar aspect of the fifth finger and hand in writing. Neurologists are sometimes puzzled by his attitude to "levels" of function. For example, he writes (p. 235): "It seems fair to conclude that within the diencephalon there are neurone circuits which may be considered the highest level of neuronal representation and re representation." Here he seems to be using "highest level" in an entirely different sense from that which HUGHLINGS JACKSON gave it long ago. Modern neurophysiology teaches that cortical mechanisms are outgrowths and elaborations of diencephalic structures. These structures therefore form a vital hub for human brain activity; but they are surely more the "telephone exchange" or the "furnace" for human endeavour than a "high level" in JACKSON's sense.

Curiously enough, however, the functions of the much-studied motor cortex have been the centre of most neurological controversy in recent years. The experimental contraction of a single muscle by electrical stimulation of the precentral gyrus has been cited as evidence of discrete muscle representation in the motor cortex, but the clinicians have staunchly defended the view that the motor cortex must control movements rather than individual muscles. LIDDELL and PHILLIPS,[4] in their paper on thresholds of cortical representation, show how these conflicting views have arisen. They found that the traditional map of motor points could be reproduced in the motor cortex of the baboon by repetitive stimulation at, say, 50 cycles per sec. But a stimulus consisting of a single weak "square-wave" produced an entirely different response. They now found wide areas covering the whole of the motor cortex from which one of three responses could easily be obtained. Far the most readily and widely elicitable was a contraction of the thumb index-minimus muscles. The other two areas were concerned with hallux toe movement and secondly with tongue and face movement. By demonstrating that thumb index-minimus movements can be obtained from an immensely wider cortical area than has hitherto seemed possible, this Oxford work has exposed a complexity of cortical motor function which must change and ultimately clarify our ideas of the functions of the motor cortex. In stimulating the motor cortex, the physiologist is clearly "butting in" on a complex mechanism of motor patterns which we are very far from understanding.

---

[1] Fritsch G Hitzig E *Arch Anat Physiol wiss Med Leipzig* 1870 p 300

[2] Penfield W Rasmussen T The Cerebral Cortex in Man New York and London Macmillan 1950 Pp 248 48*s* 6*d*

[3] Penfield W., Boldrey E *Brain* 1937 60 389

[4] Liddell E C T Phillips C G *Ibid* 1950 73 125

1 the serum globulin decreased and bone pain was relieved, but the marrow picture remained unchanged

Outside the reticulosis group of diseases, A C T H and cortisone have been used successfully in only two blood diseases DAMESHEK[6] reports that in 2 patients with idiopathic acquired hæmolytic anæmia who had not responded to splenectomy, A C T H treatment seemed to suppress the active agglutinins or hæmolysins and no further blood transfusions were needed, GARDNER[7] obtained similar results in 3 patients who were given 60–100 mg A C T H daily The other condition that has been treated with A C T H is Henoch Schonlein purpura, and since this is not a true "blood disease" but a disease of blood-vessels possibly related to the collagen diseases, a response might well be expected STEFANINI et al[8] reported the effect of A C T H on a boy of three who had skin purpura and intestinal affection, the child had been ill for six weeks when treatment was begun, the cutaneous lesions cleared and abdominal pains ceased within six days It is of course difficult to assess the effect of treatment in a condition so liable to spontaneous remission and STEFANINI thinks that the A C T H simply relieved the vasculitis without eradicating the disease

It is thus clear that the application of A C T H and cortisone in blood diseases has produced some hopeful results, and that further studies of their effect in acute leukæmia and anaphylactoid purpuras are well justified In particular we shall look forward to learning whether, by themselves or in combination with folic acid antagonists, A C T H or cortisone offer a chance of controlling acute leukæmia

Professional Privilege Abroad

IT is an ancient rule in professions that secrecy must be preserved about all facts coming to the practitioner's knowledge in the exercise of his duties But whereas members of the legal profession cannot in any circumstances be forced to divulge information entrusted to them for the purpose of obtaining advice, the law of this country does not extend protection to doctors A medical man summoned to give evidence in a court of law in any criminal or civil matter enjoys no privilege that will secure him against questions tending to elicit information, however confidential, obtained in the consulting room The law on this point was expressed in the leading case of Wheeler *v* Le Marchant (1881) as follows

> "The communications made to a medical man whose advice is sought by a patient with respect to the probable origin of the disease as to which he is consulted, and which must necessarily be made in order to enable the medical man to advise or to prescribe for the patient, are not protected "

and a textbook on modern medical jurisprudence advises members of the profession bluntly "A witness must remember that there are no medical secrets" There is no doubt that a doctor refusing to disclose confidential information in the witness box renders himself liable, if the judge is so minded, to be sent to prison for contempt of court To this state of affairs medical men have long objected, and the British Medical Association advises that "professional secrecy should be contravened only under protest after direction from the presiding judge." The law or its interpretation may yet be changed, and some light on the considerations that should guide future policy may be gained from a survey of foreign legal systems which have deliberately adopted a different attitude

In France, as elsewhere on the Continent, medical secrecy has been recognised as requiring and deserving the protection of the law No measures to maintain and improve public helath, and no health service, can, it is held, be fully effective unless the public has complete confidence in the medical profession and will invoke its help as soon as the need becomes apparent In the case of venereal diseases, for instance, experience is said to show that early attendance at a clinic can be expected only if secrecy is assured Moreover, medicine is a science which requires facts to work on, and to enable the doctor to decide what treatment is best he often needs from his patient a frank account of all the physical and mental symptoms Such a history may not be obtained unless there is a firm belief that the doctor will keep strictly to himself whatever he is told Taking it as axiomatic that unreserved communication is an essential condition of successful medical treatment, French law considers that protection against unauthorised revelations is not only indispensable to the patient but also important to the doctor and a safeguard of public health Accordingly, French law—like the law of Italy, Germany, Switzerland, and many American States—has been so framed as to place confidential medical information beyond the risk of casual disclosure, and to reconcile, as far as possible, the demand for secrecy with the needs of justice An article of the Criminal Code (art 378) renders punishable by imprisonment and fine not only medical practitioners but also pharmacists, midwives, and other related persons who without express authority reveal confidential communications made to them by patients In addition, any voluntary disclosure of such information lays a medical man open to a claim for damages at the suit of the aggrieved party—whether or not silence has been expressly imposed before the particular consultation These remedies are so clearly understood on the Continent that occasion rarely arises to enforce them, but they give doctors full sanction to refuse disclosure of confidential information, even if the demand is made in a court of law

The right to refuse to answer questions of this sort in the witness box may be of two kinds it may be absolute or it may depend on the attitude of the person most directly concerned Both systems are represented in the law as it now stands in various Continental countries German law, for instance, holds that the duty of secrecy is imposed solely for the protection of the patient Like professional privilege covering legal advisers in English courts, the privilege that can be claimed by medical men in German courts gives way, therefore, as soon as the patient releases his adviser from the duty of silence Such consent entirely destroys the justification for the doctor's refusal to speak about the privileged matter, it not only entitles the doctor to testify, but obliges him to do so even if he thinks that this is not in the true interest of his patient A similar situation prevails in most Swiss cantons The French medical profession, the age of 4 years, separation from home was the principal cause of anxiety, whereas in children aged 6–12 fear of anæsthesia was prominent. The child's reaction corresponded to the soundness of his personality structure. Furthermore, of 28 who adjusted themselves well to hospital conditions only 1 had an unsatisfactory relationship with his parents, whereas of 13 who did not adjust themselves, 10 had an unsatisfactory relationship. It was concluded that in the well-adjusted child tonsillectomy is least likely to produce psychic trauma between the ages of 5 and 10 years, and operation should be postponed if the child has suffered any recent traumatic experience. To overcome apprehension the child should be told in advance something of what to expect in hospital; this information should be given by some trusted person, usually the mother. With a 24-hour waiting-period in hospital before operation most children over 4 years of age became somewhat acclimatised, but younger children, who suffer more from separation, do not benefit from such a period.

---

[6] Dameshek, W *Blood* 1950, 5 791

[7] Gardner F *Ibid*, p 791

[8] Stefanini, M Roy, C A Zannos L Dameshek W *J Amer med Ass* 1950 **144** 1372

CONTROL OF BRUCELLOSIS

EARLY in 1950 the World Health and Food and Agriculture Organisations (W.H.O. and F.A.O.) were asked by their member-countries to produce a plan for combating brucellosis. Their immediate response was to select a panel of experts on the disease and designate 12 centres in various countries which would stimulate research and training in field and laboratory methods. The report[1] of the panel's first meeting in Washington makes encouraging reading because it squares up to a world-wide problem. In the United States, halving the number of cattle infected with brucella has saved 50 million dollars annually, and eradication of the disease from Norway has cost less than a year's toll among farm animals. Since brucellosis does not pass from man to man, the human infection can best be controlled by eradicating the disease from animals; but for this accurate diagnosis and reporting are essential. The panel recommends that all governments should make brucellosis, whether in man or in animals, a reportable disease; and it proposes a central pool of information on which all countries may draw. With probably at least 20% of British cows infected, we have a stake in this campaign; and it deserves the widest support.

As an earnest of its practical intentions the panel includes in its report an excellent account of current knowledge of the disease, though it says little on the clinical side. Brucellosis in this country means infection with *Brucella abortus*, but *Br. melitensis* has been isolated from cow's milk in some areas and we cannot dismiss the possibility that this organism may become more widespread. The report deals with modes of transmission to man, including entry through the mucous membranes and the conjunctiva and airborne spread. Modern laboratory methods of diagnosis are described, as are the newer methods of treatment, though none of these have yet proved really satisfactory. The main burden of the report bears, as it should, on brucellosis in farm animals, on the methods of diagnosing such infections, and on the production and control of strain-19 vaccine which is widely used in cattle. The panel is well aware of the variations in the method and in the antigens now used for agglutination tests and in the techniques for culturing the organism. It offers to distribute stock cultures and sera, and these should help to improve laboratory standards of diagnosis. It also describes the new ring or A.R.B. test, in which a stained antigen is added to whole milk and, if positive, the antigen collects on the fat globules to give a coloured cream line. This is a fairly sensitive test and should simplify field tests on infected herds. The detailed instructions for the control of brucellosis in swine will interest the agricultural and public-health authorities in countries where *Br. suis* infections are widespread. There are many distinguished names on this international panel of experts, and the report shows that they mean to get on with the job.

CRITICS OF PSYCHO-ANALYSIS

FREUD'S teaching has now been widely, if thinly, spread over life in the United States, and perhaps the missionary spirit of some of its transatlantic exponents is the cause of some recent critical reactions by eminent thinkers on the Continent, where Freud came into fashion many years earlier.

Gruhle[1] attacks the philosophical validity of psycho-analytic interpretations:

> Freud says of the dream that it protects sleep. This is Freud's interpretation of its objective purpose; the dreamer knows nothing of it. Freud refers to his own observation, but wrongly, for no observation can support his thesis. Freud also says the dream is wish fulfilment, an interpretation of subjective purpose again unknown to the dreamer. Freud tells him: You don't know it, but I know. This Freud calls observation; he calls observation his own experience of evidence.

Gruhle sees in psycho-analytic teaching only the enchanting play of magic, poetry, and myths, which places it outside science and scientific criticism. He warns us against drawing any conclusion from therapeutic results which may be equally achieved by all kinds of procedures and creeds, though the rational appeal in the cloak of science is probably the most effective mode of faith-healing today. He insists that Jung, for instance, persuades his patient that his dream images are of deep significance and reveal eternal truths. When the patient has been converted to this belief he thinks he has access to deep knowledge and secret meanings, and finds peace in this, his own religion. According to Gruhle, one has to see clearly the dividing line between the adept, who is stirred and may be deeply moved, and the sober scientist who can discover only misguided imagination.

Karl Jaspers, now professor of philosophy in Basle, was at one time a psychiatrist. His criticism[2] is distinguished by its moral undertone. He cannot find any criterion of true or false in the boundless interpretations, distortions, oppositions, and over-interpretations of everything used by psycho-analysts; there is no standard of discernibility in the infinite flux of meanings they may find. To consider illness as guilt, as Freud sometimes does, and to extend this view more or less to all diseases is, in Jasper's opinion, a wholly unmedical attitude. It leads to an inhuman philosophy contrary to the physician's ethics. Jaspers sees in some analytical writings a destructive fanatical tendency to use therapeutic methods in order to gain power over human souls. His strongest protest, however, is directed against the growing orthodoxy and intolerance of analytical societies and schools. A successful teaching analysis as the condition of full membership and of registration as an analyst becomes more and more a sacrifice of personal freedom in thinking comparable with the monastic exercises of the Jesuits or the practices of the Yogi. Jaspers has great doubts whether it is compatible with the freedom of a university in Western civilisation that the psycho-analytical institute of the university should ask its students to undergo a teaching analysis which is only declared successful if the candidate accepts the faith. His principal contention is similar to Gruhle's —that psycho-analysis, using pseudoscientific terms, claims to solve problems in human existence that science cannot solve without weakening its foundations and abandoning part of its freedom.

---

[1] Joint F.A.O./W.H.O. Expert Panel on Brucellosis. Report of the first session. Washington, November 1950.

[1] Gruhle, H. W. *Studium Generale*, 1950, 3, 380.
[2] Jaspers, K. *Nervenarzt*, 1950, 21, 465.

now used as a plasma substitute in many hospitals in this country, with apparent success It restores plasma volume satisfactorily, it remains in the circulation long enough to sustain the circulation until the amount of circulating plasma protein is again sufficient for this purpose, and so far as is known its use is unattended by unpleasant immediate or delayed effects It has certain disadvantages common to many plasma substitutes it is a substance foreign to the body and cannot be expected to perform all the functions of plasma protein, it has no buffering power, and probably no nutritive value, and though it seems to disappear slowly from the body, its fate is not known with certainty But if these shortcomings are understood and it is used with discretion, dextran has a useful part to play as a means of raising depleted blood volume, especially in emergencies when the natural fluids, blood and plasma, cannot be obtained in sufficient quantity But dextran also has other less obvious uses As a relatively inert substance, which disappears slowly from the tissues until only traces remain, and can be made in a wide range of molecular sizes, it can be employed as a tool for investigating problems such as the permeability of membranes, the properties of the reticulo endothelial system (by which dextran is taken up and from which it is gradually lost), and the behaviour of certain cell surfaces Moreover, when converted to a sulphuric ester, dextran becomes an anticoagulant On Feb 13 the Royal Society of Medicine's section of experimental medicine heard accounts of experimental work on these lines now being done at the Birmingham Medical School and by the Medical Research Council's burns unit in Birmingham

The most complete report was that of Dr KENNETH WALTON on the anticoagulant activity of dextran sulphate Dextran itself, which is uncharged, has a negligible effect on blood clotting, but the electro negatively charged sulphate exerts an antithrombin action, like that of heparin, which it structurally resembles GRONWALL et al[1] reported in 1945 that sulphuric esters of dextran acted as anticoagulants, but they did not pursue the discovery, because these esters also had undesirable effects Since inulin sulphate, which is of smaller molecular size, was even more toxic, they concluded that toxicity was unrelated to molecular size WALTON deduced from the Swedish data that the molecular weight of the toxic dextran sulphate used by GRONWALL et al was at least twice that of heparin, and he decided to examine dextran sulphates with a lower molecular weight His experiments disclosed that below a molecular weight of about 20,000 these had an anticoagulant action in animals without the toxic effects associated with esters of molecular weight 35,000 and above The latter group of substances, unlike the former, caused a precipitation of fibrinogen, agglutination of platelets, and the deposition of metachromatic staining material in the reticulo endothelial system The resulting fibrinogenopenia and thrombocytopenia explain the liability of this group of large molecular weight esters deposits in the reticulo endothelial system

The dextran sulphate finally selected at Birmingham for fuller investigation is free from these undesirable actions It can be given to animals in doses at least 100 times greater than the least effective anticoagulant dose, and it has a potency of some 17–20 I U per milligramme when assayed against the standard heparin Inactive by mouth, it can be sterilised by autoclaving without loss of potency if suitably buffered, and it has been given in doses up to 500 mg per kg body weight to mice, rats, rabbits, dogs, and monkeys without toxic effects, though the guineapig is an exception With doses of 40 mg per kg body weight, the blood pressure and pulse and respiration rates of anæsthetised dogs are unaffected, and at concentrations sufficient to produce an anticoagulant effect the alterations in erythrocyte sedimentation are negligible The dextran has not been demonstrated *histologically as metachromatic material in any of* the tissues examined, after single and repeated injections and over periods ranging from some hours to some months after injection Some 25% of the material is excreted in the urine in the first fifteen minutes after injection Its effect on clotting seems to be similar to that of heparin It will not prevent the clotting of pure fibrinogen by thrombin, unless a co factor associated with α globulin or the α lipoprotein fraction of plasma or serum is present, but in the presence of this factor it acts as an antithrombin A clinical trial of dextran sulphate is in prospect and the results will be awaited with interest, for there is a place for a relatively cheap, effective, and uniform anticoagulant as free from undesirable actions as dextran sulphate seems to be

Dr JOHN HARDWICKE described the further progress of his investigation[2] of the effects of dextran of various molecular sizes on erythrocyte sedimentation, and Dr D B BREWER recounted experiments on the excretion of dextran by the kidney from which he hopes eventually to derive information about the size of glomerular pores Dextran is apparently excreted chiefly by filtration through the glomerulus, the tubules playing little or no part either in excretion or reabsorption

The Aged

WORK done in Birmingham to provide the basis of a coherent administrative policy for the care of the aged was described by Prof A P Thomson addressing the Manchester Medical Society on Feb 7 It had been found, he said, that three fifths of the patients in the infirmaries required neither frequent medical attention nor skilled *nursing*, and if those were the criteria for continued stay in hospital more than half the patients *now in* the infirmaries should be accommodated either in their own homes, with the help of improved social services from local authorities or voluntary agencies, or in institutions (other than hospitals) which provide domestic services and simple nursing (washing, feeding, and dressing) Of applicants for admission to the infirmaries, at least half had no need of hospital accommodation though they required help of a different kind

---

[1] Gronwall, A Ingelman B, Mosimann H *Uppsala LäkFören Förh* 1945, 51, 397

[2] Hardwicke J Ricketts C, Squire J R *Nature Lond* 1950 166, 988

A C T H can also prevent the formation of a pyogenic membrane and scar tissue, and apparently it can do this even when given in a dosage below that which would inhibit all healing There is also a possibility that its lymphocytolytic action may so modify antigen antibody reactions as to prolong survival of homografts The daily dosage of the hormone (120 mg) in cases of severe burns was hoped to be not so large, or so long continued, as to cause side-effects But Converse[3] reports adverse effects on withdrawal of the hormone, and Moore[4] says that A C T H is not a panacea in burns By decreasing capillary permeability A C T H may also have a rôle in controlling the hæmorrhages of severe radiation sickness

PRIMARY LOCAL TREATMENT

Under civilian conditions local treatment in the primary phase is not of major importance, provided that the method used is clean and reversible (tanning is irreversible) The concept of the burned area as a parasite whose removal terminates the disease lends attraction to the idea of primary excision This is in fact the method of choice with localised deep contact burns such as those which may befall unconscious patients

With more diffuse burns the chief difficulties about primary excision are (1) the unreliability of early diagnosis of full thickness skin loss, and, even more, (2) the hazard to life and to the success of primary grafts, from applying this method to a burned surface of any extent (10% or more of full thickness skin loss) while the subcutaneous tissues are still firmly attached and intensely inflamed and hyperæmic At operation hæmorrhage may be profuse, and the risk is particularly great for the young and for the aged

In addition to A C T H two methods are known to limit extravasation of fluid at the site of the burn, thus helping to limit the constitutional reaction These methods are (1) cooling and (2) pressure, and local cooling is generally impracticable Local pressure has been extensively employed in America This method is time consuming and expensive in material, and except with small burns it does not prevent local fluid accumulation Applied to the neck the method is associated with irreducible hazards to life, and applied about the elbow or knee, peroneal or ulnar palsy may ensue

The main objective of local treatment is to keep the surface sterile and dry Physical protection by covering the burned area is essential for some patients—those who are being evacuated or who are not admitted to hospital, and Service casualties who must for a time remain in action Treatment would be greatly simplified by composite dressings with an intimate layer of an atraumatic fine gauze mesh supported by packed cellulose, whose outer layers were rendered water repellent by impregnation with silica, these dressings should be prefabricated into shapes and sizes to fit special parts (such as the hand or trunk) with tapes attached for secure, but not tight, fixation What is wanted is an inexpensive dressing thick enough to give some physical protection but not too thick for easy storage, it should be vapour permeable, but fluid impermeable The 'Nylon' derivative dressing, which has been tried extensively does not seem to be sufficiently permeable to water vapour to prevent maceration when it is applied over a fluid producing lesion An ideal dressing should make it possible to combine the first aid and the definitive local primary treatment of all burns

It is not necessary to cover the burned skin to obtain local dryness and sterility Indeed there is much evidence that for hospital patients simple exposure of the area is the best, as well as the cheapest, means of obtaining these conditions and so limiting the complications of infection (secondary skin loss and constitutional reactions) DeVirginia Blocker has reminded us that the exposure method was once widely practised in America, Copeland[5] first described its use in 1887, and Halder Sneve[6] underlined its practical advantages in 1905 Ten years later Haas[7] remarked exposure "is an ancient method quite ancient enough to be new" We owe it to A B Wallace, of Edinburgh, that this method has been reinvestigated and its full value established This is possibly the best of all local primary treatment for burns of the perineum and face in children, and of the face in adults—that is, in sites where soiling of dressings is difficult to avoid

Exposure is always a hospital procedure, it should be combined with early immobilisation of the part in the position of function, since cracks in the coagulum may lead to infection The burn can be exposed at any stage to ward atmosphere Circumferential trunk burns are unsuitable for exposure unless the patients are ambulatory, because body pressure or friction of sheets on the coagulum may lead to infection With exposure there forms a flexible coagulum, this is apparently free of the tourniquet dangers of tanning, but it is slow to separate Superficial burns treated by exposure are a week to ten days slower in healing than similar burns treated with tulle gras, and often it takes longer to ascertain the depth of the burn when the area is dry

What local treatment should be given in addition to exposure or absorptive dressings is debatable Most workers agree with Pulaski that lavage with a detergent is desirable Truman Blocker in Texas, however, often leaves the burned surface exposed without preliminary toilet and the incidence of early infection in his cases is certainly very low Penicillin cream has the disadvantages that an increasing proportion of patients are sensitive to it, its activity does not continue long enough to give security from infection of the sterilised burned surface from deeper layers of skin or from marginal areas, during the week or more that the first dressing should be left undisturbed, and its semi fluid composition encourages maceration Pulaski[8] has shown that penicillin carbonate by mouth provides adequate blood-penicillin levels for most patients, and it seems that this will more certainly sterilise the deeper layers of a burn than will topical penicillin

The risk of tetanus in burns was mentioned by Dupuytren over a hundred years ago, but has since often been overlooked Altemeier[1] recently reported an incidence of contamination by tetanus organisms of 3% in routine smears from primary burns Anti tetanus serum should certainly be given in all cases, and the advisability of active immunisation of the whole population should be seriously considered

TREATMENT IN THE HEALING PHASE

It is on the surgical programme in the healing phase, and only rarely on faults in local primary care, that the prognosis in deep burns depends after the second week The negative nitrogen and electrolyte balances, the disturbances of endocrine function, and the profound and resistant anæmia seen in the healing phase are all chiefly caused by the presence of dead tissue, or from the later persistence of granulations uncovered by skin I have suggested that primary excision of burns should not be practised routinely, but equally in the healing phase the removal of sloughs and the provision of a fresh skin surface should not be unduly delayed The vegetable collagenase described by Altemeier holds great promise, but this and other enzymic debridement agents are still at the

---

[3] Converse J Personal communication 1951
[4] Moore F Personal communication, 1951
[5] Copeland W P *Med Rec* May 1887
[6] Sneve H *J Amer med Ass* 1905 45 1
[7] Haas S V *Amer J Surg* 1915 29 61
[8] Pulaski E J Personal communication 1950

Special Articles

BURNS

A REVIEW OF THEIR MANAGEMENT

PATRICK CLARKSON
M B E , M B Lond , F R C S
CASUALTY SURGEON, GUY'S HOSPITAL, LONDON

IN the past the treatment of burns has not always reflected credit on the medical profession , for the issues have too often been debated with emotion rather than detached judgment True, mortality and morbidity have steadily fallen in the past thirty years , but even quite lately the profession has sponsored the local application of tannic acid despite its very harmful effects, and probably many patients have died needlessly because of excessive and protracted administration of fluid intravenously

The urgent topicality with which modern weapons have invested the subject of burns is illustrated by the symposium held last year in Washington,[1] by the meeting on Feb 9 of the United Services' section of the Royal Society of Medicine, and by a number of publications—notably one by Colebrook [2]

THE PROBLEMS OUTLINED

An extensive deep burn has a natural clinical course in three overlapping phases The primary phase of shock and counter shock lasts up to ten days and results in either exhaustion or survival It may be followed by the second, or healing, phase, which is of indefinite length depending on the depth, size, site, and treatment of the raw areas , this phase, in which dead tissues separate and the raw areas are re surfaced, is often characterised by profound metabolic disturbances and anæmia When re surfacing is complete there follows the third phase, in which attention turns to rehabilitation or to reconstructive surgery

In the primary phase the objects of treatment are, briefly, to preserve life by maintaining the circulation, and to prevent infection Maintenance of the circulation involves (1) restoring water, electrolyte, and colloid balance by administering fluids , and (2) attempting to control the humoral factors in this mechanism by dialysis or by administering hormones, such as the adreno corticotropic hormone (A C T H) The prevention of infection is chiefly a matter of local primary care If this is adequate, superficial burns heal without residual disability by the second or third week , and the deeper burns are then ready for surgical treatment in the healing phase In this phase treatment consists in removing dead tissues and re surfacing the raw areas by healing techniques, combined with measures to correct the metabolic disorders and anæmia

Today the possibility of war time atomic explosions and of burns from jellied petrol or from flame throwers poses additional problems These include the effects of simultaneous exposure to ionising and thermal radiations , the effects on the lung of inhaling hot air or steam , the effects on heart and brain of acute hyperthermia , the effect on mortality of impaired renal function , and the relation of depth of burn to early mortality, particularly where there is heat coagulation of muscle With regard to these war time risks, the need is, not to discover the ideal treatment, but to decide what is practicable In other words, what can best be planned for mass casualties ?

FLUID, ELECTROLYTE, AND COLLOID BALANCE

The question of fluid, electrolyte, and colloid balance in the primary phase has been reinvestigated by isotope techniques The need for careful control is emphasised by Cope, Moore, Pennell, and others,[1] who sharply restrict the amount of fluids administered intravenously once the local capillary permeability has returned to normal and diuresis has started—which is usually about the end of the second day

The main therapeutic index is still the percentage of body-surface burned—i e , replacement therapy is based on the calculated extravascular loss of the fluid, salt, and colloid constituents of the blood A formula commonly used for this purpose is 1–3 ml of fluid per 1% body surface burned per kg body weight on the first day, and 1–2 ml per 1% per kg on the second day Probably however, an empirical scale, decided rather by the response of the blood pressure and the urinary output, provides better for the individual patient's needs Whichever method is followed, the amount administered to adults should rarely exceed 3000 ml each of colloid and electrolyte solutions intravenously, plus 2000 ml. of water by mouth, during each of the first two days commonly more is given in the first twenty four hours when the need is more urgent, than in the second When oliguria is replaced by diuresis, restriction of fluids is very necessary, to avert the risk of fatal pulmonary œdema The optimum electrolyte solution varies in different patients, and sometimes from time to time in the same patient Under ideal conditions repeated estimations of the blood content of sodium, potassium, and chloride should be done if the risk of serious electrolyte depletion or intoxication is to be avoided

The colloid fluids of choice are blood and plasma Cope [1] has, however, reminded us that these have a higher protein content than has blister fluid, and therefore they may not be ideal Blood transfusions in the first forty eight hours seem to delay and reduce the anæmia of the healing phase In planning for mass casualties plasma substitutes have an important place, and the substitutes that have been most widely investigated are gelatin, globin, and dextran Both Ravdin and Everett Evans [1] report favourably on gelatin, they used the Knox P20 preparation—a relatively homogeneous molecular solution of a degraded ossein gelatin Strumia [1] points to the value of globin, which affords the only means of salvaging red blood cells in stale stored blood Both gelatin and globin are protein substitutes for a protein loss, and are at least partly metabolised by the body Dextran, on the other hand, is a polysaccharide , but there is a good deal of evidence of its effectiveness as a short term plasma substitute (Bull and Thorsen [1]) It dilutes the plasma protein, affects the blood sedimentation rate, gives rise to occasional reactions, and by causing rouleaux formation makes blood grouping difficult Its fate in the body is not fully understood , it is still expensive We need to know more about its polymer chemistry and its metabolism before pressing for its general adoption as a plasma substitute.

The value of dialysis by the artificial kidney in the oliguric phase of patients with impaired renal function has been investigated by Thorn and Moore, who have shown that in the primary phase this procedure may remove from the circulation depressor substances secreted by the liver as well as excess water and electrolytes

Of the other humoral factors concerned in this aspect of the primary phase, the most important is A C T H This seems to block the body's reaction to injury Its possible effects, in addition to an anti hyaluronidase action, which limits early capillary permeability, include reduction of histamine synthesis and suppression of the early constitutional reactions, such as pyrexia, tachycardia, and malaise Even with burns of 40–60% of the body surface, administration of this hormone may permit ambulation and full sleep, with appetite for food, from the first day , and its gluconeogenic action helps to protect liver proteins Later, during the healing phase, about the need for specialists in reaching diagnoses, but perhaps the best way of judging their value is to consider certain notoriously difficult diagnostic situations which nevertheless *can* yield some sort of definite solution

---

[1] See *Lancet* 1950 ii 635
[2] Colebrook, L A New Approach to the Treatment of Burns and Scalds London 1950

Any middle aged or old person with a chest illness which does not rapidly clear up must be considered a cancer suspect But to determine whether or not he has cancer may be very hard The plain chest X ray film may merely reveal an indeterminate shadow, and the sputum examination a mixed growth of common organisms and no malignant cells, the lesion may be out of reach of the bronchoscope, and the bronchogram findings may be equivocal One may therefore ask whether a physician who spent all his time in dealing with patients affected by chest diseases would be more likely to reach the right diagnosis than the general physician It seems highly doubtful whether he would be appreciably more successful And since precise diagnosis is here impossible, the correct attitude to adopt is either to recommend exploration of the chest or to admit doubt until unequivocal evidence pointing to cancer or benign inflammatory disease develops It is equally doubtful whether the chest physician would be superior to the general physician in deciding whether to refer the case to a thoracic surgeon (in whose hands the final decision as to chest exploration must rest) or to await developments.

A similar situation is provided by many subjects with acute intra abdominal disease No one can be sure of the diagnosis, and the best that can be said of the specialist surgeon by comparison with the sound general practitioner is that his guess will turn out correct more frequently Here the important practical questions to be asked are not the finer points of diagnosis but should a laparotomy be done ? and, if it should, where should the incision be made ? It is doubtful whether the specialist would give markedly superior answers to these questions. Indeed, it is extremely difficult to say in retrospect, when the patient is either dead or better, what was the correct answer to the first question, for the laparotomy which did not help the patient may still have been a wise precaution, and the failure to operate which was *not* followed by the patient's death may still have been an unjustifiable risk

One may next ask how the specialist and the general physician compare in their ability to label obscure syndromes which cannot usually be given confident ætiological diagnoses The case of "brachial neuralgia" may be taken here Subjects so affected may be labelled very differently by different physicians, while fashions in diagnosis have come and gone in recent years and have included "true neuritis," vitamin B_1 deficiency, cervical rib, septic tooth sockets, and prolapsed cervical intervertebral disc In the light of existing knowledge, probably the soundest attitude towards at least many cases of "brachial neuralgia" is to admit that beyond this label no diagnosis can be made The general physician will be more likely to adopt this modest view than the physical medicine specialist or even, perhaps, the neurologist

The field of rarities provides examples in which several doctors may be quite in the dark, while another confidently, and correctly, makes a diagnosis on purely clinical grounds In these circumstances the supremely important aid to diagnosis is previous personal experience of the particular syndrome in question Here the specialist will as a rule have a clear advantage over the general physician, unless the syndrome is some general disturbance claimed by no specialty But such circumstances are very rare They seem much commoner than they are because they provide opportunities for startling diagnostic tours de force which may be remembered and admired in medical schools for many years The story is sometimes heard of a great clinical giant, long since dead, who entered a ward, looked fixedly at a sick man, felt his pulse and studied his tongue, made a few dramatic gestures, and then boldly announced to his astonished clerks that the diagnosis was X's syndrome—a diagnosis triumphantly verified post mortem

The specialist may be in a much more favourable position than the general physician when the practice of his specialty involves a knowledge of some difficult technique. In the case of "? simple ulcer, ? carcinoma of the stomach" which is being studied clinically and radiologically, the gastro enterologist would probably not guess right any more often than the general physician But if the former is an expert gastroscopist he may sometimes be able to reach a confident diagnosis Similarly, when studying conditions of the large bowel, the expert with the sigmoidoscope will give a better opinion than the physician who has rarely used that instrument Nevertheless, leaving aside ear, nose, and throat, eye, neurosurgical, and perhaps genito urinary specialists, such special techniques carried out by the clinician himself do not, as a rule, play a very important part in reaching diagnoses In so far as special studies are required, X rays, blood counts, microscopical and cultural examinations of the urine, determination of blood chemistry figures, and others not normally undertaken by clinicians are generally far more important Admittedly, the clinician should study X ray films himself, and not merely accept the radiologist's opinion This conclusion is especially true of chest radiographs, and here the chest specialist may be a little more accurate than the general physician in the doubtful case In respect of the other tests mentioned, the clinician merely has to interpret figures, and that feat should almost always be performed as accurately by the non specialist as by the specialist

In the narrow diagnostic field of determining the nature of the lesion, the specialist, then, is as a rule markedly superior to the general physician only when the mastery of some special technique is necessary

DIAGNOSIS IN THE BROAD SENSE

It was said above that, whereas in the diagnosis of the acutely sick the only relevant question is as a rule "what is the exact nature of the lesion ?" in diagnosing the chronically sick it may also be necessary to ask one or more of the following three questions

1 Is a significant organic lesion present ?

2 If such a lesion is present, are the symptoms at all due to it ?

3 If the answer to question 2 is Yes, to what extent should the symptoms be ascribed to the lesion and to what extent to the state of mind ?

Errors in answering all these questions are extremely common Patients who are in fact free of organic disorder may be given such labels as strained heart, myocarditis, intestinal auto intoxication, and early hyperthyroidism The symptoms are often ascribed wrongly to astigmatism, retroverted uterus, deflected nasal septum, visceroptosis, gastritis, hypertension, and innumerable other conditions It is widely assumed that all the symptoms have an organic basis whereas in fact they are largely of psychological origin This mistake is typically made in the case of those with well compensated heart lesions

Such wholly wrong diagnoses as strained heart and myocarditis are perhaps usually made by general practitioners But the wrong ascription of symptoms to astigmatism and other similar disorders is particularly a specialist's mistake The general physician faced with experimental stage With most deep burns in adults the dead tissue has to be excised by knife and scissors (when possible under a tourniquet) This should be done in the second, or early in the third, week At this stage the raw area so exposed is very receptive to a free graft cover, which is best applied at the operation for slough removal, but if oozing is excessive, or the area large, it may be delayed two to four days With refrigeration of skin grafts[9] these procedures can easily be staged the skin may be applied later without anæsthetic The electric dermatome has greatly simplified the problem of cutting grafts and has made it more often possible to provide cover with continuous sheets of split skin grafts rather than with discontinuous patches The surgical programme for deep burns should be arranged so that the raw area substantially healed within a month of the burn Some very extensively burnt patients, and the very young and very old, have to be handled at a slower pace, but rarely is there any good reason for deferring slough excision and completion of the primary skin graft cover beyond eight to twelve weeks, however extensive the burn

The management of cases admitted with granulations already present has become more radical[8,10] It is neither necessary nor desirable to continue dressings and cultures in order to obtain the ideal of bacterial sterility before surgery, for then, apart from the expense in materials and in labour, the graft is deposited on a fibrous base thicker than it need, or should, be for stability In the last seven years surgeons, with the combined benefits of antibiotics and of blood for replacement therapy, have tended increasingly to excise forthwith the whole granulating area down to unaffected deep tissues, thus providing a soft clean base for immediate cover by graft or flap[8,10]

---

9 Matthews D N *Lancet* 1945 i 775

10 Clarkson P Lawrie R S *Brit J Surg* 1946 33, 311

Points of View

SPECIALISATION

John W Todd

M.D Lond, M R C.P

CONSULTANT PHYSICIAN, FARNHAM HOSPITAL, SURREY

Of late years a steadily increasing proportion of young doctors have become specialists rather than general practitioners or, in the old sense of the term, consultants The number of recognised specialties has also greatly increased In the last century there were merely physicians, surgeons, ophthalmologists, ear, nose, and throat surgeons, dermatologists, obstetricians, alienists and perhaps a few others There are now in addition radiologists, radiotherapists, orthopædic surgeons, neurosurgeons, thoracic surgeons, faciomaxillary surgeons, neurologists, cardiologists, endocrinologists, gastroenterologists, psycho analysts, venereologists, anæsthetists, physiotherapists, and many more The patient who attends hospital may be seen not by one doctor but by a whole series of specialists, each of whom provides a report about the state of the particular region in whose study he is an expert It has even been suggested, especially in America, that general practice as it is now known is obsolescent and that a system of "group practice," each member of the group being a specialist, should take its place The patient would then have not his own doctor but his own group, the appropriate member of which would be summoned, according to the nature of the symptoms

With these changes specialism has acquired a heightened prestige The name specialist possesses a glamour which appeals alike to the young doctor and to the layman Probably few medical students now begin their studies intending to go into general practice, and they are apt to develop a contempt for the unfortunate G P, whose errors may be pointed out so disparagingly by clever young registrars and housemen (though perhaps with the admission that he should be more pitied than condemned, lacking as he does X rays and other facilities necessary to modern scientific medicine) After qualification, only those who fail, through lack of brains, luck, money, or influence, to become specialists regretfully fall back on to general practice The knowledgeable layman, who reads of the elaborate new machines needed for diagnosis, may concede that his old G P is well able to deal with a cold in the head or a bout of indigestion, but will insist that for a serious complaint a specialist is clearly necessary "After all," it may be said in excuse for the G P's failings, "he can't be expected to know as much about the heart as the heart specialist who has spent half his life in a close study of the disorders of that organ" A recent radio serial (*The Malindens*) contains a poignant scene in which an old man on his death bed sadly tells his daughter that his life has been a failure, because he aspired to be a surgeon but only became a general practitioner

In Britain, according to many observers, the new National Health Service has accentuated the decline of general practice and the advance of specialism, by making the lives of G P's even more harassing, while providing a large and certain income for young specialists with hospital appointments as consultants

The Specialist and Diagnosis

The immediate object of diagnosis is, as a rule, to explain the patient's symptoms Now, the symptoms can never be wholly explained by a single organic cause, the state of mind must also be taken into consideration The degree of pain felt by an injured man does not depend on the nature of his injury alone If he is of sensitive temperament he may suffer great pain, if he is phlegmatic and unimaginative his pain may be slight When diagnosing the acutely sick it may nevertheless be correct to leave psychological considerations out of account For example, it is of small moment from the diagnostic (though perhaps not from the therapeutic) standpoint that a man's highly sensitive temperament causes him to describe the pain of a whitlow as overwhelmingly severe But the symptoms of many of those with chronic organic lesions should be ascribed far less to the lesion itself than to the state of mind, to ignore the latter is a grave mistake Moreover, symptomless organic disorders are commonly associated with symptoms whose origin is wholly to be sought in the mind In diagnosing the chronically sick, therefore, the following four questions may each need to be answered

1 Is a significant organic lesion present ?

2 If such a lesion is present are the symptoms at all due to it ?

3 If the answer to question 2 is Yes, to what extent should the symptoms be ascribed to the lesion and to what extent to the state of mind ?

4 What is the exact nature of the lesion ?

In the study of the acutely sick only the fourth question is usually relevant

DIAGNOSIS IN THE NARROW SENSE

The process of reaching diagnoses in the narrow sense of discovering the nature of the lesion presents greatly differing problems In some cases a complete and satisfactory diagnosis can easily be reached, in others nothing better than a descriptive label can ever be given It is therefore very difficult to generalise

Similar considerations apply to other conditions whose treatment is apparently complicated, such as peptic ulcer, congestive heart failure, and rheumatoid arthritis One gastro enterologist will treat a peptic ulcer patient with prolonged rest in bed, no smoking, two hourly feeds of citrated milk and no other food, olive oil, belladonna, and mag carb co thrice daily, another will treat an identical case with a diet from which little is forbidden but which is taken at frequent intervals, will give no olive oil or belladonna, will allow smoking, and will encourage the patient to remain up and about One physical medicine specialist will order a victim of rheumatoid arthritis to bed for weeks and give him in turn short wave diathermy, massage, wax baths, and gold injections, another who practises in a spa will keep a similar patient out of bed throughout and give him warm baths, the appropriate saline drinks, and vaccines derived from organisms in the stools, and will eradicate his septic foci Indeed, in respect of diet, régime, and other general forms of treatment, the greatest experts notoriously disagree with each other at any one time, while the experts of today disagree even more violently with the teachings of the experts of yesterday

It seems absurd to pretend, therefore, that *because* a man is a specialist in some disease, his opinion as to the value of one of these general remedies for this disease is superior to that of the general physician The one form of medical treatment on whose merits there is wide spread agreement among all the experts is specific drugs, and it could not be pretended that a specialist is necessary to order them

Elsewhere[1] I advanced the view that most patients should be given simple psychotherapy, in the shape of an explanation of their symptoms, reassurance, and encouragement Clearly such psychotherapy does not require the services of a specialist in some bodily region, and still less need a psychiatrist be called in to reassure a patient who has a fear of cancer or other similar worry But psychotherapy of this kind is commonly omitted, and if it is given, it may consist in nothing more than a brusque statement to the effect that nothing serious has been found, the physician making no attempt either to discover whether the patient has some particular worry which can be eased or to tell him why he has his symptoms The specialist, so often wrapped up in the minutiæ of the system to which he devotes his life, is more apt to fail here than is the general physician For example, the cardiologist faced with the patient who complains of palpitation, weakness, giddiness, and the usual emotional symptoms, may correctly say that the heart is organically normal, but he may easily fail to discover that the patient's father died a sudden cardiac death at the age the patient has now attained, and he may fail to explain that such symptoms are merely the manifestations of a nervous temperament In consequence the patient may be unconvinced that his heart is normal and continue to fear that he will share his father's fate It has already been noted that the specialist is particularly liable to ascribe all the symptoms to some organic lesion affecting his own system, when in fact they are largely of psychological origin In so far as he does this, so will he omit the psychotherapy which can often minimise the disability of those with organic diseases

The Specialist and Research

Specialism is sometimes defended on the ground that without it progress in medicine could hardly occur The doctor who only sees an occasional example of some disease can rarely reach useful conclusions about its ætiology, pathology, natural history, and treatment Advances in such knowledge have often been made by painstaking workers in hospitals who collected cases of the disease and then subjected them to a careful inquiry, investigated them thoroughly, treated them with some new specific drug by the alternate case method, or followed them up over the course of years Moreover, as Cohen[2] has pointed out, in some fields “ specialisation in research is perhaps inevitable because of the intricacy of many of the modern instruments of research, e g, the electron microscope, special methods of histopathology and bacterial culture or spectroscopic analysis ”

But even the most fervid advocates of specialism would not say that clinicians should be subdivided into disseminated sclerosis specialists, heart block specialists, varicellologists, ulcerative colitologists, and so forth And equally it could not be pretended that the young man who is keen on research should devote the whole or many years of his life to doing nothing else but studying a single disease The clinical research worker, for the sake of his enthusiasm, sanity, and judgment, should clearly do something besides his particular investigation

The following question therefore arises is the specialist in a certain region any better able than the general physician to carry out a research into a single disease affecting that region? For example, if a neurologist and a general physician both spent, say, a third of their time for a period of ten years in seeking the cause of disseminated sclerosis, is there any reason to suppose that the former would be more successful? Or would a cardiologist who followed up a large number of patients with rheumatic heart disease for half his life reach nearer the truth than the general physician who did the same? There is no apparent reason for giving an affirmative answer to such questions as these The necessity of special studies for the purpose of advancing knowledge provides no justification for specialisation in the ordinary meaning of that term

The Legitimate Medical Specialties

Although (if my arguments are sound) the main justification for specialisation among clinicians is the necessity for mastering difficult surgical techniques, there are nevertheless perhaps a few legitimate specialties inside medicine An obvious example is pædiatrics, for it cannot be objected that a pædiatrician is encouraged to devote his whole interest to some small region of the body, or that through following his specialty he is liable to develop a distorted viewpoint And the problems presented by infants and very young children are undoubtedly very different from those presented by adults It may nevertheless be wondered whether even here the physician who spends all his time among children is likely to be better than the physician who also deals with adults A similar “ defence ” may be made of geriatrics—a specialty of which more and more has been heard of late But the justification for geriatrics is far less than for pædiatrics There are few if any diseases peculiar to old people For example, non fatal strokes leaving paralysis, which provide one of the most common and difficult problems of old age, are seen occasionally in people below 50 and quite often in the under 60s And one often sees men in the 80s who are vigorous in mind and body while others in their 60s are living a vegetative existence It is sometimes suggested that special wards should be set aside for geriatric cases But is it not far better for old men with the more acute and recoverable conditions—and it is they who should be given most consideration—to share wards with the young? Is not the atmosphere thereby improved, and are they not thereby encouraged to recover? I believe too that, in spite of the “ write a patient complaining of a feeling of pressure on top of the head would probably conclude that no organic diagnosis could be made But if the patient chanced to have half a dioptre of astigmatism in one eye, or an opaque antrum in the radiograph, an ophthalmologist or otorhinolaryngologist might easily reach the erroneous conclusions that these conditions were the cause of the headache Similarly, few but gynæcologists would deduce that chronic low backache was due to a retroverted uterus, and few but gastro enterologists who possessed gastroscopes would attribute vague dyspepsia to chronic hypertrophic gastritis The third and more subtle error of ascribing symptoms wholly to organic disease when in fact they are partly or largely of psychological origin is also characteristically made by the specialist The cardiologist, for instance, with his attention fixed on the murmurs, the blood pressure readings, the pulse, the radiological appearances of the heart, and the fascinating defects in the electrocardiogram, may assume that a patient's dyspnœa and palpitation are wholly due to rheumatic heart disease when in fact they are predominantly emotional

---

[1] Todd J W Rational Medicine Bristol 1949

[2] Cohen H *Proc R Soc Med* 1949 42 1035

Errors such as these are often not recognised , and a doctor may perpetrate them over and over again in the course of years and never realise that he has made a mistake The essential reason for making them is the widespread inability to see the whole patient in proper perspective , for too many doctors, and particularly specialists, are only aware of a *conglomeration of organs* facing them across the consulting room table It is sometimes said of a man who has been appointed to a hospital as a general physician that " he isn't interested in stomachs, chests, and nerves, but only in hearts and kidneys " These words are a grave indictment, for they imply that he cannot be interested in people, but only *in certain bits of their bodies*

The Specialist and Treatment

SURGERY

The ordinary practitioner cannot master every detail of surgical technique Even the whole time surgeon cannot become proficient in the performance of every operation in every region of the body The fact that a surgeon is exceedingly skilful in doing a prostatectomy provides no evidence that he can efficiently excise a pituitary tumour And the simplest operations may be carried out very badly by experts in some branch of major surgery The master of gastrectomy may admit that when a patient requires an intravenous saline infusion, his house surgeon can give it better than he can himself

In surgery, therefore, specialisation is desirable—even the ultraspecialisation which has been so often condemned in recent years The general surgeon who is willing to tackle everything—and even more the general practitioner who is willing to do the same—are rightly obsolescent figures If further difficult surgical techniques are elaborated in the future, surgical specialisation of a degree even greater than that usual now may become justified

But in that part of surgery which is at least as important as the actual technical procedure—i e , the selection of cases for operation *and the selection of the appropriate* operation for the particular case—the situation is very different The fact that a surgeon can brilliantly perform a gastrectomy is no reason for supposing that he will select the cases most suitable for this operation And of the factors which should determine whether an operation is indicated, a study of the diseased region (in which *the specialist may be most proficient*) is often not the most important For example, in deciding whether herniorrhaphy should be done, the patient's age, build, and occupation, whether he has a cough, and his personal wishes may all rightly be taken into consideration, in addition to the local condition Sometimes a most important factor in determining the need for surgery is the patient's state of mind This may be so in the case of torn internal cartilage of the knee, for the subject of sound personality who strives to recover, perseveres with his exercises, and ignores his pain makes far better progress than the weak willed dullard with a similarly *damaged* knee who is satisfied *to remain a semi invalid*

In the ability to see all these factors in the right perspective, *the specialist surgeon, so far from being* superior, may be much inferior to the non specialist The very fact that he is an expert on some small region of the body tends to make him reach his conclusions from a study of this region alone There is, moreover, a natural tendency to exaggerate the importance of operations in one's own territory

An important reason why operations are wrongly done lies in the error previously discussed of making wrong diagnoses in the broad sense of improperly relating some lesion to the symptoms The *otorhinolaryngologist* may be right in saying that an antrum is infected, but is wrong in performing antrostomy, when the infection is not the cause of the headache of which the patient complains Or the neurovascular surgeon may do an extensive sympathectomy on a patient whom he rightly deems to have hypertension The blood pressure consequently falls, but the patient is no better, because his symptoms were not caused by the hypertension This sort of error is particularly made by the specialist

MEDICINE

Considerations such as these have no relevance to the physician, except in so far as he performs *such surgical* procedures as inducing artificial pneumothoraces Giving his remedies—drugs, régimes, diets, and psychotherapy—involves no technical skill Moreover, provided the diagnosis is correct, *any newly qualified* house physician can prescribe the drugs specific against infections just as well as can the highly experienced specialist , and such drugs provide the most striking triumphs of therapy Yet one encounters the notion that the treatment of those sick of certain conditions is difficult because of its complexity, and therefore that the specialist may succeed *better* than the *general physician* One such condition is diabetes mellitus

One diabetician will admit the newly diagnosed case of severe diabetes to a ward staffed by sisters and dietitians with long experience of looking after diabetics, for the purpose of " stabilisation " A dietary prescription containing the exact quantities of carbohydrate, fat, and protein is written , and afterwards at each meal a neat tray arrives from the diet kitchen on which are several aluminium dishes each containing the appropriate *amount of some* basic foodstuff Should the patient ask for more, his plea will be refused The insulin dosage will then be raised until the state of " stabilisation " has been achieved, as proved by the absence of sugar from all or nearly all the urine specimens On being discharged the patient will be provided with a scale, on which all his food except perhaps green vegetables *and* fruit has to be weighed, and a long diet-sheet giving details of the quantities of each foodstuff he should eat at each meal He is naturally profoundly depressed at the prospect before him Subsequently he attends the clinic and has *to be* " re stabilised " as he develops frequent hypoglycæmic attacks But another diabetician will utterly condemn a scheme of the kind just described He will keep such a patient out of hospital altogether (unless he is *ketotic) and* tell him to continue to eat his normal diet while increasing his insulin until his symptoms have gone

Similar considerations apply to other conditions whose treatment is apparently complicated, such as peptic ulcer, congestive heart failure, and rheumatoid arthritis. One gastro-enterologist will treat a peptic ulcer patient with prolonged rest in bed, no smoking, two-hourly feeds of citrated milk and no other food, olive oil, belladonna, and mag. carb. co. thrice daily; another will treat an identical case with a diet from which little is forbidden but which is taken at frequent intervals, will give no olive oil or belladonna, will allow smoking, and will encourage the patient to remain up and about. One physical medicine specialist will order a victim of rheumatoid arthritis to bed for weeks and give him in turn short-wave diathermy, massage, wax baths, and gold injections; another who practises in a spa will keep a similar patient out of bed throughout and give him warm baths, the appropriate saline drinks, and vaccines derived from organisms in the stools, and will eradicate his septic foci. Indeed, in respect of diet, régime, and other general forms of treatment, the greatest experts notoriously disagree with each other at any one time, while the experts of today disagree even more violently with the teachings of the experts of yesterday.

It seems absurd to pretend, therefore, that *because* a man is a specialist in some disease, his opinion as to the value of one of these general remedies for this disease is superior to that of the general physician. The one form of medical treatment on whose merits there is widespread agreement among all the experts is specific drugs; and it could not be pretended that a specialist is necessary to order them.

Elsewhere[1] I advanced the view that most patients should be given simple psychotherapy, in the shape of an explanation of their symptoms, reassurance, and encouragement. Clearly such psychotherapy does not require the services of a specialist in some bodily region; and still less need a psychiatrist be called in to reassure a patient who has a fear of cancer or other similar worry. But psychotherapy of this kind is commonly omitted; and if it is given, it may consist in nothing more than a brusque statement to the effect that nothing serious has been found, the physician making no attempt either to discover whether the patient has some particular worry which can be eased or to tell him why he has his symptoms. The specialist, so often wrapped up in the minutiæ of the system to which he devotes his life, is more apt to fail here than is the general physician. For example, the cardiologist faced with the patient who complains of palpitation, weakness, giddiness, and the usual emotional symptoms, may correctly say that the heart is organically normal; but he may easily fail to discover that the patient's father died a sudden cardiac death at the age the patient has now attained, and he may fail to explain that such symptoms are merely the manifestations of a nervous temperament. In consequence the patient may be unconvinced that his heart is normal and continue to fear that he will share his father's fate. It has already been noted that the specialist is particularly liable to ascribe all the symptoms to some organic lesion affecting his own system, when in fact they are largely of psychological origin. In so far as he does this, so will he omit the psychotherapy which can often minimise the disability of those with organic diseases.

The Specialist and Research

Specialism is sometimes defended on the ground that without it progress in medicine could hardly occur. The doctor who only sees an occasional example of some disease can rarely reach useful conclusions about its ætiology, pathology, natural history, and treatment. Advances in such knowledge have often been made by painstaking workers in hospitals who collected cases of the disease and then subjected them to a careful inquiry, investigated them thoroughly, treated them with some new specific drug by the alternate-case method, or followed them up over the course of years. Moreover, as Cohen[2] has pointed out, in some fields "specialisation in research is perhaps inevitable because of the intricacy of many of the modern instruments of research, e.g., the electron microscope, special methods of histopathology and bacterial culture or spectroscopic analysis."

But even the most fervid advocates of specialism would not say that clinicians should be subdivided into disseminated sclerosis specialists, heart-block specialists, varicellologists, ulcerative colitologists, and so forth. And equally it could not be pretended that the young man who is keen on research should devote the whole or many years of his life to doing nothing else but studying a single disease. The clinical research worker, for the sake of his enthusiasm, sanity, and judgment, should clearly do something besides his particular investigation.

The following question therefore arises: is the specialist in a certain region any better able than the general physician to carry out a research into a single disease affecting that region? For example, if a neurologist and a general physician both spent, say, a third of their time for a period of ten years in seeking the cause of disseminated sclerosis, is there any reason to suppose that the former would be more successful? Or would a cardiologist who followed up a large number of patients with rheumatic heart disease for half his life reach nearer the truth than the general physician who did the same? There is no apparent reason for giving an affirmative answer to such questions as these. The necessity of special studies for the purpose of advancing knowledge provides no justification for specialisation in the ordinary meaning of that term.

The Legitimate Medical Specialties

Although (if my arguments are sound) the main justification for specialisation among clinicians is the necessity for mastering difficult surgical techniques, there are nevertheless perhaps a few legitimate specialties inside medicine. An obvious example is pædiatrics, for it cannot be objected that a pædiatrician is encouraged to devote his whole interest to some small region of the body, or that through following his specialty he is liable to develop a distorted viewpoint. And the problems presented by infants and very young children are undoubtedly very different from those presented by adults. It may nevertheless be wondered whether even here the physician who spends all his time among children is likely to be better than the physician who also deals with adults. A similar "defence" may be made of geriatrics—a specialty of which more and more has been heard of late. But the justification for geriatrics is far less than for pædiatrics. There are few if any diseases peculiar to old people. For example, non-fatal strokes leaving paralysis, which provide one of the most common and difficult problems of old age, are seen occasionally in people below 50 and quite often in the under 60s. And one often sees men in the 80s who are vigorous in mind and body while others in their 60s are living a vegetative existence. It is sometimes suggested that special wards should be set aside for geriatric cases. But is it not far better for old men with the more acute and recoverable conditions—and it is they who should be given most consideration—to share wards with the young? Is not the atmosphere thereby improved, and are they not thereby encouraged to recover? I believe too that, in spite of the "write up " which geriatrics has recently had, it may be depressing to deal with none but the old, and that the physician who has patients of all ages is likely to handle his old patients better than the specialist geriatrician

---

[1] Todd, J. W. Rational Medicine. Bristol, 1949.

[2] Cohen, H. *Proc. R. Soc. Med.* 1949, 42, 1035.

Of the other medical specialties, perhaps dermatology is the easiest to justify, for the diseases of the skin form a genuinely distinct group which are comparatively rarely related to other bodily diseases The dermatologist, moreover, can hardly reach the wrong conclusion that a patient with obscure symptoms has a skin condition, and he must be extraordinarily blind to overlook the psychiatric aspects of skin diseases, for it is obvious that they may have a disastrous effect on the psyche, while sometimes emotional and hysterical disorders are apparently important in their ætiology

Another possibly legitimate specialty is neurology Certain diseases of the nervous system cause manifestations whose assessment and analysis requires much practice and an intimate knowledge of the anatomy and physiology of the nervous system—a knowledge which the ordinary physician rarely possesses Nevertheless, the bounds of neurology are very indistinct, and the victims of many neurological diseases require to a particularly high degree that sympathetic understanding from their medical advisers which the specialist so typically lacks The best neurologist, therefore, is probably not he who devotes his whole attention to the nervous system but he who is a general physician as well

Selection and Training of Specialists and Consultants

In recent years in Britain the typical potential specialist or consultant does some house appointments after qualification, obtains higher degrees or diplomas, becomes a registrar and, after three or more years, is appointed to hospitals with the title of consultant This process no doubt turns out men who are very knowledgeable in their subjects and (if they are surgeons) have mastered some technique But I believe it fails to give men the ability to see the problems of medicine in proper perspective It has often struck me that the average surgical registrar tends to be interested in operating, to the exclusion of all else The interest of the average medical registrar, on the other hand, is particularly aroused by the very rare and obscure case Some general physicians and surgeons may in course of time overcome the defects of their early training, but the whole manner of working of the ultraspecialists tends to distort their perspective, with the result that they may fail to inculcate the right attitude into their own registrars, whose attitude at the beginning of *their* consultant careers may in consequence be particularly distorted

The problem would, I believe, be largely solved if all clinical registrars were selected from the ranks of the general practitioners The minimum period spent in general practice should be, say, three years (It should not merely be a matter of months, for then it might easily be considered as a wasted interlude before returning to hospital and doing once more "real medicine," in the shape of inserting cardiac catheters, studying electro encephalograms, estimating 17 ketosteroids in the urine, and other similar procedures) Every medical student who intended to become a clinician would then naturally acquire the idea that the purpose of his training was to make him a competent general practitioner

Specialists recruited in this way could hardly be interested in the defects of some small region of the body to the exclusion of all else, but would also be interested in *patients* They would not be so blind to the psychiatric aspects of organic disease or the disturbing effects of psychiatric upsets on the bodily organs And they would better appreciate that the good general practitioner wishes to have advice as to how his patients can be helped, not a learned dissertation on some obscure aspect of a rare disease

The majority of general practitioners would applaud such a scheme as this and would accept more readily the opinions of consultants who had themselves been in general practice than of those who had spent their whole careers in the artificial atmosphere of a hospital If their patients were seen by a registrar instead of by the chief, they would not—as they often are now—be particularly annoyed The scheme would carry with it the further advantage of discouraging the recently qualified from hanging about teaching hospitals doing odd jobs as clinical assistants while waiting for registrarships to become vacant, and the ex registrars from acting similarly while waiting for dead men's shoes Perhaps general practice would become, not the last refuge of those who could do nothing else, but the usual goal of a high proportion of medical students

Conclusion

The main justification for specialisation among clinicians is the necessity for mastering difficult techniques The various branches of surgery are all legitimate specialties for therapeutic reasons, and ophthalmology, otorhinolaryngology, and perhaps a few others are also legitimate for diagnostic reasons The same considerations apply to anæsthetics and radiotherapy But in the field of medicine as opposed to surgery, and also in the important part of surgery which precedes the actual operation, there is little to be said in favour of specialisation, and much to be said against it The modern tendency to subdivide physicians into cardiologists, gastro enterologists, phthisiologists, diabeticians, rheumatologists, kidney specialists, and the rest is regrettable Even in so far as certain medical specialties, such as pædiatrics and neurology, are justifiable, those who practise them would usually be better if they were also general physicians

The value of the physician is derived far more from what may be called his general qualities than from his special knowledge A sound knowledge of the ætiology, pathology, and natural history of the commoner diseases is a necessary attribute of any competent clinician. But such qualities as good judgment, the ability to see the patient as a whole, the ability to see all aspects of a problem in the right perspective, and the ability to weigh up evidence are far more important than detailed knowledge of some rare syndrome, or even the possession of an excellent memory and a profound desire for learning Many of the eminent consultant physicians of the 19th century were said to be quite aware of their superior general qualities One gathers that they did not hesitate to reach confident conclusions about their cases, while lesser men unhesitatingly obeyed their orders The average modern physician appears more modest (perhaps because he is aware that some later investigation may disprove any confident statement on his part), and prefers to accept the view that his detailed knowledge rather than his superior mental prowess justifies his position If he is a gastro enterologist, he may refuse even to look at a patient who has cardiac symptoms, but may be resentful if a physician who is not a gastro enterologist questions his verdict on a dyspeptic subject But if a consultant physician lays no claim to infallibility in any situation and essays to do no more than give general practitioners a second *opinion* in cases where they are in difficulty, there is no implication that his mental prowess is of a different order to that of those he is advising

If these views are sound, even the general practitioner (except in so far as he may lack certain facilities) is often in as good a position as the most learned specialist to reach the right conclusions about his cases. I am not concerned here with the question of whether or not the standard of general practice is in fact high. But I believe that the patient with a "medical" condition is far better off under the care of a first-rate general practitioner than of an indifferent specialist who is an authority on the particular condition under consideration. On the other hand, no general practitioner is competent to do a difficult surgical operation.

Much has been heard in recent years in Britain of the shortage of specialists. As regards physicians, I do not believe that there is any real shortage. The medical outpatient departments of many hospitals are no doubt overcrowded, but much of the overcrowding is due to the attendance of patients whose general practitioners desire, not a second opinion, but an investigation which they cannot get done themselves. More overcrowding is due to the public's insistence on seeing a specialist, and to bad general practitioners who refer cases unnecessarily.

The present difficulties should, I believe, be overcome not by multiplying specialists, but by increasing the number and improving the quality of general practitioners, by giving them the facilities which so many now lack, and by a propaganda campaign to persuade the public that there is no magic in the name specialist. Top priority in the capital development schemes of the National Health Service should be given to the provision of health centres where general practitioners could have the more important investigations done. For even when the present-day enthusiasm for investigating is discounted to the utmost, no doctor can be efficient without the aid of certain X-ray films, blood counts, urinary examinations, and a few other tests.

Summary

The need for specialisation in diagnosis, treatment, and research is considered.

The conclusion is reached that the main justification for specialisation among clinicians is the necessity for mastering difficult surgical techniques, and that in medicine specialisation is in general harmful. The view is advanced that registrars should be selected from the ranks of the general practitioners.

I wish to thank Sir Henry Cohen for his encouragement and my father for his help in revision.

Parliament

Penicillin (Merchant Ships) Act

In the House of Lords on Feb. 15 the Royal Assent was given by commission to this Act.

QUESTION TIME

Hospitals and Electricity Cuts

In answer to a question Mr Alfred Robens, parliamentary secretary to the Ministry of Fuel and Power, said that the system of telephone warnings of power cuts to hospitals and other large users was being extended and experiments were being made with special short-wave radio transmitting and receiving sets. There were, however, still formidable difficulties to be overcome.

Children's Emergency Fund

In answer to a question Mr Ernest Davies, under-secretary of state for foreign affairs, stated that the Government were proposing to ask parliamentary authority for a further contribution to be made to the United Nations International Children's Emergency Fund of £100,000.

Tuberculous Pensioners

Brigadier A. H. Head asked the Minister of Pensions what were the numbers of tuberculous pensioners of the 1914–19 war and the 1939–45 war, respectively, and the total numbers of those two categories who were classified as 100% disabled.—Mr G. A. Isaacs replied: The numbers are estimated to be 17,000 and 52,000 respectively; of these pensioners 3800 and 28,700 respectively are estimated to be in receipt of pension at the 100% disablement rate.

100 per cent Disablement Pensions

Brigadier Head asked the Minister how many pensioners were now receiving the 100% rate, plus both the unemployability supplement and constant attendance allowance.—Mr Isaacs replied: 4550.

Marriage Allowances of National Service Medical Officers

Dr Charles Hill asked the Minister of Defence whether he was aware that married National Service medical officers, aged 25 years or over, received a marriage allowance of 12*s.* 6*d.* a day, as compared with a corresponding allowance of 18*s.* 6*d.* a day payable to short-service or permanent officers; and whether he would remove this anomaly, having regard to the fact that the upper age limit for the conscription of medical practitioners was 30 years, as against 26 years for other sections of the community.—Mr Emanuel Shinwell replied: The increases in marriage allowance given to regular officers in November, 1948, were intended to meet exceptional expenses which are not normally incurred by National Service officers, whether medical officers or not. It is, therefore, not possible to treat medical officers in this respect more favourably than other National Service officers. Dr Hill: Bearing in mind that the upper age for conscription for medical officers is 30, and, further, that the cost of maintaining a wife, special expenses, and other burdens is no less to a National Service officer than to a short-term officer, will the Minister reconsider the position? Mr Shinwell: We went into the matter very carefully in order to avoid all possible hardship. The fact is that the liabilities of the Regular medical officer are much more severe than in the case of the National Service officer.

Identification of Gas Cylinders

Dr Hill asked the Minister of Health whether he was aware of the recommendations proposed by a representative conference of the medical profession to introduce at an early date an agreed code of colour markings of gas cylinders and for the manufacture and use of a non-interchangeable valve that could be attached to United States and British cylinders with the object of avoiding fatal accidents as a result of the misidentification of a cylinder prior to or during the administration of an anæsthetic; and what steps he proposed to take to provide doctors within the National Health Service with the cylinders and valves they desired to eliminate fatal accidents.—Mr H. A. Marquand replied: I am aware of the recommendations referred to. A colour code and non-interchangeable valves are under consideration by the British Standards Institution and the International Organisation for Standardisation. When agreement is reached urgent consideration will be given to revision of the existing British Standards.

Cost of Drugs

Mr H. Hynd asked the Minister of Health what was the average cost per patient of drugs supplied direct to the patient by chemists under the National Health Act for the last 12 months for which figures are available.—Mr Marquand replied: The average cost (including chemists' remuneration) of drugs supplied per person on prescribing doctors' lists for the year ending Dec. 31, 1949, was 15*s.* 7½*d.*

Hospital Accommodation for Chronic Sick

In answer to a question Mr Marquand stated that 7712 chronic sick persons in England and Wales were awaiting admission to hospital on Dec. 31, 1949, the latest date for which complete returns were available. On the same date there were in chronic sick hospitals 7575 empty beds, more than half of which were unstaffed.

War-time Lists in Tuberculosis Treatment

In answer to a question Mr Marquand stated the number of cases of tuberculosis awaiting admission to hospitals or sanatoria at Dec. 31 last in the North-west, North-east, South-east, and South-west metropolitan areas respectively were 1566, 933, 1087, and 1200.

Medicine and the Law

Ministry's Liability for Hospital Staff's Negligence

As long as the authority of Hillyer *v* St Bartholomew's Hospital (decided in 1909) prevailed, it could be contended that a hospital had the duty to use care in selecting the surgeons, doctors, or nurses on its professional staff, but was not liable if the staff acted negligently in a matter of professional care or skill Lord Justice Kennedy's judgment said so , Lord Justice Farwell decided the case on narrower grounds In Gold *v* Essex County Council in 1942[1] the Court of Appeal reviewed Hillyer's case and chose to follow Lord Justice Farwell , it declared that Lord Justice Kennedy, in his remarks about nurses, went far wider than the scope of the case required, and that, as Lord Dunedin observed in Lavelle *v* Glasgow Royal Infirmary, those remarks were mere *obiter dicta*

It is now certain that the liability of a hospital is much more extensive than was supposed in Hillyer's case in 1909 This was made clear afresh by the Court of Appeal in Cassidy *v* Ministry of Health on Feb 15 Mr Cassidy went into a Liverpool hospital with a condition of his left hand which was diagnosed as Dupuytren's contracture An operation was carried out , the treatment involved keeping the hand and lower arm rigid in a splint for several days When the hand was released after 14 days, two fingers (those operated upon) were completely stiff and two others were affected , the left hand had become useless He sued Liverpool Corporation, which then owned and controlled the hospital , later, when the National Health Service was initiated, the Ministry of Health was substituted as defendant , the Ministry brought in a Canadian doctor, at the time of the operation a whole time assistant medical officer of the hospital, as third party The doctor's evidence was taken on commission in Vancouver

At the trial Mr Justice Streatfield, without deciding whether the doctor was a servant or agent of the Ministry or whether the Ministry would be liable for his negligence in that capacity, held that no negligence had been established against the doctor or any other member of the hospital staff The Court of Appeal says this was wrong it seemed to be a case of *res ipsa loquitur*—the thing spoke for itself—and a jury could have found negligence on the facts as stated But, if so, was the Ministry liable ? The doctor was employed, like the nurses, as part of the permanent staff of the hospital If, in the phrase used by Lord Greene in Gold's case, a patient knocked on the door of a hospital, he would expect to find inside medical and surgical treatment and nursing , if the treatment or the nursing were negligent, the hospital must be liable, whether the fault was that of a nurse or of the permanent medical staff Lord Justice Denning, whose powerful argument at the bar in Gold's case will be remembered, said that a hospital endeavours to cure by means of the staff which it employs , it has no ears of its own with which to listen through the stethoscope, and no hands to hold the knife If its staff is negligent, it is just as much liable for the negligence as is anyone else who employs others to do his work for him If a patient himself selects and employs doctor or surgeon (as in Hillyer's case), the hospital is not liable , but, if doctor or surgeon, whether a consultant or not, is employed and paid by the hospital and not by the patient, the hospital is liable for his negligence in treating the patient The Ministry of Health, it seems, can now sue the Canadian doctor, if it so desires

---

[1] See *Lancet*, 1942 ii, 127

In England Now

A Running Commentary by Peripatetic Correspondents

We cannot eat but little meat ,
The ration is not big
We try no end to make a friend
Of one who keeps a pig
The butchers' shops contain no chops,
Nor luscious offals hold
I ask you, Webb, at this low ebb
—If I may make so bold

Back and sides go where, go where ?
For export ? Are they sold
For bully ? God knows who consumes the stuff
—Pass me the prunes and mould

We have no roast to play the host
—We dare not light the fire—
But ancient ewe we have in lieu
Such ewe we not desire
We have no stint of spuds or mint
But no allaying lamb,
And, as I live, what wouldn't we give
For a jolly good chunk of ham ?

Back and sides go where, go where ?
For export ? Are they sold
For bully ? God knows who consumes the stuff
—Pass me the prunes and mould

* * *

It would be nice if the committee now considering general practice could find some way of rewarding practitioners according to the responsibilities they really undertake rather than by mere head counting A little while ago I was called in consultation by an elderly doctor practising in an unprosperous suburb " I have never seen a case like this before," he told me, " but I have read of them I think it is a spontaneous pneumothorax. We were not taught about that in my student days." At the patient's house we found a young man who gave us the characteristic history of sudden pain in the chest and shortness of breath, and he had the textbook signs. After giving him a few words of reassurance and arranging for a chest X ray later, we left

The point of the story is that there was no suggestion that the patient's proper place was in hospital—and this in an area where doctors send people to the outpatient department to have their urine tested One does not want to tempt any man to assume responsibilities beyond his skill, but surely my elderly friend deserves a larger reward than those who cannot treat a straightforward pneumonia without the aid of the Emergency Bed Service ?

* * *

Doctor's letter to his executive council

" This is not a complaint but a record of Mr T, who sent for me to visit him at home, but who happened to be arriving on his bicycle as I arrived to see him He was informed that if he was fit to ride a bicycle on a frosty day he ipso facto is fit to attend this surgery, and I did not go upstairs to see him Please do not trouble to reply as I consider this sort of happening to be part of our daily relationship with the public as a whole "

Medical benefit committee's comment

The Service regulations make no provision for the investigation of a complaint by a practitioner against a patient

And that's that

* * *

When my wife drew attention to his little pigs in our garden, Mr Larks did not, as expected, engage to keep these animals on his own side of our fence All he said was " Wonderful what they do in the time ! "

One's wife of course is prejudiced, living on the spot , and I like to take a broader view In the past few thousand years, I said to myself, this situation must have arisen before There must be a Precedent , and wherever freeborn Englishmen gather they will know about pigs invading gardens Encountering some free-born Englishmen in the train, I was glad to find that Mr Larks hadn't a leg to stand on. Rabbits—yes Rabbits are creatures of the wild, and if I want to keep them out I must make my fence rabbit-proof But pigs—no The pigs of Sussex are now definitely domesticated, and their owners are therefore bound to see that they don t ravage neighbouring property

Very true said I But just for confirmation I raised the question again in the help-yourself department of my club—which not only contains freeborn Englishmen but is practically the remains of the old Saxon Witanagemot After tactfully offering to advise a solicitor on how to get his ward trained as a hospital dietitian, I felt I could decently broach my pigs What, then, was my horror—and that of many clubmen present—to hear him say at once that anyone who wants to keep an animal (or, no doubt, several animals actually in this one litter there are 11, and more are promised) off his property must erect and maintain a fence that will keep it (them) out' But suppose Mr Larks bred vipers, I cried must I then reinforce my fence with zinc gauze ? Vipers are different, said the lawyer, they are Dangerous Animals If my present fence does not keep out small pigs (and it certainly doesn t) and if such pigs effect an entry (as they certainly do) I may not even eat them. all I may do is impound them and ask the owner to take them away, or see that they are conducted back to the boundary without unnecessary use of force (Actually I have already entrusted this latter duty to our dear dog)

All this information sounds simple in the clear way I've set it down, but it was complicated by the interjections of a kind but slightly deaf man a little way up the table who thought I was seeking help over the old problem of keeping cats from asphyxiating my baby He suggested a net over the pram He also thought that dogs should not be kept for pleasure, and that the care so often lavished on pet animals should be devoted to our own species

I should be more upset about all this but for a very wise remark made by one of the most venerated members of the Witan He recommended me to revenge myself on Mr Larks by keeping on my premises, not necessarily under complete control, a number of animals of a kind more subtle and more destructive even than pigs It was then I remembered that my wife and I did in fact choose our present home largely because we thought it would be nice for Andrew, Duncan, Colin, and Robin to see a good deal of the farm

* * *

During the Christmas holidays the family took me for my annual visit to the pictures There was an excellent programme, but what interested me particularly was a short film produced under the auspices of the New Zealand government, which vividly portrays the voyage made four times a year by an auxiliary ketch, the *New Golden Hind*, as a relief ship to some of the distant Pacific islands administered by the Dominion I have been reading, more or less in their original form, Captain Cook's diaries of his voyages among these very islands Besides being fascinating adventure stories these diaries contain much medical information For Cook was not only a superb seaman but also remarkably well versed in preventive medicine In applying the medical knowledge of the time he was ably supported by the surgeons who sailed with him, and their joint efforts were a major factor in the success of the expeditions The film shows what hazards this great navigator had to face in the Pacific and his descriptions apply equally well today If he had come with me to the cinema though he would have been astonished at the changed conditions of life on the islands and dumbfounded at the medical and dental services supplied for the inhabitants by the New Zealand government. If all the Europeans who visited the Pacific in early days had been of Cook s calibre the islanders would have escaped a great deal of disease and ill-treatment, but it is comforting to know that so much is being done to atone for the past evils

* * *

Aphorism of the Week

Lay the ghost of your buried mistake next time

Letters to the Editor

DIAMINODIPHENYLSULPHONE

SIR,—I am sorry that my old friend Dr R G Cochrane (in your issue of Feb 3) reported so much difficulty with the treatment of leprosy with D.A.D P S in India This treatment might well claim him as its father, for he was the first worker to use it,[1] unfortunately in doses too high to avoid toxicity Even now, with a much reduced dosage, he finds his child troublesome, and would apparently rather like to disown it There are, however, plenty of other workers who are keen to adopt it, some of them in India [2–5] In the Nigeria Leprosy Service it is the standard treatment, and now, in February, 1951, 17,000 cases are receiving this treatment Several other published reports [6–15] and several personal communications are favourable, and, in fact, of all the many workers who have now tried it, only one group—the group in India headed by Cochrane—has reported rather adversely on it and prefers to inject ' Sulphetrone ' As already stated, other workers in India have reported favourably on D A.D.P.S

There is general agreement that the maximum well-tolerated dose is 200–300 mg a day [6–15] Indians apparently tolerate rather less, 100–200 mg a day [2–5] The minimum active dose is very low, 50 mg a day is effective [3 16] I have found even 30 mg a day to exert a definite action As I have indicated,[9 10] the optimum dose is not yet fixed Our standard dose for mass treatment in Nigeria is now 800 mg a week (400 mg twice a week) very slowly attained, which is the same as that now suggested as the maximum by Cochrane himself There seems little difference of opinion here

But there is one important point on which I do differ from Cochrane He states that the main objection to sulphetrone treatment is its high cost which can be remedied by using injections of much smaller doses than those used orally This matter was fairly fully discussed by me in your pages [9] There is now very strong evidence to support the view then expressed, that disubstituted sulphones, such as sulphetrone, act only by being hydrolysed to D.A.D P S, that when they are given orally this hydrolysis occurs mainly in the stomach, and that the injection of drugs such as sulphetrone prevents this hydrolysis All the evidence on this point cannot be quoted here, but the recent papers of American,[17 18] French,[15 19] and British [20] workers may be studied on this point, all these papers report studies, in vitro and in animals, indicating that without hydrolysis to D.A.D.P S, sulphetrone is not active In a paper now in preparation I am reporting similar results in vitro and in man Opinion on these matters now seems unanimous

---

1 Cochrane R G Ramanujan K Paul H, Russell D *Leprosy Rev* 1949 20 4
2 Dharmendra *Leprosy in India* 1950 (not yet received)
3 Muir E *Int J Leprosy* 1950 p 298
4 Muir E *Leprosy in India* 1950 p 106
5 Muir E *Ibid* (in the press)
6 Floch H Destombes P *Int J Leprosy* 1949 p 367
7 De Souza P R Lima L Abstracted in *Leprosy Rev* 1950 21 45
8 Molesworth B D Narayanaswami P S *Int J Leprosy* 1950 17 197
9 Lowe J *Lancet* 1950 i 145
10 Lowe J *Ibid* Jan 6 1951 p 18
11 Lowe J Smith M *Int J Leprosy* 1949 17 181
12 Chaussinand R La Lèpre published by L Expansion Scientifique Francaise
13 Smith M *Leprosy Rev* 1949 20 78 129 *Ibid* 1950 p 17
14 Rist N Cottet J *Pr Méd* 1949 157 743
15 Boyer F Rist N Saviard M *Ann Inst Pasteur* 1949 p 680
16 Chatterji S N *Leprosy in India* 1949 p 53
17 Smith M I Jackson E I Junge J M Bhattacharya B K *Amer Rev Tuberc* 1949 60 62
18 Titus E Bernstein J *Ann N Y Acad Sci* 1949 52 719
19 Boyer F Troestler J Rist N Tabone *Ann Inst Pasteur* 1950 78 140
20 Francis J Spinks A *Brit J Pharmacol Chemotherapy* 1950 5 565

It now appears that injections of sulphetrone probably act by means of D.A.D.P.S., some being present as an impurity in the sulphetrone, some being produced by hydrolysis during sterilisation, and perhaps a little being produced by hydrolysis in the body.

The main objection to the use of sulphetrone, particularly by injection, is not its high cost; the main objection is that it is irrational, and not in accord with the steadily increasing knowledge of the mode of action of sulphones. It is such a roundabout and inefficient way of securing the action of D.A.D.P.S. in the body.

Cochrane hesitates to accept Muir's statement about the effectiveness of D.A.D.P.S. in low doses (300 mg. a week), but Muir has been treating some hundreds of cases; moreover Molesworth has been using doses not very much higher for at least two and a half years, and his cases must now number well over a thousand; he reports excellent results.[8] In experiments carried out here, we find that the D.A.D.P.S. blood-level on 300 mg. a week is considerably higher than on the 6 g. a week of injected sulphetrone that Cochrane recommends.

By being the first leprosy worker to draw attention to the possible usefulness of D.A.D.P.S. in the treatment of leprosy, Cochrane rendered a great service. We hope that he will soon be able to agree with the large and increasing number of workers who find that this treatment, which he did so much to initiate, is safe and widely applicable, especially if modified to meet local conditions.

Finally, while all will agree with Cochrane that sulphone treatment does not present the solution of the leprosy problem, properly used it is being found a great help to all aspects of anti-leprosy work, even to attempts to segregate infectious cases. In Nigeria, the prospect of a shorter period of segregation, and the painlessness and greater efficacy of the treatment, as compared with the past, are encouraging more patients to come for segregation and treatment, and to come at an earlier stage of the disease.

We are all trying to find a more rapidly effective remedy than sulphones, or an agent to augment and speed up the action of sulphones, and the thiosemicarbazones are giving promising results. In the meantime it is not by failing to acknowledge the great advances already made that we shall attract the badly needed medical staff to the leprosy services (the Nigeria Leprosy Service has less than one doctor to every 2000 patients!) or the patients to make full and proper use of those services.

Research Unit, Leper Colony,
Uzuakoli, N.E.R., Nigeria.
JOHN LOWE.

DEFINITION OF TUBERCULOSIS

SIR,—Dr. Barran (Feb. 10) has rightly called attention to the widely differing criteria used in the notification of tuberculosis. It will be generally agreed that it is undesirable that all persons should be notified who have suffered a tuberculous infection, just as it would be equally useless to notify only those who are infectious. However, some degree of uniformity is desirable. The following criteria, as used in the Ipswich and East Suffolk Chest Service, are put forward as practical:

(a) All patients from whom tubercle bacilli are isolated.
(b) All patients suffering from tuberculous disease who are in need of treatment.

By treatment is meant any change in the working or home life necessary to encourage healing of the disease, as well as the more definite forms of treatment, such as bed rest and "relaxation" therapy. This would include Dr. Barran's "minimal tuberculous lesion of the lung found to be healing without active treatment", for surely such a patient would be advised to rest in his off duty time and even perhaps to take a day in bed at the weekend. It would also include active primary tuberculous infections of childhood where it was necessary to modify school life by recommending an open air school, or a regular rest period, as well as the more specific forms of treatment.

In all these cases it may be necessary at some time to issue certificates *indicating that a patient is suffering* from tuberculosis.

I would add that I think it essential to examine the household contacts of all patients diagnosed as having suffered or as suffering from tuberculous disease, even if they have only a calcified primary lesion (this could be done by mobile mass radiography). Notification of healed cases is not necessary, since after explanation most patients and their relatives readily agree to examination.

Chest Clinic,
Foxhall Road, Ipswich.
CHARLES J. STEWART.

ÆTIOLOGY OF CHRONIC GASTRIC ULCER

SIR,—Mr. Doran's paper of Jan. 27 requires brief comment. Mr. Doran claims to show, by injection techniques, that the mucosa of the lesser curve has a "lower vascular density" than has the rest of the stomach mucous membrane. This would be an attractive finding, in view of the present re-emphasis on vascular factors as a cause of peptic ulceration, but it is unfortunately not correct. Injection techniques require careful control before quantitative differences can be claimed between different preparations. Such factors as the time interval between removal of the tissue and its *injection*, the particle size of the silver iodide preparation, the pH of the injection mass, and, above all, the pressure at which injection is carried out are factors which can profoundly modify the degree of filling of the vessels of the injected tissue.

Mr. Doran uses for injection a syringe and fine hypodermic needle, continuing the injection until a "slight resistance" is felt. The human thumb is a fallible organ as a scientific instrument. If the gastro-epiploic arterial chain of a resected stomach is injected with 10% colloidal silver iodide, using a 20 ml. 'Record' syringe and a hypodermic needle no. 17 (0.5 mm. diameter, standard wire gauge [S.W.G.] 25), the pressure within the chain is:

	mm. Hg
Moderate pressure, one thumb	20
Maximum pressure, one thumb	52
Maximum pressure, both thumbs	78

Using a "fine" hypodermic needle no. 20 (0.45 mm. diameter, S.W.G. 26), the figures are:

	mm. Hg
Moderate pressure, one thumb	16
Maximum pressure, one thumb	45
Maximum pressure, both thumbs	54

In each case there is a wide variation in pressure at which the injection mass may be introduced, and even the maximum pressure of 78 mm. Hg using a hypodermic needle no. 17 and the full strength of two *hands* is inadequate to fill completely the vessels of the *stomach*, as experience shows.

Mr. Doran is comparing specimens of stomach wall in which the vessels are filled with varying degrees of success. Precise technique shows that the size, arrangement, and density of vessels within the mucosa is the same in the lesser curve region as in the anterior and posterior walls of the stomach; and the number of mucosal arteries supplying each square centimetre of mucosa is the same in the different parts. There are differences in the vascular supply to the lesser curve, but these lie within the submucous layer and outside the muscle coat, and do not result in any difference in the vascular pattern of the mucous membrane.

So far as we know, the significance of arteriovenous shunts in the stomach wall in the causation of peptic ulceration has only been mentioned by Dr. W. C. Alvarez, of the Mayo Clinic, in a discursive leading article, and there is much that can be argued against this view.

eriovenous anastomoses are shown most accurately the stomach wall by micro dissection They are g direct channels, up to 140 μ in diameter in life, nning from mucosal artery to vein, and it is usually sible to find one arising from each mucosal artery in submucosa Examples are reproduced in the *Journal Anatomy*[1] They are present equally in the anterior d posterior walls and in the lesser curve regions It necessary to understand the architecture of the vessels, t the problem remains one of blood flow under different nditions and it is no doubt because we know so little out this that speculation, both negative and positive, s its opportunity

F H BENTLEY
T E BARLOW

Medical School
Newcastle upon Tyne

NORADRENALINE AND THE SUPRARENAL MEDULLA

SIR,—Holtz and Schümann[2] reported that noradrena ne is present with adrenaline in the normal suprarenal edulla of man, but it is not accurately known what roportion of each amine is present We have investigated y biological assay and chromatographic methods the atechol content of extracts of suprarenal glands obtained ost mortem

In 17 adult cases (ages 45–79) secured 2–49 hours fter death, noradrenaline was present to the extent of bout 14% of the total amines (mean value of noradrenaline = 29 μg per g fresh tissue) In 9 children nder 1 year, however, the mean value of noradrenaline as 65 μg per g fresh tissue, representing 90% of the otal amines present These latter samples were secured 4–22 hours after death

The significance of this finding is not yet clear

G B WEST
R B HUNTER

Department of Pharmacology and Therapeutics
University of St Andrews Medical School
Dundee

THE INVESTIGATION OF SUGAR TOLERANCE

SIR —Dr Friend's article of Jan 27 should not pass unchallenged as it denies any value of a full blood sugar curve in the following words "Complete standard tolerance tests cannot be justified, since the only information obtained from the five blood and three urine examinations of the test can be found equally well by estimation of a single 2 hour blood sugar level"

True, one admits the great importance of a return to normal in 2 hours, but mistakes will be made from this figure alone and much information omitted which can be obtained from a full blood sugar curve For example

1 No explanation of glycosuria—and it is to explain symptomless glycosuria that blood sugar investigations are undertaken—is given by the 2 hour figure Dr Friend does not mention glycosuria in his suggested test and hence would have no clear evidence on renal glycosuria or oxyhyperglycæmia

2 Without the fasting level, starvation curves (not uncommon apart from absolute starvation) would be labelled as diabetic from the raised 2 hour figure alone

3 The same would apply to thyrotoxic and certain toxæmic disturbances of the blood sugar curve

4 I am certain that I would often be misled in life assurance and other work by one 2 hour figure instead of a full curve which shows the total response to glucose tolerance by five or six blood sugar estimations and simultaneous urine tests

In any full assessment, knowledge of general health factors not mentioned in Dr Friend's analysis, is also most important

London W 1

R D LAWRENCE

VACCINATION AGAINST SMALLPOX

SIR,—Allow me to reply to letters arising from my article of Jan 13

Dr Dixon (Jan 20) says "Dr Millard's main argument is that mild cases of variola major only occur in the vaccinated In my opinion this is fundamentally wrong" Dr Dixon has not got me correctly I said of the unvaccinated "The mild and trifling cases [I was referring to the ultra mild cases which are so easily missed] very rarely occur when we are dealing with true major smallpox but only when we have to do with a mild strain of the disease, and, when this is so, the mildness tends to breed true"

Dr Dixon quotes some figures from his own experience of smallpox in Tripolitania, where out of 300 unvaccinated cases 105 were classed as types 6 and 7 (discrete and mild) Such cases would be very different from the trivial cases I was considering, which are so mild and modified that they may deceive even experts Moreover, as he does not mention the number of fatal cases we have no means of knowing whether they could rightly be regarded as true major smallpox such as occurs in India I doubt very much if they were

As regards India, Dr Dixon takes exception to my suggestion that it might be worth while trying the experiment of substituting inoculation with variola minor for vaccination He thinks it would "confuse patient and medical profession alike" This surely is hardly an insuperable objection! He further writes "It is very doubtful if 5% of India's total population are immune at any one time One would not expect this to have any appreciable effect on incidence, but the fault is not with vaccination" I cannot agree that vaccination is not to blame It is because the protection conferred by vaccination is so short lived in the face of really virulent smallpox that so small a proportion of the population is efficiently protected Let there be no mistake vaccination has been "pushed" in India for very many years as far as is practicable, so what more does Dr Dixon suggest? There has been more vaccination in India in proportion to population, than there has been in this country, certainly during the past half century The latest figures I have by me are for the year 1936 taken from the Bengal health report for that year On p 40 I read ' Smallpox 46,267 deaths were due to smallpox in the province yielding a death rate of 9 per 1,000 Smallpox accounted for 3 8% of the total provincial mortality" The population of Bengal is given as 51,000 000, which is very little more than that of the United Kingdom plus Eire If we had 46,000 deaths from smallpox in this country in one year, or only a fraction of that number, we should certainly regard our preventive measures as a ghastly failure And here are the vaccination figures (p 116)

Vaccination in Bengal 1935–36

Total number of persons vaccinated	9 106 830
Total number of vaccinations performed	9 114 092
(*a*) Primary	2 907 210
Successful	2 557 300
(*b*) Revaccinations	6 206 882
Successful	2 216 873
Ratio of successful vaccinations per 1000 population	95 3
Total number of births	1 673 206

I think that these figures may surprise some people, they certainly surprised me

I think we may assume that the reason why preventive measures have failed so lamentably in India are (1) the obvious impracticability of carrying out those measures which have been so signally successful in this country (hospital isolation and tracing and surveillance of contacts), (2) the extreme virulence of the disease, against which only recent vaccination is effective As I mentioned in my paper, British troops in India had to be revaccinated every two years It would obviously be quite impossible in India, or indeed in any country, to apply this to the general population

---

[1] J Anat 1951 85 1
[2] Holtz P Schümann H J *Nature Lond* 1950 165 683

It now appears that injections of sulphetrone probably act by means of D A D P S, some being present as an impurity in the sulphetrone, some being produced by hydrolysis during sterilisation, and perhaps a little being produced by hydrolysis in the body

The main objection to the use of sulphetrone, particularly by injection, is not its high cost, the main objection is that it is irrational, and not in accord with the steadily increasing knowledge of the mode of action of sulphones It is such a roundabout and inefficient way of securing the action of D A D P S in the body

Cochrane hesitates to accept Muir's statement about the effectiveness of D A D P S *in low doses (300 mg a week)*, but Muir has been treating some hundreds of cases, moreover Molesworth has been using doses not very much higher for at least two and a half years, and his cases must now number well over a thousand, he reports excellent results [8] In experiments carried out here, we find that the D A D P S blood level on 300 mg a week is considerably higher than on the 6 g a week of injected sulphetrone that Cochrane recommends

By being the first leprosy worker to draw attention to the possible usefulness of D A D P S in the treatment of leprosy, Cochrane rendered a great service We hope that he will soon be able to agree with the large and increasing number of workers who find that this treatment, which he did so much to initiate, is safe and widely applicable, especially if modified to meet local conditions

Finally, while all will agree with Cochrane that sulphone treatment does not present the solution of the leprosy problem, properly used it is being found a great help to all aspects of anti leprosy work, even to attempts to segregate infectious cases In Nigeria, the prospect of a shorter period of segregation, and the painlessness and greater efficacy of the treatment, as compared with the past, are encouraging more patients to come for segregation and treatment, and to come at an earlier stage of the disease

We are all trying to find a more rapidly effective remedy than sulphones, or an agent to augment and speed up the action of sulphones, and the thiosemicarbazones are giving promising results In the meantime it is not by failing to acknowledge the great advances already made that we shall attract the badly needed medical staff to the leprosy services (the Nigeria Leprosy Service has less than one doctor to every 2000 patients [7]) or the patients to make full and proper use of those services

Research Unit Leper Colony,
Uzuakoli, N E R , Nigeria

JOHN LOWE

DEFINITION OF TUBERCULOSIS

SIR,—Dr Barran (Feb 10) has rightly called attention to the widely differing criteria used in the notification of tuberculosis It will be generally agreed that it is undesirable that all persons should be notified who have suffered a tuberculous infection, just as it would be equally useless to notify only those who are infectious However, some degree of uniformity is desirable The following criteria, as used in the Ipswich and East Suffolk Chest Service, are put forward as practical

(*a*) All patients from whom tubercle bacilli are isolated

(*b*) All patients suffering from tuberculous disease who are in need of treatment

By treatment is meant any change in the working or home life necessary to encourage healing of the disease, as well as the more definite forms of treatment, such as bed rest and "relaxation" therapy This would include Dr Barran's "minimal tuberculous lesion of the lung found to be healing without active treatment", for surely such a patient would be advised to rest in his off duty time and even perhaps to take a day in bed at the weekend It would also include active primary tuberculous infections of childhood where it was necessary to modify school life by recommending an open air school, or a regular rest period, as well as the more specific forms of treatment

In all these cases it may be necessary at some time to issue certificates indicating that a patient is suffering from tuberculosis

I would add that I think it essential to examine the household contacts of all patients diagnosed as having suffered or as suffering from tuberculous disease, even if they have only a calcified primary lesion (this could be done by mobile mass radiography) Notification of healed cases is not necessary, since after explanation most patients and their relatives readily agree to examination

Chest Clinic
Foxhall Road Ipswich

CHARLES J STEWART

ÆTIOLOGY OF CHRONIC GASTRIC ULCER

SIR,—Mr Doran's paper of Jan 27 requires brief comment Mr Doran claims to show, by injection techniques, that the mucosa of the lesser curve has a "lower vascular density" than has the rest of the stomach mucous membrane This would be an attractive finding, in view of the present re emphasis on vascular factors as a cause of peptic ulceration, but it is unfortunately not correct Injection techniques require careful control before quantitative differences can be claimed between different preparations Such factors as the time interval between removal of the tissue and its injection, the particle size of the silver iodide preparation, the pH of the injection mass, and, above all, the pressure at which injection is carried out are factors which can profoundly modify the degree of filling of the vessels of the injected tissue

Mr Doran uses for injection a syringe and fine hypodermic needle, continuing the injection until a "slight resistance" *is felt* The human thumb is a fallible organ as a scientific instrument If the gastro epiploic arterial chain of a resected stomach is injected with 10% colloidal silver iodide, using a 20 ml 'Record' syringe and a hypodermic needle no 17 (0 5 mm diameter, standard wire gauge [S W G] 25), the pressure within the chain is

	mm Hg
Moderate pressure, one thumb	20
Maximum pressure, one thumb	52
Maximum pressure, both thumbs	78

Using a "fine" hypodermic needle no 20 (0 45 mm diameter, S W G 26), the figures are

	mm Hg
Moderate pressure, one thumb	16
Maximum pressure, one thumb	45
Maximum pressure, both thumbs	54

In each case there is a wide variation in pressure at which the injection mass may be introduced, and even the maximum pressure of 78 mm Hg using a hypodermic needle no 17 and the full strength of two hands is inadequate to fill completely the vessels of the stomach, as experience shows

Mr Doran is comparing specimens of stomach wall in which the vessels are filled with varying degrees of success Precise technique shows that the size, arrangement, and density of vessels within the mucosa is the same in the lesser curve region as in the anterior and posterior walls of the stomach, and the number of mucosal arteries supplying each square centimetre of mucosa is the same in the different parts There are differences in the vascular supply to the lesser curve, but these lie within the submucous layer and outside the muscle coat, and do not result in any difference in the vascular pattern of the mucous membrane

So far as we know, the significance of arteriovenous shunts in the stomach wall in the causation of peptic ulceration has only been mentioned by Dr W C Alvarez, of the Mayo Clinic, in a discursive leading article, and there is much that can be argued against this view

A VISIT TO INDIA

SIR,—Last October and November I was privileged to take a party of medical practitioners from this country for a goodwill tour of India The trip, I am glad to say, was most successful, and the welcome and hospitality extended to us by my countrymen in India were so unstinting and sincere that I am now making arrangements to repeat the tour over a period of six weeks during October and November of this year

The party will travel by air between London and Bombay, and all journeys during our stay in India will be made either by air or by rail Our itinerary will include visits to places of historical and archæological interest as well as to universities hospitals, and cultural centres in Bombay, Mysore, Bangalore Hyderabad, Madras, Delhi, Agra, Kashmir, Calcutta, and Darjeeling The total cost will be approximately £250 per person

My primary objective in organising the tour is to stimulate full comprehension of India's vast potentialities in those persons who, through active work in their profession, are most favourably placed to strengthen the ties of friendship between Great Britain and India Inquiries from doctors wishing to join the party should reach me before March 31

128 Harley Street
London W 1

R HINGORANI

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—Our cases of hypertension treated with methonium compounds now number 50, and many of them have been followed as outpatients for almost six months Most of these were cases of essential hypertension with severe headache or left ventricular failure, 2 had had bilateral sympathectomy without benefit, and 1 had malignant hypertension

Our method of administering the drug was to give 25 mg by injection intramuscularly and observe the blood pressure at fifteen minute intervals for the next two hours If this initial dose was unsatisfactory it was increased by 10 mg or more and the procedure was repeated until we obtained what we felt was a satisfactory fall in blood pressure The drug was then given by injection six-hourly, and as tolerance increased the intervals were reduced until in some cases the patients were having as much as 100 mg three hourly After seven to fourteen days on injection the patient was transferred to the drug by mouth We considered that a suitable dose to commence with would be 250 mg by mouth at the same time interval as every 50 mg was given by injection In some cases the patients had as much as 7–8 g daily by mouth

Before any patient was started on methonium treatment he was given a fortnight's rest in bed, and his blood pressure was taken at frequent intervals during the day When the patient was put on the drug his blood-pressure was taken even more frequently All the injections were given with the patient sitting up, and a few patients were ambulatory After four weeks in hospital all the patients were up and about They were then seen as outpatients fortnightly or more often

Since finding a case of bromide poisoning about five months ago we have estimated the serum bromide level fortnightly on every patient receiving hexamethonium bromide We found that every patient had a reasonably high serum bromide level, and owing to the slow excretion of bromide these serum bromide levels tended to increase at about the same rate, irrespective of the dose of the drug, or at least provided the dose was between certain fairly wide limits We have recently had a second case of bromide intoxication in a patient whose blood pressure did not fall in spite of the fact that he was receiving at one time 12 g of hexamethonium bromide by mouth

Our results, which we hope to publish in detail shortly, have been unsatisfactory Unquestionably injections of the drug, and in some few cases oral administration, will produce an acute fall in blood pressure Sometimes, however, in spite of large doses of the drug, even this acute fall did *not* occur In all cases except 1, oral administration of the drug failed to keep the blood-pressure down, and every patient so far seen at outpatients has had a blood pressure at the same level as it was before treatment was commenced, though many patients admitted to feeling much better The initial fall in blood pressure obtained with methonium compounds is often, in our experience, no greater than that produced in many patients by rest in bed

We agree with the writers who have suggested that at present these compounds should only be used under hospital observation The production of a drug which has a longer action than the hexamethonium compound and which does not contain the bromide radicle, or alternatively is effective in much smaller doses, would be the ideal to aim at

Oldchurch Hospital
Romford Essex

S LOCKET
Senior Physician

SIR,—After Kay and Smith [1] observed that the potency of the halide salts of hexamethonium given orally, expressed in terms of the cation, was highest for the iodide and lowest for the chloride, with the bromide intermediate, clinical studies of this drug have been made mostly with the bromide or iodide It seems improbable, however, that the halide anion of such a salt, which must be completely dissociated in solution, can exert any significant effect on the activity of the hexamethonium cation, or even on its absorption In view of the possibilities of bromism [2] and of iodism from the use of the bromide or iodide, we have been prompted to test the purity of some of the available preparations in order to determine whether the reputed inefficacy of the chloride was associated with any impurity, and to verify whether, with pure salts, the biological activity of the cation did indeed vary with the different halide ions We have determined the halide content of samples of hexamethonium salts, and have assayed biological activity, using the antagonism of hexamethonium to the action of acetylcholine on the frog's rectus abdominis (limits of error 7–10%, P = 0 05) The results were as follows

Hexamethonium salt		*Biological activity*	*Halide content (% theoretical)*
1	Iodide	93	94
2	Iodide	100	99
3	Iodide	100	100
4	Bromide	90	94
5	Bromide	100	99
6	Chloride	80	84
7	Chloride	97	99

Biological potency is given (in terms of the cation) as percentage of that of the pure iodide (Salts 2 and 3)

It will be seen that biologically several of the salts were below theoretical potency, and that in each case there was evidence of impurity One particular cause of apparent inefficacy of the chloride came to our attention We obtained a sample of chloride which had been made up as a powder in a waxed paper, in which it had remained for some months On opening the paper no powder could be seen, but simple extraction of the paper with saline, followed by biological assay, produced 91% of the quantity of hexamethonium stated to be within the paper The chloride, therefore, is sufficiently hygroscopic to take up so much water vapour that it can go into solution and impregnate the wrapping paper

We believe, therefore, that the results of Kay and Smith may have been due to a failure to give the full dose intended, because of some impurity in the chloride

---

[1] Kay A W Smith A N *Brit med J* 1950 ii 807

[2] Rosenheim M L *Lancet* Feb 10 1951 p 347 Holt M. C Litchfield J W *Ibid*

It is here that inoculation with variola minor might well have a great advantage over vaccination The resulting protection against variola major would, I believe, be at least as great as that conferred by vaccination, indeed it might be much greater Furthermore, variola minor being highly infectious, a baby who was inoculated would spread the infection to other members of the family and to neighbouring families who had never been protected or whose protection had lapsed There would indeed be no limit to the effect And it should be remembered that clinically variola minor is little, if any, more serious than vaccination I speak here from my personal experience of the Gloucester epidemic of 1923 (over 1000 cases with practically no fatality)

Dr Watts (Feb 3) makes the surprising assertion that no practical alternative to vaccination has been put forward I would ask him what he supposes has enabled this country to control smallpox so successfully during the past half century He can hardly contend that it is vaccination of the general population, for this has been steadily and rapidly declining, and now that compulsory infant vaccination has been abandoned it is likely to decline still further No, the real cause of our success has been prompt isolation plus the searching out and close surveillance of contacts, and the only thing which defeats these measures is the missed case, which, as I tried to show in my paper, vaccination of the general population tends to encourage

May I remind Dr Watts that during the last century before efficient modern measures were introduced vaccination of the general population, though carried out far more thoroughly than during the present century, entirely failed to protect this country from really severe epidemics of smallpox accompanied by a heavy death roll, as reference to the Registrar General's reports will show

Dr Woolman (Feb 10) thinks that I invalidate my thesis by saying that I am in favour of all who visit the East being protected by recent vaccination I am also in favour of such people being inoculated against typhoid, but I do not think it necessary that everyone in this country should be similarly inoculated

Leicester C KILLICK MILLARD

SECRECY OF SERVICE MEDICAL REPORTS

SIR,—Your timely article of Feb 10 (p 343) calls attention to an increasingly unsatisfactory position

The reference to the inquest on the soldier who dropped dead during a course at the Guards' depot, Caterham, may, I think give the impression that privilege was claimed for the evidence of the Army doctor for whose attendance, among other things, the inquest was adjourned, this is not so, nor would it be possible to claim privilege in this way The Army doctor was summoned to the inquest from Germany He duly attended, and gave most comprehensive evidence of his previous examinations

Privilege was in fact claimed, supported by a certificate signed by the Secretary of State for War, for the production of the medical history sheet of the deceased soldier Counsel who appeared on behalf of the War Office *at the inquest stated that privilege was always* claimed for documents of this kind, and the fact that privilege is automatically claimed in every case irrespective of the particular facts, seems to be one of the more objectionable features of this practice Lord Simon's judgment in Duncan *v* Cammell Laird makes it clear that the refusal to produce must not be arbitrary, but must be on the grounds of injury to national defence or to diplomatic relations, or because secrecy is necessary for the proper functioning of the public service

Can it really be said that the production of a medical history sheet to a soldier (or to his relatives, when he is dead) falls within any of these classes of cases? Unfortunately the decided cases make it clear that the certificate of the responsible Minister is conclusive, and that, whatever view may be taken of the real reason for the claim of privilege, no court may go behind the certificate and inquire into the Minister's reasons

Coroner's Office, East Horsley CYRIL BARON

NURSING INFECTIOUS DISEASES

SIR,—The letters of Dr Stanley Banks (Feb 3) and Prof A V Neale (Feb 17) raise many problems, not least that a general trained nurse can admit "that she has never had any practice in handling a baby, or in the principles of infant feeding"

Candidates who enter for the final general examination of the General Nursing Council for England and Wales must have had experience—not only lectures—in medical and surgical nursing, in gynæcological nursing, and in the nursing of sick children The head of the training school, usually the matron, must send a signed certificate to this effect before the candidate is accepted

Members of former councils, myself included, have often proposed that general training schools should be asked to give some details of the experience candidates have had, including experience in the nursing of sick *infants and children, and the real solution to the present lack in training is for the General Nursing Council to* bring this measure into effect With good will and good administration it could be achieved almost overnight It may mean that some of our large and well known training schools will have to second their nurses for specialised experience in this field, but the ultimate benefit would far outweigh any temporary inconvenience

London W 8 EVELYN C PEARCE

SURGICAL RELIEF OF MYOCARDIAL ISCHÆMIA

SIR,—In his intriguing paper last week Mr Mason expresses his belief that treatment of angina (and, incidentally, of heart failure) by reduction of metabolic activity has now been discarded He also considers that *this treatment condemns the* patient to "a reduced level of existence"

Reduction of basal metabolism in cardiac disability is nowadays carried out by thiouracil medication, not by thyroidectomy, and it is certainly not discarded I know that at least one of the leading cardiologists of this country practises the method widely I have used it in a small series of cases selected by the crippling nature of their condition, and by the failure of all other treatment to enable the patient to lead a working, or at least an ambulant, life, or to maintain life at all in the face of advancing and intractable congestive failure Of 12 such patients, 1 died of (his second) coronary thrombosis after three years of freedom from angina The other 11 have continued the active life they were on the point of giving up, or have resumed activities previously beyond their scope In each case the *maintenance* treatment was, either purposely or accidentally, reduced below the required level at one time or another without the patient's knowledge The relapse that follows within one or two weeks, and the rapid restoration upon resumption *of adequate treatment*, are a dramatic therapeutic test One of my patients, a man with a rheumatic aortic stenosis, went into failure in the autumn of 1946, became bedridden within a few months with massive œdema, anasarca, and a right sided pleural effusion (tapped, $1^1/_2$ pints) Under thiouracil, instituted in the nick of time, he lost all his accumulated fluid and has not again required digitalis or mersalyl Like all these patients, he is maintained just *above* myxœdema level, and, so far from living "on a reduced level," he has in the meantime become my very efficient secretary

London W 1 G SCHOENEWALD

A VISIT TO INDIA

SIR,—Last October and November I was privileged to take a party of medical practitioners from this country for a goodwill tour of India The trip, I am glad to say, was most successful, and the welcome and hospitality extended to us by my countrymen in India were so unstinting and sincere that I am now making arrangements to repeat the tour over a period of six weeks during October and November of this year

The party will travel by air between London and Bombay, and all journeys during our stay in India will be made either by air or by rail Our itinerary will include visits to places of historical and archæological interest, as well as to universities hospitals, and cultural centres in Bombay, Mysore, Bangalore Hyderabad, Madras, Delhi Agra, Kashmir, Calcutta and Darjeeling The total cost will be approximately £250 per person

My primary objective in organising the tour is to stimulate full comprehension of India's vast potentialities in those persons who, through active work in their profession, are most favourably placed to strengthen the ties of friendship between Great Britain and India Inquiries from doctors wishing to join the party should reach me before March 31

128 Harley Street
London W 1

R HINGORANI

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—Our cases of hypertension treated with methonium compounds now number 50, and many of them have been followed as outpatients for almost six months Most of these were cases of essential hypertension with severe headache or left ventricular failure, 2 had had bilateral sympathectomy without benefit, and 1 had malignant hypertension

Our method of administering the drug was to give 25 mg by injection intramuscularly, and observe the blood pressure at fifteen minute intervals for the next two hours If this initial dose was unsatisfactory it was increased by 10 mg or more and the procedure was repeated until we obtained what we felt was a satisfactory fall in blood pressure The drug was then given by injection six hourly, and as tolerance increased the intervals were reduced until in some cases the patients were having as much as 100 mg three hourly After seven to fourteen days on injection the patient was transferred to the drug by mouth We considered that a suitable dose to commence with would be 250 mg by mouth at the same time interval as every 50 mg was given by injection In some cases the patients had as much as 7–8 g daily by mouth

Before any patient was started on methonium treatment he was given a fortnight's rest in bed, and his blood pressure was taken at frequent intervals during the day When the patient was put on the drug his blood pressure was taken even more frequently All the injections were given with the patient sitting up, and a few patients were ambulatory After four weeks in hospital all the patients were up and about They were then seen as outpatients fortnightly or more often

Since finding a case of bromide poisoning about five months ago we have estimated the serum bromide level fortnightly on every patient receiving hexamethonium bromide We found that every patient had a reasonably high serum bromide level, and owing to the slow excretion of bromide these serum bromide levels tended to increase at about the same rate, irrespective of the dose of the drug, or at least provided the dose was between certain fairly wide limits We have recently had a second case of bromide intoxication in a patient whose blood pressure did not fall in spite of the fact that he was receiving at one time 12 g of hexamethonium bromide by mouth

Our results, which we hope to publish in detail shortly have been unsatisfactory Unquestionably injections of the drug, and in some few cases oral administration, will produce an acute fall in blood pressure Sometimes, however, in spite of large doses of the drug, even this acute fall did not occur In all cases except 1, oral administration of the drug failed to keep the blood pressure down, and every patient so far seen at outpatients has had a blood pressure at the same level as it was before treatment was commenced, though many patients admitted to feeling much better The initial fall in blood pressure obtained with methonium compounds is often, in our experience, no greater than that produced in many patients by rest in bed

We agree with the writers who have suggested that at present these compounds should only be used under hospital observation The production of a drug which has a longer action than the hexamethonium compound and which does not contain the bromide radicle, or alternatively is effective in much smaller doses, would be the ideal to aim at

Oldchurch Hospital
Romford Essex

S LOCKET
Senior Physician

SIR,—After Kay and Smith[1] observed that the potency of the halide salts of hexamethonium given orally, expressed in terms of the cation, was highest for the iodide and lowest for the chloride, with the bromide intermediate, clinical studies of this drug have been made mostly with the bromide or iodide It seems improbable, however, that the halide anion of such a salt, which must be completely dissociated in solution, can exert any significant effect on the activity of the hexamethonium cation, or even on its absorption In view of the possibilities of bromism[2] and of iodism from the use of the bromide or iodide, we have been prompted to test the purity of some of the available preparations in order to determine whether the reputed inefficacy of the chloride was associated with any impurity, and to verify whether, with pure salts, the biological activity of the cation did indeed vary with the different halide ions We have determined the halide content of samples of hexamethonium salts, and have assayed biological activity, using the antagonism of hexamethonium to the action of acetylcholine on the frog's rectus abdominis (limits of error 7–10%, $P = 0\ 05$) The results were as follows

Hexamethonium salt		*Biological activity*	*Halide content (% theoretical)*
1	Iodide	93	94
2	Iodide	100	99
3	Iodide	100	100
4	Bromide	90	94
5	Bromide	100	99
6	Chloride	80	84
7	Chloride	97	99

Biological potency is given (in terms of the cation) as percentage of that of the pure iodide (Salts 2 and 3)

It will be seen that biologically several of the salts were below theoretical potency, and that in each case there was evidence of impurity One particular cause of apparent inefficacy of the chloride came to our attention We obtained a sample of chloride which had been made up as a powder in a waxed paper, in which it had remained for some months On opening the paper no powder could be seen, but simple extraction of the paper with saline, followed by biological assay, produced 91% of the quantity of hexamethonium stated to be within the paper The chloride, therefore, is sufficiently hygroscopic to take up so much water vapour that it can go into solution and impregnate the wrapping paper

We believe, therefore, that the results of Kay and Smith may have been due to a failure to give the full dose intended, because of some impurity in the chloride

---

[1] Kay A W Smith A N *Brit med J* 1950 ii 807
[2] Rosenheim M. L *Lancet* Feb 10 1951 p 347 Holt M. C Litchfield, J W *Ibid*

It is here that inoculation with variola minor might well have a great advantage over vaccination The resulting protection against variola major would, I believe, be at least as great as that conferred by vaccination, indeed it might be much greater Furthermore, variola minor being highly infectious, a baby who was inoculated would spread the infection to other members of the family and to neighbouring families who had never been protected or whose protection had lapsed There would indeed be no limit to the effect And it should be remembered that clinically variola minor is little, if any, more serious than vaccination I speak here from my personal experience of the Gloucester epidemic of 1923 (over 1000 cases with practically no fatality)

Dr Watts (Feb 3) makes the surprising assertion that no practical alternative to vaccination has been put forward I would ask him what he supposes has enabled this country to control smallpox so successfully during the past half century He can hardly contend that it is vaccination of the general population, for this has been steadily and rapidly declining, and now that compulsory infant vaccination has been abandoned it is likely to decline still further No, the real cause of our success has been prompt isolation plus the searching out and close surveillance of contacts, and the only thing which defeats these measures is the missed case, which, as I tried to show in my paper, vaccination of the general population tends to encourage

May I remind Dr Watts that during the last century before efficient modern measures were introduced vaccination of the general population, though carried out far more thoroughly than during the present century, entirely failed to protect this country from really severe epidemics of smallpox accompanied by a heavy death roll, as reference to the Registrar General's reports will show

Dr Woolman (Feb 10) thinks that I invalidate my thesis by saying that I am in favour of all who visit the East being protected by recent vaccination I am also in favour of such people being inoculated against typhoid, but I do not think it necessary that everyone in this country should be similarly inoculated

Leicester **C Killick Millard**

SECRECY OF SERVICE MEDICAL REPORTS

Sir,—Your timely article of Feb 10 (p 343) calls attention to an increasingly unsatisfactory position

The reference to the inquest on the soldier who dropped dead during a course at the Guards' depot, Caterham, may, I think give the impression that privilege was claimed for the evidence of the Army doctor for whose attendance, among other things, the inquest was adjourned, this is not so, nor would it be possible to claim privilege in this way The Army doctor was summoned to the inquest from Germany He duly attended, and gave most comprehensive evidence of his previous examinations

Privilege was in fact claimed, supported by a certificate signed by the Secretary of State for War, for the production of the medical history sheet of the deceased soldier Counsel who appeared on behalf of the War Office at the inquest stated that privilege was *always* claimed for documents of this kind, and the fact that privilege is automatically claimed in every case irrespective of the particular facts, seems to be one of the more objectionable features of this practice Lord Simon's judgment in Duncan *v* Cammell Laird makes it clear that the refusal to produce must not be arbitrary, but must be on the grounds of injury to national defence or to diplomatic relations, or because secrecy is necessary for the proper functioning of the public service

Can it really be said that the production of a medical history sheet to a soldier (or to his relatives, when he is dead) falls within any of these classes of cases? Unfortunately the decided cases make it clear that the certificate of the responsible Minister is conclusive, and that, whatever view may be taken of the real reason for the claim of privilege, no court may go behind the certificate and inquire into the Minister's reasons

Coroner's Office East Horsley **Cyril Baron**

NURSING INFECTIOUS DISEASES

Sir,—The letters of Dr Stanley Banks (Feb 3) and Prof A V Neale (Feb 17) raise many problems, not least that a general trained nurse can admit "that she has never had any practice in handling a baby, or in the principles of infant feeding"

Candidates who enter for the final general examination of the General Nursing Council for England and Wales must have had experience—not only lectures—in medical and surgical nursing, in gynæcological nursing, and in the nursing of sick children The head of the training school, usually the matron, must send a signed certificate to this effect before the candidate is accepted

Members of former councils, myself included, have often proposed that general training schools should be asked to give some details of the experience candidates have had, including experience in the nursing of sick infants and children, and the real solution to the present lack in training is for the General Nursing Council to bring this measure into effect With good will and good administration it could be achieved almost overnight It may mean that some of our large and well known training schools will have to second their nurses for specialised experience in this field, but the ultimate benefit would far outweigh any temporary inconvenience

London W 8 **Evelyn C Pearce**

SURGICAL RELIEF OF MYOCARDIAL ISCHÆMIA

Sir,—In his intriguing paper last week Mr Mason expresses his belief that treatment of angina (and, incidentally, of heart failure) by reduction of metabolic activity has now been discarded He also considers that this treatment condemns the patient to "a reduced level of existence"

Reduction of basal metabolism in cardiac disability is nowadays carried out by thiouracil medication, not by thyroidectomy, and it is certainly not discarded I know that at least one of the leading cardiologists of this country practises the method widely I have used it in a small series of cases selected by the crippling nature of their condition, and by the failure of all other treatment to enable the patient to lead a working, or at least an ambulant, life, or to maintain life at all in the face of advancing and intractable congestive failure Of 12 such patients, 1 died of (his second) coronary thrombosis after three years of freedom from angina The other 11 have continued the active life they were on the point of giving up, or have resumed activities previously beyond their scope In each case the maintenance treatment was, either purposely or accidentally, reduced below the required level at one time or another without the patient's knowledge The relapse that follows within one or two weeks, *and the rapid restoration upon resumption of adequate treatment, are a dramatic therapeutic test One of my patients, a man* with a rheumatic aortic stenosis, went into failure in the autumn of 1946, became bedridden within a few months with massive œdema, anasarca, and a right sided pleural effusion (tapped, $1^1/_2$ pints) Under thiouracil, instituted in the nick of time, he lost all his accumulated fluid and has not again required digitalis or mersalyl. Like all these patients, he is maintained just *above* myxœdema level, *and*, so far from living "*on a reduced level*," he has in the meantime become my very efficient secretary

London W 1 **G Schoenewald**

A VISIT TO INDIA

SIR,—Last October and November I was privileged to take a party of medical practitioners from this country for a goodwill tour of India The trip, I am glad to say, was most successful, and the welcome and hospitality extended to us by my countrymen in India were so unstinting and sincere that I am now making arrangements to repeat the tour over a period of six weeks during October and November of this year

The party will travel by air between London and Bombay and all journeys during our stay in India will be made either by air or by rail Our itinerary will include visits to places of historical and archæological interest, as well as to universities, hospitals, and cultural centres in Bombay, Mysore, Bangalore Hyderabad, Madras, Delhi Agra, Kashmir, Calcutta, and Darjeeling The total cost will be approximately £250 per person

My primary objective in organising the tour is to stimulate full comprehension of India's vast potentialities in those persons who, through active work in their profession, are most favourably placed to strengthen the ties of friendship between Great Britain and India Inquiries from doctors wishing to join the party should reach me before March 31

128 Harley Street
London W 1

R HINGORANI

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—Our cases of hypertension treated with methonium compounds now number 50, and many of them have been followed as outpatients for almost six months Most of these were cases of essential hypertension with severe headache or left ventricular failure, 2 had had bilateral sympathectomy without benefit, and 1 had malignant hypertension

Our method of administering the drug was to give 25 mg by injection intramuscularly and observe the blood pressure at fifteen minute intervals for the next two hours If this initial dose was unsatisfactory it was increased by 10 mg or more and the procedure was repeated until we obtained what we felt was a satisfactory fall in blood pressure The drug was then given by injection six hourly, and as tolerance increased the intervals were reduced until in some cases the patients were having as much as 100 mg three hourly After seven to fourteen days on injection the patient was transferred to the drug by mouth We considered that a suitable dose to commence with would be 250 mg by mouth at the same time interval as every 50 mg was given by injection In some cases the patients had as much as 7–8 g daily by mouth

Before any patient was started on methonium treatment he was given a fortnight's rest in bed, and his blood pressure was taken at frequent intervals during the day When the patient was put on the drug his blood pressure was taken even more frequently All the injections were given with the patient sitting up, and a few patients were ambulatory After four weeks in hospital all the patients were up and about They were then seen as outpatients fortnightly or more often

Since finding a case of bromide poisoning about five months ago we have estimated the serum bromide level fortnightly on every patient receiving hexamethonium bromide We found that every patient had a reasonably high serum bromide level, and owing to the slow excretion of bromide these serum bromide levels tended to increase at about the same rate, irrespective of the dose of the drug, or at least provided the dose was between certain fairly wide limits We have recently had a second case of bromide intoxication in a patient whose blood pressure did not fall in spite of the fact that he was receiving at one time 12 g of hexamethonium bromide by mouth

Our results, which we hope to publish in detail shortly, have been unsatisfactory Unquestionably injections of the drug, and in some few cases oral administration, will produce an acute fall in blood pressure Sometimes, however, in spite of large doses of the drug, even this acute fall did not occur In all cases except 1, oral administration of the drug failed to keep the blood-pressure down, and every patient so far seen at out patients has had a blood pressure at the same level as it was before treatment was commenced, though many patients admitted to feeling much better The initial fall in blood pressure obtained with methonium compounds is often, in our experience, no greater than that produced in many patients by rest in bed

We agree with the writers who have suggested that at present these compounds should only be used under hospital observation The production of a drug which has a longer action than the hexamethonium compound and which does not contain the bromide radicle, or alternatively is effective in much smaller doses, would be the ideal to aim at

Oldchurch Hospital
Romford Essex

S LOCKET
Senior Physician

SIR,—After Kay and Smith[1] observed that the potency of the halide salts of hexamethonium given orally, expressed in terms of the cation, was highest for the iodide and lowest for the chloride with the bromide intermediate, clinical studies of this drug have been made mostly with the bromide or iodide It seems improbable, however, that the halide anion of such a salt, which must be completely dissociated in solution, can exert any significant effect on the activity of the hexamethonium cation, or even on its absorption In view of the possibilities of bromism[2] and of iodism from the use of the bromide or iodide, we have been prompted to test the purity of some of the available preparations in order to determine whether the reputed inefficacy of the chloride was associated with any impurity, and to verify whether, with pure salts, the biological activity of the cation did indeed vary with the different halide ions We have determined the halide content of samples of hexamethonium salts, and have assayed biological activity, using the antagonism of hexamethonium to the action of acetylcholine on the frog's rectus abdominis (limits of error 7–10%, P = 0 05) The results were as follows

Hexamethonium salt		*Biological activity*	*Halide content (% theoretical)*
1	Iodide	93	94
2	Iodide	100	99
3	Iodide	100	100
4	Bromide	90	94
5	Bromide	100	99
6	Chloride	80	84
7	Chloride	97	99

Biological potency is given (in terms of the cation) as percentage of that of the pure iodide (Salts 2 and 3)

It will be seen that biologically several of the salts were below theoretical potency, and that in each case there was evidence of impurity One particular cause of apparent inefficacy of the chloride came to our attention We obtained a sample of chloride which had been made up as a powder in a waxed paper, in which it had remained for some months On opening the paper no powder could be seen, but simple extraction of the paper with saline, followed by biological assay, produced 91% of the quantity of hexamethonium stated to be within the paper The chloride, therefore, is sufficiently hygroscopic to take up so much water vapour that it can go into solution and impregnate the wrapping paper

We believe, therefore, that the results of Kay and Smith may have been due to a failure to give the full dose intended, because of some impurity in the chloride

---

[1] Kay A W Smith A N *Brit med J* 1950 ii 807
[2] Rosenheim M L *Lancet* Feb 10 1951 p 347 Holt M. C, Litchfield J W *Ibid*

It is here that inoculation with variola minor might well have a great advantage over vaccination The resulting protection against variola major would, I believe, be at least as great as that conferred by vaccination, indeed it might be much greater Furthermore, variola minor being highly infectious, a baby who was inoculated would spread the infection to other members of the family and to neighbouring families who had never been protected or whose protection had lapsed There would indeed be no limit to the effect And it should be remembered that clinically variola minor is little, if any, more serious than vaccination I speak here *from my* personal experience of the Gloucester epidemic of 1923 (over 1000 cases with practically no fatality)

Dr Watts (Feb 3) makes the surprising assertion that no practical alternative to vaccination has been put forward I would ask him what he supposes has enabled this country to control smallpox so *successfully* during the past half century He can hardly contend that it is vaccination of the general population, for this has been steadily and rapidly declining, and now that compulsory infant vaccination has been abandoned it is likely to decline still further No, the real cause of our success has been prompt isolation plus the searching out and close surveillance of contacts, and the only thing which defeats these measures is the missed case, which, as I tried to show in my paper, vaccination of the general population tends to encourage

May I remind Dr Watts that during the last century before efficient modern measures were introduced vaccination of the general population, though carried out *far more* thoroughly than during the present century, entirely failed to protect this country from really severe epidemics of smallpox accompanied by a heavy death roll, as reference to the Registrar General's reports will show

Dr Woolman (Feb 10) thinks that I invalidate my thesis by saying that I am in favour of all who visit the East being protected by recent vaccination I am also in favour of such people being inoculated against typhoid, but I do not think it necessary that everyone in this country should be similarly inoculated

Leicester C KILLICK MILLARD

SECRECY OF SERVICE MEDICAL REPORTS

SIR,—Your timely article of Feb 10 (p 343) calls attention to an increasingly unsatisfactory position

The reference to the inquest on the soldier who dropped dead during a course at the Guards' depot, Caterham, may, I think, give the impression that privilege was claimed for the evidence of the Army doctor for whose attendance, among other things, the inquest was adjourned, this is not so, nor would it be possible to claim privilege in this way The Army doctor was summoned to the inquest from Germany He duly attended, and gave most comprehensive evidence of his previous examinations

Privilege was in fact claimed, supported by a certificate signed by the Secretary of State for War, for the production of the medical history sheet of the deceased soldier Counsel who appeared on behalf of the War Office at the inquest stated that privilege was *always* claimed for documents of this kind, and the fact that privilege is automatically claimed in every case irrespective of the particular facts, seems to be one of the more objectionable features of this practice Lord Simon's judgment in Duncan *v* Cammell Laird makes it clear that the refusal to produce must not be arbitrary, but must be on the grounds of injury to national defence or to diplomatic relations, or because secrecy is necessary for the proper functioning of the public service

Can it really be said that the production of a medical history sheet to a soldier (or to his relatives, when he is dead) falls within any of these classes of cases? Unfortunately the decided cases make it clear that the certificate of the responsible Minister is conclusive, and that, whatever view may be taken of the real reason for the claim of privilege, no court may go behind the certificate and inquire into the Minister's reasons

Coroner's Office, East Horsley CYRIL BARON

NURSING INFECTIOUS DISEASES

SIR,—The letters of Dr Stanley Banks (Feb 3) and Prof A V Neale (Feb 17) raise many problems, not least that a general trained nurse can admit "that she has never had any practice in handling a baby, or in the principles of infant feeding"

Candidates who enter for the final general examination of the General Nursing Council for England and Wales must have had experience—not only lectures—in medical and surgical nursing, in gynæcological nursing, and in the nursing of sick children The head of the training school usually the matron, must send a signed certificate to this effect before the candidate is accepted

Members of former councils, myself included, have often proposed that general training schools should be asked to give some details of the experience candidates have had, including experience in the nursing of sick infants and children and the real solution to the present lack in training is for the General Nursing Council to bring this measure into effect With good will and good administration it could be achieved almost overnight. It may mean that some of our large and well known training schools will have to second their nurses for specialised experience in this field, but the ultimate benefit would far outweigh any temporary inconvenience

London W 8 EVELYN C PEARCE

SURGICAL RELIEF OF MYOCARDIAL ISCHÆMIA

SIR,—In his intriguing paper last week Mr Mason expresses his belief that treatment of angina (and, incidentally, of heart failure) by reduction of metabolic activity has now been discarded He also considers that this treatment condemns the patient to "a reduced level of existence"

Reduction of basal metabolism in cardiac disability is nowadays carried out by thiouracil medication, not by thyroidectomy, and it is certainly not discarded I know that at least one of the leading cardiologists of this country practises the method widely I have used it in a small series of cases selected by the crippling nature of their condition, and by the failure of all other treatment to enable the patient to lead a working, or at least an ambulant, life, or to maintain life at all in the face of advancing and intractable congestive failure Of 12 such patients, 1 died of (his second) coronary thrombosis after three years of freedom from angina The other 11 have continued the active life they were on the point of giving up, or have resumed activities previously beyond their scope In each case the maintenance treatment was, either purposely or accidentally, reduced below the required level at one time or another without the patient's knowledge The relapse that follows within one or two weeks, and the rapid restoration upon resumption of adequate treatment, are a dramatic therapeutic test One of my patients, a man with a rheumatic aortic stenosis, went into failure in the autumn of 1946, became bedridden within a few months with massive œdema, anasarca, and a right sided pleural effusion (tapped, $1^1/_2$ pints) Under thiouracil, instituted in the nick of time, he lost all his accumulated fluid and has not again required digitalis or mersalyl Like all these patients, he is maintained just *above* myxœdema level, and, so far from living "on a reduced level,' he has in the meantime become my very efficient secretary

London W 1 G SCHOENEWALD

A VISIT TO INDIA

SIR,—Last October and November I was privileged to take a party of medical practitioners from this country for a goodwill tour of India. The trip, I am glad to say, was most successful, and the welcome and hospitality extended to us by my countrymen in India were so unstinting and sincere that I am now making arrangements to repeat the tour over a period of six weeks during October and November of this year.

The party will travel by air between London and Bombay and all journeys during our stay in India will be made either by air or by rail. Our itinerary will include visits to places of historical and archæological interest, as well as to universities, hospitals, and cultural centres in Bombay, Mysore, Bangalore, Hyderabad, Madras, Delhi, Agra, Kashmir, Calcutta, and Darjeeling. The total cost will be approximately £250 per person.

My primary objective in organising the tour is to stimulate full comprehension of India's vast potentialities in those persons who, through active work in their profession, are most favourably placed to strengthen the ties of friendship between Great Britain and India. Inquiries from doctors wishing to join the party should reach me before March 31.

125, Harley Street,
London, W.1. R. HINGORANI.

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—Our cases of hypertension treated with methonium compounds now number 50, and many of them have been followed as outpatients for almost six months. Most of these were cases of essential hypertension with severe headache or left ventricular failure; 2 had had bilateral sympathectomy without benefit, and 1 had malignant hypertension.

Our method of administering the drug was to give 25 mg. by injection intramuscularly and observe the blood pressure at fifteen-minute intervals for the next two hours. If this initial dose was unsatisfactory it was increased by 10 mg. or more and the procedure was repeated until we obtained what we felt was a satisfactory fall in blood pressure. The drug was then given by injection six-hourly, and as tolerance increased the intervals were reduced until in some cases the patients were having as much as 100 mg. three-hourly. After seven to fourteen days on injection the patient was transferred to the drug by mouth. We considered that a suitable dose to commence with would be 250 mg. by mouth at the same time interval as every 50 mg. was given by injection. In some cases the patients had as much as 7–8 g. daily by mouth.

Before any patient was started on methonium treatment he was given a fortnight's rest in bed, and his blood pressure was taken at frequent intervals during the day. When the patient was put on the drug his blood-pressure was taken even more frequently. All the injections were given with the patient sitting up, and a few patients were ambulatory. After four weeks in hospital all the patients were up and about. They were then seen as outpatients fortnightly or more often.

Since finding a case of bromide poisoning about five months ago we have estimated the serum-bromide level fortnightly on every patient receiving hexamethonium bromide. We found that every patient had a reasonably high serum bromide level, and owing to the slow excretion of bromide these serum bromide levels tended to increase at about the same rate irrespective of the dose of the drug, or at least provided the dose was between certain fairly wide limits. We have recently had a second case of bromide intoxication in a patient whose blood pressure did not fall in spite of the fact that he was receiving at one time 12 g. of hexamethonium bromide by mouth.

Our results, which we hope to publish in detail shortly, have been unsatisfactory. Unquestionably injections of the drug, and in some few cases oral administration, will produce an acute fall in blood pressure. Sometimes, however, in spite of large doses of the drug, even this acute fall did not occur. In all cases except 1, oral administration of the drug failed to keep the blood-pressure down, and every patient so far seen at outpatients has had a blood-pressure at the same level as it was before treatment was commenced, though many patients admitted to feeling much better. The initial fall in blood-pressure obtained with methonium compounds is often, in our experience, no greater than that produced in many patients by rest in bed.

We agree with the writers who have suggested that at present these compounds should only be used under hospital observation. The production of a drug which has a longer action than the hexamethonium compound and which does not contain the bromide radicle, or alternatively is effective in much smaller doses, would be the ideal to aim at.

Oldchurch Hospital,
Romford, Essex. S. LOCKET
Senior Physician.

SIR,—After Kay and Smith[1] observed that the potency of the halide salts of hexamethonium given orally, expressed in terms of the cation, was highest for the iodide and lowest for the chloride, with the bromide intermediate, clinical studies of this drug have been made mostly with the bromide or iodide. It seems improbable, however, that the halide anion of such a salt, which must be completely dissociated in solution, can exert any significant effect on the activity of the hexamethonium cation, or even on its absorption. In view of the possibilities of bromism[2] and of iodism from the use of the bromide or iodide, we have been prompted to test the purity of some of the available preparations in order to determine whether the reputed inefficacy of the chloride was associated with any impurity, and to verify whether with pure salts the biological activity of the cation did indeed vary with the different halide ions. We have determined the halide content of samples of hexamethonium salts, and have assayed biological activity, using the antagonism of hexamethonium to the action of acetylcholine on the frog's rectus abdominis (limits of error 7–10%, $P = 0{\cdot}05$). The results were as follows:

Hexamethonium salt	*Biological activity*	*Halide content (% theoretical)*
1 Iodide	95	94
2 Iodide	100	99
3 Iodide	100	100
4 Bromide	90	94
5 Bromide	100	99
6 Chloride	80	84
7 Chloride	97	99

Biological potency is given (in terms of the cation) as percentage of that of the pure iodide (Salts 2 and 3).

It will be seen that biologically several of the salts were below theoretical potency, and that in each case there was evidence of impurity. One particular cause of apparent inefficacy of the chloride came to our attention. We obtained a sample of chloride which had been made up as a powder in a waxed paper, in which it had remained for some months. On opening the paper no powder could be seen; but simple extraction of the paper with saline, followed by biological assay, produced 91% of the quantity of hexamethonium stated to be within the paper. The chloride therefore is sufficiently hygroscopic to take up so much water-vapour that it can go into solution and impregnate the wrapping paper.

We believe, therefore, that the results of Kay and Smith may have been due to a failure to give the full dose intended because of some impurity in the chloride

---

1. Kay, A. W., Smith, A. N. *Brit. med. J.* 1950, ii, 807.
2. Rosenheim, M. L. *Lancet*, Feb. 10, 1951, p. 347. Holt, M. C., Litchfield, J. W. *Ibid.*

used—probably water We suggest that the chloride, offering as it does freedom from actions other than those of the hexamethonium cation, should be more fully tested therapeutically The compound should be issued in a form in which it is not liable to absorb moisture, leading to errors in dosage

National Institute for Medical Research
London N W 7
W D M PATON
J WALKER

INTRAVENOUS IRON FOR ANÆMIA OF PREGNANCY

SIR,—I should like to thank Dr Scott and Dr Govan for their report last week on the use of intravenous iron therapy For the past year now I have been trying this method with cases which do not respond to iron by mouth, or where time was short The second condition is common in this practice because of unmarried mothers whom I do not have under my care until eight to six weeks before delivery

I am very pleased with the rapid response to this treatment, but I agree that occasionally a patient who has had other injections without a reaction may have a vasovagal attack In preventing local pain and reactions it is essential, in my opinion, that there should be no leakage from the vein For this I recommend that a very small (immunisation type) needle should be used and that the injection should be given very slowly indeed

York F CHARLOTTE NAISH

MUNCHAUSEN'S SYNDROME

SIR,—Dr Asher is to be congratulated on his timely description and apt christening of this curious syndrome Few hospital medical officers are unfamiliar with it, and with the extent to which its sufferers (for surely it is a disease) waste our already overtaxed hospital resources

One additional feature is that these patients usually present in hospital casualty departments either late at night or at weekends—times when young and inexperienced housemen are often left "holding the fort" At many hospitals these cases are so often seen that an unofficial register of them is kept, though its usefulness is vitiated because these patients seldom "try it on" at the same hospital twice, but go on circuit An accessible central register, at least in the London area, would be of the greatest value to casualty officers because once caught out these patients usually go, quietly and quickly The E B S. would seem to be the obvious place for such a register to be kept, reports being sent there from all local hospitals I believe that by this means the syndrome could be almost wiped out

The following case is atypical in that the patient did not take his own discharge

A 43 year old man arrived in the casualty department of St Giles' Hospital, Camberwell, at 8 15 P M on Jan 9, complaining of sudden onset of severe epigastric pain and vomiting Three upper and one lower abdominal scars were said to be due to operations on the stomach, gallbladder, and right inguinal hernia, one of these having been done at Mansfield Hospital in 1945 He was admitted with a provisional diagnosis of perforated peptic ulcer Although he had marked upper abdominal guarding and rigidity, gut sounds were heard, and there was no rise in temperature or pulse rate He was treated by continuous gastric suction, which he tolerated unexpectedly well

Inquiry revealed that he was never operated on at Mansfield Hospital A barium meal was entirely negative, and he was reassured and discharged on Jan 27, when he agreed that his pain was better

The same evening he arrived at Dulwich Hospital with the same story When he was on the point of being admitted, a nurse noticed a certificate of the same date from St Giles in his pocket A telephone call followed after which his pain mysteriously vanished and he left He was last seen walking down the road divesting himself of handfuls of tell tale certificates, evidently determined not to be caught out like that again

I wonder who's treating him now

St Giles Hospital,
London, S E 5
J E H STRETTON

SIR,—A good example of this syndrome was to be found in a ship's steward, of about 40, who haunted London hospitals about 1920 to 1934

He presented as a case of acute amœbic hepatitis, and he was able to produce just that element of "artistic verisimilitude" which could deceive at first the most experienced clinician, and which Dr Asher (Feb 10) mentions as a feature of the syndrome

His stay in hospital seldom lasted more than three days, and usually culminated in his throwing any convenient china utensil at the nearest nurse I met him first when he was admitted under the care of the late Dr F J Poynton at University College Hospital in 1920, pathological investigations had not got far when he threw a sputum mug at some unoffending nurse in the vicinity and was immediately discharged, though I cannot recollect whether we succeeded in dismissing him before he removed himself of his own accord.

I met him again about 1934 in St Mary Abbots Hospital, there having meanwhile been a number of interesting reports of his antics in other hospitals On this occasion, although amply forewarned, as a young admitting officer I was still not proof against his wiles and did not have the courage to refuse him admission, such refusal was not encouraged by authority and was apt to be followed by reproof In any case, I thought, after all the man *might* have a real hepatitis, one of those weird tropical diseases of which before the late war so many of us were ignorant On this occasion, however, I drew his attention to his previous unsatisfactory record of behaviour and besought him in his own interests to allow diagnosis and treatment, if required, to proceed The sequel was according to his usual form, he was admitted I think on a Friday and on Sunday morning the ward telephoned me as I was sitting down to lunch "Arthur has just thrown his dinner at a nurse!" (The plate was included in the missile) Before I could get to the ward he had taken himself off, gravy and potatoes on a nice clean apron were the only damage

I wonder if he is doing it still

Leamington Spa W M PRIEST

SIR,—From Dr Asher's graphic description in his article (Feb 10), it is clear that his first patient spent a few days in Oxford last May, after leaving St James' Hospital, Balham, and before his abdomen was explored at Harrow Hospital

He gave a name readily associated with "Beeches" and his age as 47, and was admitted to the Radcliffe Infirmary on May 9, 1950, with the symptoms of acute intestinal obstruction, and a scarred, distended tender abdomen There were, however, no fluid levels on a plain radiograph He gave a similar story, with a wealth of circumstantial detail, from having his 'stomach blown to pieces" by a torpedo when chief engineer on the last ship from Singapore, to the eleven operations at Freemantle He explained the evidence of recent transfusions, presumably given at St James', as part of conservative treatment for a similar recent attack at sea, saying that his ship had docked only the previous night

He was treated conservatively, but his pain continued, this was unrelieved by pethidine, but was eased by injections of morphine or sterile water Next day he threatened to leave hospital as he considered that he had been insulted His distension and complaints increased, and a barium-enema examination was made. This showed a long filling defect in the rectum and sigmoid colon strongly suggestive of intussusception but on rectal examination nothing could be found to account for this It seemed that we had misjudged this suspicious character, and because of the well known danger of overlooking an organic lesion in such patients, operation was now advised He refused treatment, however, and was last seen on May 12 boarding a no 3 bus The following day his abdomen was explored at Harrow Hospital, as we have read, with no abnormal findings

The effect of anæsthesia on another recent patient with this syndrome was interesting

A nurse of 48, a known drug-addict, was admitted while convalescent from a compound fracture of her tibia with all the symptoms of acute intestinal obstruction Her distended, scarred abdomen bore witness to six abdominal operations, and there was tenderness in the left iliac fossa There was no evidence of nerve damage Although bowel sounds were increased, and there was gaseous distension on a plain radiograph, there were no fluid levels After the induction of anæsthesia and without the passage of flatus her abdomen became soft and flat She was allowed to regain consciousness, and as she did so her uncovered abdomen appeared rapidly to swell This seemed to be due to contraction of her diaphragm and lateral abdominal muscles rather than to aerophagy She seemed disappointed that an operation was not considered necessary, and for a time continued to complain of pain. A barium series was normal, and she was discharged a few days later, still with apparent distension

Radcliffe Infirmary Oxford. NEIL WARD MCQUAID

SIR,—A woman of 45 was admitted to this hospital on Feb 14, complaining of a fæcal fistula She gave a history of eighteen operations, all performed at the Royal Devon and Exeter Hospital, and said that for the last four days there had been a profuse discharge of foul dark material from an ulcerated area in the lower abdomen It was not until we read Dr Asher's article that we realised exactly what we were dealing with When she received no operative treatment she became very resentful and was discharged the day after admission

Lambeth Hospital
Brook Drive S E 11

J WILKS
Surgical Registrar

SIR,—To assist recognition of Munchausen's syndrome, may I recommend an old Barts custom For generations the Barts surgery has possessed a "black-book" in which descriptions of such hardy annuals are entered From it casualty officers have derived assistance, and readers have derived much amusement [1]

My first encounter with this disease (sub species, laparotomophilia) fooled me completely But the second time he was entered in the black book and introduced to the casualty porter, who was told to remember him in future Three years later he again deceived a new houseman, and was enjoying a very thorough abdominal examination in casualty, when the same porter looked through the screens He was instantly recognised by the patient who shouted "Blimey, it's you again," and bolted into the street like a startled hare I do not know the subsequent history of this patient, but it might have been of interest because his trousers remained on the couch.

London W 8 JAMES T HAROLD

RESULTS OF SURGERY IN SCIATICA AND LOW BACK PAIN

SIR,—In their interesting article of Feb 3 Mr Burns and Mr Young make two statements which, in my opinion, are not entirely correct—namely, that it is usually impossible to foretell which of the lower two discs is affected, and that at operation it is essential to explore both discs I agree that it is usually impossible to foretell, from orthopædic or neurological *signs*, which of the lower two discs is affected, but surely this can often be decided, before starting the physical examination, from the distribution of the sciatic pain ? This, of course, does not apply to patients with low back pain only The majority of patients, if carefully questioned, localise the sciatic pain accurately to the distribution of the 5th lumbar or 1st sacral nerve root, pain due to protrusion at the 4th disc is situated mainly on the lateral side of the buttock in the region of the greater trochanter, down the lateral aspect of the limb, and in front of the lateral malleolus, whereas pain due to protrusion from the 5th disc is on the medial side of the buttock in the region of the ischium, down the posterior aspect of the limb, and behind the lateral malleolus [1]

It is hardly necessary to emphasise the great value of a careful neurological history about the pain (which is usually the only complaint and sole reason for treatment), its distribution, how it has affected the patient's life, and the result of previous treatment This information not only provides the main considerations in deciding treatment, but, at the same time, it gives a better guide than physical signs to the level of the protrusion

When the pain is localised accurately to a typical root distribution, as in the majority of cases, only the affected disc need be explored, it is certainly not essential to explore both 4th and 5th lumbar spaces

Leeds W R HENDERSON

BIRTHMARKS AND MOLES

SIR,—Your annotation of Jan 20 is of interest and importance Since there is still no general agreement on the treatment of the common (or "cavernous") hæmangioma of infancy and childhood, I investigated their natural history by leaving a series untreated in 1945–46 (thus repeating the experiment of Lister [1]) together with a control series treated by the usual radiation methods

Lister's findings were confirmed, of 83 cases followed for three years 45 (54%) regressed spontaneously, and of 69 followed for five years 66 (96%) had more or less disappeared Radiation or other treatment can make them disappear faster, but this is usually unnecessary and therefore may well be considered undesirable unless there are positive reasons for treatment

These results were communicated to the fifth International Congress of Radiology in London last year, and I hope to publish the full details before long

Sheffield National Centre
for Radiotherapy

J WALTER

BEDPAN EXERCISE

SIR,—Your annotation of Jan 27 does not refer to the type of bedpan under observation The slipper model, which can be slid beneath the recumbent patient, is much less exhausting for females who (since they cannot use a bottle) may need to hop on and off the conventional type several times in the day It is also easier for the nurse

London N W 1 STELLA CHURCHILL

ELECTRIC POWER SHORTAGE AND HOSPITAL PLANNING

SIR,—During the last twenty years, at least, a trend has been apparent in hospital design, in the direction of greater concentration in higher buildings Much can be said in favour of this, and something, also, against it, but all I wish to do in this letter is to call attention to the bearing on the question of a new factor, or at any rate of a factor which has forced itself on our notice The higher the building the more is it dependent on lifts and the more paralysing is the effect of a failure of electric power A two storey hospital without the use of its lifts suffers nothing much worse than serious inconvenience, even a three storey one can struggle along, but the mere thought of a hospital of six or more storeys deprived of its lifts makes one shudder Hitherto, the risk of anything worse than rare and brief failures of electric power has been remote enough to be taken without much misgiving, but now there seems to be reason to fear that we have entered upon an era of recurring power shortage, possibly getting worse as time goes on The bearing of this on hospital design has therefore become a matter calling for serious consideration

The question may seem a little academic at present, when the prospect of building the much needed new hospitals seems to be moving into an ever more distant future with each year that passes It would, however, be well to take advantage of the period of enforced inactivity, to discuss such questions and be ready with conclusions, in case happier times ever come again

---

[1] Flavell G *St Bart's Hosp Rep* 1937 45 187

[1] Lister W A. *Lancet* 1938 i 1429

London T S McINTOSH

TRAINING OF INVALID CHILDREN

SIR,—In Prof Alan Moncrieff's address to the 62nd annual general meeting of the Invalid Children's Aid Association (*Lancet*, 1950, ii, 494) he remarked that "the state of civilisation of a community can be deduced from the way it looks after its lame ducks—and ducklings" This statement raises many important issues on which I would like your readers' advice What is the best way of looking after lame ducklings? In your report of the meeting you say that an appeal for £15,000 was made for a holiday home for invalid children, but that it had previously been disclosed that the I C A Association has an overdraft of about £12,000 and the excess of expenditure over income last year was £3000 Working in a country where many services for lame ducklings require development, I wonder how far it is justifiable to expend the time and energy of skilled workers and public money on children who can never utilise the training they receive All that these invalid children require is someone to care for them and make them happy, and I feel sure this could be done on a more economical basis than the one now recommended, though I would welcome the opinion of your readers on this subject In Malaya most of these children are cared for in their own homes, where some are well and others less well looked after, but the majority seem happy I have no hesitation in recommending training for the blind and deaf and for certain classes of cripples who can become useful citizens, but what of the others?

General Hospital, Penang, Malaya. C ELAINE FIELD

TREATMENT OF THE AGED SICK

SIR,—In his letter last week Dr Brown refers to senile mental changes as a reason for a patient being confined to bed Has he considered the other aspect of senile patients in this relation—confinement to bed as a cause of senile mental changes, ranging from exaggeration of normal involution to the "vegetable" state? Lord Amulree and his colleagues (Jan 20) do in fact mention the desirability of keeping the elderly patient mobile for physical, as distinct from mental, reasons

I feel that the relation between enforced bed rest and mental deterioration is not adequately stressed in our teaching or practice In my opinion the mental failure is a direct result of the lowered blood pressure, which follows rest, failing to force blood through the smaller cerebral vessels The fact that visitors to the bedfast patient steadily decrease in numbers as the months and years go by, with a consequent reduction of the stimulus and outside interest which they afford, is a recognisedly important factor, but it is not nearly the whole story

Blackrock, co Dublin JOHN F FLEETWOOD

SIR,—As one of those concerned with the care of the aged sick, I found Lord Amulree's article (Jan 20) interesting but somewhat disappointing In his survey he failed to mention that important clinical entity—the aged psychiatric patient In my experience the ambulant senile confusional patient presents one of the major problems in geriatrics, but one that must be tackled if we envisage a comprehensive service in this branch of medicine

It is hoped to publish shortly the results achieved in the psychiatric department attached to the geriatric unit at this hospital These results should prove encouraging, and help to illuminate a dark corner in geriatrics

J DE LARGY
Senior Medical Officer

Geriatric Unit
Langthorne Hospital London E 11

Public Health

Smallpox

WHEN S S *Strathmore* arrived from Australia in the Port of London on Feb 12, a 12 year-old girl passenger, who had embarked at Bombay on Jan 26 was removed to St Andrew's Hospital annexe, Billericay, Essex, where she was diagnosed as smallpox She was admitted to Long Reach Hospital, Dartford, on Feb 14

She had sickened on Jan 28, and a rash appeared on the 30th On that day she was isolated in the ship's hospital as a case of chickenpox She was admitted as such to the hospital in Essex, but on Feb 13 a review of the case and information that she had previously suffered from chickenpox led to a suspicion of smallpox. She had been vaccinated in infancy (two scars) and again before leaving India The recent vaccination was unsuccessful

S S *Strathmore* called at Aden on Jan 30, Suez on Feb 2, Port Said on Feb 3, and Marseilles on Feb Up to Feb 20 there had been no further reports of smallpox or suspected smallpox among the passengers and crew

Influenza

In England and Wales during the week ended Feb 10, influenza deaths in the Great Towns fell from 61 2 to 41 7 per million The number of deaths fell most steeply in the East and West Ridings, the North Western, North Midland, Midland, Eastern, London, and South Eastern regions, and in Wales There were smaller decreases in the remainder except the Northern region where there was an insignificant increase of 2 deaths The proportion of influenza deaths in the age-groups 55 and over rose to 91 5%

In the Great Towns pneumonia deaths fell from 830 (last week) to 662 Pneumonia notifications in England and Wales also fell from 3513 (last week) to 3091

In London there was a continued decline in the number of removals to hospital for pneumonia, influenza, and bronchitis, as also in pneumonia and influenza deaths

Weekly claims on the National Insurance funds for the week ending Feb 6 continued to fall There were 288,940 as against 350,714 the previous week

Influenza Abroad—There is evidence of a high prevalence of influenza in certain parts of Canada, which is understood to be due to virus A-prime It is now reported that cases in the Yugoslavia outbreak have been due to virus B, and that virus A-prime has been identified in Italy The disease is also reported in Germany, but the viral type has not, as far as is known, yet been established

Poliomyelitis

In England and Wales notifications of poliomyelitis during the week ended Feb 10 were as follows paralytic 12 (21), non-paralytic 7 (11), total 19 (32) Figures for the preceding week are in parentheses The total is the lowest since the week ended April 8, 1950

Difficulties in the School Health Service

In his report for 1949 on the school health service in Worcestershire, Dr Wyndham Parker, the county and school medical officer draws attention to three difficulties

1 *Dental Service*—As elsewhere in the country, the difficulty of retaining the school dental staff has become acute "Efforts have been made to try to maintain the service by approaching private dental practitioners, but the results in this connection have been small to date"

2 *Hospital Treatment*—Information is no longer readily available, as it was when the county council, through its education committee, paid for such treatment 'Reports are irregular and often very delayed"

3 *Specialist Service*—Specialists, notably ophthalmologists and to a lesser extent orthopædists, are now so busy with other duties that the school health service has had to take second place

Obituary

HORACE MIDDLETON VERNON

M.A D.M Oxfd

Dr H M Vernon for many years a member of the ientific staff of the Industrial Health Research Board as a pioneer in the application of scientific method and search to the problems of the conditions affecting hose who work in factories

Born in 1870 he was educated at Dulwich College and erton College, Oxford to which he obtained a science cholarship In 1891 he took first-class honours in the hemistry and physiology schools. As an added interest e studied biology and with a biological scholarship in 894 he worked at the Marine Biological Station at Naples, where he specialised in a statistical study of the effects of environment and cross fertilisation on the growth of sea-urchin larvæ He obtained the Rolleston prize the George Henry Lewes scholarship and a Radcliffe travelling fellowship, and he held a university lectureship in chemical pathology before taking his medical degree in 1898

Shortly afterwards he was elected to a fellowship at Magdalen College, Oxford which he held till 1920 There he settled down to teaching and research work in physiology But the 1914–18 war diverted his interest and he became for a time a worker in a munition factory in Birmingham His medical and scientific training opened his eyes to the environmental problems of industrial workers When the Health of Munition Workers Committee was appointed in 1915 to study the human problems of the industry Dr Vernon was one of the first investigators appointed His early work on hours of labour has been of great practical importance, and he also introduced a method of studying the effects of hours of work on health and output These findings were embodied in his official memoranda on Industrial Efficiency and Fatigue in Munition workers published between 1915 and 1918

When the Industrial Fatigue (Health) Research Board was instituted at the end of the war, Dr Vernon was offered a post The rest of his working life was spent in research concerned with tinplate workers, blast-furnace workers and coalminers particularly from the point of view of atmospheric conditions heating and ventilation in potters shops, rest pauses accidents, and allied subjects

After he retired in 1932 he occupied himself in writing and he also found more time to watch the cricket matches which he so greatly enjoyed Apart from articles in scientific journals he published in these years authoritative books on *The Principles of Heating and Ventilation* (1934) *The Shorter Working Week* (1934), *Accidents and their Prevention* (1936), *Health in Relation to Occupation* (1939) All these works show clearly how Dr Vernon s scientific training both in the organic and inorganic field helped him to recognise allied problems in a different field and gave him the tools with which to collect and analyse his data He died on Feb 11 after a long life spent in work he loved

Dr Vernon married Miss Katharine Ewart She survives him with a son and three daughters

CHARLES PYE OLIVER

C.B C.M.G M D Lond., D P.H

Dr Pye Oliver who died on Jan. 28 in his 90th year, had served Maidstone as a townsman and a doctor for well over half a century His family had a tradition of civic service for his father Dr J Oliver, was an alderman and mayor of Maidstone

Dr Oliver received his medical education at Charing Cross Hospital and University College Hospital As soon as he obtained the L.S.A. in 1885 he started in practice at Gabriel s Hill, Maidstone, but he continued with his studies and he obtained in turn the Conjoint qualification in 1887, the M B in 1885, and the M.D in 1892 His interest in public health had already been aroused and in 1896 he took the D P H. and his M D in State medicine in 1902

Meanwhile in 1899 he had been appointed medical officer of health for Maidstone Contemporary interest in raising standards of health and hygiene gave him opportunities which he was quick to seize, and he started the maternity and school medical services of the town on a sound foundation Besides these official duties he acted as physician to the West Kent Hospital, in addition to running his practice, and in these early days most of his visits were paid on horseback

As early as 1887 he had joined the Old Maidstone company of the Volunteer Medical Staff Corps Later he became surgeon of the corps and eventually succeeded to the command with the rank of major He represented the corps at the funeral of Queen Victoria In 1913 he was appointed honorary surgeon to the King for his work for the field ambulance service in Kent

During the 1914–18 war he served in France with the 67th division and he was three times mentioned in despatches Later he became A.D.M.S of the 67th division and the 23rd Army Corps In 1918 he was appointed C.M.G and in 1927 C B After the war he continued his association with the Regular and Territorial Armies and he became honorary colonel of the R.A.M C units of the 44th division of the Territorial Army

Dr Oliver worked for his county as well as his town and in 1920 he became a J.P for Kent, sitting regularly on the Bearsted bench In 1931 when he retired he was appointed a deputy lieutenant of the county During the late war though he was in his 80s, he was county controller of the V.A.D, and he also worked for the British Red Cross Society and the Order of St John of Jerusalem

Since 1919 Dr Oliver had been a widower, but he leaves four sons and one daughter A son has followed his father in practice in Maidstone.

Dr ALBERT JACOBUS STALS the South African minister of health and social welfare who died at Cape Town on Feb 5, was a graduate of medicine and law of the University of Dublin. He qualified in 1909, taking his M D the following year He was a member of the South African parliament from 1924 to 1933 and again from 1943 onwards Dr Stals was made minister of education and of health and social welfare when the Nationalist government was formed in 1948, but he gave up the portfolio of education in 1949

Appointments

ADAMS A V., M.A M.B. Camb resident M O Ipswich Borough General Hospital

BIGGAM JAMES M C M.B Edin D O.M.S asst ophthalmologist Glasgow Eye Infirmary

CROWLEY NORA M.B N U I asst M O maternity and child welfare and school medical inspection Northampton

GILMOUR DAVID M.D Edin D.P.M consultant psychiatrist Glasgow Royal Mental Hospital Killearn Hospital and Lansdowne Clinic Glasgow

MCALPINE D F M.B Glasg D A anaesthetist Ballochmyle Hospital

PHILLIPS T J M R.C.S consultant ophthalmic surgeon St Helens Hospital and Newton le-Willows Hospital

PIZEY N C D M B Lond F.R.C.S house surgeon (senior house-officer grade) Hospital for Sick Children Great Ormond Street London

RANKIN A L K M.D Edin D.P.H physician-superintendent Belvidere Infectious Diseases Hospital Glasgow

RITCHIE W M M B Aberd D.L.O consultant ear nose and throat surgeon Falkirk and district hospitals and Stirling and Clackmannan hospitals

SHANKS A G M.B Glasg D.P.H D O.M.S ophthalmologist, hospital and school eye service Lanarkshire

SHEPHERD J A. M D St And., F.R.C.S.E. consultant general surgeon Broadgreen Hospital Liverpool

STANLEY D A M.D Lond consultant pathologist Bootle General and Waterloo and District Hospital Liverpool

TAYLOR IAN M.D Lond M.R.C P senior M.O (epidemiology) London County Council

Colonial Service

CUMMINS GERALDINE, M.B. Camb M.R C.P M O Federation of Malaya

DAVIES, C S M.R.C.S D.P.H. asst director of medical services Nyasaland

LAWSON T L. M.B. M CH. Dubl F.R.C.S.E. D T.M & H senior specialist Nigeria

MACKINTOSH G S M. M.B. Aberd. M O., Nigeria

Notes and News

APPROVED NAMES FOR DRUGS

THE British Pharmacopœia Commission have added five approved names to the supplementary list they published last year (*Lancet* 1950, ii, 422)

Approved names	*Other names*
Paramethadione	5 Ethyl 3 5 dimethyloxazolidine 2 4 dione Paradione
Ethopropazine	N (2 Diethylamino *n* propyl) phenothiazine Lysivane is the hydrochloride
Diethylcarbamazine	1 Diethylcarbamyl 4 methylpiperazine Banocide is the dihydrogen citrate Hetrazan is the dihydrogen citrate
Lucanthone	1 2 Diethylaminoethylamino 4 methyl thiaxanthone Nilodin is the hydrochloride
Solapsone	Tetrasodium 4 4 bis (γ phenylpropyl amino) diphenylsulphone α γ α γ tetrasulphonate Sulphetrone

TUBERCULOSIS

"I DO not admit of pessimism, but optimism is difficult," a correspondent recently wrote to Sir John Charles, chief medical officer of the Ministry of Health In quoting the letter at the annual luncheon of the Joint Tuberculosis Council, on Feb 17, Sir John remarked on his own different outlook "I do not admit of complacency, but pessimism is difficult" Since July 5, 1948, he said, over 3500 tuberculosis beds have been added to the complement in England and Wales, and further additions are expected in the next six months, in the past year whole time tuberculosis nurses have increased by 700, and part time nurses by 150, B C G vaccination is now well established, 30,000 people having received it already, and an immunisation rate of 5000 a month is contemplated in the near future Since the start of the National Health Service the number of mass radiography units in action has risen from 30 to 60, and some $1^1/_2$ million people are now being examined yearly

Dr Peter Edwards, the chairman, in answer to Sir John Charles's toast of The Council, made a rallying reply on the recent mitosis at the Ministry Sir Robert Young, in a kind and elegant speech, proposed the toast of The Guests, and Dr Hugh Clegg, replying, related a parable Two skeletons, he said, hanging in a remote corner of an old mansion, were arguing about their situation "Say what you like," one of them finally declared "if we had any guts we could get out of this —— cupboard"

MEDICAL GAS CYLINDERS

A FURTHER meeting of the Conference on Medical Gas Cylinders was convened by the Association of Anæsthetists on Jan 24 The conference received a report that provisional agreement had been reached between representatives of the United Kingdom and the U S A, at a meeting of the International Standards Organisation, regarding the introduction of certain colour markings and of non interchangeable couplings for medical gas cylinders, with a view to eliminating the possibility of using the wrong gas The agreement requires ratification by the appropriate bodies in each country This is now being sought, and it is hoped that these proposals, which have been accepted by the International Standards Organisation, will soon take effect

TOXIC SPRAYS

THE *Manchester Guardian* (Feb 16) reports that the National Farmers' Union have recommended that farmers using toxic sprays should ensure that

Operators wear protective clothing

Proper facilities for washing are provided near the scene of spraying operations

Limits are placed on the period of work each day and the total period in each week

Adequate supervision of workers using toxic substances is made

No food or drink is consumed within the spraying zone

Proper decontamination of machinery and equipment is carried out immediately after use

Attention was drawn last year to the dangers of some of the newer insecticides by Dr James Wilson, secretary of the American Medical Association's council on pharmacy, and by Dr Donald Hunter in his Ernestine Henry lecture to the Royal College of Physicians (*Brit med J* 1950, i, 449, 506, *Lancet* 1950, i, 407)

WEST LONDON RHEUMATISM DEPARTMENT

MORE than a thousand new patients are seen each year at the West London Hospital's department of rheumatic diseases, and the department's attractively designed report for 1950 illustrates the many different activities of workers in this field The papers published in the report include a lecture given by Prof Philip Hench when he visited the department, an account of a tour in America by one of the staff, and the diary of a patient with rheumatoid arthritis while under treatment with 'Cortisone' and A C T H

DIRECTORY OF INTERNATIONAL SCIENTIFIC ORGANISATIONS

DETAILS of the aims, facilities, publications, and governing bodies of more than 150 international scientific bodies are given in this UNESCO handbook, which is now available at H.M. Stationery Office (6s) The organisations are grouped under three headings basic sciences, applied sciences, and the ever hospitable "miscellaneous" Medicine takes its place among the applied sciences, and 59 organisations are listed The handbook offers a great deal of information, not otherwise readily accessible, in a convenient and readable form

OFFICE ROOMS NEEDED

THE British Epilepsy Association, founded last year as a memorial to Dr Tylor Fox, has made good progress So far it has been housed in the building occupied by the National Association for Mental Health, but there is only room for one worker in the space available, and the time has now come when the British Epilepsy Association needs clerical staff if its plans are to develop The honorary secretary asks for news of one or two office rooms in a central position, and at a moderate rent, which might be suitable for this young and growing body Anyone able to suggest appropriate quarters is asked to write to Miss Irene Gairdner, at 39, Queen Anne Street, London, W 1

PROSPECTS IN THE DESERT

"IF ye be willing and obedient, ye shall eat the good of the land, but if ye refuse and rebel, ye shall be devoured with the sword for the mouth of the Lord hath spoken it" Thus wrote Isaiah over 2600 years ago

Today the prophets exhort us to apply scientific principles and techniques to farming throughout the world, that we may become well fed and prosperous, otherwise we shall die in our millions of starvation and in the civil wars and epidemics that accompany famine The message is clear and simple, if we die, it will not be for lack of forewarning The chief prophet Lord Boyd Orr, speaks to the world with the full vigour of stern Scottish evangelism, minor prophets follow with varying success Among these Ritchie Calder with his new study of desert civilisations,[1] is assured of a high place Calder was asked by UNESCO to investigate the problem of developing for human use the vast desert surfaces of our planet He limited his study to the deserts of North Africa and the Middle East, visiting Algeria, Tunisia, Tripolitania, Cyrenaica, Egypt, Iraq, Iran, Israel, and Cyprus He used every ancient and modern means of transport and was accompanied only by Raymond Kleboe, whose beautiful photographs help towards a proper understanding of the book Calder has a sense of science and a sense of history and also a peculiar appreciation of values in a civilisation From all his cameos there stand out in close association the art and skill of the water engineer, the efficiency of the farmer, the health and energy of the people, and the level of their culture Throughout history these are intimately interwoven, and there seems no escape from the conclusion that water engineering was and remains the foundation on which all our high civilisations ultimately stand If the water engineer fails, then mankind cannot prosper and the arts die

Calder gives his message simply, even ruthlessly, but the breadth of his knowledge and the sureness of his judgments make the book fascinating and exciting Although in most places he visited the state of agriculture and the condition of the people was poor and often pitiable, yet in every country he met a few scientific people captivated by the desert and confident that much of it could be reclaimed for agriculture Applied science has already yielded impressive results There is, for example, the great work of the Jewish collective settlements (kibbutzim) in bringing the deserts of Palestine back into cultivation and also the successful banishment of alaria from Cyprus The book ends with the words of an d French Colonial officer, just about to retire on parting om Calder in the Kasserine Gap 'Tell me that there are the world ten men who believe that the desert can be made blossom—ten men who believe that we can redeem the upidities of mankind—and I shall die happy

---

[1] Calder R Men against the Desert London George Allen & Unwin 1951 Pp 186 12s 6d

---

niversity of Cambridge

On Feb 9 the following degrees were conferred

M.D—* J P Bull M. M. Bull J A Cosh C A. de Candole M. Hay Robert Hodkinson * J A R Miles F G Sita Lumsden H C Upjohn John Vallance Owen

M.B B Chir—* Vera Armett, *Rosemary A Cooper * I M. ulver *W R. Jockes * C D Lacey K G P Mackenzie *H F W ribram * G E Sayce

* By proxy

niversity of London

The governing body of the British Postgraduate Medical ederation has awarded travelling fellowships for 1951–52 enable for one year to W A Briscoe B.M., of the Post raduate Medical School of London (respiratory function, S.A), H. McK. Carey, M B., F.R C S.E , M.R C O G , of the nstitute of Obstetrics and Gynæcology (uterine physiology, anada and U S A.) J A Carr, F.R.C S , of the Institute f Urology (calculus formation, U S.A.) , J O Laws, M.R C.P , f Guy s Hospital Medical School (cytology France) , R B ynn, M.D F.R.C S , of the Postgraduate Medical School of ondon (cardiovascular surgery, U S.A.)

niversity of Birmingham

Dr A. P Thomson professor of therapeutics in the university has been appointed dean of the faculty of medicine in uccession to the late Sir Leonard Parsons

University of Manchester

The Queen will attend a congregation to be held on May 13 n celebration of the centenary of the Owens College, to eceive the honorary degree of LL.D The other graduands will include Sir John Stopford F R.S vice chancellor of the university since 1934

Royal College of Surgeons

At a dinner held on Feb 14, to mark the 223rd anniversary of John Hunter s birth, Mr H A. Marquand, the new Minister of Health, said that a great opportunity lay before him. The transfer of responsibility for housing to the Ministry of Local Government and Planning left him free to concentrate on the health services as could no Minister since Mr Lloyd George formed the department in 1919 with Lord Addison at its head. (Lord Addison, a fellow of the college was present at the dinner) Mr Marquand declared that his aim was to learn, not only about the National Health Service and its various institutions but also about the traditions of the medical and allied professions With his university background he would be especially sympathetic towards claims for medical education or research and he appealed for the coöperation of all doctors to build up a service that would be of real value to the people Mr Marquand was proposing The College and in his reply Sir Cecil Wakeley the president dwelt on the activities of the past year In 1950, he said the law decided that the college was a charity and that the Middlesex Hospital was not nationalised, while in 1951 the law decided that the Middlesex Hospital was nationalised and the college was not a charity [*Lancet* 1950, ii, 155 , Feb 17, 1951, p 405] 'Very perplexing' the college at any rate is not letting its uncharitable status pass unchallenged and is taking the question to the House of Lords ' Turning to examinations Sir Cecil remarked that an agreement for reciprocity of primary fellowship examinations had been reached by the three Royal Colleges of Surgeons and the Royal Faculty of Physicians and Surgeons of Glasgow ' This arrangement will alleviate the hardship caused to men who at present feel the need to pass more than one primary examination while still not in a position to know which fellowship they will eventually wish to hold As to finance, the college, with great projects in hand had its anxieties a further £400 000 or so was needed for building alone In replying for The Guests to a toast by Prof Ernest Finch the Archbishop of York owned that he had found some difficulty in briefing himself for a well known book of quotations cited among many references to surgeons, only one that was laudatory Mr P H Mitchiner proposed the Hunterian Orator and Sir Max Page, this year s orator replied

University of Sheffield

Dr C M Scothorne has been appointed honorary demonstrator in bacteriology, Dr Cedric Harvey clinical teacher in child health, and Dr J Walter clinical teacher in radiology

Royal College of Physicians of London

Prof K. J Franklin will deliver the Oliver-Sharpey lectures on Tuesday and Thursday, March 13 and 15, at 5 P.M at the college, Pall Mall East, S W 1 He is to speak on Aspects of the Circulation s Economy

Ministry of Health

The Minister of Health Mr H. A Marquand M P , has appointed Mr A. R W Bavin to be his principal private secretary, and Miss L R Prescott to be his assistant private secretary

Harveian Society of London

Sir James Learmonth will deliver the Harveian lecture to this society on Thursday March 15, at 8 15 P.M. at the Royal College of Surgeons, Lincoln s Inn Fields, London, W C.2 He is to speak on the Surgery of the Spleen

Ulster Pædiatric Society

At a meeting of this society on Feb 7, with Dr Rowland Hill in the chair Dr Joan Logan spoke on Renal Acidosis, Dr R J Young on Cystic Disease of the Lung Dr A. W Dickie on B C G Vaccination in Tuberculous Families in Sweden

Ophthalmologists Fees

At a meeting on Feb 9 the N O T B Association unanimously resolved that they could not accept the validity of a reduction in the fee for medical examination through the supplementary ophthalmic service to £1 They held that any fee below 25*s* was inequitable and would not be accepted save under duress The association is circularising all its medical members giving full particulars of the stand taken

Kingston Victoria Hospital

After discussions between the Minister of Health and a deputation led by Mr J Boyd Carpenter, M.P , on the plan to convert the Kingston Victoria Hospital from a general hospital into a gynæcological unit the following agreed statement was issued

> The Minister explained the general proposals of the south west metropolitan regional hospital board which have led to the present situation Members of the deputation put a number of points to the Minister and the Minister undertook to consider these points

A New Chair at Yale

Dr J F Fulton has retired from the chair of physiology at Yale to accept a new appointment, also at Yale as Sterling professor of the history of medicine It is expected that Dr Fulton will develop a small university department in the field of the history of medicine and science in the historical division of the Yale medical library He will have an honorary appointment in his old department and will continue with certain phases of physiological research important for the present war emergency

Slimming on Television

For the next three to four months viewers will be able to watch the progress of two women who are taking part in a slimming experiment under the supervision of Dr David Edwards of University College Hospital On Feb 27, a television cookery expert will discuss a special diet and Dr Edwards will explain the medical aspects of slimming The two women will appear in future *Designed for Women* programmes, when they will be weighed and measured and will describe their reactions to the diet

£1000 to be Recovered from Dentist

Mr Hector McNeil Secretary of State for Scotland, has directed the Executive Council for Ayr County to recover £1000 from a dentist The dental service committee had found that in treating six of his patients this dentist had failed to employ proper skill and attention. His offences included failure to undertake fillings which were obviously necessary, and proposals to carry out multiple extractions and to provide full dentures in excess of the treatment required Four of the six patients he failed to advise as to the whole treatment necessary He also failed to produce records when asked for them by a dental officer of the Department of Health , and he admitted that all his records had been destroyed

Society of Chiropodists

The annual convention of the society will take place on April 26, 27, and 28, at Friends House, Euston Road, London, N W 1 Sir Henry Cohen will open the convention, and other speakers will include Lord Amulree and Mr T T Stamm

Association of French-speaking Pædiatricians

The association will hold its 13th congress at Algiers from May 7 to 9 Further particulars may be had from the Expansion Scientifique Française, 23, rue du Cherche Midi, Paris, vi

International Congress of Gynæcology

To celebrate their jubilee the French Society of Gynæcology, in collaboration with UNESCO, are holding an international congress at the Centre Marcellin Berthelot, 28 bis, Rue St Dominique, Paris, from June 23 to 29 Further information may be had from Dr Maurice Fabre, secretary general, 1, rue Jules Lefebvre, Paris, ixe

South African Minister of Health

Dr Karl Bremer has been appointed South African minister of health and social welfare in succession to the late Dr Stals Dr Bremer obtained his M B degree at Cape Town University in 1935 and his F R C S in 1938 On his appointment as minister he resigned from the presidency of the South African Medical Council, an office which he had held for many years

C M F /M E F Physicians' Reunion Dinner

This dinner will be held this year in the hall of the Royal College of Physicians of Edinburgh on Saturday, May 12 Any physician who served in these Commands during the war should write to the Edinburgh secretary, Dr R W D Turner, 20, Warriston Crescent, Edinburgh

South Wales Medical Ex-Service Association

This association will hold their annual reunion dinner on Saturday, March 3, at the Park Hotel, Cardiff, at 7 45 P M Colonel D P Holmes will be in the chair Tickets (12*s* 6*d*) may be had from the hon secretary, Mr C W D Lewis, surgical unit, Royal Infirmary, Cardiff

The Minister's Reception

On Friday last Mr Hilary Marquand, the Minister of Health, held a reception at the new office of his Ministry in Savile Row The move from Whitehall, where the Ministry's present offices will be occupied by the Minister of Local Government and Planning, is taking place gradually over the next few weeks

London Hostel for Tuberculous

At the end of last year the Ministry of Health approved in principle of the London County Council's proposal to provide hostel accommodation for people with tuberculosis who are infectious but are unlikely to benefit by further sanatorium treatment and who have no suitable home of their own (see *Lancet*, 1950, ii, 779) The L C C announce that they are now setting up a hostel of this kind for 35 men in Islington

World Health Organisation

Japan has applied for full membership in W H O The application has been placed on the agenda of the World Health Assembly due to open on May 7 in Geneva According to the W H O constitution, States not belonging to the United Nations can be admitted as members by simple majority vote of the assembly To date, 74 countries have joined W H O and one country, Southern Rhodesia, has been admitted as an associate member

---

Mr C Price Thomas, under the auspices of the British Medical Association and the British Council, is spending two weeks in Yugoslavia lecturing and giving demonstrations of the surgical treatment of tuberculosis He is accompanied by Dr Robert Machray and Mr Peter Jones

The Royal Society for the Prevention of Cruelty to Animals has issued the 7th edition of its booklet on First-Aid and Fire Precautions Copies may be obtained, price 6*d* , from the society, 105, Jermyn Street, London, S W 1

CORRIGENDUM : *Potassium Deficiency in Idiopathic Steatorrhœa* —Dr Lubran and Dr McAllen inform us that in the report on the blood chemistry of their patient (*Lancet*, Feb 10, p 321) the figures for sodium should have been 301 mg (130 9 m eq), for calcium 7 6 mg (3 8 m eq), and for phosphorus 3 2 mg (1 8 m eq)

Diary of the Week

FEB 25 TO MARCH 3

Monday, 26th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene, Keppel Street W.C.1) Prof J Engelbreth Holm (Copenhagen) Folic Acid and Growth of Tumours, especially Rous Sarcoma
INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Mr R C Davenport Clinical Picture of the Normal and Abnormal Macular Region
HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Mr William Tanner The Man John Hunter Rejected The Man John Hunter Selected Retrospect and Prospect (Hunterian oration)

Tuesday, 27th

UNIVERSITY COLLEGE Gower Street, W C 1
5 15 P M Dr McKeen Cattell (New York) Observations on the Mechanism of Action of the Digitalis Glycosides on Cardiac Muscle
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene) Dr J R Squire The Reactions to Protein Sensitisation
INSTITUTE OF NEUROLOGY The National Hospital Queen Square W C 1
5 P M Prof H Hyden (Gothenburgh) Chemical Changes in Nerve Cells with Respect to Function and Age

Wednesday, 28th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields W C 2
5 P M Dr Ruth Bowden Factors Influencing Functional Recovery of Peripheral Nerve Injuries in Man (Hunterian lecture)
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr Norman Ashton New Vessel Formation in the Retina
MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr S Cochrane Shanks Influence of Radiology on the Diagnosis of Abdominal Disease (Second Lettsomian lecture)
UNIVERSITY OF GLASGOW
4 30 P M (Chemistry Department) Dr H P Himsworth Nutritional Factors in Liver Disease (Noah Morris lecture)

Thursday, 1st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Prof T McKeown Congenital Malformations.
INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Street, W C 2
5 P M Dr S C Gold Eruptions of the Hands
LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant Liverpool 3
8 P M Prof R A Willis Diagnostic Errors in Tumour Cases.
UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd Dundee) Dr H P Himsworth Nutritional Factors and Liver Injury

Saturday, 3rd

ST STEPHEN'S HOSPITAL, Fulham Road S W 10
10 A M Dr W Russell Brain P R C.P Cervical Spondylosis. (Introductory address to a weekend course on the rheumatic diseases)

Births, Marriages, and Deaths

BIRTHS

GLYN —On Feb 14 in London the wife of Dr John H. Glyn —a son
LISTER —On Feb 15 at Plymouth, the wife of Dr H K. N Lister —a daughter
MACKELLAR —On Feb 13 at Heckmondwike, the wife of Dr John MacKellar—a daughter
MANN —On Feb 6 in London, the wife of Dr Trevor P Mann—a son
RODGERS —On Feb 9, the wife of Dr W B Rodgers—a son

MARRIAGES

CALDER—REW —On Feb 10 at Appleshaw Hants Kenneth Vassall Calder M B to Cynthia Branfill Rew
JOHNSON—NOBLE —On Feb 10, at Newcastle upon Tyne, Gordon Trevor Johnson M B to Helen Margaret Noble M B

DEATHS

BRAYNE —On Feb 2 William Frederick Brayne, M.B Edin., lieut.-colonel I.M S retd
BROWN —On Feb 14 in London Henry Robert Brown, O.B.E. L R C P E lieut -colonel, I M.S retd
BROWN —On Feb 11 in London William Armour Brown M.B. Edin. F R C S E
BUCKLEY —On Feb 13 at Onchan Isle of Man Charles Herbert Buckley M R C S L D.S , aged 85
COGHILL.—On Feb 14 in London Violet Alice Penrose Coghill, M B Edin aged 83
LOCKWOOD —On Feb 13 at Worthing Dora Elizabeth Lockwood L R.C P E aged 88
MAINPRISE —On Feb 10 at Aldershot, Cecil Wilmot Mainprise D.S O major general A M S retd
REWCASTLE —On Feb 18 Attracta Genevieve Rewcastle, O.B E. M B N U I

SOME RECENT STUDIES OF PORPHYRIN METABOLISM AND PORPHYRIA*

C J WATSON
M.D., Ph.D Minn., F.A.C.P
ROFESSOR OF MEDICINE UNIVERSITY OF MINNESOTA MEDICAL SCHOOL AND HOSPITAL, MINNEAPOLIS

I HAVE chosen the subject for this lecture with a very real sense of humility, having in mind the many outstanding contributions made by London porphyrin scholars over the last half century I am the proud ossessor of a reprint from THE LANCET of Sir Archibald Garrod's Bradshaw lecture for 1900 on the Urinary Pigments in their Pathological Aspects This contains remarkable number of interesting observations on what as then mistakenly termed hæmatoporphyrin, now alled coproporphyrin The more recent studies in this eld by London investigators, notably Rimington Harrison, Gray, and Prunty and their associates, have provided a great stimulus to all who, like myself, are interested in the clinical and fundamental aspects of the porphyrins

CLASSIFICATION

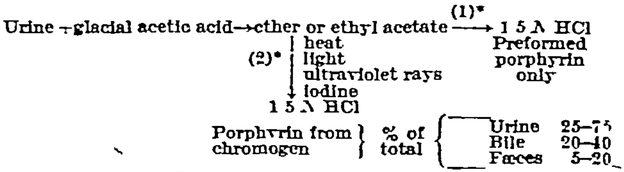
It is perhaps not surprising that the earlier studies of he porphyrins confused the artificial hæmatoporphyrin with those which occur in Nature This difficulty may be ascribed at least in large part to the relatively crude pectroscopes available at the turn of the century, hese were too insensitive to detect the slight differences n absorption spectra especially between hæmatoporphyrin and coproporphyrin, whose spectra are almost dentical. Hans Fischer was the first to put this matter on a firm footing, by crystallising the more important of he naturally occurring porphyrins and clearly establishing their identity on the basis of various physical criteria Fischer 1915, 1930, Fischer and Orth 1937) Coproporphyrin, so called because it was first found in the fæces, was noted to be ether-soluble, whereas uroporphyrin, first isolated from the urine, was insoluble in ether The most widely represented porphyrin, that of the hæmoglobin molecule and of other iron porphyrin enzymes, was appropriately named protoporphyrin This was also found to be ether soluble, but easily separated from coproporphyrin by being extracted from ether only by more concentrated hydrochloric acid, by exhibiting an insoluble sodium salt, and by chloroform solubility

Fischer (1930) recognised a "dualism" of the porphyrins in Nature—i e, the existence of two isomeric series which he believed to be synthesised independently, a concept which has been fully borne out by subsequent work The classification of the porphyrin isomers depends on the four artificial ætioporphyrins prepared by Fischer and his associates The structural formulæ are given by Fischer and Orth (1937) and Watson and Larson (1947), and it will suffice to recall now that the ætioporphyrins have only methyl and ethyl groups on the eight positions of the four pyrrol nuclei, the latter being joined by methene (CH) bridges to form the porphyrin ring There are but four possible differing combinations, and hence isomers, of the ætioporphyrins The protoporphyrin of the hæmoglobin molecule corresponds in configuration to ætioporphyrin III, and, as we shall note in a moment, there is also a type III coproporphyrin which is probably of considerable importance in hæmoglobin metabolism Coproporphyrin I differs only by reversal of the side groups on pyrrol nucleus IV This difference, nevertheless, is such that type I could not be derived from type III without complete disruption and resynthesis, hence the formation of type I is generally regarded as an independent synthesis Types II and IV have not so far been encountered in Nature, either as a coproporphyrin or any other form of porphyrin Sufficient data have now accumulated to indicate the unlikelihood that either II or IV will be found, and it is now reasonably clear that the enzyme systems necessary to porphyrin formation relate only to types I and III Uroporphyrin I has four acetic acid groups instead of the four methyl groups of coproporphyrin, since it also has the four propionic acid groups it is an octacarboxyl porphyrin, whereas the coproporphyrins are tetracarboxyl. The question of occurrence of a uroporphyrin III will be considered subsequently

URINARY EXCRETION

The study of the urinary excretion of coproporphyrin has been based mainly on fluorimetry, because the porphyrins generally exhibit an intense red fluorescence when exposed to light of about 4000 Å Various modifications of Fikentscher's (1932) method have been proposed In all of them it is assumed that any porphyrin excreted as chromogen or leuco-compound is converted to porphyrin during extraction and purification Recently, however we have "rediscovered" a fact that was undoubtedly known to Saillet (1896), although his terminology and description were somewhat obscure Saillet recognised that his "urospectrine" or "urohematoporphyrine normal" occurred in part in the urine as a colourless chromogen which was not readily extracted from ether or from ethyl acetate by hydrochloric acid. There appears to be little doubt that Saillet's "urospectrine" is identical with coproporphyrin Studies in our laboratory in the past two years have revealed entirely similar behaviour The chromogen does not fluoresce in Wood's light, and in the modification of Fikentscher's method that we have hitherto used (Schwartz et al. 1947) it is left behind undetected in the ether We have now determined that the conversion of chromogen to porphyrin is promoted by light, heat, and many dehydrogenators (Watson et al. 1951, Schwartz et al 1950)[1] These relationships are briefly summarised as follows

Coproporphyrin chromogen or precursor
(colourless and non fluorescing)



*Indicates order of procedures

Iodine in very dilute solution has so far proved most efficient (Schwartz et al. 1950) Titrations with iodine have clearly shown that coproporphyrinogen, as formed in vitro by the sodium-amalgam reduction of coproporphyrin, has six hydrogen atoms, of which four are probably added to the four methene bridges and two to the free nitrogens A new method of quantitative determination, devised by Dr Schwartz in this laboratory and described in detail by Watson et al. (1951), uses iodine to convert chromogen to porphyrin, and is not only considerably simpler and more reliable than previous methods but also much more sensitive, requiring only 5 ml. of urine, this advantage being due to the use of a

---

* Given in part as a University of London lecture on June 27, 1950 The work was aided by grants from the United States Public Health Service (RG no 345) and from the Medical Research Fund of the Graduate School University of Minnesota

[1] Since this lecture was given an abstract has appeared by D N Raine (*Biochem J* 1950, 47, xiv) in which the natural occurrence of a chromogen of coproporphyrin is discussed, also a method of conversion to porphyrin by the use of quinhydrone Our own experience with quinhydrone indicates that it is not as efficient as iodine

Society of Chiropodists

The annual convention of the society will take place on April 26, 27, and 28, at Friends House, Euston Road, London, N W 1 Sir Henry Cohen will open the convention, and other speakers will include Lord Amulree and Mr T T Stamm

Association of French-speaking Pædiatricians

The association will hold its 13th congress at Algiers from May 7 to 9 Further particulars may be had from the Expansion Scientifique Française, 23, rue du Cherche Midi Paris, VI

International Congress of Gynæcology

To celebrate their jubilee the French Society of Gynæcology, in collaboration with UNESCO, are holding an international congress at the Centre Marcellin Berthelot, 28 bis, Rue St Dominique, Paris, from June 23 to 29 Further information may be had from Dr Maurice Fabre, secretary general, 1, rue Jules Lefebvre, Paris, IXe

South African Minister of Health

Dr Karl Bremer has been appointed South African minister of health and social welfare in succession to the late Dr Stals Dr Bremer obtained his M B degree at Cape Town University in 1935 and his F.R C S in 1938 On his appointment as minister he resigned from the presidency of the South African Medical Council, an office which he had held for many years

C M F /M E F Physicians' Reunion Dinner

This dinner will be held this year in the hall of the Royal College of Physicians of Edinburgh on Saturday, May 12 Any physician who served in these Commands during the war should write to the Edinburgh secretary, Dr R W D Turner, 20, Warriston Crescent, Edinburgh

South Wales Medical Ex-Service Association

This association will hold their annual reunion dinner on Saturday, March 3, at the Park Hotel, Cardiff, at 7 45 P M Colonel D P Holmes will be in the chair Tickets (12*s* 6*d*) may be had from the hon secretary, Mr C W D Lewis, surgical unit, Royal Infirmary, Cardiff

The Minister's Reception

On Friday last Mr Hilary Marquand, the Minister of Health, held a reception at the new office of his Ministry in Savile Row The move from Whitehall, where the Ministry 's present offices will be occupied by the Minister of Local Government and Planning, is taking place gradually over the next few weeks

London Hostel for Tuberculous

At the end of last year the Ministry of Health approved in principle of the London County Council's proposal to provide hostel accommodation for people with tuberculosis who are infectious but are unlikely to benefit by further sanatorium treatment and who have no suitable home of their own (see *Lancet*, 1950, ii, 779) The L C C announce that they are now setting up a hostel of this kind for 35 men in Islington

World Health Organisation

Japan has applied for full membership in W H O The application has been placed on the agenda of the World Health Assembly due to open on May 7 in Geneva According to the W H O constitution, States not belonging to the United Nations can be admitted as members by simple majority vote of the assembly To date, 74 countries have joined W H O and one country, Southern Rhodesia, has been admitted as an associate member

---

Mr C Price Thomas, under the auspices of the British Medical Association and the British Council, is spending two weeks in Yugoslavia lecturing and giving demonstrations of the surgical treatment of tuberculosis He is accompanied by Dr Robert Machray and Mr Peter Jones

The Royal Society for the Prevention of Cruelty to Animals has issued the 7th edition of its booklet on First Aid and Fire Precautions Copies may be obtained, price 6*d* , from the society, 105, Jermyn Street, London, S W 1

CORRIGENDUM : *Potassium Deficiency in Idiopathic Steatorrhœa* —Dr Lubran and Dr McAllen inform us that in the report on the blood chemistry of their patient (*Lancet*, Feb 10, p 321) the figures for sodium should have been 301 mg (130 9 m eq), for calcium 7 6 mg (3 8 m eq), and for phosphorus 3 2 mg (1 8 m eq)

Diary of the Week

FEB 25 TO MARCH 3

Monday, 26th

UNIVERSITY OF LONDON
5 30 P.M (London School of Hygiene, Keppel Street W.C1 Prof J Engelbreth Holm (Copenhagen) Folic Acid t Growth of Tumours especially Rous Sarcoma.

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Mr R C Davenport Clinical Picture of the N and Abnormal Macular Region

HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Mr William Tanner T Man John Hunter Rejected The Man John H Selected Retrospect and Prospect (Hunterian or

Tuesday, 27th

UNIVERSITY COLLEGE Gower Street, W C 1
5 15 P M Dr McKeen Cattell (New York) Observations o Mechanism of Action of the Digitalis Glycosides on Ca Muscle

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene) Dr J R Squire T Reactions to Protein Sensitisation

INSTITUTE OF NEUROLOGY The National Hospital Queen Sq W C 1
5 P M Prof H Hyden (Gothenburgh) Chemical Chan Nerve Cells with Respect to Function and Age

Wednesday, 28th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Dr Ruth Bowden Factors Influencing Functi Recovery of Peripheral Nerve Injuries in Men (Hunter lecture)

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr Norman Ashton New Vessel Formation i Retina

MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr S Cochrane Shanks Influence of Radiology on Diagnosis of Abdominal Disease (Second Letts lecture)

UNIVERSITY OF GLASGOW
4 30 P M (Chemistry Department) Dr H P Himswort Nutritional Factors in Liver Disease (Noah M lecture)

Thursday, 1st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Prof T McKeown Congenital Malformations.

INSTITUTE OF DERMATOLOGY St John's Hospital Lisle Str W C 2
5 P M Dr S C Gold Eruptions of the Hands

LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant, Liverpool
8 P M Prof R A Willis Diagnostic Errors in Tumour Cases

UNIVERSITY OF ST ANDREWS
5 P M (Medical School, Small's Wynd Dundee) Dr H. P Himsworth Nutritional Factors and Liver Injury

Saturday, 3rd

ST STEPHEN'S HOSPITAL, Fulham Road S W 10
10 A M Dr W Russell Brain F R.C P Cervical Spondylosis (Introductory address to a weekend course on the rheumatic diseases)

Births, Marriages, and Deaths

BIRTHS

GLYN —On Feb 14 in London the wife of Dr John H. Glyn —a son

LISTER —On Feb 15 at Plymouth the wife of Dr H K N Lister —a daughter

MACKELLAR —On Feb 13 at Heckmondwike the wife of Dr John MacKellar—a daughter

MANN —On Feb 6 in London the wife of Dr Trevor P Mann—a son

RODGERS —On Feb 9, the wife of Dr W B Rodgers—a son

MARRIAGES

CALDER—REW —On Feb 10 at Appleshaw Hants, Kenneth Vassall Calder M B to Cynthia Branfill Rew

JOHNSON—NOBLE —On Feb 10, at Newcastle upon Tyne, Gordon Trevor Johnson M B , to Helen Margaret Noble, M B.

DEATHS

BRAYNE —On Feb 2 William Frederick Brayne M.B. Edin., lieut -colonel I.M.S retd

BROWN —On Feb 14 in London Henry Robert Brown O.B.E., L.R.C.P E , lieut -colonel I M.S retd

BROWN —On Feb 11 in London William Armour Brown M.B. Edin., F R C.S E

BUCKLEY —On Feb 13 at Onchan Isle of Man, Charles Herbert Buckley, M R C.S L.D S , aged 85

COGHILL —On Feb 14 in London Violet Alice Penrose Coghill M B Edin aged 83

LOCKWOOD —On Feb 13 at Worthing Dora Elizabeth Lockwood, L.R C P E aged 88

MAINPRISE —On Feb 16 at Aldershot Cecil Wilmot Mainprise D S O major-general, A.M.S retd

REWCASTLE —On Feb 18 Attracta Genevieve Rewcastle O B.E., M B N U I

SOME RECENT STUDIES OF PORPHYRIN METABOLISM AND PORPHYRIA*

C J WATSON
M.D, Ph.D Minn, F.A C P
)FESSOR OF MEDICINE UNIVERSITY OF MINNESOTA MEDICAL
SCHOOL AND HOSPITAL, MINNEAPOLIS

I HAVE chosen the subject for this lecture with a very .l sense of humility, having in mind the many out- nding contributions made by London porphyrin iolars over the last half-century I am the proud ssessor of a reprint from THE LANCET of Sir Archibald rrod's Bradshaw lecture for 1900 on the Urinary gments in their Pathological Aspects This contains emarkable number of interesting observations on what is then mistakenly termed hæmatoporphyrin, now lled coproporphyrin. The more recent studies in this ld by London investigators, notably Rimington arrison, Gray, and Prunty and their associates, have ovided a great stimulus to all who, like myself, are erested in the clinical and fundamental aspects of the rphyrins

CLASSIFICATION

It is perhaps not surprising that the earlier studies of e porphyrins confused the artificial hæmatoporphyrin th those which occur in Nature This difficulty may be cribed at least in large part to the relatively crude ectroscopes available at the turn of the century, ese were too insensitive to detect the slight differences absorption spectra, especially between hæmato rphyrin and coproporphyrin, whose spectra are almost entical Hans Fischer was the first to put this matter ı a firm footing, by crystallising the more important of ie naturally occurring porphyrins and clearly establish- g their identity on the basis of various physical criteria ischer 1915, 1930, Fischer and Orth 1937) Copro- orphyrin, so called because it was first found in the ces, was noted to be ether soluble, whereas uropor- hyrin, first isolated from the urine, was insoluble in her The most widely represented porphyrin, that of ie hæmoglobin molecule and of other iron porphyrin zymes, was appropriately named protoporphyrin his was also found to be ether soluble, but easily parated from coproporphyrin by being extracted from ther only by more concentrated hydrochloric acid, by xhibiting an insoluble sodium salt, and by chloroform olubility

Fischer (1930) recognised a "dualism" of the por- hyrins in Nature—i e, the existence of two isomeric eries which he believed to be synthesised independently, concept which has been fully borne out by subsequent vork The classification of the porphyrin isomers depends n the four artificial ætioporphyrins prepared by Fischer nd his associates The structural formulæ are given y Fischer and Orth (1937) and Watson and Larson 1947), and it will suffice to recall now that the ætio orphyrins have only methyl and ethyl groups on the ight positions of the four pyrrol nuclei, the latter being oined by methene (CH) bridges to form the porphyrin ing There are but four possible differing combinations, nd hence isomers, of the ætioporphyrins The proto- porphyrin of the hæmoglobin molecule corresponds in configuration to ætioporphyrin III, and, as we shall note in a moment, there is also a type III coproporphyrin which is probably of considerable importance in hæmo globin metabolism Coproporphyrin I differs only by reversal of the side groups on pyrrol nucleus IV This difference, nevertheless, is such that type I could not be derived from type III without complete disruption and resynthesis, hence the formation of type I is generally regarded as an independent synthesis Types II and [illegible] have not so far been encountered in Nature, either as coproporphyrin or any other form of porphyrin. Sufficient data have now accumulated to indicate the unlikelihood that either II or IV will be found, and it is now reasonably clear that the enzyme systems necessary to porphyrin formation relate only to types I and III Uroporphyrin has four acetic acid groups instead of the four [illegible] groups of coproporphyrin, since it also has [illegible] propionic acid groups it is an octacarboxyl porphyrin whereas the coproporphyrins are tetracarboxyl [illegible] question of occurrence of a uroporphyrin III will be considered subsequently

URINARY EXCRETION

The study of the urinary excretion of coproporphyrin has been based mainly on fluorimetry, because [illegible] porphyrins generally exhibit an intense red fluorescence when exposed to light of about 4000 Å Various [illegible] tions of Fikentscher's (1932) method have been [illegible] In all of them it is assumed that any porphyrin [illegible] as chromogen or leuco compound is converted [illegible] phyrin during extraction and purification [illegible] however we have "rediscovered" a fact [illegible] undoubtedly known to Saillet (1896), although [illegible] minology and description were somewhat [illegible] recognised that his "urospectrine" or [illegible] porphyrine normal" occurred in part [illegible] colourless chromogen which was not [illegible] from ether or from ethyl acetate by [illegible] There appears to be little doubt that [illegible] trine" is identical with coproporphyrin [illegible] laboratory in the past two years have [illegible] similar behaviour The chromogen [illegible] Wood's light, and in the modification [illegible] method that we have hitherto used [illegible] it is left behind undetected in the [illegible] determined that the conversion of [illegible] is promoted by light, heat, and [illegible] (Watson et al 1951, Schwartz [illegible] relationships are briefly summarised [illegible]

Coproporphyrin [illegible]
(colourless [illegible]

Urine + glacial acetic acid→ether [illegible]

(?)* [illegible]

Porphyrin [illegible]
chromogen [illegible]

*Indicates [illegible]

Iodine in very dilute [illegible] efficient (Schwartz et al [illegible] have clearly shown that [illegible] in vitro by the sodium [illegible] phyrin, has six hy[illegible] probably added to the [illegible] the free nitrogens. [illegible] mination, devised by [illegible] described in detail [illegible] convert chromogen [illegible] siderably simpler [illegible] methods but also [illegible] 5 ml. of urine, the [illegible]

n)
do
inco
por
opor,
en more
ices may
, whereas
contains
ion to the
phyrin and
to a striking
itive studies
well provide
ria[3]
is been recog-
the occurrence
ogen, both for
type porphyrin
on of the urine
ith acetic acid
regularly finds
is not removed
n washed with
chromogen to
ed with HCl
the Ehrlich
phyrin pre
d Vahlquist
pe porphyrin
an Ehrlich
lectrophoretic
hlquist (1930)
phobilinogen has
be studied as a
n unanswered
t, depending
ng Ehrlich
es as the
mittent
licates

---

* Given in part as a University of London lecture on June 27, 1950 The work was aided by grants from the United States Public Health Service (RG no 345) and from the Medical Research Fund of the Graduate School University of Minnesota

[1] Since this lecture [illegible] D N Raw[illegible] natural occurrence [illegible] is discussed [illegible] by the use [illegible] quinhydrone [illegible]

Society of Chiropodists

The annual convention of the society will take place on April 26, 27, and 28 at Friends House, Euston Road, London, N W 1 Sir Henry Cohen will open the convention, and other speakers will include Lord Amulree and Mr T T Stamm

Association of French-speaking Pædiatricians

The association will hold its 13th congress at Algiers from May 7 to 9 Further particulars may be had from the Expansion Scientifique Française, 23, rue du Cherche Midi, Paris, vi

International Congress of Gynæcology

To celebrate their jubilee the French Society of Gynæcology, in collaboration with Unesco, are holding an international congress at the Centre Marcellin Berthelot, 28 bis, Rue St Dominique, Paris, from June 23 to 29 Further information may be had from Dr Maurice Fabre, secretary general, 1, rue Jules Lefebvre, Paris, ixe

South African Minister of Health

Dr Karl Bremer has been appointed South African minister of health and social welfare in succession to the late Dr Stals Dr Bremer obtained his M B degree at Cape Town University in 1935 and his F R C S in 1938 On his appointment as minister he resigned from the presidency of the South African Medical Council, an office which he had held for many years

C M F /M E F Physicians' Reunion Dinner

This dinner will be held this year in the hall of the Royal College of Physicians of Edinburgh on Saturday, May 12 Any physician who served in these Commands during the war should write to the Edinburgh secretary, Dr R W D Turner, 20, Warriston Crescent, Edinburgh

South Wales Medical Ex-Service Association

This association will hold their annual reunion dinner on Saturday, March 3, at the Park Hotel, Cardiff, at 7 45 P M Colonel D P Holmes will be in the chair Tickets (12*s* 6*d*) may be had from the hon secretary, Mr C W D Lewis, surgical unit, Royal Infirmary, Cardiff

The Minister's Reception

On Friday last Mr Hilary Marquand, the Minister of Health, held a reception at the new office of his Ministry in Savile Row The move from Whitehall, where the Ministry's present offices will be occupied by the Minister of Local Government and Planning, is taking place gradually over the next few weeks

London Hostel for Tuberculous

At the end of last year the Ministry of Health approved in principle of the London County Council's proposal to provide hostel accommodation for people with tuberculosis who are infectious but are unlikely to benefit by further sanatorium treatment and who have no suitable home of their own (see *Lancet*, 1950, ii, 779) The L C C announce that they are now setting up a hostel of this kind for 35 men in Islington

World Health Organisation

Japan has applied for full membership in W H O The application has been placed on the agenda of the World Health Assembly due to open on May 7 in Geneva According to the W H O constitution States not belonging to the United Nations can be admitted as members by simple majority vote of the assembly To date, 74 countries have joined W H O and one country, Southern Rhodesia, has been admitted as an associate member

---

Mr C Price Thomas, under the auspices of the British Medical Association and the British Council, is spending two weeks in Yugoslavia lecturing and giving demonstrations of the surgical treatment of tuberculosis He is accompanied by Dr Robert Machray and Mr Peter Jones

The Royal Society for the Prevention of Cruelty to Animals has issued the 7th edition of its booklet on First-Aid and Fire Precautions Copies may be obtained, price 6*d*, from the society, 105, Jermyn Street, London, S W 1

CORRIGENDUM › *Potassium Deficiency in Idiopathic Steatorrhœa* —Dr Lubran and Dr McAllen inform us that in the report on the blood chemistry of their patient (*Lancet*, Feb 10, p 321) the figures for sodium should have been 301 mg (130 9 m eq), for calcium 7 6 mg (3 8 m eq), and for phosphorus 3 2 mg (1 8 m eq)

Diary of the Week

FEB 25 TO MARCH 3

Monday, 26th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene Keppel Street W.C.1 Prof J Engelbreth Holm (Copenhagen) Folic Acid Growth of Tumours especially Rous Sarcoma

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Mr R C Davenport Clinical Picture of the No and Abnormal Macular Region

HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4) Mr William Tanner T Man John Hunter Rejected The Man John Hu Selected Retrospect and Prospect (Hunterian ora

Tuesday, 27th

UNIVERSITY COLLEGE Gower Street, W C 1
5 15 P M Dr McKeen Cattell (New York) Observations on Mechanism of Action of the Digitalis Glycosides on Car Muscle

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene) Dr J R Squire Ti Reactions to Protein Sensitisation

INSTITUTE OF NEUROLOGY, The National Hospital Queen S W C 1
5 P M Prof H Hyden (Gothenburgh) Chemical Change Nerve Cells with Respect to Function and Age.

Wednesday, 28th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Dr Ruth Bowden Factors Influencing Funct— Recovery of Peripheral Nerve Injuries in Men (Hunte— lecture)

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr Norman Ashton New Vessel Formation in t Retina

MEDICAL SOCIETY OF LONDON 11 Chandos Street, W 1
8 30 P M Dr S Cochrane Shanks Influence of Radiology on Diagnosis of Abdominal Disease (Second Letts lecture)

UNIVERSITY OF GLASGOW
4 30 P M (Chemistry Department) Dr H P Himsworth Nutritional Factors in Liver Disease (Noah M lecture)

Thursday, 1st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M Prof T McKeown Congenital Malformations.

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Str W C 2
5 P M Dr S C Gold Eruptions of the Hands

LIVERPOOL MEDICAL INSTITUTION 114, Mount Pleasant Liverpool
8 P M Prof R A Willis Diagnostic Errors in Tumour Cas

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Dr H P Himsworth Nutritional Factors and Liver Injury

Saturday, 3rd

ST STEPHEN'S HOSPITAL Fulham Road S W 10
10 A M Dr W Russell Brain F R C P Cervical Spondylosis (Introductory address to a weekend course on the rheumatic diseases)

Births, Marriages, and Deaths

BIRTHS

GLYN —On Feb 14 in London the wife of Dr John H Glyn —a son

LISTER —On Feb 15 at Plymouth, the wife of Dr H K. N Lister —a daughter

MACKELLAR —On Feb 13 at Heckmondwike, the wife of Dr John MacKellar—a daughter

MANN —On Feb 6, in London, the wife of Dr Trevor P Mann—a son

RODGERS —On Feb 9, the wife of Dr W B Rodgers—a son

MARRIAGES

CALDER—REW —On Feb 10 at Appleshaw Hants Kenneth Vassall Calder M B to Cynthia Branfill Rew

JOHNSON—NOBLE —On Feb 10 at Newcastle upon Tyne Gordon Trevor Johnson M B to Helen Margaret Noble M B

DEATHS

BRAYNE —On Feb 2 William Frederick Brayne M B. Edin lieut -colonel I M S retd

BROWN —On Feb 14 in London, Henry Robert Brown, O B E., L.R C P F, lieut -colonel, I M.S retd

BROWN —On Feb 11 in London William Armour Brown M B Edin., F R C.S E

BUCKLEY —On Feb 13 at Onchan Isle of Man Charles Herbert Buckley M R C S L D.S , aged 85

COGHILL.—On Feb 14 in London Violet Alice Penrose Coghill, M B Edin aged 83

LOCKWOOD —On Feb 13 at Worthing Dora Elizabeth Lockwood L R.C P E aged 88

MAINPRISE —On Feb 16 at Aldershot, Cecil Wilmot Mainprise D.S O major general, A M.S retd

REWCASTLE —On Feb 18 Attracta Genevieve Rewcastle, O B E., M B N U I

CLASSIFICATION AND MAIN FEATURES OF PORPHYRIA

Type and incidence	Clinical	Chemical
1 PHOTOSENSITIVE (congenital) Rare	Somewhat more common in males Onset early in life either prenatal or postnatal Hydroa æstivale eventual scarring and mutilation of exposed skin erythrodontia Splenomegaly and hæmolytic anæmia not infrequently splenectomy may relieve and cause porphyria to become latent with disappearance of photosensitivity	Absence of Ehrlich reacting porphobilinogen in urine Presence of large amounts of uroporphyrin and coproporphyrin I both excreted in part as colourless Ehrlich negative chromogens (in urine urocopro in fæces vice versa) Slight or negative zinc complex formation by these porphyrins Uroporphyrin I methyl ester M.P 284°C
2 INTERMITTENT ACUTE (acute or toxic ') Relatively common	Somewhat more common in females Abdominal pain of various types Peripheral neuropathy with pain in extremities Varying neuropsychiatric disturbances weakness *paralyses* hysterical behaviour or outspoken psychoses Pigmentation of skin in some cases	Porphobilinogen usually present in urine at least during attacks (Ehrlich $CHCl_3$ insoluble aldehyde) Non Ehrlich reacting chromogen → Porphobilinogen (colourless) ↓ $-H_2$ ← ? Waldenström uro type porphyrin (zinc *complex*) *methyl ester* M P 258–260 C Porphobilinogen ↓ Porphobilin (dark brown) non porphyrin probable *dipyrryl methene or* polymer thereof coproporphyrin III usually excessive
3 MIXED (' chronic) Relatively uncommon	Differing sex incidence not clearly defined probably somewhat more common in males Late appearance of photosensitivity (so called cutanea tardive type) Relatively benign course Liver disease or functional impairment frequent Attacks of abdominal pain neuropsychiatric disturbances infrequent	Porphobilinogen inconstant. Varying appearance of Waldenström uro *type* porphyrin or uroporphyrin I with various mixtures of coproporphyrins I and III

than with the concept of Lemberg and Legge (1949) that one member of a pair of specific dipyrryl methene precursors capable of condensing to form coproporphyrin III is normally converted to a dipyrryl methene precursor of protoporphyrin by decarboxylation Among other features which this theory was believed to explain is the very small amount of coproporphyrin III normally encountered in the urine and fæces, but it does not harmonise as well with the finding of coproporphyrin in the bone marrow and erythrocytes and the increases observed when erythropoiesis is stimulated even in a relatively normal way, as after blood loss or reduction of oxygen tension (Schmid et al 1950) Perhaps even more important is the lack of any increase of coproporphyrin III in the urine in posthæmorrhagic or hæmolytic anæmias, since, if it were merely a side product of hæmoglobin synthesis, significant increases in these circumstances would be anticipated, but they have not been observed (Watson and Larson 1947, Dobriner and Rhoads 1940) The recent hypothesis of porphyrin biosynthesis proposed by Neuberger et al (1950) looks on coproporphyrin III as intermediary in the formation of protoporphyrin, and is thus in better agreement with the various findings just referred to which relate to this area of the biosynthesis As is noted below, the rôle of uroporphyrin is still very difficult to assess, although Neuberger et al believe that uroporphyrin III is a normal precursor of coproporphyrin and protoporphyrin

PORPHYRIA

We may turn now to the problem of porphyria which, as Garrod (1923) recognised, is a special situation, an inborn error of metabolism" A classification of porphyria is submitted in the accompanying table, together with the outstanding clinical and chemical features

As noted in the table, the "cutanea tarda" form, which in some instances presents nothing more than photosensitive manifestations, is nevertheless classified with the mixed type Probably this form differs essentially from the infantile or so called congenital photosensitive variety As Brunsting et al (1950) have emphasised, these patients commonly present (1) evidence of liver disease, (2) a violaceous hue of the exposed skin with or without pigmentation and/or hypertrichosis, and (3) bullæ caused by heat and trauma as well as light From a fundamental standpoint it is perhaps even more important that the bone marrow in such instances may not contain any increased amount of porphyrin, whereas the liver, examined at about the same time, contains large amounts of porphyrins, in contradistinction to the pure photosensitive disease in which coproporphyrin and uroporphyrin are formed in the bone marrow to a striking degree (Aldrich et al 1950) Further comparative studies of this type, which are now in progress, may well provide a much more basic classification of porphyria[3]

A fact which is noted in the table and has been recognised but recently (Schwartz et al 1950) is the occurrence of a chromogen, other than porphobilinogen, both for uroporphyrin I and the Waldenström uro type porphyrin This is readily demonstrated by extraction of the urine with ethyl acetate after acidification with acetic acid Porphobilinogen is not extracted, but one regularly finds a chromogen in the ethyl acetate which is not removed by 1 5 *N* HCl until the solution has first been washed with 0 05% iodine solution This converts chromogen to porphyrin, after which it is readily extracted with HCl This finding makes it uncertain whether the Ehrlich reacting porphobilinogen is actually a porphyrin precursor as has been believed (Waldenström and Vahlquist 1939), or its apparent transition to a uro type porphyrin is simply a matter of being accompanied by an Ehrlich negative porphyrinogen The careful electrophoretic purification of Waldenström and Vahlquist (1939) supported the former belief, but porphobilinogen has not been crystallised, and, until it can be studied as a chemical entity, this question must remain unanswered Meanwhile the porphobilinogen aldehyde test, depending on the chloroform insolubility of the resulting Ehrlich compound (Watson and Schwartz 1941), serves as the simplest method in the diagnosis of the intermittent acute type of porphyria Present experience indicates that the reaction, though not wholly pathognomonic characterises the intermittent acute form of porphyria was believed by Waldenstrom (1937), Mertens (1937), and Chandler et al (1939) to represent uroporphyrin-III Studies in this laboratory have shown, however, that it is a curious mixture or molecular complex of uroporphyrin I with a type III porphyrin which probably has less than eight carboxyl groups Prunty (1946), McSwiney et al (1950), and Gray (personal communication) have confirmed the finding of uroporphyrin I as an important constituent of the Waldenstrom porphyrin Recent methoxy determinations have borne out our earlier finding of a heptamethyl ester (melting point 208°C) The nature of the combination of this porphyrin with uroporphyrin I in the Waldenstrom porphyrin is not clear, but it may be noted that in some cases, and even at certain times in the same case, it has been impossible to separate the uroporphyrin I from the admixed type III porphyrin on the $CaCO_3$ column (So far a separation by paper chromatography has not been reported) This inseparable behaviour has been referred to as the type-B Waldenstrom porphyrin in contradistinction to type A, in which uroporphyrin I is readily separated from the 208 or heptacarboxyl porphyrin A binding factor may operate to a variable extent in conditioning these differences Gibson and Harrison (1950) have observed that a porphyria urine which initially yielded uroporphyrin I (ester melting point 282–5°C) yielded seven times as much porphyrin after being boiled, but now the ester melting point was lowered to 264–5°C This behaved as a type B Waldenstrom porphyrin, and a 208 porphyrin was not observed Additional studies of this type are needed with urine from various cases of porphyria Recently the administration of N^{15} tagged uroporphyrin I (methyl ester melting point 284°C) in a case of intermittent acute porphyria has yielded significant data The patient was excreting large amounts of porphobilinogen and Waldenstrom porphyrin The latter was separable on the Tswett column into uroporphyrin I and the 208 or heptacarboxyl porphyrin The uroporphyrin I which was administered had been crystallised from the urine of a girl, aged 5 years, with photosensitive porphyria with splenomegaly and hæmolytic anæmia (Grinstein et al 1949) N^{15} glycine had been fed to this girl a few days earlier, as a result of which the uroporphyrin I contained 3 2 atom per cent excess of N^{15} (Grinstein et al 1949, 1950a) 7 mg of this material was given intravenously in divided doses over three days The uro type porphyrin isolated from the recipient of the uro I during this period had an ester melting point of 260–4°C, but it behaved as an entity on the Tswett column The crystals obtained from urine and fæces contained 0 032 and 0 045 atom per cent excess of N^{15} respectively, whereas the value for the urine and fæces coproporphyrin isolated simultaneously was 0 00 atom per cent excess Thus it was clear that at least the N^{15}, and quite probably the tagged uroporphyrin I in toto, had become incorporated to some extent in the Waldenstrom porphyrin which was isolated It was not clear, however, whether the administered porphyrin had occasioned the behaviour as an entity, or whether this was a pure coincidence As already mentioned, such variations in behaviour have been observed in other instances It was thought significant that the coproporphyrin I isolated after the administration of the N^{15} uroporphyrin did not contain any excess of N^{15} Though this finding does not weigh too heavily against a uro copro transition it clearly does not support it Since this patient could make considerable excesses of both coproporphyrin isomers, it seems that more biological than the carboxylation of four to four acetic acid groups, as would be necessar conversion of coproporphyrin to uroporphyrin however, no decisive evidence of either sequence h described Of the three studies so far reported ir porphyria has been studied with glycine contain those of Grinstein et al (1949, 1950a) and Gr Neuberger (1949) have revealed an earlier and peak concentration of N^{15} in the coproporphyrin the uroporphyrin This relates to the urine por only, the variable lag in excretion in the fæces comparison of urinary and fæcal porphyrin N^{15} difficult if not impossible In the third of these (London et al 1950) the peak concentration developed earlier in the uroporphyrin than in the porphyrin, but the latter value depended on th rather than the urinary coproporphyrin Even the data are quite comparable, as in the first two referred to, the possibility must be considere uroporphyrin has a later and lesser peak concen of N^{15} owing to a larger "pool" or a greater and slower release of uroporphyrin than of co phyrin This consideration prevents conclusions possibility must also be borne in mind that uropor and coproporphyrin are only related on the b common precursors, neither being the parent sub of the other This concept is given prominent pl Lemberg and Legge (1949)

---

[3] Since this was written Dr Schmid has studied liver biopsy material from additional cases of the 'mixed" type This study revealed large amounts of porphyrin in the liver, with slight or no increase in the bone marrow The term 'porphyria hepatica ' is tentatively considered most suitable for this group, while, conversely, "porphyria erythropoietica" seems to designate most accurately the fundamental disturbance in the pure photosensitive or congenital form

CONCLUSION

In closing, it is desirable to refer again to the t thesis of the porphyrins recently proposed by Neu et al (1950) This postulates an initial synth uroporphyrin III, hence the identification o substance seems to be a primary requisite to the of their hypothesis This porphyrin might be a p logical precursor but not demonstrable owing to of reaction One might anticipate, however, that it be found in certain conditions, such as lead pois which are characterised by excessive type III cop phyrins, since there is much reason to believe that excesses are due to an enzymatic disturbance i synthesis of hæmoglobin

Finally, it is a pleasure to acknowledge that in desc work from our laboratory I have simply been the spok for a number of my associates, in particular Dr S Schwartz, Dr Moises Grinstein, Dr Robert Aldrich, Dr Lowry, Dr Rudi Schmid, Miss V E Hawkinson, Miss Bossenmaier, and Mrs Rita Hughes

REFERENCES

Aldrich R A Grinstein M Hawkinson V E Watson,
(1950) in the press
Brunsting L A Mason H Aldrich R A (1950) in the pr
Castex M R Lopez Garcia A Zolasco, J F (1948) *Prens argent* 35, 907
Chandler F G Harrison, G A, Rimington, C (1939) *Brit* ii 1173
Dobriner K, Rhoads C P (1940) *Physiol Rev* 20 416
— — Hummel, L E (1938) *J clin Invest* 17, 125
Fikentscher R (1932) *Biochem Z* 249 257
Fischer H (1915) *Hoppe Seyl Z* 95, 34 96 148
— (1930) in Oppenheimer's Handbuch der Biochem Menschen und der Tiere 2nd ed Jena p 72
— Orth, H (1937) Die Chemie des Pyrrols Leipzig, vo
Garrod, A E (1900) *Lancet* ii 1323
— (1923) Inborn Errors of Metabolism 2nd ed London
Gibson Q H Harrison D C (1950) *Biochem J* 46 154
Gray C H Neuberger A (1949) *Ibid* 44, xlvii
Grinstein, M. Aldrich R A, Hawkinson V E, Watson,
(1949) *J biol Chem* 179 983
— — — — (1950a) *Ibid* (in the press)
— Kamen, M D Wikoff H M. Moore C V (1950b) *Ibi* 715

Continued at foot of next column

SENSIBILITY OF THE RECTUM AND COLON

ITS RÔLE IN THE MECHANISM OF ANAL CONTINENCE

J C Goligher
Ch M. Edin , F R C S
ASSISTANT SURGEON ST MARY'S HOSPITAL AND ST MARK'S HOSPITAL FOR DISEASES OF THE RECTUM AND COLON, LONDON

E S R Hughes
M.S-Melb , F.R C S
ASSISTANT SURGEON, ROYAL MELBOURNE HOSPITAL , FORMERLY SURGICAL REGISTRAR, ST MARK S HOSPITAL

It is known from the work of Lennander (1901), Hurst (1911), and others that, with the exception of the anal canal, the gut is largely insensitive to stimuli capable of producing pain or other sensation when applied to a cutaneous surface It is, however, sensitive to distension by an experimental balloon introduced through the mouth, the anus, or a colostomy, though it is not clear whether it is the stretching or reflex contraction of the gut wall, or the distortion of the mesentery that produces the pain The same doubt exists as to the mechanism of the pain in ordinary intestinal colic According to Hurst (1911), the sensation of fullness in the rectum that constitutes the normal call to defæcation is also due to distension, and is caused by the sudden entry of fæces into this segment of the bowel

In this paper we describe some observations on the sensations produced by balloon distension of the rectum and distal colon in normal subjects and in patients who have had the nerve supply to the bowel interrupted or varying portions of the rectum removed. In the latter group we try to correlate our findings with the functional result obtained The balloon, mounted on the end of a narrow graduated rubber tube, was inserted into the rectum and the lower part of the sigmoid colon through a sigmoidoscope , the instrument was then withdrawn over the tube, and the tube was connected to a pair of bellows and a mercury manometer The balloon was inflated at the highest level reached by the sigmoidoscope —usually 25 cm , sometimes only 20 cm, from the anus —and the minimum pressure required to produce sensation and the patient's description of the sensation were recorded It was then deflated and the process repeated at 5 cm intervals right down to the anus In the few cases where the balloon was introduced through a colostomy, the same technique of insertion with the aid of a sigmoidoscope was employed Distension was then performed at measured distances from the actual opening

It will be apparent that the recordings made by this apparatus do not accurately represent the tension exerted on the gut wall, because some of the pressure is engaged in overcoming the resistance of the balloon itself Preliminary tests showed that inflation of the balloon to a size sufficient to distend the colon at all—diameter about 3 cm —required a pressure of approximately 20 mm Hg, but that further dilatation to a diameter of 9 cm required a rise of pressure of only about 5 mm Hg Practically all the pressures recorded with the balloon in situ lay between 60 and 150 mm Hg, so the differences between them may be accepted as reflecting with reasonable accuracy the variations in the sensibility of the bowel

FINDINGS IN NORMAL SUBJECTS

The following account is based on the results obtained in forty normal people

Colonic Sensation

Distension of the sigmoid colon, and occasionally the upper part of the rectum, caused a sensation in the lower abdomen, either in the midline suprapubically or in the left iliac fossa Usually considerable pressure was required to elicit this sensation (average 80 mm Hg , extremes 40 and 140 mm Hg), and there was a lag of 2 or 3 seconds between the inflation of the balloon and its appreciation by the patient If no further inflation was carried out the pressure gradually fell, presumably owing to relaxation of the intestinal wall, and this fall was associated with a waning of sensation, which eventually disappeared in 30 or 40 seconds unless the threshold had been much exceeded in the first instance The sensation was sometimes described by the patient as being like "wind" in the bowel , at other times as a definite pain, rather like a colic but constant and not spasmodic On increasing the pressure the sensation always became painful

Rectal Sensation

Distension of the rectum proper caused a characteristic sensation referred to the rectum itself or the sacral region The pressure needed to elicit this sensation was usually lower—sometimes considerably lower—than that required to produce colonic sensation in the same individual (average 62 mm Hg , extremes 25 and 130 mm Hg) The latent interval between the inflation of the balloon and its perception by the patient seemed to be slightly shorter than with the colon It was noted that the pressure threshold for sensation was slightly lower when the balloon was distended rapidly instead of slowly As with the colon, once the sensation had been established, and in the absence of further distension, the pressure gradually sank and the sensation steadily diminished in intensity over a period of $^1/_2$–1 minute or more, perhaps finally disappearing altogether Like Gaston (1948a), we found that the sensibility of the rectum increased as the anus was approached, for the average pressures needed to produce sensation at 20, 15, 10 and 5 cm from the anal orifice were 67, 63, 61 and 56 mm Hg respectively

The patients' description of the sensation varied A few stated that they had never experienced anything quite comparable before, but the majority likened it to that of wind or motion in the rectum requiring evacuation In more than half the cases it was found that lesser

---

PROFESSOR WATSON REFERENCES—*continued*

Hammond R L Welcker M. L (1948) *J Lab clin Med.* 33 1254
Hijmans van den Bergh H H Grotepass W Revers F E (1932) *Klin Wschr* 11 1534
— Hyman, A J (1928) *Dtsch med. Wschr* 54 1492
Klüver H (1944) *Science* 99 482 *J Psychol* 17 209
Kvasničková, V (1947) *Cas Lék. ces* 87 633 abstr *Blood* 1949 4 987
Lemberg R. Legge J W (1949) Hematin Compounds and Bile Pigments New York
London I M West R Shemin D Ritterberg D (1950) *J biol Chem.* 184 365
McSwiney R R Nicholas R E H Prunty F T G (1950) *Biochem J* 46 147
Mertens E (1937) *Hoppe Seyl Z* 250 57
Neuberger A Muir H M. Gray C H (1950) *Nature Lond* 165, 948
Pimenta de Mello, R (1949) *Proc Soc exp Biol. N Y* 72 292
— (1950) in the press
Prunty F T G (1946) *Arch intern Med* 77 623
Saillet (1896) *Rev Méd* 16 542.
Salzburg, P Watson C J (1941) *J biol Chem.* 139 593
Schmid R Schwartz S Watson C J (1950) *Proc Soc exp Biol N Y* 75 705
Schwartz, S Hawkinson V E Cohen S Watson C J (1947) *J biol Chem* 168 133
— Wikoff, H M (1950) in the press
— Zieve L Everts C Watson C J (1950) in the press.
Sutherland, D S Watson C J (1951) *J Lab clin Med* 37 29
Waldenström J (1937) *Acta med scand.* suppl 82
— Vahlquist B (1939) *Hoppe-Seyl. Z* 260 189
Watson C J (1950) *Trans Ass Amer Phys* (in the press)
— Hawkinson, V E Capps R B Rappaport E M (1949) *J clin Invest* 28 621
— Larson E A (1947) *Physiol Rev* 27 478
— Pass I J Schwartz, S (1941) *J biol Chem* 139 583
— Pimenta de Mello R Schwartz S Hawkinson V E Bossenmeier I (1950) in the press.
— Schulze W Hawkinson V E Baker A B (1947) *Proc Soc exp Biol N Y* 64 73
— Schwartz, S (1941) *Ibid* 47 393
— Sutherland D S Hawkinson V E (1951) *J Lab clin Med.* 37 8

degrees of pressure caused a sensation of flatus in the rectum; when the pressure was increased by 10 or 20 mm. Hg, however, the sensation became more urgent and the patients now stated that they felt they wanted to pass a motion. In some cases the distinction between flatus and fæces did not seem to depend on differences of pressure, the patients feeling one or other throughout or being unable to state with confidence which they thought was present in the rectum.

When the balloon was inflated in the anal canal an entirely different sensation from that created in the rectum proper was produced. Instead of having a desire to defæcate or pass wind, the patient now felt that the motion was actually escaping from the anus, and indeed unless special care was taken to maintain the balloon in position it was automatically evacuated.

Localisation of Colonic and Rectal Types of Sensation

The line of demarcation between the zones in which rectal and colonic sensation could be elicited did not always correspond accurately to the anatomical division into rectum and colon. The rectosigmoid junction is usually taken to lie between 12 and 15 cm. from the anus. In our 40 subjects the boundary between the zones of rectal and colonic sensation lay more than 25 cm. from the anus in five, between 25 and 20 cm. away in nine, between 20 and 15 cm. in ten, and between 15 and 10 cm. in four. In twelve cases there was a zone where colonic and rectal sensation overlapped for 10 to 15 cm. between the 25 cm. and 10 cm. levels.

Reflex Contraction of the External Sphincter Ani during Balloon Distension

Garry (1933) showed that in animals distension of the rectum with a balloon evokes a reflex contraction of the external sphincter, and this has also been elicited by Gaston (1948a) in human beings. The behaviour of the external anal sphincter was therefore noted during our investigations. No elaborate recording apparatus was employed: the tip of the index finger was simply placed at the anal orifice in contact with the subcutaneous external sphincter. Even slight contraction of the muscle could be readily appreciated. It was found that balloon distension producing rectal sensation invariably caused contraction of the external sphincter. Occasionally, indeed, the muscle contraction seemed to precede appreciation of sensation by a second or so. Distension of the segments of bowel causing colonic sensation was not accompanied by contraction of the sphincter.

FINDINGS AFTER INTERRUPTION OF NERVE SUPPLY

The nerve supply to the rectum and sigmoid colon is derived from the sympathetic and parasympathetic nervous systems, and from the inferior hæmorrhoidal branches of the pudendal nerves. According to Gask and Ross (1937), the *sympathetic* fibres originate in the lower 6 thoracic and upper 2 lumbar segments of the spinal cord and pass via the thoracic and lumbar splanchnic nerves to join the aortic plexus. Some then proceed along the presacral nerve; this divides into right and left branches which combine with the parasympathetic branches from the 2nd and 3rd sacral segments to form the pelvic plexuses, from which in turn branches are distributed to the rectum and other pelvic organs. Other fibres pass from the aortic plexus to the inferior mesenteric plexus, which accompanies the inferior mesenteric artery and is distributed along the branches of that vessel to the colon and rectum.

The *parasympathetic* supply comes from the 2nd, 3rd, and 4th sacral segments of the cord (*Gray's Anatomy* 1949). Some fibres proceed directly to the pelvic plexuses and are distributed from these; others, as Telford and Stopford (1934) have shown, form a trunk which passes upwards to join the inferior mesenteric plexus and are conveyed in its branches to the left half of the colon and the rectum. It is not believed that the vagi send fibres farther distally than the splenic flexure of the colon—if indeed as far as this.

The *inferior hæmorrhoidal* branches of the pudendal nerves (S2, 3 and 4) cross the ischiorectal fossæ to supply the external sphincter ani; they also contain sensory fibres from the skin, and possibly from the mucosa of the anal canal and lower rectum (*Gray's Anatomy* 1949).

Afferent nerve impulses from the rectum and distal colon must be transmitted along one or more of these routes. To determine the relative importance in this respect of the three pathways, experiments were carried out in which each was blocked in turn and the effect on the sensibility of the rectum and colon was observed.

Inferior Hæmorrhoidal Block

In six patients requiring surgical treatment for rectal conditions, such as anal warts or external hæmorrhoids, which can be dealt with very satisfactorily under local anæsthesia, the opportunity was taken to block the inferior hæmorrhoidal nerves. Anæsthesia was achieved by the injection through a puncture 1 in. behind the anus of 20 ml. of 2% procaine on either side of the anal canal. Complete paralysis of the external sphincter indicated that conduction in the inferior hæmorrhoidal nerves had been successfully interrupted. Balloon distension of the rectum and colon was carried out before and after the injection. The only change noted after blocking the inferior hæmorrhoidal nerves was a very slight lowering of the pressure threshold for sensation in both rectum and colon.

Parasympathetic Block

The parasympathetic outflow from S2 and 3 can be interrupted by a low spinal anæsthetic such as is commonly used for minor rectal operations, &c. 0·8 ml. of 1/2000 heavy 'Nupercaine' solution is injected into the subarachnoid space between the 3rd and 4th lumbar spinous processes, the patient being kept sitting up for four minutes afterwards. Anæsthesia develops up to the 2nd or 1st sacral nerve segments, which suffices to block the sacral parasympathetic nerves (and also incidentally the pudendal nerves and their inferior hæmorrhoidal branches) but does not affect the sympathetic supply to the colon and rectum.

Six cases were investigated by balloon distension before and after induction of low spinal anæsthesia. It was found that colonic sensation was quite unaffected by the anæsthetic but that rectal sensation was completely abolished. The most vigorous distension of the rectum after the injection caused no sensation whatsoever, though in two cases the colon and rectum were stimulated thereby to expel fæces and flatus, the patients being quite unaware of this till the flatus was heard escaping from the anus.

Sympathetic Block

In the surgical treatment of essential hypertension the extensive sympathectomy advocated by Grimson—division of the sympathetic outflow from T3 to L3 on both sides—is now frequently employed. This operation also deprives the entire colon and rectum of their sympathetic supply. Six cases of hypertension which had had a bilateral denervation of this type were examined by balloon distension of the rectum and colon. Unfortunately, in five of the patients it was found impossible, for technical reasons, to insert the sigmoidoscope further than 15 cm.; balloon distension up to this level gave a rectal sensation of flatus or fæces. In the sixth patient the sigmoidoscope was passed to 25 cm.; balloon distension as far as this point produced a rectal sensation but no abdominal pain. It should be added that all six patients had normal rectal function.

FINDINGS AFTER PARTIAL OR COMPLETE EXCISION OF RECTUM

Complete Abdominoperineal Excision with Terminal Iliac Colostomy

In six patients who had had this operation some months or years previously, balloon distension of the segment of colon leading to the colostomy was carried out; only a sensation of pain referable to the hypogastric or umbilical region was elicited. Even when the balloon was withdrawn so as to lie immediately adjacent to the anterior abdominal wall there was never any sense of fullness in the vicinity of the colostomy, and this was in keeping with the experience of these patients that the escape of fæces or flatus from their colostomies was never preceded by any warning sensation.

Partial Excision with Preservation of Anal Sphincters

Abdomino anal excision of "pull through" type (Bacon 1945, Babcock 1947).—In this operation the lower sigmoid colon, all the rectum proper, and the anal mucosa as far as the mucocutaneous junction are removed, the stump of colon is pulled down through the anal orifice, and the anal sphincter which has been divided in the midline posteriorly, is sutured around it. Eventually the projecting portion of bowel sloughs off or is removed by diathermy or snare, leaving the state of affairs shown in fig 1.

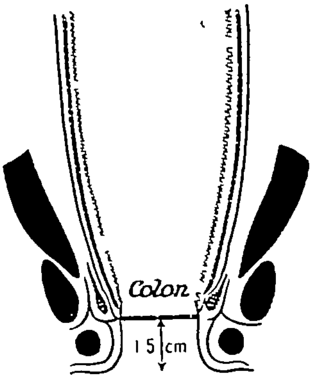


Fig 1—Diagram showing the state of affairs after the Bacon Babcock operation when the excess of bowel projecting through the anus has been removed.

Four patients who had been subjected to this procedure were examined. The anastomosis between the colon and the anal canal was situated 0·5–1·5 cm from the anal orifice; two cases had a fairly tight fibrous stenosis at this level. In all cases the tone of the external sphincter was very poor and its contractile power slight or non existent. The puborectalis muscle showed better tone and could contract—in two cases quite strongly. In view of the atonic, often patulous, condition of the anus it was not surprising that all four patients were incontinent; careful interrogation disclosed further that they were devoid of ordinary rectal sensation. Three stated that they sometimes had a vague sense of discomfort in the perineal or sacral region immediately before the expulsion of fæces or flatus. More often a "windy" sensation in the lower abdomen due to active colonic peristalsis indicated that a motion or escape of flatus was imminent but they had come to dispense with sensation as a guide in these matters and had endeavoured, by attention to diet, to establish a routine like that followed by colostomy cases. They found it necessary, however, to wear a perineal pad constantly during the day to protect their clothing from soiling, and a bout of diarrhœa confined them to the house. It was difficult to see how such a patient was any better off than one with an abdominal colostomy.

Balloon distension of the colon from 15 cm down to the suture line elicited an abdominal sensation in all four cases; when the pressure was increased to 180 mm Hg a very vague rectal sensation was also experienced in three subjects.

Abdomino anal excision of invagination type (Maunsell 1892, Weir 1901).—In this procedure the lower part of the sigmoid colon and the greater part of the rectum are excised through the abdomen, the subsequent anastomosis between the colon and lower fringe of rectum being accomplished by everting the anorectal stump through the anus and drawing the colon down through it so that their cut edges can be approximated by suture outside the anus; afterwards the suture line is replaced within the pelvis. By this technique the anal sphincters and lower anorectum are retained undamaged (see fig 2).

Nine such cases were considered. The bowel suture line was usually situated about 6 or 7 cm from the anal orifice. The tone and contractile power of the sphincters and puborectales were normal in all cases. Rectal function was excellent in all but two patients, who found that they were unable to control flatus or liquid fæces. One of these incontinent patients was able to tell when wind or motion was present in the bowel, but in the other rectal sensibility seemed to be grossly impaired.

Balloon distension with the balloon lying just above the anorectal ring, and therefore partly or entirely below the suture line, always produced a sensation of rectal fullness. With the balloon above the suture line an abdominal sensation was invariably elicited, but in six of the nine cases this was accompanied by a rectal sensation as well.

Abdominal or anterior resection.—Here the resection of the cancerous segment per abdomen is followed by a sutured anastomosis between the colon and the rectal stump from above, a substantial portion of rectum usually being retained, as in fig 3.

Examination of ten patients subjected to this operation yielded the following information: the suture lines lay between 7·5 and 13 cm—usually 9 or 10 cm—from the anal orifice. The tone and contractility of the sphincters and puborectales were invariably excellent, and the functional result could be classed as perfect in all cases. Balloon distension below the suture line caused a purely rectal sensation; above the suture line it always caused an abdominal sensation, but in two cases a rectal sensation as well.

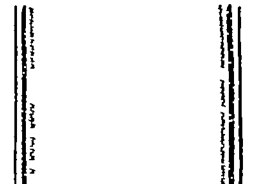


Fig 2—Diagram showing the result of abdomino-anal excision of invagination type with suture line replaced through the anus.

DISCUSSION

Distinction between Colonic and Rectal Sensation

This investigation confirms in the main Hurst's (1911) contention that balloon distension of the colon in normal subjects produces a purely abdominal sensation of "flatulent" discomfort or pain, whereas rectal distension causes a feeling of fullness in the rectum interpreted by the patient as a desire to pass wind or motion. It shows, however, that the distribution of the two types of sensation in the bowel does not always coincide accurately with the anatomical division into rectum and colon It also demonstrates that the rectum is more sensitive and discriminating than the colon this is indicated by the lower pressure at which sensation can be elicited in the former, and by the ability of the rectum to distinguish between flatus and fæces, which the colon cannot do Some evidence is presented which suggests that flatus normally produces a slightly lower degree of intrarectal tension than does fæces, and that the rectum is able to appreciate these minor differences of pressure but it may well be that the distinction depends, at least in part, on the recognition by the rectum of some other physical or chemical quality in its contents, not considered in this study

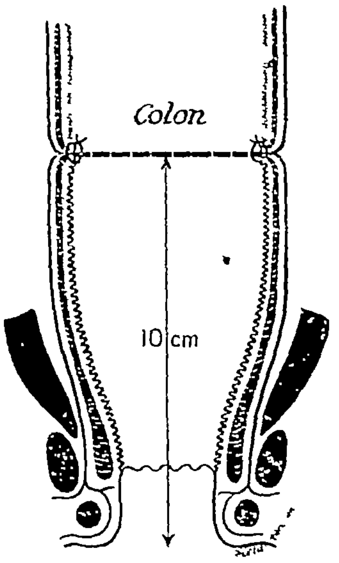


Fig 3—Diagram showing state of affairs after abdominal resection with intrapelvic anastomosis

This difference in the sensitivity of the rectum and colon is also seen under ordinary functional conditions During normal peristalsis considerable tension is presumably generated in the colon, but this usually produces no sensation, apart from occasional slight abdominal discomfort It is only when peristalsis becomes greatly exaggerated, as with drastic purgation, that actual pain is experienced The rectum, by contrast, is able to detect quite small quantities of flatus, and to distinguish them reliably from fæces, except perhaps during an attack of diarrhœa

Site of Origin of the Stimulus Producing Sensation in the Colon and Rectum

It has never been satisfactorily established where precisely the nerve endings are situated which transmit sensations from the bowel The matter cannot be decided anatomically because there are no recognisable sensory nerve endings in the bowel wall Presumably, therefore, afferent nerve impulses originate in free unencapsulated nerve terminals, which unfortunately cannot be distinguished from the nerve endings of intramural plexuses Hurst (1911) claimed, without producing any real evidence, that sensation was experienced in the muscularis, while Garry (1933) tried to show by experiments, in which he painted the rectal mucosa with a cocaine solution, that afferent impulses originated in the mucous membrane However, the anæsthetic solution might conceivably have been absorbed into the muscle coat as well, as Garry admits, and his work cannot be regarded as conclusive

It has been suggested by Lennander (1901), and more recently by Lewis and Kellgren (1939), that bowel pain does not originate in the gut wall at all, but is due to stretching of the sensitive mesentery We refer to this possibility because of our observation—which incidentally conflicts with the findings of Hurst (1911) and Gaston (1948b)—that stumps of colon brought down into the pelvis to restore continuity after sphincter saving resections of the rectum often acquire an imperfect sort of rectal sensation The fact that patients with an abdominal colostomy never develop a rectal type of sensation in the piece of colon leading to the colostomy suggests that the location of the stump in the pelvis is in some way responsible It is possible that pressure on surrounding parts is a factor in the production of rectal sensation in normal subjects, but it cannot be the only factor since the rectal sensation elicited in these colon stumps is much less delicate and discriminating than normal rectal sensation and requires a higher pressure to elicit it It also seems to be of little value to the patient as a substitute for the sensory function of the normal rectum

Nerve Pathways

Bentley and Smithwick (1940) showed that the pain resulting from balloon distension of the small gut was conveyed by the sympathetic system and was not felt after bilateral resection of the splanchnic nerves and thoracic sympathetic chains Ray and Neill (1947) demonstrated that colonic pain followed the same route and could be blocked by a similar operation if the upper 2 lumbar sympathetic ganglia on both sides were removed as well We had hoped to make some observations on colonic sensation in patients subjected to Grimson's extensive sympathectomy for hypertension but were prevented by technical difficulties from so doing

The pathway for the sensation of rectal fullness has not hitherto been known for certain Our investigations have established that neither the sympathetic system nor the inferior hæmorrhoidal and pudendal nerves play any part in this sensation, which is transmitted solely by the parasympathetic fibres connecting the rectum to the 2nd and 3rd sacral segments

Importance of Rectal Sensibility in the Maintenance of Anal Continence

The lower end of the rectum is embraced by three muscles—the internal and external anal sphincters and the puborectales, which, according to Milligan and Morgan (1934), may also act as a sphincter The internal sphincter is an involuntary muscle, and it has been established by Garry (1933), Denny Brown and Robertson (1935), and Gaston (1948a) that when the rectum is distended this sphincter, far from contracting to resist the raised pressure, undergoes reflex relaxation to facilitate defæcation For these reasons we find it difficult to see what part the internal sphincter can play in controlling the escape of fæces and flatus in accordance with the conventions of civilised life

Anal continence must in our view depend on the action of the external anal sphincter and the puborectales These are voluntary muscles capable of vigorous active contraction They rapidly tire, however, and can maintain this contraction for only a few minutes, as Gaston (1948a) has shown very clearly in the case of the external sphincter In the ordinary way, therefore, they exhibit only moderate resting tone, but when the pressure in the rectum rises suddenly owing to the entrance of flatus or fæces their tone is instantly reinforced, and maintained at this heightened level for a short period, to give the rectal wall time to relax and accommodate the new contents at lower pressure

There has been some dispute as to whether the sphincter contraction in response to rectal distension is purely reflex or whether it involves cortical participation and voluntary effort Gaston (1948a) showed that contraction did not follow balloon distension of the rectum in a patient with a complete lesion of the cord at the level of the 8th thoracic vertebra, it is not, therefore, a spinal cord reflex The same worker, however, claims to have elicited external sphincter contraction by rectal distension in a patient who was asleep, and who had no subsequent memory of a desire to defæcate, which suggests that contact between the sensory and motor sides of the arc can be effected at a subcortical level It will be recalled that, in our investigations, reflex contraction of the external sphincter occasionally seemed to precede by an instant or so conscious appreciation of fullness We have also observed during fistula tions that, when the anæsthesia is sufficiently light, lation of the lower rectum regularly evokes contrac- f both the external sphincter and the puborectales, h the patient is of course still unconscious There e little doubt, therefore, that the initial contraction e sphincter apparatus in response to a rise of intra- l tension is entirely reflex, but this is almost immedi- supplemented by a voluntary contraction as the l sensation reaches consciousness Further, the fine rentiation between fæces and flatus and the subse t decision as to whether sphincter contraction should naintained or relaxed—indispensable components of mechanism of continence—are entirely conscious esses We therefore regard the exercise of anal nence as an essentially conscious activity

nal incontinence may obviously be produced by ry to the motor mechanism, as by injudicious division he anal musculature during fistula operations It is haps not sufficiently widely recognised, however, that nay equally certainly result from damage to the sory apparatus even though the muscles may be intact capable of strong voluntary contraction This may pen in sphincter saving excisions of the rectum, ere a scrupulous preservation of the external sphincter scle, the levatores ani, and the motor nerves may none less be followed by a poor functional result This is cause the rectum, with its essential sensory nerve- dings, has been largely or entirely sacrificed the nsequence is that the patient receives inadequate rning of a sudden accumulation of flatus or fæces d so cannot contract his sphincters in time Our amination of patients who had undergone sphincter ving resections of the rectum showed that, though a gue rectal sense was not infrequently developed in the wer part of the colon anastomosed to the rectal stump r anus, this did not seem to be of much practical value the patient, the quality of the functional result was ill dependent on the amount of anorectum preserved elow With an anorectal stump of not less than 8–10 cm, neasured from the anal orifice, function was invariably ood a stump of 6–7 cm usually gave good function, hough sometimes rectal sensibility and control were nadequate especially for flatus or liquid fæces Finally patients in whom the whole rectum proper and the anal mucosa as far as the mucocutaneous junction had been excised had no useful rectal sensation or control and would pass flatus or fæces quite unconsciously It is only fair to mention that in these latter cases the external sphincter had invariably been divided and resutured round the projecting colon and was found to be in an atonic weak condition, which undoubtedly contributed to the inadequacy of anal control, but it should not have affected sensation

Another way in which "sensory incontinence" may be produced at operation is by damage to the parasympathetic and associated afferent nerves from the rectum, Considering the extensive mobilisation of the rectum with division of the lateral ligaments, that is so frequently necessary in resection operations, it might be expected that the remaining rectal stump would often be completely deprived of its sensory nerve supply It was surprising therefore to find that in our resection cases the rectal stump was always sensitive to balloon distension, and poor functional results could not be attributed to denervation of this structure However, the following case record shows that incontinence may result from interference with the sensory nerves of the rectum

A woman of 55 complained of prolapse of rectum at defæcation and on exertion during the day for 10 years She was unable to control flatus or fæces when bowel was extruded but fully continent when prolapse was reduced She had complete rectal prolapse projecting 2 in. beyond anus on straining Sphincter tone fair contractile power good, normal tone and contractile power in puborectalis

On Jan. 6, 1949, combined Roscoe Graham and Moschowitz type of abdominal repair performed under spinal and general anæsthesia Abdomen opened by left paramedian incision, peritoneum divided on either side of the rectum and across the pouch of Douglas rectum mobilised behind and in front, and lateral ligaments completely divided on either side By further dissection, levator ani muscles clearly defined on each side, the puborectales being especially well seen forming sling at anorectal junction. Contiguous edges of these muscles approximated with 4 floss-silk sutures in rectovaginal space, pouch of Douglas obliterated by purse string sutures of fine silk, and finally fundus of uterus fixed to anterior abdominal wall just above pubes by 2 silk sutures Abdomen closed in layers

Patient made good recovery and postoperative examination showed strong pelvic floor, well marked anorectal ring vigorous anal sphincter, and no further rectal prolapse Unfortunately, after operation patient had no control over wind or motion Flatus passed quite unconsciously and involuntarily Unless she was given daily washout to regulate bowel action motion would likewise escape and soil bed linen. Balloon distension was carried out on Feb 2, 1949 and showed that rectum was completely anæsthetic up to 15 cm. Owing to the narrowing produced by operation, it was impossible to pass sigmoidoscope beyond this point to test colonic sensation

Twelve months after operation there is still no sensation of wind or motion in the rectum, and she is virtually incontinent. Copes with disability by enemata, by frequent defæcation and by straining to empty rectum without waiting for large fæcal accumulation to occur Fortunately never has much intestinal flatus Is completely incapacitated by an attack of diarrhœa or by over purgation.

SUMMARY

Experiments are described in which patients' sensations were recorded while the lower sigmoid colon and rectum were distended by inflation of a balloon introduced through a sigmoidoscope.

Distension of the bowel up to 15 cm from the anal orifice (occasionally only 10 cm or as much as 25 cm) caused a sensation of fullness in the rectum giving the patient a desire to pass wind or motion—*rectal type of sensation* Distension above this level produced a purely abdominal sensation, referred to the suprapubic or left iliac region, and simulating a "wind" pain or intestinal colic—*colonic type of sensation*

Interruption of the nerve supply to the rectum and colon by anæsthetic block or operative division showed that the colonic type of sensation is mediated by the sympathetic and the rectal type by the parasympathetic system

Balloon distension causing rectal sensation evoked a contraction of the external sphincter ani which appeared to be partly reflex and partly voluntary This was never produced by colonic distension

A rectal type of sensation never develops in the terminal colon of colostomy cases, but may develop to a small degree in stumps of colon drawn down into the pelvis in cases treated by sphincter saving resections This is probably due to pressure of the distended colon on adjoining pelvic structures and not to a change in the type of sensibility normally inherent in the bowel.

This spurious rectal sensation is unfortunately no adequate substitute for genuine rectal sensation in the maintenance of anal continence Hence, in the performance of sphincter saving excisions, if a good functional result is to be ensured and "sensory incontinence" avoided, it is essential to preserve undamaged not only the sphincter muscles but also at least 6 cm, and preferably 8 cm or more, of anorectal stump with its parasympathetic nerve supply

We are greatly indebted to our colleagues at St. Mark's and St Mary's Hospitals for permission to investigate their cases and to Prof G W Pickering for helpful criticism.

References overleaf

RAPID AND SIMPLE METHOD OF ESTIMATING HÆMOGLOBIN

G KEMBLE WELCH
M B N Z
LATE REGISTRAR

W W WALTHER
M B Lond
PATHOLOGIST

GROUP 10 AREA LABORATORY WHIPPS CROSS HOSPITAL, LEYTONSTONE

LABORATORIES are now called upon to do so many hæmoglobin estimations that the saving of time without loss of accuracy must be the main consideration in the choice of method Macfarlane et al (1948) showed that, with a neutral grey standard, photometric or colorimetric methods which estimate hæmoglobin as oxyhæmoglobin are as reliable as any routine method and have the additional advantage that hæmoglobin in solution can be converted to oxyhæmoglobin without any special treatment

Using an oxyhæmoglobin method, Bell et al (1945) found that even if 10% of the hæmoglobin is converted into carboxyhæmoglobin or methæmoglobin the alteration in the density reading will be less than 1% They claimed that this is true only if 0 007 *N* ammonia is used as the solvent We have confirmed the magnitude of the error, but with our colorimeter the readings were identical whether 0 007 *N* or 1% ammonia was used King (1946) cites Ammundsen (1939, 1941) as saying that 2–12% of a normal adult's hæmoglobin may be in inactive forms, chiefly carboxyhæmoglobin, methæmoglobin, and sulphæmoglobin But up to 10% of carboxyhæmoglobin will raise the density reading by less than 1% and the same proportion of methæmoglobin will lower it by the same amount, so the errors arising from mixtures of these two substances will tend to cancel each other out Even in a person with severe carbon monoxide poisoning, half of whose hæmoglobin is in the form of carboxyhæmoglobin, when any exertion will precipitate a fainting attack, an uncorrected hæmoglobin estimation would be only 5% too high on the Haldane scale, a correct reading could of course be obtained by passing oxygen through the solution beforehand

E E L TEST TUBE COLORIMETER

With these considerations in view we decided to use the colorimetric oxyhæmoglobin method, and chose the photo electric principle for the sake of accuracy, though errors are more likely to arise in collecting the blood than in estimating the hæmoglobin The simplest instrument seemed to be the 'E E L' test tube colorimeter based on a design of Prof E J King's This is really an absorptiometer, in that it measures the light absorbed by a coloured solution compared with the colourless solvent The light from an incandescent filament passes in turn through a colour filter, a variable aperture, and the test tube containing the solution to be tested, to fall on a light sensitive cell The current produced is measured with a micro ammeter whose scale registers from 0 absorption at full deflection to 100 at no deflection when absorption complete, and the readings on the scale are in direct proportion to the amount of light absorbed In use, the colourless solvent (in this case weak ammonia solution) is put into a standard test tube, and, with the green filter in position, the light is adjusted by varying the aperture until the scale reads 0 The test tube is then replaced by one containing dilute laked blood, and the scale is read again

Reading

There were two ways of obtaining hæmoglobin readings with this instrument (1) One might construct a graph converting the scale readings into hæmoglobin concentrations in this case one would either use dry tubes and measure the appropriate amount of solvent into each with a pipette, necessitating a large stock of tubes, or one would have the tubes marked at an appropriate level when there would be no need for a pipette and undried tubes could be used (2) One might calibrate the tubes in such a way that the result could be found by a simple conversion factor (× 2 for the Haldane scale) The second method is the one of choice, because each tube is calibrated separately, thus eliminating errors due to variations in bore, &c, the tubes need not be dried, and no time is wasted through using pipettes for measuring the solvent

Materials

For this method the following materials are needed

(1) E E L photo-electric test tube colorimeter fitted with an adaptor to take $^7/_{16}$ inch test-tubes
(2) Colorimeter test tubes, $^7/_{16}$ inch (matched)
(3) Green filter (tricolour no 404)
(4) Standard 20 c mm pipettes
(5) Approximately 1% solution of ammonium hydroxide in distilled water

Details of Operation

To 1 ml of the ammonia solution in a calibrated colorimeter tube (see below) add 20 c mm of the blood to be tested and mix Then add ammonia solution to the mark, mix the contents again, and wipe the outside of the tube clean

TABLE I—COMPARISON OF PROPOSED METHOD WITH AN ALKALINE HÆMATIN METHOD ON IDENTICAL DILUTIONS OF THE SAME SAMPLE OF HUMAN BLOOD

Concentration of sample of blood %	Hb reading on Haldane scale	
	By method described	By alkaline hæmatin method
Undiluted	114	114
90	103	102
80	92	92
70	80	80
60	69	68
50	58	56
40	46	46
30	34	34
20	23	23
10	12	11

There is sufficient oxygen dissolved in the solution to oxidise the hæmoglobin present, as may be shown by passing oxygen for 10 minutes through the solution, which will not alter the reading To obtain the zero reading, place a matched tube (kept apart for the purpose), filled with dilute ammonia solution and wiped clean, in the colorimeter, with the green filter in position, switch on the light and open the aperture until the needle registers 0 and remains steady Then replace the matched tube by the tube containing the blood and note the new scale reading (*x*) Repeat the zero reading, and if the needle does not register 0, as may happen if the light sensitive cell has not had time to "settle

---

MR GOLIGHER, MR HUGHES REFERENCES

Babcock W W (1947) *Surg Gynec Obstet* **85** 1
Bacon H E (1946) *Ibid* **81** 113
Bentley F H Smithwick R (1940) *Lancet* ii 389
Denny Brown D Robertson E G (1935) *Brain* **58** 256
Garry R C (1933) *J Physiol* **78** 208
Gask G E, Ross J P (1937) The Surgery of the Sympathetic Nervous System 2nd ed London
Gaston E A (1948a) *Surg Gynec Obstet* **87** 280
— (1948b) *Ibid* p 669
Gray's Anatomy (1949) 30th ed London
Hurst A F (1911) The Sensibility of the Alimentary Canal London
Lennander, K G (1901) *Zbl Chir* **28** 209
Lewis, T, Kellgren J H (1939) *Clin Sci* **4** 47
Maunsell H W (1892) *Lancet* ii 473
Milligan E T C Morgan, C N (1934) *Ibid* ii 1150
Ray B S Neill C L (1947) *Ann Surg* **126** 709
Telferd E D Stopford J S B (1934) *Brit med J* i 572
Weir, R. F (1901) *J Amer med Ass* **37** 801

down," discard the previous test reading and repeat the process. Finally, % Hb (Haldane) = $x \times 2$. This follows from the calibration method described below.

Table I shows how hæmoglobin estimations by this method compare with the alkaline hæmatin method (Gibson and Harrison 1945) on identical dilutions of human blood.

Correction for bile pigments or other coloured substances may be made by taking a further 20 c mm of blood into physiological salt solution in a calibrated tube, diluting the contents to the mark with salt solution, mixing, and spinning in the centrifuge at 2000 r p m for a minute. The reading given by the cell free supernatant fluid is subtracted from the total hæmoglobin reading before the conversion factor is applied, or the supernatant fluid may be used as a blank for zero setting the colorimeter.

In cases of severe anæmia it is advisable to use 40 c mm of blood diluted in the usual way, when % Hb = x.

Calibration of Tubes

(1) 10 ml of venous blood from a healthy person is taken into a tube containing 100 units of heparin and mixed.

(2) The hæmoglobin value of this blood is found by the alkaline hæmatin method, the Gibson Harrison standard being used in the photo electric colorimeter. This is converted to the Haldane scale.

(3) 1 ml of the heparinised blood is added to 90 ml of 1% ammonium hydroxide solution in a volumetric flask, and the volume is made up to 100 ml.

TABLE II—VARIATIONS IN READINGS OBTAINED BY SERIOUS INTERFERENCE WITH THE SOURCE OF LIGHT

Concentration of sample of blood (% approx)	Hæmoglobin % on Haldane scale in different lights				Error in coloured lights compared with normal reading in white light (%)		
	White	Yellow	Blue	Red	Yellow	Blue	Red
Undiluted	86	86	86	70	0	0	−19
80	70	70	70	60	0	0	−14
60	52	52	52	46	0	0	−12
40	36	36	36	30	0	0	−17
20	18	18	19	16	0	+ 5 5	−11
10	9	9	10	9	0	+ 11	0

(4) 2 ml quantities of this solution (containing 20 c mm of blood) are placed in the colorimeter tubes to be calibrated.

(5) The zero reading is obtained as set out above, then each tube in turn is placed in the colorimeter and its contents are diluted until the scale reading is exactly half the known hæmoglobin percentage (Haldane) of the sample of blood. With a little practice this can be done very quickly. The tubes are then marked at the lower level of the meniscus. If hæmoglobin readings in g per 100 ml are required, the tubes may be calibrated so that the scale reading divided by 4 gives the hæmoglobin in g per 100 ml.

DISCUSSION

It will be seen that no standard solution is used for comparison with the unknown, apart from the dilute ammonia solution which gives the zero reading. This is because standard conditions are imposed by adjusting the light to give the zero reading, and thereafter identically coloured solutions will always give the same scale reading for each particular instrument. Gross variations in light conditions, obtained by tinting the electric light bulb which is the source of light, gave surprisingly low errors (see table II), and such variations would never be attained in normal practice since the energy for the lamp is obtained from the mains via a constant voltage transformer. We have used this type of instrument for several years, and an unvarying standard always gives identical readings. To test the instrument for accuracy such a standard may be used from time to time, and if the readings always agree one may use the instrument with confidence.

The advantages claimed for the method are as follows:

Speed.—A large number of estimations can be done in a short time. The colorimeter tubes need not be dried before use.

Accuracy.—In table I the results are compared with those of a standard alkaline hæmatin method (which takes much longer). The individual calibration of the tubes excludes the effects of variations in size and shape.

Stability.—Tubes containing the oxyhæmoglobin solution left standing over night at room temperature gave the same reading next day.

Simplicity.—The method is reliable in unskilled hands. With calibrated tubes there is no need to prepare a graph. Even student technicians have obtained consistently accurate results.

REFERENCES

Ammundsen, E. (1941) *J. biol. Chem.* 138, 563.
— Trier, M. 1939 *Acta med. scand.* 101, 451.
Bell, G. H., Chambers, J. W., Waddell, M. B. R. (1945) *Biochem. J.* 39, 60.
Gibson, Q. H., Harrison, D. C. (1945) *Ibid* p. 490.
King, E. J. (1946) Micro Analysis in Medical Biochemistry. London.
Macfarlane, R. G., King, E. J., Wootton, I. D. P., Gilchrist, M. (1948) *Lancet*, i, 282.

THE HYPOTENSIVE ACTION OF VERILOID (VERATRUM VIRIDE)

A CLINICAL INVESTIGATION

RALPH KAUNTZE
M B E, M D Camb, F R C P
ASSISTANT PHYSICIAN

JOHN TROUNCE
M D Lond, M R C P
MEDICAL REGISTRAR

GUY'S HOSPITAL, LONDON

HELLEBORE, a name anciently given to species of helleborous and veratrums (O E D) has a long established, if somewhat dubious, reputation in the treatment of such diversities as madness, cerebral hæmorrhage, dropsy, and worms. *Veratrum album* L and the American hellebore, *V viride* Aiton, contain among others the crystalline alkaloids jervine, protoveratrine, and protoveratridine, and an amorphous alkaloid, veratroidine. The extracts, tinctures, or powder, made from the rhizome and roots were hard to prepare in uniform potency, and in 1769 J Cook, writing of *Helleborus fœtidus* in particular, observed: "Where it kills not the patient, it would certainly kill the worms, but the worst of it is, it will sometimes kill both." Nevertheless, it has long been known that veratrum viride could lower the blood-pressure, and in consequence it has been administered on occasion to check the convulsions of puerperal eclampsia (Bryant 1935) and the pain of thoracic aneurysm. It is of interest that bradycardia was emphasised as an indication of adequate dosage in eclampsia.

More recently, on account of its digitalis like action, veratrum has been used in congestive heart failure (Löffler et al 1948). The promising results obtained by Freis and Stanton (1948) with veratrum viride in hyperpiesia were followed by studies of its hæmodynamic effects in man (Freis et al 1949) and the preparation by Stutzman et al (1949) of a stable, reproducible, and highly potent extract which was given the proprietary name 'Veriloid'.

Veriloid is a mixture of amorphous alkaloids obtained by fractionation, and contains none of the potent alkaloids mentioned above. It is biologically standardised according to its vasodepressor effect in dogs. Previously veratrum had been assayed in various small animals, a Craw unit being the least amount which would arrest the daphnia heart in systole. Since the dog's reactions to veratrum are similar to those in man, it is a more suitable animal for use in standardisation.

PHARMACOLOGY

The pharmacological action of the veratrine group of drugs has been studied extensively since purification has made practical their use in hypertension. The present position is a little obscure, for the numerous fractions known all have much the same action but with minor and not unimportant differences.

RAPID AND SIMPLE METHOD OF ESTIMATING HÆMOGLOBIN

G. KEMBLE WELCH
M.B. N.Z.
LATE REGISTRAR

W. W. WALTHER
M.B. Lond.
PATHOLOGIST

GROUP 10 AREA LABORATORY, WHIPPS CROSS HOSPITAL, LEYTONSTONE

LABORATORIES are now called upon to do so many hæmoglobin estimations that the saving of time without loss of accuracy must be the main consideration in the choice of method. Macfarlane et al. (1948) showed that, with a neutral grey standard, photometric or colorimetric methods which estimate hæmoglobin as oxyhæmoglobin are as reliable as any routine method and have the additional advantage that hæmoglobin in solution can be converted to oxyhæmoglobin without any special treatment.

Using an oxyhæmoglobin method, Bell et al. (1945) found that even if 10% of the hæmoglobin is converted into carboxyhæmoglobin or methæmoglobin the alteration in the density reading will be less than 1%. They claimed that this is true only if 0.007 *N* ammonia is used as the solvent. We have confirmed the magnitude of the error, but with our colorimeter the readings were identical whether 0.007 *N* or 1% ammonia was used. King (1946) cites Ammundsen (1939, 1941) as saying that 2–12% of a normal adult's hæmoglobin may be in inactive forms, chiefly carboxyhæmoglobin, methæmoglobin, and sulphæmoglobin. But up to 10% of carboxyhæmoglobin will raise the density reading by less than 1% and the same proportion of methæmoglobin will lower it by the same amount, so the errors arising from mixtures of these two substances will tend to cancel each other out. Even in a person with severe carbon monoxide poisoning, half of whose hæmoglobin is in the form of carboxyhæmoglobin, when any exertion will precipitate a fainting attack, an uncorrected hæmoglobin estimation would be only 5% too high on the Haldane scale; a correct reading could of course be obtained by passing oxygen through the solution beforehand.

E.E.L. TEST TUBE COLORIMETER

With these considerations in view we decided to use the colorimetric oxyhæmoglobin method, and chose the photo-electric principle for the sake of accuracy, though errors are more likely to arise in collecting the blood than in estimating the hæmoglobin. The simplest instrument seemed to be the 'E.E.L.' test tube colorimeter based on a design of Prof. E. J. King's. This is really an absorptiometer, in that it measures the light absorbed by a coloured solution compared with the colourless solvent. The light from an incandescent filament passes in turn through a colour filter, a variable aperture, and the test tube containing the solution to be tested, to fall on a light-sensitive cell. The current produced is measured with a micro-ammeter whose scale registers from 0 absorption at full deflection to 100 at no deflection when absorption complete, and the readings on the scale are in direct proportion to the amount of light absorbed. In use, the colourless solvent (in this case weak ammonia solution) is put into a standard test tube, and, with the green filter in position, the light is adjusted by varying the aperture until the scale reads 0. The test tube is then replaced by one containing dilute laked blood, and the scale is read again.

Reading

There were two ways of obtaining hæmoglobin readings with this instrument. (1) One might construct a graph converting the scale readings into hæmoglobin concentrations: in this case one would either use dry tubes and measure the appropriate amount of solvent into each with a pipette, necessitating a large stock of tubes, or one would have the tubes marked at an appropriate level when there would be no need for a pipette and undried tubes could be used. (2) One might calibrate the tubes in such a way that the result could be found by a simple conversion factor (× 2 for the Haldane scale). The second method is the one of choice, because each tube is calibrated separately, thus eliminating errors due to variations in bore, &c., the tubes need not be dried, and no time is wasted through using pipettes for measuring the solvent.

Materials

For this method the following materials are needed:

(1) E.E.L. photo-electric test tube colorimeter fitted with an adaptor to take $^7/_{16}$ inch test tubes.
(2) Colorimeter test tubes, $^7/_{16}$ inch (matched).
(3) Green filter (tricolour no. 404).
(4) Standard 20 c.mm. pipettes.
(5) Approximately 1% solution of ammonium hydroxide in distilled water.

Details of Operation

To 1 ml. of the ammonia solution in a calibrated colorimeter tube (see below) add 20 c.mm. of the blood to be tested and mix. Then add ammonia solution to the mark, mix the contents again, and wipe the outside of the tube clean.

TABLE I—COMPARISON OF PROPOSED METHOD WITH AN ALKALINE HÆMATIN METHOD ON IDENTICAL DILUTIONS OF THE SAME SAMPLE OF HUMAN BLOOD

Concentration of sample of blood %	Hb reading on Haldane scale	
	By method described	By alkaline hæmatin method
Undiluted	114	114
90	103	103
80	92	92
70	80	80
60	69	68
50	58	56
40	46	46
30	34	34
20	23	23
10	12	11

There is sufficient oxygen dissolved in the solution to oxidise the hæmoglobin present, as may be shown by passing oxygen for 10 minutes through the solution, which will not alter the reading. To obtain the zero reading, place a matched tube (kept apart for the purpose), filled with dilute ammonia solution and wiped clean, in the colorimeter; with the green filter in position, switch on the light and open the aperture until the needle registers 0 and remains steady. Then replace the matched tube by the tube containing the blood and note the new scale reading (*x*). Repeat the zero reading, and if the needle does not register 0, as may happen if the light-sensitive cell has not had time to "settle

---

MR. GOLIGHER, MR. HUGHES: REFERENCES

Babcock, W. W. (1947) *Surg. Gynec. Obstet.* 85, 1.
Bacon, H. E. (1945) *Ibid*, 81, 113.
Bentley, F. H., Smithwick, R. (1940) *Lancet*, ii, 389.
Denny-Brown, D., Robertson, E. G. (1935) *Brain*, 58, 256.
Garry, R. C. (1933) *J. Physiol.* 78, 208.
Gask, G. E., Ross, J. P. (1937) The Surgery of the Sympathetic Nervous System. 2nd ed. London.
Gaston, E. A. (1948a) *Surg. Gynec. Obstet.* 87, 280.
— (1948b) *Ibid*, p. 669.
Gray's Anatomy (1949) 30th ed. London.
Hurst, A. F. (1911) The Sensibility of the Alimentary Canal. London.
Lennander, K. G. (1901) *Zbl. Chir.* 28, 209.
Lewis, T., Kellgren, J. H. (1939) *Clin. Sci.* 4, 47.
Maunsell, H. W. (1892) *Lancet*, ii, 473.
Milligan, E. T. C., Morgan, C. N. (1934) *Ibid*, ii, 1150.
Ray, B. S., Neill, C. L. (1947) *Ann. Surg.* 126, 709.
Telford, E. D., Stopford, J. S. B. (1934) *Brit. med. J.* i, 572.
Weir, R. F. (1901) *J. Amer. med. Ass.* 37, 801.

in blood-pressure Ultimately the patient was observed as an outpatient

CASE RECORDS

Case 1 —A male bank clerk, aged 39, had complained of frontal headaches in the morning since an attack of amblyopia, lasting two hours, three months previously Although an athlete, he had noticed undue dyspnœa on exertion for six months His mother suffered from hypertension.

On Examination —Optic fundi normal, left ventricle moderately enlarged cardiothoracic ratio 52, blood pressure 240/130 mm Hg, electrocardiogram (E C G) normal Urine contained 0·1 g of albumin per 100 ml., deposit normal Blood urea 35 mg per 100 ml. Intravenous pyelogram showed poor concentration.

Result —During his observation period as an inpatient this man's blood pressure ranged from 200/125 to 180/120 mm. Hg The effect of giving 0 6 mg of veriloid intravenously over a period of 10 min. is shown in fig 1, the systolic and diastolic pressures fell to 70 and 50 mm. Hg at 20 min but were 122 and 88 mm. Hg an hour after the injection Coincident with the fall in blood pressure there was a slowing of the pulse In fig 2 the effects of atropine and ephedrine are shown. Atropine rapidly restored the pulse-rate to normal and at the same time caused a small rise in both systolic and diastolic pressures Ephedrine produced a rapid rise in the blood pressure to above the resting levels

We did not consider that the hypertension and circumstances of this patient warranted treatment with veriloid.

Case 2 —A boy, aged 19, was admitted to hospital in August, 1950, with hypertensive encephalopathy There was no family history of hypertension In 1946 he had acute nephritis, for which he was treated in bed for four months The urine continued to contain albumin and a few red cells, and once there was a frank hæmaturia, so that the boy was in bed for further long periods In February, 1950 he was found semi-conscious, and since then most of his time has been spent in hospital Latterly he has had attacks of headache and vomiting

On Examination.—Poor physique, pallid, with 10·3 g of Hb per 100 ml. No œdema Left ventricle slightly enlarged cardiothoracic ratio 46 Optic fundi papill œdema with exudates and hæmorrhages Urine 0 6 g of albumin per 100 ml red cells and granular casts Blood urea 102 mg per 100 ml standard urea clearance 15% of normal Blood pressure, recorded daily for a month before treatment with veriloid 235–220 mm systolic and 165–130 mm. diastolic, with mean 245/150 mm Hg

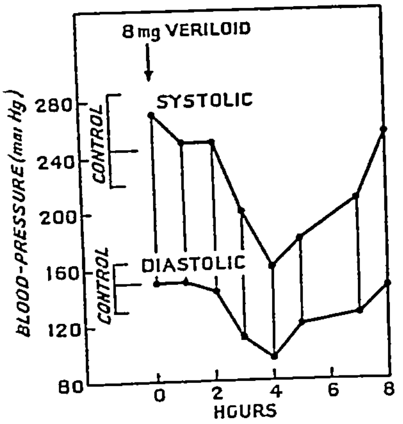


Fig 3—Effect of veriloid 8 mg by mouth on blood pressure (case 2)

The highest lowest, and mean blood pressure readings during the control period are included at the side of this and subsequent graphs.

Result —The patient responded readily to veriloid and fig 3 shows the effect of a single dose of 8 mg by mouth To avoid the possible embarrassment of renal function from sudden lowering of systemic pressure, his blood pressure levels were kept on the high side (fig 4) He has been maintained on veriloid for ten weeks without any significant change in his urinary output or blood urea. There has been much subjective improvement Withdrawal of veriloid was followed by recurrence of the headache and immediate return of the blood pressure to former levels The optic fundi remain unaltered.

Case 3 —A male confectioner, aged 46, who had been known to have hypertension since 1948, was admitted to hospital in 1950 for frontal headaches and shortness of breath. His headaches had begun six months before his admission, and latterly had become so severe as to interfere with his work. He had noted dyspnœa on effort for more than ten years, but in the last five weeks this had become more troublesome and he had taken to his bed In addition, he had angina of effort which came on if he walked 50 yards or so His father died at 46 from hypertensive heart-failure, and his mother at 33 from Bright's disease, one sister had kidney trouble

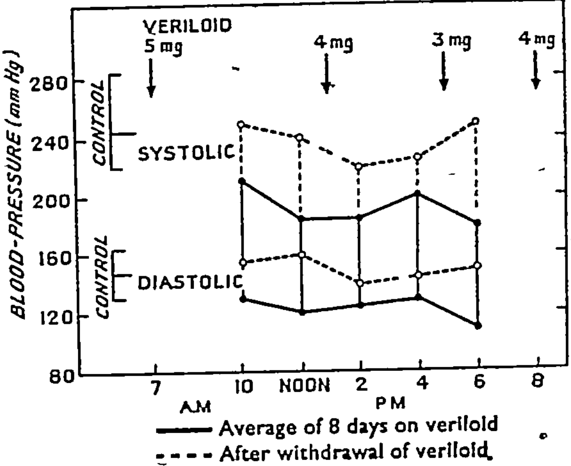


Fig 4—Blood-pressure during eight days on veriloid (continuous lines) and one day without veriloid (interrupted lines) in case 2.

On Examination —Obese and orthopnœic Optic fundi showed grade IV changes (Wagener and Keith 1939) Presystolic triple rhythm present, blood pressure 260/150 mm. Hg Cardiothoracic ratio 54, no hilar congestion. E C G left heart strain Kidneys concentrated to sp gr 1 025 and diluted to sp gr 1 002 Urine 0 1 g albumin per 100 ml, no casts or red cells Blood urea 40 mg per 100 ml During observation period at rest, blood pressure range was 240–210 mm systolic and 130–110 mm. diastolic, with mean of 225/120 mm Hg

Result —This was the first patient on whom we used veriloid, so the initial dose was small and single Less than 10 mg, however, had little effect Fig 5 shows the results of an attempt to adjust the concentration of veriloid so as to keep his blood pressure at a lower level throughout the day When his blood pressure fell to 160/100 mm Hg he felt faint and dizzy With this patient there was considerable variation both in the hypotensive effect obtained and the time taken for the drug to act Fig 6 gives the results with veriloid during five days while he was up and about Coincident with the fall in blood pressure his headaches were considerably relieved and his effort dyspnœa was less marked During ten weeks' observation as an outpatient his progress has been as follows

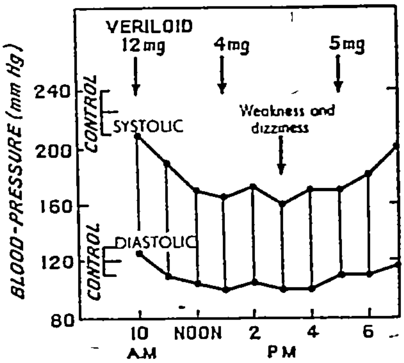


Fig 5—Result of attempt to control blood pressure throughout the day (case 3).

Dose of veriloid (mg)			*Blood pressure (mm Hg) at*	*Toxic effects*
8 A.M	2 P.M.	8 P.M.	5 P.M.	
10	4	2	175/105	Morning vomiting faintness
8	6	4	175/105	Nausea after two weeks
6	3	4	215/115	
6	3	4	175/110	

The patient has resumed his work as a confectioner He has a sense of fullness in his head on waking, but his headaches are less severe His angina of effort is now the same as before his admission.

Case 4 —A builder, aged 62, had had severe paroxysmal headaches for two years. His father died from hypertension, The three major effects of veriloid in man and the dog are hypotension, emesis, and bradycardia

Hypotension —Stutzman et al (1949) suggested that the hypotension is caused by dilatation of the arterioles in skeletal muscle, the splanchnic area, and the skin, together with venous constriction This action is unaltered in dogs by complete atropinisation, bilateral cervical vagotomy, or bilateral denervation of the carotid sinus and body (Stutzman et al 1950), moreover, veriloid produces a further fall of blood pressure in animals already rendered hypotensive by an amount of tetraethylammonium chloride sufficient to block the bradycardia from peripheral vagal stimulation and the pressor response from bilateral carotid occlusion In this respect veriloid seems to differ from the crystalline alkaloids, protoveratrine and veratridine, studied by Meilman and Krayer (1950), who found that their action was largely reflex, involving the peripheral endings of the vagus nerve There is no evidence that veriloid is sympatholytic, the postural and vasomotor reflexes are left intact, and the hypotension is counteracted by ephedrine

Emesis —The emetic action of veriloid, which has been studied in dogs, occurs with either oral or intravenous administration and is unaffected by atropine or ephedrine (Stutzman et al 1950) As would be expected, the drug is less liable to produce vomiting when given after food

Bradycardia —The third effect, bradycardia, has been investigated in dogs and to some extent in man It is probably mediated through the vagus, being abolished by vagectomy in dogs and by atropine in man, and it does not occur in the isolated perfused rabbit heart (Stearns 1950) Increasing dosage in the anæsthetised dog leads to prolongation of the P–R interval, partial heart block, and atrioventricular nodal rhythm, finally 200–500 times the minimal effective dose causes ventricular fibrillation, though this is not seen in the unanæsthetised animal (Stutzman et al 1949) Prolonged administration of veriloid to animals has produced no apparent structural change (Stutzman et al 1950)

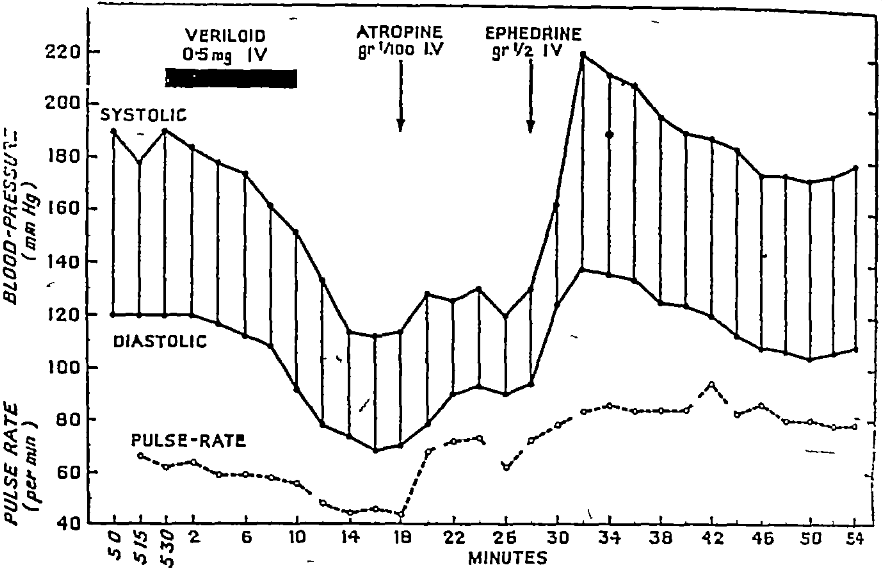


Fig 2—Effects on blood-pressure and pulse-rate of atropine gr 1/100 and ephedrine gr 1/2 i.v in hypotension after veriloid (case 1)

METHOD

Our objects have been to observe the effect on the blood-pressure of veriloid given by mouth in gradually increasing dosage thence, by spacing the administration and varying the form in which the drug was given to attempt continuous control of blood pressure at a lower level, to decide in which types of hypertension a response could be expected, to record the toxic effects and finally, when a suitable preparation became available, to study the results of a known concentration from intravenous injection

It was decided to admit the patients to hospital, so as to obtain basal conditions and continuous observation and also for safety's sake, because we were uncertain of the dosage of veriloid required and of the drug's toxicity Ten patients were observed initially in hospital and one as an outpatient only In each case the hypertension was severe, and no patient with a diastolic pressure below 120 mm Hg after five days' rest in bed with mild sedation was included

During the preliminary period in hospital clinical examination, tests of renal function, fluoroscopy of the heart, and electrocardiograms were completed, and the blood pressure was recorded twice daily, as far as possible by the same person, for even a comparative stranger may cause a considerable rise in systemic pressure

When the blood pressure seemed to have reached a stable level, treatment with veriloid was begun At first we tried single doses, but after a considerable amount of experiment we decided on three or four doses in the day When a suitable dosage had been found it was maintained for a few days with the patient ambulant (case 2 was an exception), the drug was then omitted in an attempt to exclude continued stay in hospital as the cause of the fall

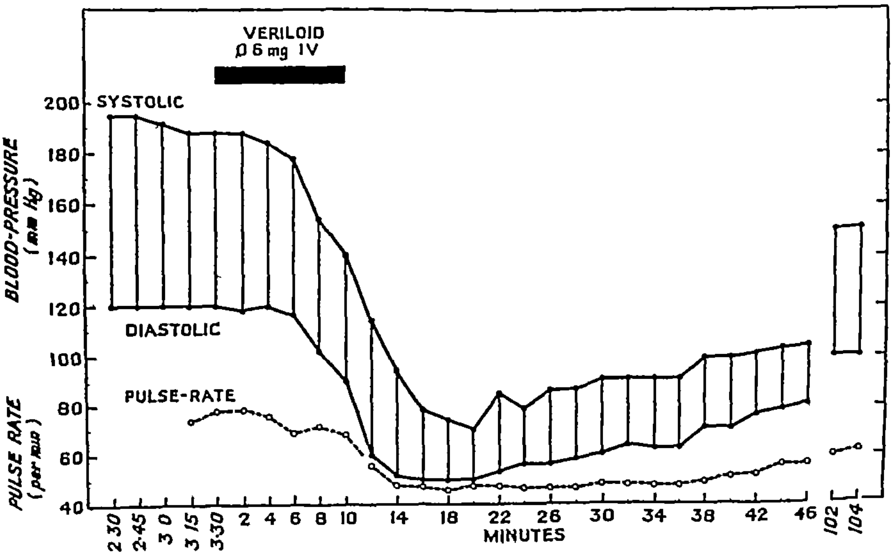


Fig 1—Effect of intravenous veriloid 0·6 mg on blood-pressure (case 1)

n blood pressure Ultimately the patient was observed as an outpatient

CASE RECORDS

Case 1 —A male bank clerk, aged 39, had complained of frontal headaches in the morning since an attack of amblyopia, lasting two hours, three months previously Although an athlete, he had noticed undue dyspnœa on exertion for six months His mother suffered from hypertension.

On Examination—Optic fundi normal, left ventricle moderately enlarged cardiothoracic ratio 52, blood pressure 240/130 mm Hg, electrocardiogram (E C G) normal Urine contained 0·1 g of albumin per 100 ml, deposit normal Blood urea 35 mg per 100 ml. Intravenous pyelogram showed poor concentration.

Result—During his observation period as an inpatient this man's blood pressure ranged from 200/125 to 180/120 mm Hg The effect of giving 0 6 mg of veriloid intravenously over a period of 10 min. is shown in fig 1, the systolic and diastolic pressures fell to 70 and 50 mm Hg at 20 min but were 122 and 88 mm. Hg an hour after the injection Coincident with the fall in blood pressure there was a slowing of the pulse In fig 2 the effects of atropine and ephedrine are shown. Atropine rapidly restored the pulse-rate to normal and at the same time caused a small rise in both systolic and diastolic pressures Ephedrine produced a rapid rise in the blood pressure to above the resting levels

We did not consider that the hypertension and circumstances of this patient warranted treatment with veriloid

Case 2 —A boy, aged 19, was admitted to hospital in August, 1950, with hypertensive encephalopathy There was no family history of hypertension. In 1946 he had acute nephritis, for which he was treated in bed for four months The urine continued to contain albumin and a few red cells, and once there was a frank hæmaturia, so that the boy was in bed for further long periods. In February, 1950, he was found semi conscious, and since then most of his time has been spent in hospital Latterly he has had attacks of headache and vomiting

On Examination—Poor physique pallid, with 10·3 g of Hb per 100 ml No œdema Left ventricle slightly enlarged cardiothoracic ratio 46 Optic fundi papillœdema with exudates and hæmorrhages Urine 0 6 g of albumin per 100 ml red cells and granular casts. Blood urea 102 mg per 100 ml standard urea clearance 15% of normal Blood pressure recorded daily for a month before treatment with veriloid 285–220 mm systolic and 165–130 mm diastolic, with mean 245/150 mm. Hg

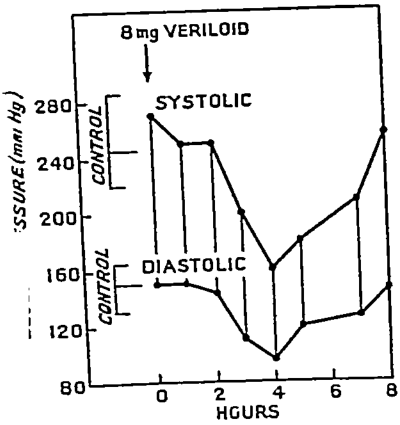


Fig 3—Effect of veriloid 8 mg by mouth on blood-pressure (case 2)

The highest lowest and mean blood pressure readings during the control period are included at the side of this and subsequent graphs.

Result—The patient responded readily to veriloid, and fig 3 shows the effect of a single dose of 8 mg by mouth To avoid the possible embarrassment of renal function from sudden lowering of systemic pressure, his blood pressure levels were kept on the high side (fig 4) He has been maintained on veriloid for ten weeks without any significant change in his urinary output or blood urea. There has been much subjective improvement Withdrawal of veriloid was followed by recurrence of the headache and immediate return of the blood pressure to former levels The optic fundi remain unaltered

Case 3 —A male confectioner aged 46, who had been known to have hypertension since 1948 was admitted to hospital in 1950 for frontal headaches and shortness of breath. His headaches had begun six months before his admission, and latterly had become so severe as to interfere with his work. He had noted dyspnœa on effort for more than ten years, but in the last five weeks this had become more troublesome and he had taken to his bed In addition he had angina of effort which came on if he walked 50 yards or so His father died at 46 from hypertensive heart-failure, and his mother at 33 from Bright s disease, one sister had kidney trouble

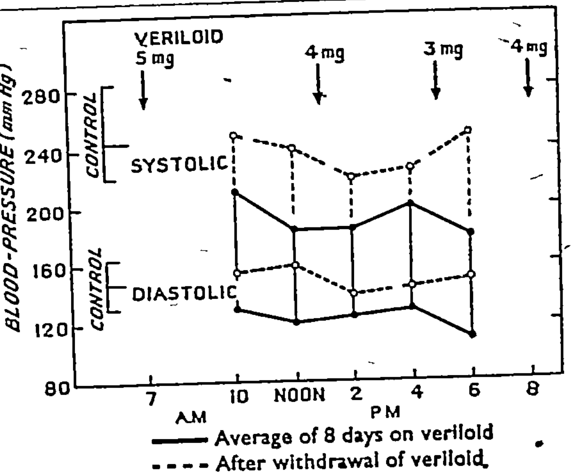


Fig 4—Blood-pressure during eight days on veriloid (continuous lines) and one day without veriloid (interrupted lines) in case 2.

On Examination—Obese and orthopnœic Optic fundi showed grade IV changes (Wagener and Keith 1939) Pre systolic triple rhythm present, blood pressure 260/150 mm. Hg Cardiothoracic ratio 54, no hilar congestion. E C G left heart strain. Kidneys concentrated to sp gr 1 025 and diluted to sp gr 1 002 Urine 0 1 g albumin per 100 ml, no casts or red cells Blood urea 40 mg per 100 ml. During observation period at rest, blood pressure range was 240–210 mm systolic and 130–110 mm. diastolic, with mean of 225/120 mm Hg

Result—This was the first patient on whom we used veriloid, so the initial dose was small and single Less than 10 mg, however, had little effect Fig 5 shows the results of an attempt to adjust the concentration of veriloid so as to keep his blood pressure at a lower level throughout the day When his blood pressure fell to 160/100 mm Hg he felt faint and dizzy With this patient there was considerable variation both in the hypotensive effect obtained and the time taken for the drug to act Fig 6 gives the results with veriloid during five days while he was up and about Coincident with the fall in blood pressure his headaches were considerably relieved and his effort dyspnœa was less marked During ten weeks' observation as an outpatient his progress has been as follows

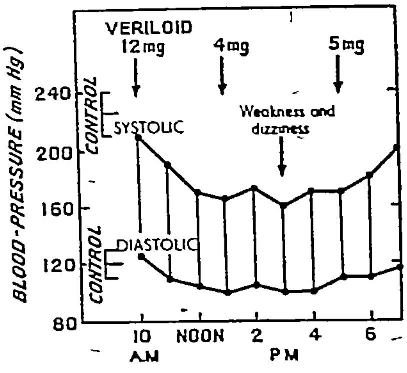


Fig 5—Result of attempt to control blood pressure throughout the day (case 3).

Dose of veriloid (mg.)			*Blood pressure (mm Hg) at*	*Toxic effects*
8 A.M	2 P.M.	8 P.M.	5 P.M.	
10	4	2	175/105	Morning vomiting faintness
8	6	4	175/105	Nausea after two weeks
6	3	4	215/115	
6	3	4	175/110	

The patient has resumed his work as a confectioner He has a sense of fullness in his head on waking, but his headaches are less severe His angina of effort is now the same as before his admission.

Case 4 —A builder, aged 62, had had severe paroxysmal headaches for two years. His father died from hypertension

The three major effects of veriloid in man and the dog are hypotension, emesis, and bradycardia.

Hypotension.—Stutzman et al. (1949) suggested that the hypotension is caused by dilatation of the arterioles in skeletal muscle, the splanchnic area, and the skin, together with venous constriction. This action is unaltered in dogs by complete atropinisation, bilateral cervical vagotomy, or bilateral denervation of the carotid sinus and body (Stutzman et al. 1950); moreover, veriloid produces a further fall of blood pressure in animals already rendered hypotensive by an amount of tetraethylammonium chloride sufficient to block the bradycardia from peripheral vagal stimulation and the pressor response from bilateral carotid occlusion. In this respect veriloid seems to differ from the crystalline alkaloids, protoveratrine and veratridine, studied by Meilman and Krayer (1950), who found that their action was largely reflex, involving the peripheral endings of the vagus nerve. There is no evidence that veriloid is sympatholytic; the postural and vasomotor reflexes are left intact, and the hypotension is counteracted by ephedrine.

Emesis.—The emetic action of veriloid, which has been studied in dogs, occurs with either oral or intravenous administration and is unaffected by atropine or ephedrine (Stutzman et al. 1950). As would be expected, the drug is less liable to produce vomiting when given after food.

Bradycardia.—The third effect, bradycardia, has been investigated in dogs and to some extent in man. It is probably mediated through the vagus, being abolished by vagectomy in dogs and by atropine in man, and it does not occur in the isolated perfused rabbit heart (Stearns 1950). Increasing dosage in the anæsthetised dog leads to prolongation of the P-R interval, partial heart block, and atrioventricular nodal rhythm; finally 200–500 times the minimal effective dose causes ventricular fibrillation, though this is not seen in the unanæsthetised animal (Stutzman et al. 1949). Prolonged administration of veriloid to animals has produced no apparent structural change (Stutzman et al. 1950).

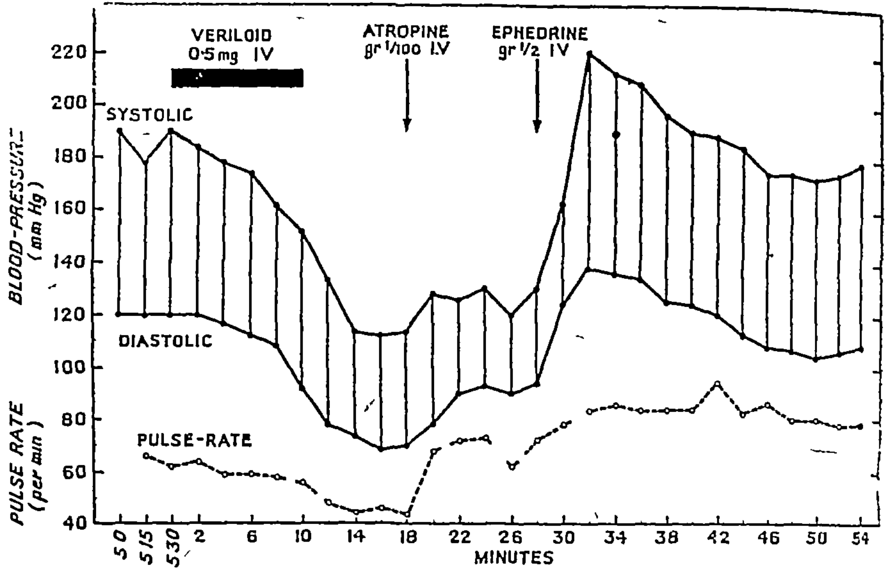


Fig. 2—Effects on blood pressure and pulse-rate of atropine gr. $^1/_{100}$ and ephedrine gr. $^1/_2$ i.v. in hypotension after veriloid (case 1).

METHOD

Our objects have been to observe the effect on the blood pressure of veriloid given by mouth in gradually increasing dosage; thence, by spacing the administration and varying the form in which the drug was given to attempt continuous control of blood-pressure at a lower level; to decide in which types of hypertension a response could be expected; to record the toxic effects; and finally, when a suitable preparation became available, to study the results of a known concentration from intravenous injection.

It was decided to admit the patients to hospital so as to obtain basal conditions and continuous observation, and also for safety's sake, because we were uncertain of the dosage of veriloid required and of the drug's toxicity. Ten patients were observed initially in hospital and one as an outpatient only. In each case the hypertension was severe, and no patient with a diastolic pressure below 120 mm. Hg after five days' rest in bed with mild sedation was included.

During the preliminary period in hospital clinical examination, tests of renal function, fluoroscopy of the heart, and electrocardiograms were completed, and the blood pressure was recorded twice daily, as far as possible by the same person, for even a comparative stranger may cause a considerable rise in systemic pressure.

When the blood pressure seemed to have reached a stable level, treatment with veriloid was begun. At first we tried single doses, but after a considerable amount of experiment we decided on three or four doses in the day. When a suitable dosage had been found it was maintained for a few days with the patient ambulant (case 2 was an exception); the drug was then omitted in an attempt to exclude continued stay in hospital as the cause of the fall

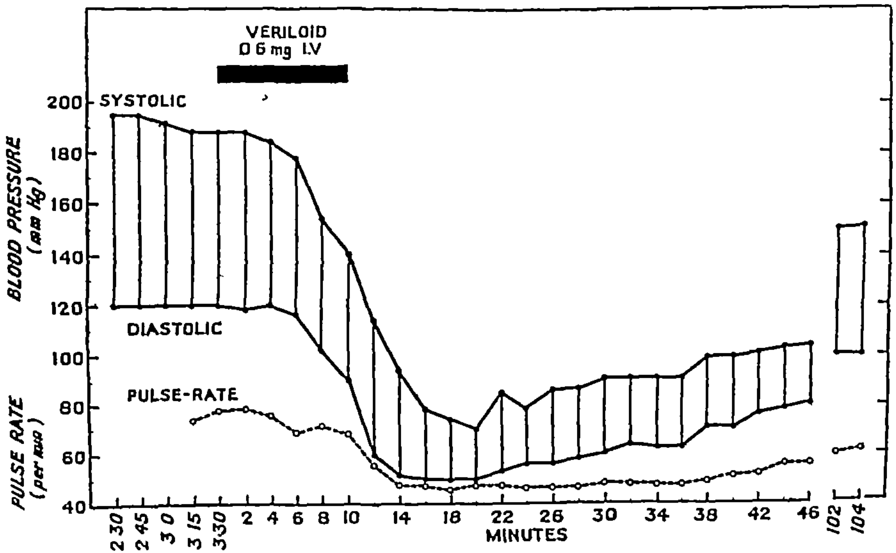


Fig. 1—Effect of intravenous veriloid 0·6 mg. on blood-pressure (case 1).

discontinue treatment This vagal effect is readily overcome by atropine, it should be borne in mind during the concurrent administration of digitalis Substernal and epigastric discomfort were most troublesome in case 7, they were relieved by hyoscyamine sulphate and were not accompanied by electrocardiographic changes

DOSAGE

Although the blood pressure can be readily lowered by the intravenous administration of veriloid, the oral route offers peculiar difficulties There is individual daily variation in the rate of intestinal absorption, as judged by the degree and duration of the drug's effect on the blood pressure In one patient we thought pylorospasm, perhaps from vagal stimulation, was a factor in delaying absorption The main action of veriloid is exerted three to six hours after ingestion, which necessitates administration three or four times a day and precludes an interval of less than four hours between doses The drug's action is partly cumulative, which calls for frequent observation of the patient in the early stages of treatment with large doses, but the cumulative effect can be used to give a loading dose in the morning The action of veriloid has much in common with that of digitalis

Our procedure is to start with 3, 2, 2, and 3 mg of veriloid given with breakfast (8 A M), lunch (12 30 P M), tea (5 P.M), and late supper (9 P M), or in three doses at breakfast, lunch, and dinner Giving veriloid with food has diminished the tendency to vomit After four days the dosage is adjusted according to the effect produced, but the adjustment must be gradual, for the difference between a profound and a slight hypotensive effect may represent an increase of only 2 mg Nevertheless, an intelligent patient can safely be treated as an outpatient.

Nausea, vomiting, or faintness, if not rapidly relieved by rest is an indication for halving, or if severe omitting, the next dose Nausea may develop in a patient who seems well stabilised, in 2 of our patients a slight reduction in the antecedent dose relieved their nausea without interfering unduly with the hypotensive action of veriloid

DISCUSSION

The precise cause of systemic arterial hypertension remains unknown, but hereditary, psychogenic, endocrine, and renal factors may each determine its production In the benign essential variety the hypertension appears to pass through a labile stage, where psychogenic and endocrine influences are largely operative, to a relatively fixed stage and finally a wholly fixed stage, associated with renal ischæmia and arteriosclerosis There seems to be scant hope of benefiting fixed hypertension, and therapy has been directed to checking the condition in its earlier stages Lumbodorsal sympathectomy seemed a logical approach because it would be expected not only to lower the blood pressure but also to increase renal blood flow But the results on the whole have been disappointing particularly after long term follow up (Evelyn et al 1949), and sympathectomy now has little to commend it, except perhaps in the rare cases of hypertension secondary to chronic pyelonephritis (Platt and Stanbury 1950)

The search for effective hypotensive drugs continues Thiocyanate was first advocated by Treupel and Edinger (1900) and has more recently been reported on by Watkinson and Evans (1947) The use of tetraethyl ammonium salts was described by Stead et al (1948) Paton and Zaimis (1949) noted that hexamethonium and pentamethonium compounds could block ganglionic transmission without exerting any significant atropine-like action Turner (1950), in a clinical study of the methonium compounds, suggested that they had as yet no place in the routine management of patients, though they might prove useful in resistant symptoms related to hypertension Campbell and Robertson (1950) have reported some spectacular results from hexamethonium bromide

If a drug is to be considered satisfactory in the treatment of hypertension it must fulfil the following criteria reduce blood pressure and maintain it at a lower level, act consistently in a high proportion of patients, cause no toxic symptoms, and be easy to administer and control

Possibly because of the more benign course of hypertension in women, it has been suggested that it is not always desirable to lower an unduly high blood pressure, but while we remain ignorant of the first causes of the condition, treatment of the hypertension direct is the sole measure we can apply to relieve the symptoms and avert the failure of heart and kidneys, or rupture of a cerebral artery, which is otherwise the final sequence That by so doing we increase the risk of cerebral thrombosis must be accepted, this risk is similarly present during sleep

The chief source of error in estimating the hypotensive effect of a drug is the considerable variation in blood-pressure throughout the day, apparently independent of external influences, such as excitement or meals, and particularly in hypertensives Evidently veriloid will lower the blood pressure in the great majority of hypertensives, even severe cases Case 6 was an exception for which we can offer no explanation As a result of the vagaries of intestinal absorption it was impossible to control the blood-pressure throughout the day by giving veriloid by mouth, but it was usually possible to convert a severe into a moderate or mild hypertension and at the same time produce well marked symptomatic relief Whether this will affect the development of cardiovascular or renal failure in the younger hypertensive can only be determined after long continued observation At the least it is reasonable to hope that these changes may be retarded

CONCLUSIONS

Veriloid is a potent hypotensive drug which on injection rapidly causes a profound fall in blood pressure For this reason it should prove of value in hypertensive encephalopathy and the convulsions of puerperal eclampsia Given by mouth its absorption is difficult to control and its effect lasts a relatively short time, with the result that uniform lowering of the blood pressure is not readily obtained, but the variations can be kept at a lower level and symptomatic relief is usually attained The margin between therapeutic and toxic levels, where high dosage is necessary, is small and makes the fixed arteriosclerotic type of hypertension unsuitable for treatment Because of vagus action, veriloid is best avoided in the presence of peptic ulceration Its main field of usefulness is in the younger patients with severe benign or malignant hypertension and possibly those with chronic nephritis

We are indebted to the Rexall Drug Co, of Los Angeles, and the Riker Laboratories Inc for supplies of veriloid

REFERENCES

Bryant R D (1935) *Amer J Obstet Gynec* 30, 46
Campbell A Robertson E (1950) *Brit med J* ii 804
Evelyn K A Alexander F Cooper S R (1949) *J Amer med Ass* 140 592
Freis, E D Stanton J R (1948) *Amer Heart J* 36 723
— — Culbertson J W Litter J Halperin N H Burnett, C H, Wilkins R W (1949) *J clin Invest* 28 353
Löffler W Essellier A F Pedrazzini A (1948) *Schweiz med Wschr* 78 1021
Meilman E Krayer O (1950) *Circulation* 1 204
Paton W D M Zaimis E J (1949) *Brit J Pharmacol* 4 381
Platt R, Stanbury S W (1950) *Lancet* i 651
Stead, W W Reiser M F Rapoport S Ferris, E B (1948) *J clin Invest* 27 766
Stearns N S (1950) *Fed. Proc* 9 318
Stutzman J W, Maison G L Bauer, R O (1950) *Proc New Engl cardiovasc Soc* February
— — Kusserow G W (1949) *Proc Soc exp Biol, N Y* 71 725
Treupel G Edinger A (1900) *Münch med Wschr* 47 717, 767
Turner R (1950) *Lancet* ii 353
Wagener H P Keith N M (1939) *Medicine Baltimore* 18 317
Watkinson G Evans G (1947) *Brit med. J* i 595

On veriloid 26 mg daily, in four doses, his blood pressure ranged from 130 to 180 mm systolic and from 80 to 110 mm Hg diastolic, with a pulse rate about 50 , there was considerable symptomatic improvement, but nausea in the forenoon was common The difficulties of continuous control of blood pressure in this patient are illustrated in fig 14

Case 11 —A female checker, aged 39, had had acute nephritis at 24 and again at 34, since when she had remained fairly well until the last three months, when she began to have hypertensive attacks characterised by sweating, palpitation, headache, pallor, and sometimes loss of consciousness

On Examination —Optic fundi grade II arteriosclerosis Heart moderately enlarged , blood pressure 220/110 mm Hg (had been 210/120 mm nine months before) Femoral pulses normal , no cardiac failure E C G left ventricular hypertrophy Urine albumin and granular casts , blood urea 47 mg per 100 ml

Result —This woman s blood pressure with mild sedation was fairly constant at 220/120 mm Hg in the month before outpatient treatment with veriloid was begun The initial dosage of 2 mg b d had no effect, but after a week on 4, 3, and 2 mg daily the blood pressure was 200/105 , a week later it was 190/115 and after a further week 135/80 Two, five, and eight weeks later the afternoon readings were 155/90, 145/90, and 150/90 mm Hg respectively During this period there was occasional transitory nausea about midday but no other symptom

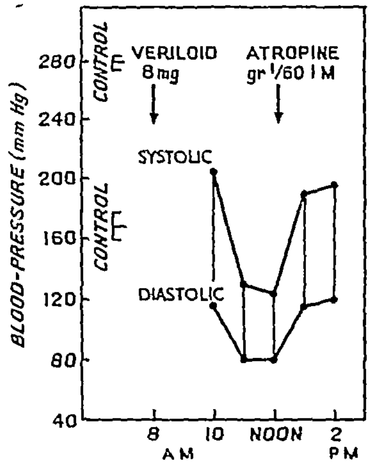


Fig 12—Effect of atropine in presence of hypotensive action of veriloid by mouth (case 9)

RESULTS

Veriloid was given by mouth to 5 men and 5 women with hypertension, and an eleventh patient (case 1) received intravenous veriloid alone The intravenous injection of 0 6 mg of veriloid over a period of ten minutes (fig 1) produced an abrupt and profound fall in the blood pressure, maximal twenty minutes from the start, with a gradual return to previous levels in about two hours There was no postural change in the blood pressure comparable with that after the injection of hexamethonium Together with the fall in blood pressure the patient experienced some flushing of the face and the pulse was slowed, but there was no other symptom Atropine abolished the bradycardia but had only a moderate effect on the blood pressure, whereas ephedrine rapidly restored the pressure to its former levels (fig 2) A single dose of veriloid by mouth may be similar in effect, the hypotensive action occurring two hours or more after ingestion and persisting up to six hours, with a maximal effect between three and five hours after intake (fig 3)

Of the 10 patients treated with veriloid by mouth, 8 showed a definite and at times considerable fall in blood pressure , in case 6 there was no response, and in case 5 the margin between therapeutic and outstanding vagal action was too small to warrant further treatment with the drug No attempt was made to restore normal tension, but it was usually possible to control the diastolic blood pressure at reduced levels and this gave considerable symptomatic relief On withdrawal of veriloid the blood pressure returned to its former levels and the symptoms recurred Case 8, who had malignant hypertension, died of a cerebral hæmorrhage while under treatment

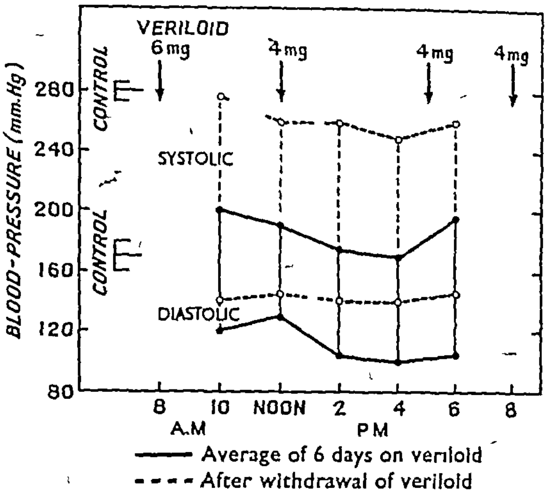


Fig 13—Blood pressures during six days on veriloid (case 9)

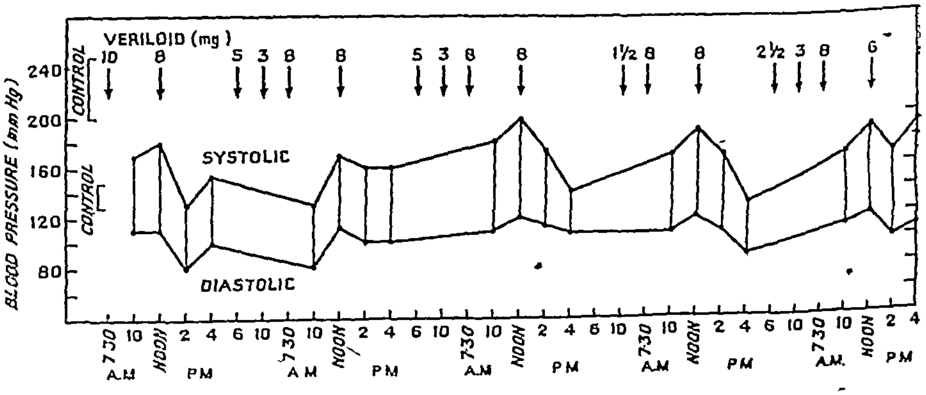


Fig 14—Case 10 shows difficulties of continuous control of blood pressure with veriloid

Of the 5 patients observed as outpatients for one to three months since their discharge from hospital, in 3 the blood pressure has been kept at a lower level, and these patients remain considerably improved, case 11 being an outstanding success Case 7, although symptomatically improved, has been difficult to maintain well because of nausea, and cannot be considered satisfactory Case 9, after being considerably improved, developed a cerebral thrombosis and treatment was discontinued

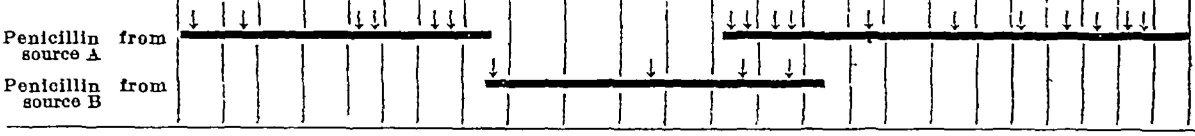
TOXICITY

The toxic effects of veriloid fall into two groups (1) nausea, vomiting, faintness, and collapse due to its hypotensive action , and (2) bradycardia and substernal and epigastric discomfort from vagal stimulation Nausea has been produced at times in all the patients, and though this is a nuisance it is also a protection against excessive dosage The nausea is not invariably the result of hypotension or of vagal stimulation, for it may still occur where neither of these effects is manifest and may then perhaps be central in origin The 6 patients who developed faintness all did so after a considerable amount of veriloid had produced a well marked hypotensive effect, and ephedrine, by abolishing the hypotension, gave immediate relief

Some slowing of the heart occurred in most patients, but in case 5 the slowing was extreme and caused us to

INCIDENCE OF ABSCESSES IN RELATION TO COURSES OF PARENTERAL PENICILLIN

—	1948										1949												1950		Total
	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	
No of abscesses presenting	—	—	—	—	—	—	—	—	3	3	5	5	5	8	10	12	3	1	—	3	4	1	2	1	66
No of patients receiving parenteral penicillin who developed abscesses *	1 (*3*)	—	2 (*4*)	1 (*1*)	—	—	2 (*3*)	1 (*2*)	5 (*14*)	4 (*14*)	2 (*6*)	3 (*7*)	1 (*1*)	2 (*2*)	2 (*7*)	—	1 (*1*)	1 (*1*)	—	—	—	—	—	—	28 (*66*)



Arrows denote arrival of new batches of aqueous yellow sodium penicillin

* *No of abscesses shown in parentheses*

MANTOUX TESTS

Of 7 children under the age of twelve years who were Mantoux tested with 1 in 1000 Old Tuberculin from one to eleven months after an abscess had formed, 2 were positive, one was aged seven, and the other, who was aged sixteen months at the time of the test, had been given penicillin at the age of five months. Unfortunately the abscess was not investigated bacteriologically, and this case was possibly tuberculous, though radiography of chest and abdomen revealed no lesions. However, it is clear that in 5 of these children the abscesses were not tuberculous.

SENSITIVITY TO PENICILLIN

All the children who were Mantoux tested were also tested for penicillin sensitivity by the intradermal injection of yellow penicillin 500 units in 0·1 ml. of distilled water, but the results were negative. Of the adult patients 3 had developed urticaria during their penicillin treatment, but 2 of these showed no sensitivity to intradermal penicillin.

HISTOLOGY

Six abscesses were excised at stages of development varying from two to twelve months from the time of the penicillin treatment.

In general terms the appearances (figs. 1 and 2) were those of a foreign-body granulomatous inflammation: infiltration by lymphocytes, plasma cells, and histiocytes; formation of giant cells; and proliferation of fibroblasts. Eosinophils were present in all sections examined and were a prominent feature in some, and there was intense polymorph infiltration of the lining wall of the earlier abscesses.

The uniformity of the histological appearances in all the sections suggests that an irritant was the common cause of the abscesses. In the older abscesses fibrosis was marked, leading eventually in the year-old lesion to a fibrous-walled cyst with amorphous contents.

No tubercle bacilli were seen in any section.

SOURCE OF PENICILLIN

No records had been kept of the source and batch number of penicillin given to each patient, but an investigation of the dates of supply of different batches of penicillin to the hospital yielded interesting information.

Before October, 1948, all our penicillin was supplied by one manufacturer (source A). Then a further supply was obtained from a second manufacturer (source B). All the penicillin used between the end of October, 1948, and the end of January, 1949, was of this particular batch. A second batch was then received from source B, and further supplies were obtained from both source A and source B in March, 1949. The accompanying table shows the monthly incidence of cases in relation to the time at which the penicillin had been given, the number of abscesses caused in these cases, and the source of penicillin. It will be seen that there was a striking increase in the incidence associated with one source of penicillin, and in particular with one batch received *at the end of October, 1948.*

There was no more penicillin issued to female than to male wards to explain the preponderance of female cases; nor was the amount of penicillin used in the six winter months sufficiently greater than that used in the six summer months to explain the increased incidence arising from injections given between November and May.

DISCUSSION

There are gaps in the account of these chronic abscesses which were unavoidable in the circumstances of the investigation. Many of the inquiries were made retrospectively after many months had elapsed.

It cannot be claimed, for instance, that a homogeneous series has been presented, or that no single case included in these observations was tuberculous. We feel, however, that we have provided enough evidence to conclude that most of the sterile chronic abscesses which develop at the site of penicillin injections are not due to the tubercle bacillus, and that they have distinct clinical and pathological features which suggest a common irritant. The evidence also indicates several *predisposing factors* in the development of these abscesses: subcutaneous rather than intramuscular injections; a large dose given in a small volume of fluid injected; and, probably most important, the particular batch of penicillin in use.

Subcutaneous instead of intramuscular injection is often made in obese patients and in children, and this probably explains the high incidence in women and children.

The question of a large dose in a small volume of injected fluid is particularly relevant at present, when the tendency in penicillin therapy is *towards large doses* at relatively long intervals, or, in dealing with penicillin-resistant strains of organisms and with gram-negative infections, to massive doses given often. For the comfort of the patient the smallest possible volume of injection is usually aimed at, but the implications of this procedure require consideration.

Commercial preparations of yellow sodium penicillin vary in potency from 1450 to 1000 units of penicillin per mg. of product. Since pure penicillin has a potency

CHRONIC NON-TUBERCULOUS ABSCESS AT SITE OF PENICILLIN INJECTIONS

J FIELDING
M R C.P , D P H
ASSISTANT PATHOLOGIST

AUDREY NORRIS
M A , M B Camb
CASUALTY REGISTRAR

PADDINGTON HOSPITAL, LONDON

THE development of tuberculous abscesses at the site of penicillin injections has been reported by Ebrill and Elek (1946), Boquien and Charbonel (1947), Forbes and Strange (1949), Hounslow (1946), Heidenach (1947), Marsh (1949), and Douglas (1950) The last named reported 9 cases

Ebrill and Elek (1946) state that " abscesses sterile on routine examination are not infrequent , but they are not always examined for tubercle bacilli " Inquiries have shown that sterile abscesses at the site of penicillin injections have been seen in many other hospitals

During the first six months of 1949 an unusually large number of abscesses in patients who had received penicillin was seen in the receiving ward of Paddington hospital Altogether 66 abscesses were seen in 28 patients between November, 1949, and February, 1950 Of those 28 patients, 21 had received penicillin as inpatients , and the remaining 7 as outpatients All the abscesses were sterile on routine examination

The following is a report of an investigation into the circumstances in which these abscesses developed

CLINICAL COURSE OF ABSCESS FORMATION

Of 21 adult patients 20 were female and 1 male , 7 were children under the age of twelve years, 4 being two years old or less

The presenting symptom was tenderness on pressure —e g , on sitting There was no spontaneous pain or local hyperæmia

The abscesses were palpable in the subcutaneous fat of the buttocks and thighs, at various depths down to the deep fascia, and varied in diameter from one to three inches No truly intramuscular abscess was seen No accompanying inguinal lymphadenitis was found

From cases of multiple abscesses, and from those in which there were one or more firm small palpable nodules, in addition to a fully formed abscess, it was possible to follow the development of these abscesses At first a non fluctuant nodule is palpable, which may resolve, and probably most of such nodules resolve without further trouble In cases which proceed to abscess formation the nodule slowly enlarges, becomes tender, gradually softens, and involves the skin In half the cases the abscesses discharged spontaneously

60% of the cases observed as fully formed abscesses developed from three to six months after the penicillin injections, but the interval has varied from one to thirteen months The commonest interval was five months

16 patients had more than one abscess, developing at different times, and one patient had as many as seven It is our impression that in patients who have received two courses of injections for different conditions abscesses have formed as a result of both courses, although it is difficult to be sure of this, owing to the multiplicity of injections at each course and the long period of development

Abscesses discharging spontaneously were usually treated with dry dressings only They healed slowly in one to six months, leaving a depressed scar Local heat and other physiotherapy had no apparent effect Incision of the abscess before spontaneous discharge did not alter this course of events, and secondary infection was common In 6 cases, in which the abscesses were aspirated without incision, resolution occurred within three months Up to 2 oz of light brown opaque fluid was removed from each abscess, varying in viscosity, but never as thick as frank pus Repeated aspiration was required in 2 cases

In a further 6 cases the abscess with its fibrous wall was excised , healing occurred by first intention in all but one, in which excision was probably incomplete and which became secondarily infected

DOSAGE AND COURSE OF PENICILLIN

Aqueous yellow sodium penicillin had been given in 63 cases, the number of injections per course varying from four to forty eight In 60 cases the dose per injection had been 200,000–300,000 units in 1 ml of distilled water , 3 patients had received 100,000 units in 1 ml per injection, and 3 had received procaine penicillin 300,000 units per injection No aqueous penicillin had been given in these cases

BACTERIOLOGICAL FINDINGS

Pus, removed after incision, by aspiration, or after excision of the abscess, from 20 abscesses in 15 patients, proved sterile, both aerobically and anaerobically, on routine examination In no case were tubercle bacilli demonstrated either directly or by culture on Löwenstein's medium, or, in 6 cases, by inoculation of guinea pigs A penicillin resistant *Staphylococcus aureus* was grown from fluid derived from a patient with several typical abscesses

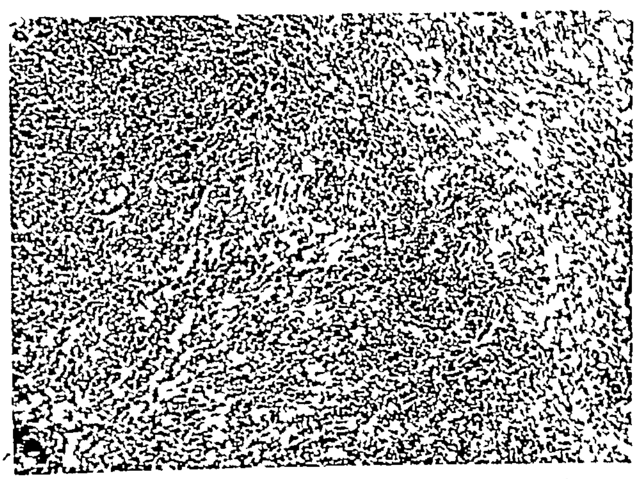


Fig 1—Abscess wall seven months after penicillin (× 70)

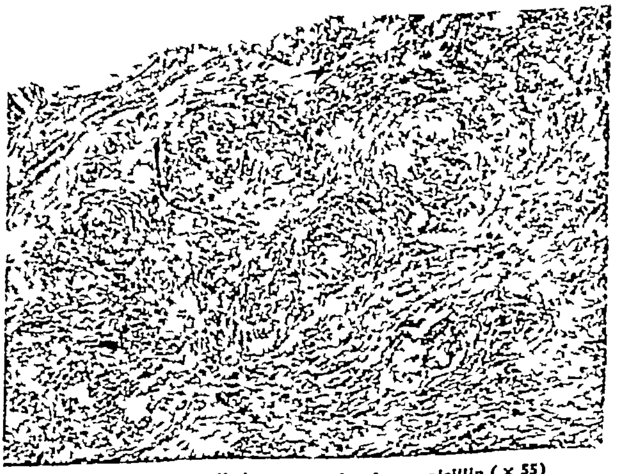


Fig 2—Abscess wall eleven months after penicillin (× 55)

Yaws

Yaws is predominantly a disease of the tropics and is distributed from Central Africa to Burma, Thailand, the East Indies, the Pacific Islands, and the West Indies There is some clinical and pathological evidence that it is distinct from syphilis, but Butler (1936) and Hudson (1946) put forward the view that it is syphilis operating in different circumstances on different soil.

Pinta

Pinta is found in Mexico, Central America, and the northern States of South America, where the number of cases has been estimated at half a million (Varela and Avila 1947) or a million or more (Holcomb 1942) It is caused by *T carateum* which, like *T pertenue* responsible for yaws, is indistinguishable morphologically from *T pallidum* Pinta differs from syphilis even more than yaws does, and perhaps most workers consider it to be a separate disease. Earlier hopes that the in-vitro immobilisation test developed by Nelson and Mayer (1949) may determine specific qualities in the responsible organisms have not yet been confirmed.

Other Examples

While yaws and pinta may have some justification to be considered as separate diseases from syphilis, there are others whose claims are less pressing Such are bejel, the extinct sibbens or button scurvy of Scotland, the radesyge of Norway, the extravenereal syphilis of Turkey (which may still be present in Turkey and possibly in Afghanistan), and the skerljevo of the Balkans, whose remnants may still be observed in Bosnia It is also likely that there are considerable islands of infection in the undeveloped areas of Africa.

In a survey of venereal diseases in Southern Rhodesia, I discovered one such nidus of extravenereal syphilitic infection whose local name is njovera (Willcox 1949) Subsequently I visited Iraq and compared this disease with bejel, which I saw not only in Baghdad but also in the rural Arab tribes of the Ramadi liwa in the Euphrates-Tigris wedge

NJOVERA

The Karanga people of the Fort Victoria and Ndanga districts of the southerly parts of Southern Rhodesia give the name "njovera" to an endemic disease indistinguishable from syphilis and usually contracted in childhood The same word is also used for the venereal syphilis of the towns, but the tribes appreciate that the juvenile disease is contracted in a different manner from the venereal form.

I saw njovera in the Ndanga district and in the satellite clinics east and south east of Fort Victoria in the Chibi and Matibi districts south of Fort Victoria, at Belingwe and Gwanda, both south of Bulawayo, and, under a different name, in the north-west of the country not far from Wankie, which is near to the Zambezi River and the Victoria Falls. Isolated examples of the same condition were observed in Salisbury and other parts, and there is no reason to assume that njovera is confined to the places mentioned but rather that with the development of the African it is tending to die out and assume the customary venereal pattern By hearsay it is also apparently prevalent in adjacent Bechuanaland (Willcox 1950)

Clinical Course

A *primary sore* is not often seen, but a "throwback" is occasionally observed, as in the north-west near Wankie, where a mother while nursing her 18-months-old baby, had a large sore on a nipple and enlarged hard non-tender axillary glands with typical secondary lesions In some clinics cracked nipples and breast abscesses were sometimes diagnosed as njovera by the African orderlies. This seems to indicate that "throwback" infection is sufficiently common for Africans to associate it with the usual form of njovera. Similar stories were told about bejel, which also rarely shows a primary sore, though Akrawi's (1949a) experiments on man indicated that, in experimental bejel at any rate, a definite primary lesion was usual, for it was obtained in 8 of 10 persons inoculated

Njovera is usually first seen in *the secondary stage* and affects the African children of rural areas Lesions are typically present within the mouth or on the lips, where there are mucous patches, and characteristic split papules or small ulcers may appear at the commissures (see figure), and be accompanied by enlargement of the cervical glands and laryngitis The external oral lesions are often confused with angular stomatitis and streptococcal fissures due to a deficiency of vitamins Exactly the same difficulties are encountered in Iraq, where the Arabs diagnosed as bejel an angular stomatitis which was regarded by physicians as due to vitamin deficiency.

Secondary lesions of njovera on lips.

The next most common secondary lesions are those of condylomata lata of the usual form on the vulva, where bilateral plaque-like lesions are not uncommon, and around the anus, groins, and armpits. From these lesions organisms indistinguishable from *T pallidum* may be obtained without difficulty The inguinal glands enlarge to a syphilitic pattern, and sore throat and osteocopic pains are not rare. Secondary lesions of the body are much less often seen, they are usually frambœsiform but diffuse and scanty The serum tests for syphilis are positive, and njovera responds to antisyphilitic drugs—e.g, penicillin, neoarsphenamine, and bismuth.

Of 50 persons questioned at Ndanga who admitted to past childhood infection, the lesions present were stated to be on lips and mouth 34, on genitalia and around anus 25, in armpits 13 on face and neck 3, on legs 5 on arms 1, and on the body 3, 1 person remembered having had laryngitis.

At a clinic near the Lundi River, some 70 miles south of Fort Victoria, where the accompanying photograph was taken, a series of children with identical oral and condylomatous lesions was encountered. These ranged from infants a few months old with mothers acknowledged to have had syphilis during pregnancy, through all the age levels to adults whose consorts had recently had syphilis There was no reason why the youngest should not have been suffering from early congenital syphilis, and the eldest from early acquired venereal syphilis, but those patients in the intervening age groups probably contracted the disease by other than sexual activity A boy, aged 7 years, with perianal condylomata, seen elsewhere, admitted to sexual interference, but it is thought that this is an unusual way to acquire njovera, and that usually dirt, flies, overcrowding, communal feeding and implements, and the fact that families sleep huddled together, are responsible for the transmission of the disease

Tertiary lesions may not always be associated with njovera by the patient, although the African may call gummata of the nose and soft palate njovera. Destruction of the nose, with a gangosa-like appearance, may occur of 1650 units per mg, it follows that yellow penicillin contains at present 120–400 mg of impurities per 1,000,000 units An injection of 250,000 units of yellow penicillin is thus accompanied by 30–100 mg of impurities This may be compared with the situation in the early days of penicillin therapy, when the potency of the product was 300–400 units per mg At that time a common dosage was 10,000 units three hourly, and each injection contained about 20 mg of impurities It is probable, too, that the high potency product of today (other than crystalline) contains impurities which have been selectively concentrated during the purification of penicillin

These impurities have not been the subject of many published studies, but they are far from being biologically inert It is well known that individual batches of yellow penicillin vary considerably in the degree of pain caused at the time of injection Ungar (1949) showed that, as measured by the cellular reaction on intraperitoneal injection in guineapigs, yellow penicillin was many times more irritant than crystalline penicillin Yellow penicillin may produce hæmorrhage and tissue necrosis on intramuscular injection in guineapigs and rabbits (Hamre et al 1943) In preliminary experiments one of us has shown that yellow penicillin, potency 1410 units per mg, is about five times more lethal to guineapigs than is the crystalline product 50,000 units intraperitoneally will kill a guineapig weighing 300 g in four to seven days with certain characteristic but inconstant intestinal lesions As little as 5000 units will kill some guineapigs

That there is a relation between tuberculous and non tuberculous abscesses at the site of penicillin injections is a possibility to be considered In the case of tuberculous abscesses the weight of evidence is in favour of exogenous infection introduced with the injected fluid, rather than hæmatogenous spread from a focus elsewhere Whichever of these is correct—possibly both happen at times—the local tissue damage caused by large doses of yellow penicillin may well be a major accessory factor in promoting the growth of a minute inoculum of tubercle bacilli

Schwabacher and Wilson (1937), investigating the minimum infective dose for the most susceptible of laboratory animals, the guineapig, found that an intramuscular inoculum of up to 100 living bacilli produced only very slowly developing disease, often with spontaneous resolution of the primary focus Ten living bacilli could not be relied on to produce disease on intramuscular injection

Kettle (1924) showed that in mice and rabbits given a tuberculous septicæmia the simultaneous subcutaneous injection of silica led to a tuberculous abscess of fixation at the site of injection, whereas some other irritants, although causing local inflammation, were indifferent in this respect

Both these observations, the one from the point of view of exogenous infection, the other from endogenous, suggest that an accessory factor is required for the successful implantation of a minute inoculum of tubercle bacilli We suggest that the irritant variably present in yellow penicillin may be such an accessory factor This would satisfactorily explain the absence of reports of tuberculous abscesses subsequent to other parenteral therapy

SUMMARY

67 chronic abscesses in 28 patients at the site of penicillin injections are reviewed

These abscesses had a characteristic clinical course and were not tuberculous

Their incidence varied with different batches of penicillin

The possible link between tuberculous and non tuberculous abscesses at the site of penicillin injection is discussed

We wish to thank Prof W D Newcomb for most helpful comments, Dr A Beck and Mr G M Gray for their coöperation, and Mr J Hunter for preparing the sections

REFERENCES

Boquien Y Charbonnel A (1947) *Bull Soc méd. Hôp Paris*, 63, 153
Douglas D M (1950) *Lancet*, i 92
Ebrill, D, Elek S D (1946) *Ibid*, ii 379
Forbes, G B, Strange, F G St C (1949) *Ibid*, i, 478
Hamre D M, Rake G, McKee C M., MacPhillamy, H B (1943) *Amer J med Sci* 206, 642
Heidenach, J C R (1947) *Proc R Soc Med.* 40 161
Hounslow A G (1946) *Lancet*, ii 617
Kettle, E H (1924) *Brit J exp Path* 5, 158
Marsh F (1949) *Lancet* i 800
Schwabacher H, Wilson G S (1937) *Tubercle*, 18, 442
Ungar J (1949) *Brit med J* i 654

NJOVERA AN ENDEMIC SYPHILIS OF SOUTHERN RHODESIA

COMPARISON WITH BEJEL

R R WILLCOX
M.D Lond

PHYSICIAN IN CHARGE OF VENEREAL DISEASES DEPARTMENT, KING EDWARD VII HOSPITAL, WINDSOR, CONSULTANT VENEREOLOGIST, ST MARY'S HOSPITAL, LONDON

> "That syphilis and sex are indissolubly linked is only half of the story The other half is that the same disease under other names runs riot through great regions of the earth as a childhood disease without reference to sex"—ELLIS H HUDSON

The problem of syphilitic or parasyphilitic extra venereal diseases caused by organisms morphologically indistinguishable from that of syphilis is world wide The question whether these diseases are syphilis or conditions similar to syphilis has engaged the minds of clinicians and pathologists for as long as the diseases have been recognised

EXTRAVENEREAL DISEASES

Bejel

The disease bejel, affecting the Arabs of the Euphrates and Tigris valleys and adjoining regions of Iraq and Syria, was first described by Hudson (1928) It is caused by an organism indistinguishable from the *Treponema pallidum* of syphilis, has a similar clinical pattern, is associated with parallel serological changes, and responds to antisyphilitic drugs

The clinical course is briefly as follows (Hudson 1946)

> "At some time in early life the Bedhouin child contracts bejel from some other child in the acute stage of the disease The spirochæte is usually passed from host to host by immediate, non sexual contact, and the transfer is favoured by general uncleanliness, total lack of segregation, and the succulence of mucocutaneous lesions Possible auxiliary factors in contagion are the use of the common drinking bowl, the habit of kissing and fondling children and the presence of the domestic fly, the louse, and the flea Lesions often first appear in the mouth but are followed by moist papules in the folds of the skin and by drier lesions on the trunk and extremities Treponemes are easily demonstrable in great numbers in all of these lesions A roseolar eruption has been observed but is rare Late lesions consist of ulceration of the palatal and nasal bones which involve pharynx and often larynx, gummata of the skin, and subcutaneous tissues producing huge ulcers and cicatrices, osteoperiostitis, particularly of the long bones with the *formation of sabre shins*, adenopathy, juxta articular nodules, hyperpigmentation, depigmentation, hyperkeratosis and alopecia An adult who has escaped bejel in childhood is likely to contract it later from a child, often his own The course of the disease in the adult does not differ essentially from that of the child "

The primary stage of the disease is seldom seen

TREATMENT OF PROLAPSED CORD

L Woodrow Cox

M B N Z, F R C S, M R C O G

OBSTETRICIAN AND GYNÆCOLOGIST, WALTON HOSPITAL, LIVERPOOL, EXTERN REGISTRAR, LIVERPOOL MATERNITY HOSPITAL

Prolapse and presentation of the umbilical cord are rare complications of labour, the incidence being 145 cases in 26,739 labours (0·54%) in twelve years in the Liverpool Maternity Hospital Since it is uncommon, and since some of the cases are seen only after cord pulsations have ceased and the fœtus is dead, obstetricians tend to regard the treatment as theoretical rather than practical

Perusal of many hospital reports shows that the fœtal mortality is commonly about 50% However, on examining the records of this hospital in recent years, I found a smaller mortality than this It seemed that by more active treatment more infants could be saved In the early weeks of my term of office at the hospital three cases were treated actively, by version, but without immediate delivery Two of the infants died It seemed possible that if these had been delivered immediately they would have survived It was therefore suggested that an attempt should be made to obtain a series of 20 or 30 cases without loss of the fœtus To do so meant that the whole team—obstetrician, residents, nurses, and theatre staff, not forgetting the ambulance and the domiciliary services—should be highly efficient

Since some cases of prolapsed cord reach hospital with the fœtus already dead, it is important that any statistical inquiry should pay most attention to those cases where there is an opportunity for treatment As an essential part of the treatment of prolapsed cord is early diagnosis, statistics should be presented with cases divided into the following groups

(1) *Cord not pulsating on admission to hospital*

(2) Cord not pulsating on discovery of prolapse (fœtus alive on admission)

(3) Cord pulsating, discovered at or near full dilatation of the cervix

(4) Cord pulsating, discovered before full dilatation of the cervix

Group 1 is of interest in so far as it is a measure of the awareness of the domiciliary attendants and of the intelligence of the patient

A member of the consultant staff was called on a domiciliary visit to a case of prolapsed cord He arrived at a house to find that the attendant had been sitting for two hours watching a pulsating cord prolapsed outside the vulva and had only called for help when the pulsations ceased *

A multigravida with a bicornute uterus the fœtal presentation being unstable in the latter weeks of pregnancy, had been warned that at the first sign of the onset of labour she must enter hospital She arrived after having had strong uterine contractions for three hours, with the cervix fully dilated, and the cord prolapsed, not pulsating

Group 2 is an index of the efficiency of the hospital attendants If heed is paid to the first signs of fœtal distress, and if vaginal examinations are made always on rupture of the membranes, it is unlikely that a case will be missed

A labour ward sister, routinely checking a fœtal heart, noticed a slight irregularity A vaginal examination had been made previously when the membranes had ruptured However, as the presenting part (a vertex) remain unfixed, the sister repeated the vaginal examination and found the cord prolapsed through a cervix dilated to admit only three fingers By the time the house surgeon arrived in the labour ward (a run up one flight of stairs), she was busy setting the operating theatre

Group 3 indicates the operative dexterity of the attendant The discovery of a prolapsed cord at full dilatation may lead him to call for forceps for a hurried delivery But it is no gain if, in extracting the child rapidly to save it, he causes a cerebral trauma and loses it

A multigravida was admitted with a pulsating prolapsed cord The cervix was fully dilated, but the head was not ready for delivery A forceps extraction was quickly performed, but the child was dead Necropsy revealed a tentorial tear *

Group 4—*Around each case in group 4 there can be a* discussion on the method of treatment, and it is to contribute to this discussion that this paper is presented.

After a study of the records of this and other hospitals, the thesis is proposed that delay is dangerous, and that the best plan for saving the fœtus is to deliver the child as soon as the diagnosis has been made From the summary of cases presented below it is seen that only 4 cases were not treated by immediate delivery

(1) A *syphilitic patient with mild toxæmia had labour* induced by rupturing the bag of forewaters The cord was felt beside the head Further examination showed a placenta prævia type I As the patient very badly wanted a living child (having had a macerated fœtus previously), although the chance of a healthy infant was poor, bipolar version was done and a leg was brought down Spontaneous delivery of a living but severely asphyxiated child took place an hour and a half later The child, after a stormy neonatal period, survived

(2) A multigravida, in whom cord prolapse had been detected when the cervix was three fingers dilated, was treated by internal version, and a leg was brought down. The fœtal heart remained regular When the cervix was nearly fully dilated fœtal distress came on and the child was extracted dead

(3) A similar case, where the cervix was four fingers dilated, was treated by internal version and breech extraction The delay in extraction was not much over half an hour from the time of discovery The child was dead.

(4) In a multigravida, having labour induced at term for toxæmia a loop of cord was found beside the head Only a small hole had been made in the bag of forewaters, so as much liquor as possible was drained away, and the cord was pushed up above the parietal eminence inside the membranes Uterine contractions had already started It was decided to await events Normal delivery of a living child took place two hours later

The remaining cases were treated by immediate delivery by whatever method seemed safe In some cases the membranes ruptured and the cord prolapsed at full dilatation of the cervix Delivery was sometimes normal, sometimes with forceps if a cephalic presentation, or by extraction of a breech Sometimes the cervix was incompletely dilated but seemed soft and stretched under anæsthesia, hence, by the time internal version had been done full dilatation was achieved and a breech extraction completed the operation If, however, the cervix was not soft, then without hesitation cæsarean section was performed Every child survived

It is to be expected that this radical treatment may receive adverse criticism because of the increased risk

---

* These cases did not occur in 1948 or 1949

DR WILLCOX REFERENCES

Akrawi F (1949a) *Brit J vener Dis* 25 115
— (1949b) Personal communication
Butler C S (1936) Syphilis Sive Morbus Humanus Lancaster, Pa.
Chambers H D (1938) Yaws (Frambœsia tropica) London
Hermans, E H (1931) Framboesia Tropica
Holcomb, R C (1942) *Nav med Bull Wash* 40 517
Hudson E H (1928) *Ibid* 26 817
— (1946) Treponematosis London p 98
Nelson R A jun. Mayer M M (1949) *J exp Med* 89 369
Varela G Avila, C (1947) *Amer J trop Med* 27 663
Willcox R R (1946) *Brit J vener Dis* 22 63
— (1949) A Venereal Diseases Survey of the African in Southern Rhodesia South Rhodesian Government.
— (1950) Textbook of Venereal Diseases London

(complete destruction was noted in a girl aged 6 years), as may gummata of the skin or the skull, or their scars, periostitis, plantar lesions, and ganglion formation. Two cases of juxta-articular nodes were observed in elderly patients.

The examples of late bejel demonstrated to me in Iraq included gummata of the soft palate and nasal septum, gangosa-like lesions in the adult, and osteoperiostitis with sabre tibiæ in the child. In both the bejel and njovera cases seen it was impossible to say that these late lesions were not syphilitic.

I have purposely omitted any expression of opinion about the possibility of involvement of the cardiovascular and nervous systems. Syphilis of both of these systems was encountered in Southern Rhodesia, but in both Rhodesia and Iraq venereal syphilis is rife in the towns, and the matter requires further elucidation, as does the question of transplacental transmission.

Incidence

There seemed to be both clinical and pathological evidence in the areas visited that the incidence of childhood njovera was on the decline. This is almost certainly due to the treatment facilities offered by the government clinics and reinforced in part by the policy adopted by one physician, which he has pursued for many years, in giving antisyphilitic drugs to all the patients admitted to his clinics.

Of 1620 adults 293 (18·1%) had had njovera in childhood and 143 (8·8%) after they had grown up. In the latter the disease may have been venereal syphilis; but, even so, it gives a total admitted previous treponematosis rate of 26·9%. It was very noticeable, when questioning these patients in 14 rural clinics, that elderly persons nearly always spoke of having had njovera, whereas the young men and women stated far less often that they had had it.

Serological surveys are biased by the possibility of yaws, the presence of malaria, and the difficulties attendant on the use of the Kahn test, which was the one generally used under truly "field" conditions. A previous history of njovera, however, even in the absence of clinical signs, predisposes to a positive serum test for syphilis. Thus Kahn tests performed on 156 persons known to have had njovera showed 40 positives (25·6%) and 14 doubtfuls, whereas of 617 persons who gave no history of njovera only 54 (8·7%) were positive and there were 36 doubtfuls.

Of serological samplings undertaken during the survey in the njovera area about 13·2% of positives were obtained in 1527 patients tested in nine rural clinics (patients with venereal disease included). If the venereal cases are omitted, the figure was 10·2%. These nine clinics were those where mass antisyphilitic treatment had been given through the years. In rural areas outside this group 1301 patients, excluding those with venereal disease, were tested in eight clinics and gave 20·3% of positives. At two of the institutions in the njovera area there were 40·0% and 49·5% positive tests in 75 and 103 patients respectively.

Other figures obtained from a Swedish mission in the njovera area south of Belingwe claimed 75·6% positive of 2140 tested at an outlying clinic in a year, while at the mission hospital in the same year there had been 39·4% positive of 4147 tested. The base hospital figure has shown a steady annual decline, having been above that of the outlying clinic in 1929—further evidence of the decreasing incidence.

Serological surveys of children in schools adjacent to the clinics where antisyphilitic drugs had been more freely dispensed than is usual gave only 1·9% positive in 360 tested, but 6·3% positive were found in 349 school children serum-tested in rural areas outside this region. All these schools, however, are situated reasonably near government clinics, and, not only as a result of the facilities offered but also because of increasing civilisation, the chance of children and their parents contracting an extravenereal infection is smaller than in former times.

DISCUSSION

Njovera is believed by some to be yaws; indeed it was in search of yaws, which had been reported as being present, that the njovera was encountered. I have seen yaws in West Africa and have compared it with syphilis (Willcox 1946). In the secondary lesions (other than condylomata), which are much less frequent in njovera and much less florid than in yaws; in the general absence of primary lesions in njovera; and in the oral manifestations which are so well marked in njovera and are said by some to be slight or even absent in yaws (Chambers 1938, Hermans 1931), the Rhodesian njovera does not closely resemble the West African yaws.

On the other hand, yaws has been said to be present not only in Southern Rhodesia but also in neighbouring Portuguese territories. Gangosa was encountered in patients from both, and goundou, although not seen by me, was reported as rarely observed. Two cases of juxta-articular nodes were, however, noted, as was one lesion resembling a primary yaw seen on the chin of an elderly lady at Belingwe.

Both diseases may therefore possibly coexist; or if Hudson's (1946) theory of treponematosis is accepted and yaws and syphilis are really the same disease modified by racial, climatic, and sociological conditions, and primitive yaws becomes venereal syphilis as the only hope of survival for the treponeme, with intermediate forms still present as bejel, then we may have here examples of the transition in progress.

Hudson (1946) considers bejel as a manifestation of treponematosis caused by *T. pallidum*, and Akrawi (1949a) believes it to be syphilis; but these viewpoints are not necessarily contradictory. I think that njovera is syphilis and probably identical with bejel. Both njovera and bejel are primarily diseases of children, and in both of them the primary stage is usually absent and "throw-backs" occasionally present; and in both of them the secondary stage is identical, with genital and anogenital condylomata, mucous patches in the mouth and on the lips, and split papules or ulceration at the commissures of the lips. In both diseases other secondary lesions on the body are less frequent. The later manifestations of bejel seen included gummata of bone and soft tissue, osteoperiostitis, gummata of the soft palate and nasal septum, and gangosa-like lesions. These, if much more numerous in the bejel area, are of the same general pattern as encountered with njovera. Juxta-articular nodes in bejel have been reported by Hudson but have not been seen by Akrawi (1949b). They were but rarely seen in Southern Rhodesia by me.

SUMMARY

Njovera, an extravenereal syphilis encountered in certain parts of Southern Rhodesia, is described. As a result of government treatment facilities and improving social conditions, its incidence is believed to be declining.

A comparison of njovera with bejel in Iraq shows that they are similar if not identical. It is believed that both conditions are in fact syphilis.

The investigation in Southern Rhodesia was part of a larger survey undertaken for the Government of that country. I am indebted to Dr. R. M. Morris, the Secretary for Health, and to many doctors there, especially Dr. J. H. Kennedy, of Ndanga, for their many kindnesses and help. The serological tests were done by Mr. E. A. Boulter. The work in Iraq was part of a mission performed for the World Health Organisation, and special thanks are given to the Ministry of Social Affairs of Iraq and to Prof. F. Akrawi, of Baghdad.

References at foot of next column

A CASE OF TRUE HERMAPHRODITISM

A W CAPON
M.A., M.B Camb., M R C.P
LATE MEDICAL REGISTRAR, MILE END HOSPITAL, LONDON

TRUE hermaphroditism is rare, only 40 authenticated cases having been published. According to Hinman (1935) it may be of three types

- A. Bilateral, with ovary and testis on both sides, either separate or united (ovotestis)
- B. Unilateral, with testis and ovary, separate or united, on one side, and an ovary or testis on the other
- C. Lateral or alternating, with a testis on one side and an ovary on the other

Of the 40 published cases 11 were bilateral, 14 unilateral (7 with an ovary, and 7 with a testis, on the opposite side from an ovotestis), 11 were lateral, and 4 had an ovotestis on one side, the other gonad remaining unidentified (Weed et al 1947). In the case reported here the right gonad was an ovotestis and the left an ovary.

CASE RECORD

The patient, aged 29, reported to the outpatient department complaining of lassitude and palpitation, symptoms which proved to be due to a mild anxiety state. Preliminary examination showed female bodily configuration and mal-developed genitalia.

History.—He was brought up as a boy. At the age of 8 he became aware of the defective development of his external genitalia, and from that age onwards he strove to prevent the defect from becoming known. He does not remember the matter being discussed at home at any time. At school he was keen on games, and was captain of the school football team, but he gave up football and swimming at the age of 15 owing to the development of his breasts. His voice altered somewhat at this age, becoming deeper, but it did not develop a normal masculine pitch. At 11 he won a scholarship to a secondary school, and he was preparing for a career as an architect, but he had to leave school at 15 owing to financial difficulties. He then started work as a plasterer, and he has continued with this occupation, though he has changed his job on many occasions because he becomes unsettled if he stays in one place for long.

His interests have always been heterosexual, and he married at the age of 26. His marriage is regarded by him as satisfactory, and intercourse is practised two or three times a month.

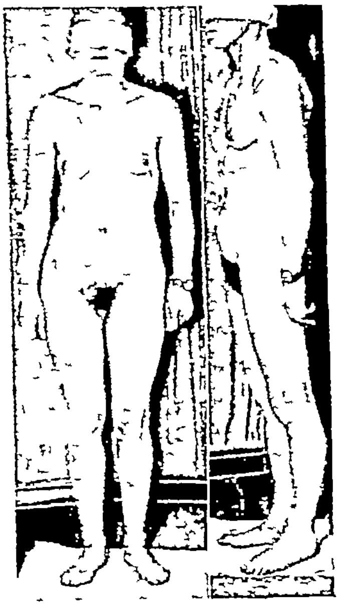


Fig. 1—Hermaphroditism, showing female bodily configuration and ill-developed genitalia.

Owing to the position of his urethra, he has always voided his urine standing up. About three years ago he noticed a slight bloodstained discharge from the urethral orifice, and this was repeated at irregular intervals. The bleeding later became more regular, with a cycle of about 28 days, and lasting 3 or 4 days. Rarely was the bleeding sufficient to appear externally, most of the discharge being passed at the time of micturition. No associated symptoms occurred at these times.

Genital and axillary hair started to grow at the age of 16, but he has rarely had to shave the soft hair which appeared somewhat later on his face. There is no history of genital defects in other members of his family.

On examination the patient was found to have a female type of body, with well-developed breasts (fig 1) containing palpable glandular tissue. His skin was smooth, and he looked younger than his age. There was a little soft hair in the beard area. The axillary hair was scanty, and the pubic hair was of female distribution. His height was 5 ft 4½ in., weight 135 lb, span 5 ft 6 in., length of upper limb 24 in., length of lower limb 37 in., and he measured 34½ in round the chest, 27½ in. round the waist, and 37 in round the hips. Muscular development was within normal limits for a man. A right incomplete indirect inguinal hernia was present. Physical examination revealed no other defects apart from those mentioned above, and those of the genitalia.

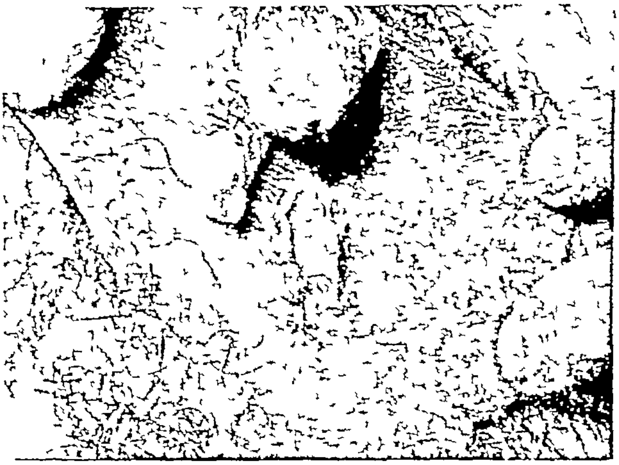


Fig 2—Hermaphroditism showing short penis and urogenital sinus leading to female genitalia.

Under general anæsthesia it was found that the labioscrotal folds met anteriorly over the root of the "penis," which was about 2 in long. No gonads were palpable in the labioscrotal folds. The glans projected beyond the folds and exhibited a small depression in the normal site of the opening of the male urethra. The glans was uncovered, the prepuce being represented by a loose fringe of skin attached all round behind a well marked corona. A tag of skin hung down from the prepuce on the right side. Rudimentary

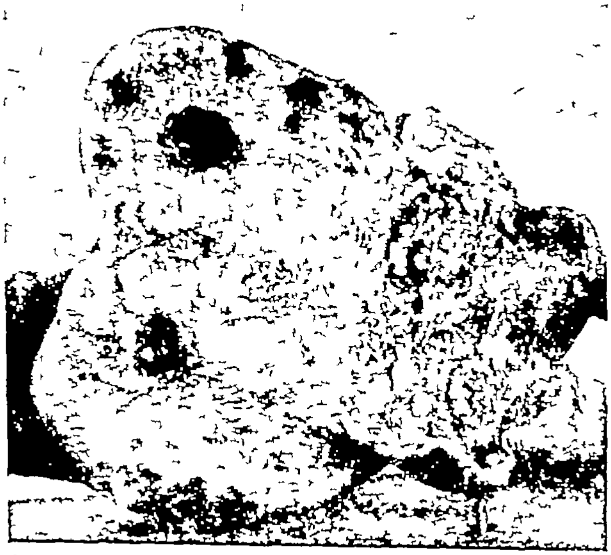


Fig 3—Right gonad, cut across. To the right of the photograph is the spherical (proximal) part, consisting of soft, velvety pale red yellow tissue. To the left is the ovoid (distal) part consisting of firmer yellow-grey tissue with some mauve mottling and containing some small cysts filled with blood clot. The two parts are separated by a narrow indefinite white zone.

of operating on a hurriedly prepared patient With modern facilities this risk should not be great Surgical instruments in most hospitals are kept sterilised ready for use Anæsthesia, when intravenous agents are used, atropine, curare, and 'Kemithal' (thialbarbitone), with intratracheal tubes and aspirators in readiness, is not the hazard of yesteryear

RESULTS

The following is a summary of the results in the period from Jan 1, 1948, to Dec 31, 1949

Number of cases	35
Infants born	39

In 4 sets of twins one infant of each set had a prolapsed cord the presentation of the remaining infant was normal and no mishap occurred in the delivery of this infant

Infants stillborn (cord pulsating on admission)	2 (5 7%)
Infants stillborn (cord not pulsating on admission)	2 (5 7%)
Neonatal deaths	0
Gross fœtal mortality	4 (*11 4%*)

Group 1 (cord not pulsating on admission to hospital) 2 cases

Stillbirths	2

Group 2 (cord not pulsating on diagnosis) 0 cases

Group 3 (cord pulsating discovered at or near full dilatation of cervix) 12 cases

Normal delivery	3
Forceps delivery	2
Breech extraction	7
Stillbirths	0

Group 4 (cord pulsating discovered before full dilatation of the cervix) 21 cases

Immediate delivery	
Cæsarean section	13
Internal version and breech extraction	4
Stillbirths	0
Delayed delivery	
Internal version and breech extraction	3
Normal delivery	1
Stillbirths	2

ILLUSTRATIVE CASES

Typical cases are the following

Case 1—A breathless urchin arrived at the hospital with a note from the district midwife that a cord had just prolapsed The house was barely a stone's throw distant While the telephonist was calling the ambulance, two house surgeons ran to the house, prepared to effect delivery immediately if conditions were suitable At the same time the operating theatre was prepared both for cæsarean section and for vaginal delivery

The patient, a multigravida, was in labour The cord was found to be pulsating strongly, but the cervix was only about four fingers dilated In a minute or two the ambulance arrived, and the patient was moved to hospital There, atropine was given intravenously, and after the usual preparations an anæsthetic was administered During internal version the cervix was dilated completely, and a living child was extracted as a breech

Case 2—A doctor telephoned to say that he had a patient in a nursing home whose waters had just broken, and the cord was prolapsed The ambulance was immediately dispatched, and preparations were made for vaginal delivery or for cæsarean section On arrival, the patient was taken directly into the operating theatre, where the pulsating cord was found to be prolapsed through a cervix dilated to admit two fingers Anæsthesia was induced with curare and thialbarbitone, and cæsarean section was done A living child was delivered

Case 3—A patient in the antenatal ward awaiting a repeat cæsarean section complained of backache It was thought that labour might be starting and a vaginal examination was made The cervix had begun to dilate, and in the intact bag of forewaters the cord was presenting Within an hour cæsarean section had been completed and a living child delivered

To save so many of these children the conditions of work must be satisfactory As nearly as possible all unnecessary risk is eliminated in this hospital The facilities for immediate vaginal or abdominal operations are always ready An expert anæsthetist is available at a moment's notice There is always in the building an obstetrician capable of taking the responsibility for, and trained to do, any operation No mishap has occurred with any mother in this series, and the puerperia have been normal

ÆTIOLOGY

Twins—Prolapse of the cord of the first twin occurred thrice, and of the second twin once

Breech Presentation—Prolapse of the cord occurred six times in cases of breech presentation In five of these the cervix was fully or almost fully dilated, and a breech extraction was done

Transverse Lie and Compound Presentations—In these cases prolapsed cord occurred four times, three times the cervix permitted vaginal delivery In addition there was one case with a bicornuate uterus where the lie was longitudinal on admission

Disproportion was associated with three cases, and cæsarean section was performed

Surgical induction of labour was followed by prolapse of the cord in six cases two were for toxæmia, two for expected erythroblastosis, and two for breech presentation (already mentioned) to avoid postmaturity Two cases were treated by cæsarean section

Cases Otherwise Regarded as Normal—Four occurred when the cervix was fully dilated, and nine when the cervix was incompletely dilated

DISCUSSION

The argument here proposed, that the child can be saved in almost every case, is applicable only to urban communities with a highly efficient hospital service Other methods, with different results, must perforce prevail in less densely populated countries In those circumstances any measure that yields a fœtal mortality of less than 100% can be said to have its place

The greater share of praise for the success gained in this series is due to the nurses and to the ambulance service for their speed in performing their tasks Only a modicum need be offered to the operators concerned in the deliveries, and that not for speed, but for forbearance from haste, so that the infants were extracted with all due care, still living It is fitting to record that, once "immediate delivery" became the practice, no infant was lost in an unbroken series of nearly 30 cases

SUMMARY

35 cases of prolapse or presentation of the cord are reviewed

The fœtus was lifeless on admission in 2 cases 5 7%

No infant was lost when delivery was performed immediately

The gross fœtal mortality was 11 4%

My thanks are due to the visiting medical staff of the Liverpool Maternity Hospital for permission to treat many of these cases and to record the results Four cases were in private patients, and were treated by the four consultants concerned

> " During my student days I had the good fortune to be taught by a physician who had a clear appreciation of the 'functional aspects of disease' A patient, say John Smith, had been allotted to me as a clinical clerk Both the history and physical examination indicated that he had lobar pneumonia, and therefore when asked by the clinician what the patient was suffering from, I confidently replied that he had pneumonia To my surprise the answer was 'No, John Smith has not got pneumonia, but pneumonia has John Smith The physician then proceeded to explain that, although John Smith did in fact have pneumonia, there were many other factors concerning him which might be of equal or even greater importance "—Dr LESLIE HURLEY, *Med J Aust* Feb 17 1951, p 254

A CASE OF TRUE HERMAPHRODITISM

A W CAPON
M.A., M.B Camb, M.R C.P
LATE MEDICAL REGISTRAR, MILE END HOSPITAL, LONDON

TRUE hermaphroditism is rare, only 40 authenticated cases having been published. According to Hinman (1935) it may be of three types

A. Bilateral, with ovary and testis on both sides, either separate or united (ovotestis)

B Unilateral, with testis and ovary, separate or united, on one side, and an ovary or testis on the other

C Lateral or alternating, with a testis on one side and an ovary on the other

Of the 40 published cases 11 were bilateral, 14 unilateral (7 with an ovary, and 7 with a testis, on the opposite side from an ovotestis), 11 were lateral and 4 had an ovotestis on one side, the other gonad remaining unidentified (Weed et al 1947) In the case reported here the right gonad was an ovotestis and the left an ovary

CASE RECORD

The patient, aged 29, reported to the outpatient department complaining of lassitude and palpitation, symptoms which proved to be due to a mild anxiety state Preliminary examination showed female bodily configuration and maldeveloped genitalia

History—He was brought up as a boy At the age of 8 he became aware of the defective development of his external genitalia and from that age onwards he strove to prevent the defect from becoming known. He does not remember the matter being discussed at home at any time At school he was keen on games, and was captain of the school football team, but he gave up football and swimming at the age of 15 owing to the development of his breasts His voice altered somewhat at this age, becoming deeper, but it did not develop a normal masculine pitch. At 11 he won a scholarship to a secondary school, and he was preparing for a career as an architect, but he had to leave school at 15 owing to financial difficulties. He then started work as a plasterer and he has continued with this occupation, though he has changed his job on many occasions because he becomes unsettled if he stays in one place for long

His interests have always been heterosexual, and he married at the age of 26 His marriage is regarded by him as satisfactory, and intercourse is practised two or three times a month.

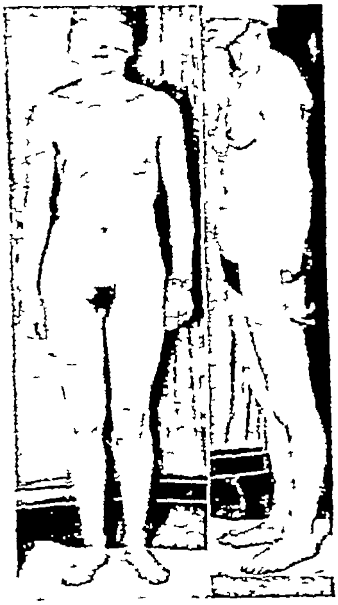


Fig. 1—Hermaphroditism showing female bodily configuration and ill-developed genitalia.

Owing to the position of his urethra, he has always voided his urine standing up About three years ago he noticed a slight bloodstained discharge from the urethral orifice, and this was repeated at irregular intervals The bleeding later became more regular with a cycle of about 28 days, and lasting 3 or 4 days Rarely was the bleeding sufficient to appear externally, most of the discharge being passed at the time of micturition. No associated symptoms occurred at these times.

Genital and axillary hair started to grow at the age of 16, but he has rarely had to shave the soft hair which appeared somewhat later on his face There is no history of genital defects in other members of his family

On examination the patient was found to have a female type of body, with well-developed breasts (fig 1) containing palpable glandular tissue His skin was smooth, and he looked younger than his age There was a little soft hair in the beard area The axillary hair was scanty, and the pubic hair was of female distribution His height was 5 ft 4½ in., weight 135 lb, span 5 ft 6 in., length of upper limb 24 in., length of lower limb 37 in., and he measured 34½ in round the chest, 27½ in. round the waist, and 37 in. round the hips. Muscular development was within normal limits for a man A right incomplete indirect inguinal hernia was present Physical examination revealed no other defects apart from those mentioned above, and those of the genitalia

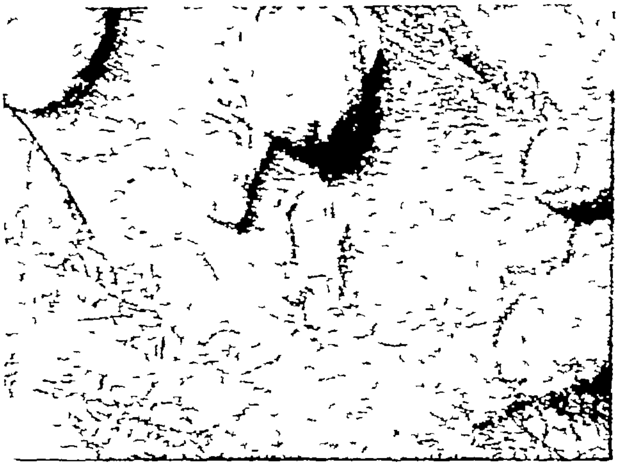


Fig 2—Hermaphroditism showing short "penis" and urogenital sinus leading to female genitalia.

Under general anæsthesia it was found that the labioscrotal folds met anteriorly over the root of the "penis" which was about 2 in. long No gonads were palpable in the labioscrotal folds The glans projected beyond the folds and exhibited a small depression in the normal site of the opening of the male urethra The glans was uncovered, the prepuce being represented by a loose fringe of skin attached all round behind a well marked corona A tag of skin hung down from the prepuce on the right side Rudimentary

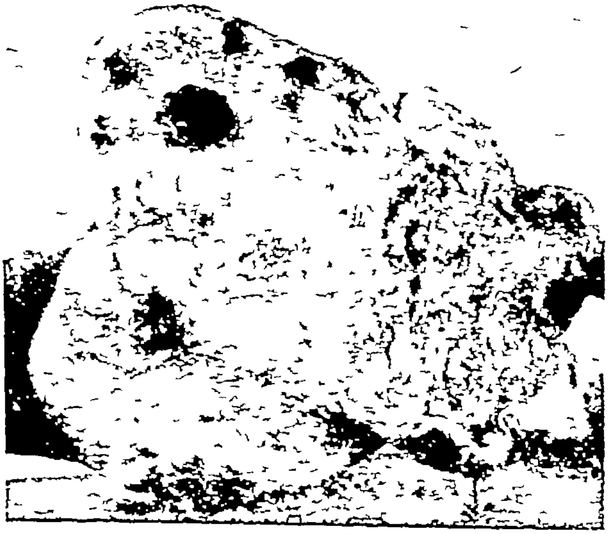


Fig 3—Right gonad, cut across. To the right of the photograph is the spherical (proximal) part, consisting of soft, velvety pale red-yellow tissue. To the left is the ovoid (distal) part, consisting of firmer yellow-grey tissue with some mauve mottling and containing some small cysts filled with blood clot. The two parts are separated by a narrow indefinite white zone.

labia minora were present, and between them posteriorly was a circular orifice $^1/_4$ in in diameter (fig 2) which opened into a cavity which was regarded as a persistent urogenital sinus A urethral orifice was observed at a depth of $^1/_2$ in from the surface Posterior to this was the vaginal opening, this being slightly constricted by a muscular ring which gripped the little finger The vaginal cavity was 4 in long and extended upwards and backwards In the vaginal vault was a small cervix with a patulous os and larger posterior, and smaller anterior, lips

Cytoscopy revealed no abnormality Iodised oil run into the vagina passed into the uterus and fallopian tubes, and radiography gave the impression of a bifid uterus, but this study was inconclusive During cytoscopy the "penis" became erect, and it was seen that erection was limited by a tight frenum Rectal examination had previously demonstrated the presence of a small uterus and cervix

Operation (Mr S Willson Holmes, F R C S)—As the patient was reluctant to submit to any major operation, he was advised to have a plastic operation on the "penis" and a repair of the right inguinal hernia At this time the diagnosis was one of ovarian pseudo male hermaphroditism Through a right inguinal incision the sac of the hernia was exposed and opened after division of the deep epigastric vessels It was not considered justifiable to damage the conjoined tendon, and examination of the pelvic contents was incomplete It was impossible to ascertain the nature of the gonad on the left side A small uterus with supravaginal cervix was palpable, the whole structure being 2 in long and 1 in broad The uterus was median and single, and the arrangement of the pelvic peritoneum was like that found in a normal female The right fallopian tube was 6 cm long and normally fimbriated, and showed the normal relationship to a gonad The right gonad, $^1/_2$ in of broad ligament with the fallopian tube and the hernial sac were removed, and the hernia was repaired The right gonad (fig 3) consisted of a spherical part 1 2 cm in diameter united to an ovoid part (2 4 × 1 7 cm) At operation there was no evidence of any intrapelvic elements of the male genital tract

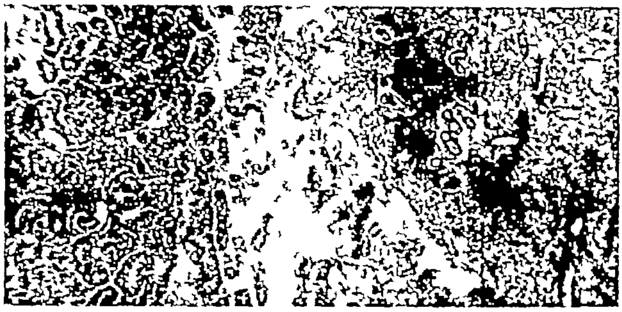


Fig 4—Ovotestis, showing both ovarian and testicular tissue (× 20)

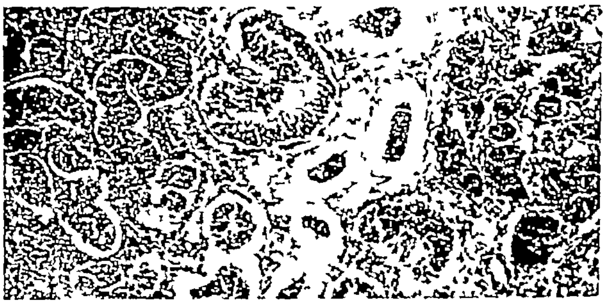


Fig 5—Ovotestis showing testicular tissue (× 100)

Histology (figs 4–7)—The spherical part of the right gonad consisted of seminiferous tubules, some well formed but mostly showing various degrees of atrophy, with replacement by hyaline tissue Islets of well defined testicular interstitial cells were present The ovoid part of the gonad was typically ovarian and showed a well formed graafian follicle with ovum, corpora albicantia, a corpus luteum undergoing change to a corpus albicans, small cystic follicles, and numerous primordial ova The specimen was therefore an ovotestis

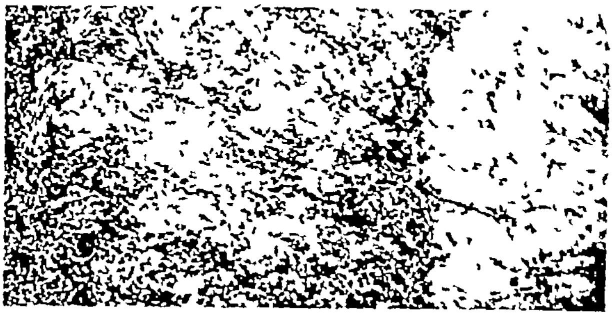


Fig 6—Ovotestis, showing ovarian tissue with a corpus luteum undergoing change to a corpus albicans (× 100)

Investigations—Radiography of the chest showed no abnormality, but radiography of the pelvis showed a partial spina bifida of the first sacral vertebra, a small sacrum, and a wide pelvis of gynæcoid type The urine contained no abnormal constituents, sp gr 1 024 A blood count showed red cells 4,440,000 per c mm, Hb 74%, colour index 0·84, and white cells 9800 per c mm (neutrophils 62%, eosinophils 3%, basophils 1%, lymphocytes 28%, monocytes 6%)

Progress—Menstrual bleeding occurred after operation and lasted six days In view of this, and the removal of testicular tissue at operation, it was decided to institute androgen therapy The patient was given injections thrice weekly of testosterone propionate 25 mg, and this treatment was continued for three months, after which an implant of 1 g was made Six months later the patient had gained 8 lb in weight, and he needed to shave once a week instead of very occasionally Menstruation was much reduced but not completely inhibited, and a year after the initial investigation more radical surgical treatment was advised and accepted

Second Operation—Mr S Willson Holmes did a total hysterectomy and left salpingoöphorectomy The uterus was slightly smaller than in the normal adult female, and the fallopian tube and ovary were grossly normal, section of the ovary showing several small cysts Microscopical examination of the uterus showed normal endometrium in the proliferative non secretory phase, and the ovarian tissue was also normal there being no evidence of testicular tissue

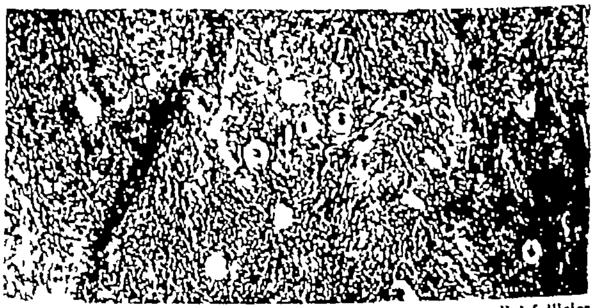


Fig 7—Ovotestis, showing ovarian tissue with primordial follicles (× 100)

COMMENTS

The general appearance and genital development in this patient are predominantly female, but the psychological outlook is male This is in accordance with the observation made by McKenna and Kiefer (1944) that in most cases of true hermaphroditism the libido and emotions depend on the person's upbringing Investigation at any early age would have disclosed the predominantly feminine sexual characteristics, and surgery could have removed the "penis" and constructed a normal opening of the vagina

In all cases the sociological background must be considered before undertaking treatment In this case the patient, aged 29, was the male partner of a marriage, and was predominantly masculine in outlook It was therefore important that he should continue to regard himself as essentially male, or impotence would almost certainly have resulted

It would have been more satisfactory to remove the uterus, fallopian tubes, and ovarian tissue at the first operation, but the patient refused this, and technically it would have been impossible to ensure an adequate blood supply to the testicular portion of the ovotestis on the right side

Replacement therapy with testosterone propionate will be necessary for the rest of the patient's life

The association of inguinal hernia with hermaphroditism has been previously reported (Weed et al 1947) It is interesting to note the association with spina bifida occulta

SUMMARY

A case of true hermaphroditism is described, including the sociological and psychological background

The main points were the presence of a true ovotestis on the right side, with an ovary on the left, associated with predominantly female physical characteristics combined with a male psychological outlook

I wish to thank Dr Raymond Greene for his guidance, Mr S Willson Holmes for the surgical investigation and treatment, Dr V Pugh for help in the preparation of the specimens, Dr Louis Steingold for the reports on the ovotestis and photomicrographs, and Dr W Gordon Sears, senior physician and medical superintendent, Mile End Hospital, for his help and encouragement The clinical photographs were taken by Nucleus Photographic Specialists Ltd, London, E C 1

REFERENCES

Hinman F (1935) Principles and Practice of Urology Philadelphia and London
McKenna C M. Kiefer J H (1944) *J Urol* 52 464
Weed, J C Segaloff, A Wiener, W B Douglas J W (1947) *J clin Endocrinol.* 7, 741

Reviews of Books

Diseases of the Heart and Circulation

PAUL WOOD, O B.E, M.D, F.R C P director, Institute of Cardiology, London. London Eyre & Spottiswoode 1950 Pp 589 70*s*

IT would be difficult to get so comprehensive an account of this subject into fewer words On many aspects of cardiology Dr Wood is able to strengthen his account from his own original work, but everywhere he quotes the views of others Indeed, perhaps fewer references and a more dogmatic statement would be better suited to the student, though it is doubtless hard to know where to draw the line when the requirements of examiners and personal modesty have to be considered Dr Wood opens with chapters on clinical examination, X-ray appearances, and electrocardiography, in which the theory of the normal curve and the principles underlying abnormalities are briefly considered, cardiograms are more fully described in the chapter on disorders of rhythm as well as throughout the book The chapter on heart-failure is excellent, but in dealing with triple heart sounds (or gallop rhythm) remarks about syllables per poetical foot only serve to mystify In the remaining sections the account is mainly on accepted lines The book is profusely and beautifully illustrated, and in every sense a fine production

Neoplasms of Bone

BRADLEY L COLEY, M D, attending surgeon, bone tumour department, Memorial Hospital for Cancer and Allied Diseases, assistant professor of clinical surgery, Cornell New York Paul B Hoeber London Cassell 1949 Pp 765 £6 10*s*

THE bone sarcoma registry, while advancing and greatly increasing our knowledge of bone pathology, has led rather to greater complexity than clarity, and what was a few years ago a very simple field in pathology has become difficult to experts and almost incomprehensible to the pathology of the practising surgeon Thus a great want has been supplied in this capable book, in which Professor Coley describes and associates the clinical and pathological features of neoplastic bone disease He is fitted by birth, interest, and exceptional experience to write such a book, and in him we have the experienced pathologist and surgeon combined In this comprehensive work he begins with the latest classification, and the biochemistry of bone neoplasms, and then deals with the various innocent, malignant, and "tumour-like" swellings (and the chapter on fibrous dysplasia is masterly) The later chapters discuss the various tumours in special situations, the various modes of treatment, and the results achieved in large series of cases Too many books on bone pathology confuse rather than clarify, but here description is uniformly full and clear, so that every type of tumour, however rare, stands out as an entity Not only orthopædic, but general surgeons—to whom bone tumours, common or exceptional, are relatively rare—will gain greatly from possession of this work

Results of Radium and X-Ray Therapy in Malignant Disease

Third Statistical Report from the Radium Institute, Manchester Compiled by RALSTON PATERSON, C.B.E, F R C S E, MARGARET TOD, F R C S E, MARION RUSSELL Edinburgh E & S Livingstone 1950 Pp 167 10*s* 6*d*

THIS is primarily a statistical report on radiotherapy at the Christie Hospital and Holt Radium Institute, Manchester, with a plea for a different way of presenting results The generally accepted method, which allows personal opinion and failure of follow-up to influence survival-rates, has been discarded, and in its place the use of crude rates, corrected by age, has been adopted. To obtain the age factor for the correction of the five-year survival rates for deaths due to intercurrent disease, age tables have been rearranged on the pattern used in the General Register Office in showing probability of dying This is done by using tables supplied by Dr Stocks [1] showing the probability of not dying of any cause within five years, and a table to correct for expectation of dying from the form of cancer present The authors claim that this method of presenting results is both scientific and exact, and undoubtedly it has advantages For example, for skin cancer the crude survival-rate is only 65% but the corrected rate 82% here the importance of the age factor is seen at once, the crude rate giving a wholly erroneous idea of the results of treatment Another change in this year's report is the substitution of the description of early and late for the four stages previously used. This simple division at once gives the contrast between the results at five years of early and late cases, and makes further tables unnecessary Commentaries on cancers in various sites are intended to interest those with no special knowledge of radiotherapy, who nevertheless want to keep themselves informed of the efforts being made to control cancer The new form of table accompanying each commentary points to the need for earlier diagnosis and to the peak age in each site.

The second part consists of a detailed report, with comparative analysis, of the various techniques employed It presents them in such a form that comparison between methods is possible, enabling radiotherapists to judge the merits of the various techniques and the lines along which progress has been made As full details of the techniques used have already been published,[2] descriptions are restricted to modifications or adjustments In this part of the report the internationally recognised method of classification into four stages is still used, because at present this is the sole means of getting an indication of the comparability of samples, where large groups are being considered For cancers in which the numbers are smaller, division is simply into early and late

During the period under review there has been an increase in the proportion of cases treated with X rays, but radium therapy is advocated by the Manchester school for all cases lending themselves to local application of radium The multiplicity of techniques used in treating cancer of the breast underlines the unsatisfactory position of radiotherapy for this cancer, and no conclusion can be reached on the relative efficacy of different techniques For tumours of the brain, it is thought that X radiation has a part to play, 31% of 187 patients treated having survived five years For cancer of the bladder, gold seed implantation is held to represent an advance on any published methods of treatment For cancer of the ovary the results of radiotherapy represent an improvement on those obtained by surgery Another interesting feature of this part of the report is the number of cases of seminoma referred to the clinic Here there has been a steady increase in number since it became known that even cases with large secondary deposits have a good chance of cure by irradiation

---

[1] Stocks P *J Fac Radiol.* 1950 1 187

[2] Radium Dosage The Manchester System Compiled by W J Meredith Edinburgh 1947

A study of the ten-year results of cases treated in 1934–38 shows that the various types of cancer tend to fall into two groups In one group, which includes cancer of the breast and cancer of the bladder, there is a continuous loss of treated cases, from recurrences, metastases, or persistence of the carcinogenic process In the second group, exemplified by cancer of the uterine cervix, lip, and larynx, if the patient survives five years without recurrence the cure is likely to be maintained Hence during the second half of the ten-year period the prognosis in this group is much better than that of the first group Cancer of the skin and mouth is nearer the second than the first group, so that it now seems possible to say that three out of the four major accessible cancers are curable by competent modern radiotherapy

The report represents the result of much careful work and is a step towards finding an internationally acceptable method of presenting results of cancer treatment, as well as being a clear and restrained statement of what can be achieved by well-planned radiotherapy

Surgery of Cataract

DANIEL B KIRBY, M D, professor of ophthalmology, College of Medicine, New York University Philadelphia and London J B Lippincott 1950 Pp 695 £12

Professor Kirby has undertaken a complete survey of the history, the development, and the modern practice of cataract surgery His book is in five parts, parts I and II covering the development of and preparation for cataract surgery, part III present-day technique, part IV the correction of aphakia, and part V the results For his facts he has searched the writings not only of our own times but of the early Hindus and Chinese, and pictures from early manuscripts are included He has much to say of all the modern types of operation, but naturally pride of place goes to the intracapsular operation and to his own methods of performing it He is a surgeon of great experience, who has given special thought to this branch of ophthalmic surgery, and his observations on modern methods, especially those pages on the mental approach of the surgeon to fine and critical work are particularly valuable His quotations from the writings of those who laid the foundations of modern ophthalmology make fascinating reading Eye surgeons will long be grateful for his presentation of the subject

Bronchoesophagology

CHEVALIER JACKSON, M D, honorary professor of bronchoesophagology, Temple University, Philadelphia, CHEVALIER L JACKSON, M D, of the same department London W B Saunders 1950 Pp 366 63*s*

THE authors of this book regard "bronchoesophagology" as "covering a department of study and a branch of medical science", and indeed it is one which has evolved largely from their extensive and almost unique experience In this work they are not only concerned with the technique and instrumentation required in dealing with the bronchial tree and the œsophagus, but indicate the points at which cooperation with other branches of medicine and surgery are necessary This does much to allay the suspicion that bronchoscopy and œsophagoscopy were becoming isolated from other branches, and that diseases of, or near, these structures were being regarded from too limited a viewpoint In this country bronchoscopy and œsophagoscopy are often routinely handled as part of general thoracic work by both physicians and surgeons, as well as by laryngologists The book is comprehensive, and is very well illustrated in line and photograph There are remarkable sections dealing with foreign bodies in the bronchus and œsophagus, and the vast experience of the authors, covering several thousand cases, is illuminating Each case is studied carefully, and if necessary the foreign body is reproduced and practised on with special forceps—newly designed, if need be This care in itself explains how such a high proportion of successes is achieved. The description of pathological conditions of the bronchial tree is full but less detailed than the section on foreign bodies, and there is possibly some undue emphasis on the value of bronchoscopic measures over those commonly practised by the thoracic surgeon The value of endoscopic treatment of bronchial adenoma can be well appreciated from the account given here If there is an extrabronchial projection of the growth, a final cure by bronchoscopy cannot be expected, but where it presents as a polyp it may well be removed successfully by bronchoscopy, or, indeed, if surgery is contraindicated, the condition may be temporarily relieved The technique of œsophagoscopy is given in detail, and attention is repeatedly drawn to the possible dangers of improper handling of the instrument Perforations are by no means unknown and many fatalities have resulted from this cause The removal of sharp foreign bodies from the œsophagus is also fraught with considerable danger All conceivable manœuvres to prevent any damage on withdrawal of foreign bodies are carefully described and illustrated

The work is well produced and some of the coloured endoscopic illustrations made by the authors are especially good

Types of Diabetes Mellitus and Their Treatment

A R COLWELL, M D, associate professor of medicine, Northwestern University Medical School, Chicago Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 97 16*s* 6*d*

THIS is a simply written general account of diabetes for those not already well acquainted with the subject. Professor Colwell deals separately with diabetes of different degrees of severity and gives useful information on diets He treats controversial topics in a disarmingly direct manner, but includes 50 key references to subjects treated summarily in the text Professor Colwell is among the foremost experts on the use of insulin mixtures, and his recommendation to use mixtures prepared previously in sterile ampoules rather than in the syringe at the time of injection could well be taken to heart by many in this country He states clearly that two doses of unmodified insulin are usually incapable of controlling the blood sugar for 24 hours—another fact which needs to be more widely appreciated He advises the use of high ratios of fat to carbohydrate, even when insulin is being taken, this does not conform to recent work relating the development of atheroma to dietary fat, but the matter is still sub judice Once the reader has accepted the term "desugarisation," and realised that the standard technique of the glucose-tolerance test differs from ours he will find that the book is as appropriate for British as for American use

John Ferriar

EDWARD M BROCKBANK, M D, F.R.C.P London Heinemann Medical Books 1950 Pp 51 6*s*

IN this little book Dr Brockbank has given us a study of a many-sided man, John Ferriar (1761–1815) As physician to the Manchester Infirmary he was the first successfully to organise measures to control the spread and the enormous death-rate of typhus and other fevers His board of health and his fever hospital, called by him hopefully "The House of Recovery," were taken as models in many other cities He was the first, or among the first, to establish the connection between acute rheumatism and heart disease A bibliophil and a poet, his knowledge of literature led to his famous exposition of the sources from which Sterne had culled his *Tristram Shandy* and his *Sentimental Journey*—sources which he used so freely that his admirers have had to change their praise of his originality to applause for the deftness with which he has blended and incorporated the imaginings of others

Sir William Osler, too, was an admirer of Ferriar, and Dr Brockbank has added the story of his visits to Manchester and of his interest in the subject.

THE LANCET

LONDON SATURDAY, MARCH 10, 1951

Industrial Health Services

To any suggestion that the industrial health services are taking doctors and nurses away from their proper work the Dale Committee [1] answers that these services are necessary, that they overlap little with other services, and that what overlapping there is benefits the National Health Service and the output from the factories. As we noted last week, the committee recommends that the development of the services should be encouraged, and proposes the formation of a standing joint advisory committee to coordinate the industrial with the general health services.

It seems strange that, at this point in the history of our highly industrialised society, it should be necessary to apologise for the existence of the services which, however inadequately, look after the health of our large industrial population. E L Collis's remarks made in 1915 about the tardy development of the industrial health services have already been quoted in these columns,[2] but they will bear repetition. Referring to Greenhow's brilliant investigations in the 1860s into the effect of occupational dusts on the lungs, he said:

> "Why work so well started was then allowed to lie dormant for so long, while other aspects of public health were being strenuously developed by medical officers of health with inspectors of nuisances appointed for every town and district, reinforced now by a battalion of tuberculosis officers, is astonishing."

There can be no doubt that the local authority public health services, hampered by local politics and influence, lost a great opportunity in the middle of the last century to develop the industrial health services, and it was left to the Factory Department with its certifying surgeons, and a few enlightened factory owners, zealous reformers, and perhaps the trade unions, to carry on the struggle for safer and healthier working conditions in factories. Nowadays, on the other hand, many organisations, groups, and Government departments, both local and central, are keen to take industrial medicine under their wings, and the report of the Dale Committee has been eagerly awaited because it was hoped that it would give a strong lead for the future. The committee was asked "to consider what measures should be taken by the Government and other parties concerned to ensure that such medical man-power is used to the best advantage," and the outcome is disappointing because the nettles of controversy have not been grasped firmly and the recommendations leave the position nearly unchanged. Perhaps because of unresolved differences of opinion within the committee, the lead given is feeble. Surely it would have been within the committee's competence to say why the Ministry of Health should or should not take over all health matters including industrial health; to give the reasons for and against the medical officers of health dealing with the subject; to discuss the suitability of the Ministry of Labour, the Ministry of Fuel and Power, or, curiously enough, the Treasury (for evidence was taken from some of its officials) for controlling the services. Again, it would have been useful to know what the committee thought about the effect of lay administrators' control over health matters—whether, for instance, it has helped or hindered the development of the industrial health services. Refraining even from a summary of the arguments, the report goes out of its way to avoid controversy. What is meant, in referring to health services for workers in shops and offices, by the statement that "the proper authorities to encourage the development would, we think, be the authorities respectively responsible for the enforcement of general health standards"? It would have been easy to say that the authorities were the Ministry of Health, the medical officers of health, the regional hospital boards, or the Ministry of Labour: as it stands, the recommendation is capable of as many interpretations as there are protagonists. Another strange sentence is "industrial health services are indeed not wholly medical in character but they are bound up with the carrying out of certain functions, largely non-medical, at the place of work." Why should the industrial health services be singled out in this implication that doctors are not really needed in dealing with all aspects of a health service? The same can be said about any health service, because doctors are always assisted by non-medical auxiliaries. The sentence smacks of the recent development in the United States of the industrial hygienists or "health engineers" who are now maintaining that in order to deal with industrial health it is unnecessary to have a medical qualification.

The committee has nevertheless done a valuable work in setting forth clearly the present position of the industrial health services and in emphasising their importance to the nation. It shows that about 250 doctors are engaged whole time in factory work, and that there are 1789 appointed factory doctors and 1287 other doctors taking part in factory medical services. Also, about 2600 State registered nurses and 1400 other nursing staff are employed in factories. Despite the shortage of nurses, the committee believes that they should be used in industry; but they should be used for strictly nursing duties—not, for instance, as welfare officers—and their labour should be diluted as much as possible by giving them subordinate staff. As regards dental, ophthalmic, ambulance, and medical auxiliary services, the committee finds that there is no overlapping with similar services for the general public. It expresses the opinion that there should eventually be comprehensive provision for occupational health, covering not only industrial establishments, both large and small, but also workers in shops and offices, to which the general health standards of the Factory Acts should be applied. But this development is regarded as remote, and not to be achieved without much more experience to be gathered from future surveys and experiments. The drawing up of any national scheme for an industrial health service would also depend on further surveys and experiments All factories are obliged by law to maintain certain standards of healthy environment, and if they employ people in certain processes with special risks, or if they employ young persons at all, they have to consult the appointed factory doctor Services like those established in some of the larger factories might be neither practicable nor appropriate in smaller factories which need some further provision Attention is drawn to the group services for smaller factories at Slough, Bridgend, and Hillington, and the committee would like to see further group experiments made on a scale that the average small employer is willing and able to afford They realise, however, that before health supervision beyond the minimum already provided can be extended, even moderately, there will have to be a big increase in the numbers of doctors and nurses available to industry "Meanwhile, any detailed planning of a nation wide scheme remains largely academic "

---

[1] Report of a Committee of Enquiry on Industrial Health Services. Cmd 8170. H M Stationery Office. Pp 35. 1*s* 3*d*.
The committee was appointed by the Prime Minister on June 1, 1949, and its members were: Judge E T Dale (chairman), Mr J T Byrne, Dr T A Lloyd Davies, Miss M M Edwards, S R N, Miss E M Gosling, S R N, Sir Robert Hyde, Dr Walter Jope, Mr K I Julian, Dame Anne Loughlin, Mr J R Pheazey, Dr Llywelyn Roberts, Dr A Talbot Rogers, and Sir Geoffrey Vickers.

[2] *Lancet* 1945, i, 151.

The one positive recommendation is that there should be a standing joint advisory committee to coordinate the development of the industrial health services it should be composed of persons appointed by the Ministry of Health and the Ministry of Labour, together with representatives of the Ministry of Fuel and Power, employers, workers, doctors, and nurses , and there should be strong medical representation on it A similar committee should be appointed for Scotland in which the Department of Health for Scotland would take the place of the Ministry of Health The chairmen of these committees should not be drawn from any of the departments represented on them The main function of the committees would be to correlate advice to be afterwards given by departments on major developments affecting industrial health, with special regard to the best use of medical man power Unfortunately, this method of coördination by advisory committees is at best only a half-hearted one, and it would probably have been better to give one department the main responsibility for the development of the services The outcome of the Dale Committee's deliberations really depends on how the Prime Minister deals with the " detailed consideration of the coordinating machinery " If this is not done effectively the Dale report will go down in the history of industrial medicine as another lost opportunity

Veratrum in Hypertension

THE blood pressure of most hypertensive patients can be lowered temporarily by rest and freedom from everyday cares, aided perhaps by venesection or drugs It is in seeking to make the change permanent, with reasonable safety, while avoiding intolerable side-effects, that difficulties arise Moreover, as TURNER[1] has pointed out, high blood-pressure is only one of the manifestations of hypertensive disease Reducing the pressure may not relieve the patient's symptoms, and may be dangerous Such considerations have not deterred clinicians from cautious trials of the potent methonium compounds, which were discussed in our leading article of Feb 17 This week two correspondents indicate that, even with supervision in hospital, administration of such compounds may have a fatal outcome , and on p 549 Dr KAUNTZE and Dr TROUNCE draw attention to the possible advantages of veratrum preparations Veratrum viride is no novelty , it was familiar to our grandfathers as a remedy for hypertension Twenty years ago Dr DOUTHWAITE[2] reported unfavourably on its efficacy in this condition, and for a time its reputation languished , but in 1949 work in America gave a fresh turn to its fortunes

How the veratrum alkaloids exert their hypotensive action is not certain It is agreed, however, that the effect is not sympatholytic According to GOUTIER[3] these drugs act largely by heightening the response of plain muscle to potassium ions WILKINS et al[4] suggest that they act through a " central " mechanism not hitherto recognised, aided perhaps by peripheral vasodilation Thus, it is claimed, they reduce hypertension while largely avoiding the undesirable side effects of the simple vasodilators , and blood pressure can be reduced without impairing the cardiac output or the circulation in the major organs The slowing of the heart which these alkaloids induce, and which is abolished by atropine, is thought by WILKINS and his associates to be due to action on the vagus centres This " prevents the tachycardia and palpitation that ordinarily results from reflexes arising in the aortic and carotid areas when such a lowering of arterial pressure occurs " Apparently, therefore, these compounds can " maintain the patient in a state of circulatory equilibrium but with a lower arterial pressure " There is evidence for this view For instance, after the blood pressure has been significantly depressed by parenteral injection of a veratrum alkaloid, a normal " cold pressor " rise can, according to MEILMAN and KRAYER,[5] be obtained from the new levels WILKINS et al reported that " postural hypotension did not develop following sub-toxic dosage " , but MEILMAN and KRAYER claimed only that the postural response " did not differ much " from that before the preparation was administered The bradycardia, they maintained, is not responsible for the lowered pressure, since this remains low after the pulse has been quickened with atropine

WILKINS and his associates insist that their laboratory work on veratrum viride was done with " the same old drug " But for their clinical trial MEILMAN and KRAYER used a pure ester alkaloid of veratrum, which they called ' Protoveratrine ' KRAYER et al[6] had previously shown experimentally that " not all veratrum alkaloids, but only some of the ester alkaloids " were " capable of eliciting the reflex decrease in blood pressure and heart rate " It has not yet proved possible to administer protoveratrine orally Given intravenously it produced virtually no side effects in doses sufficient to cause a conspicuous fall in pathologically raised blood-pressure Moreover, in a high proportion of cases the fall was accompanied by relief of headache and reversion of flat or inverted T waves in the electrocardiograph The response was evident in about ten minutes and lasted from one to three hours In America several attempts have been made to find a veratrum compound that is both effective and safe when given by mouth **FREIS** and **STANTON**[7] studied the effect of a biologically standardised preparation of veratrum in a powder with tetraiodo-pyrrole Of 34 ambulant hypertensives who received this substance, 30 had a significant fall in blood-pressure and 27 experienced subjective improvement, 13 had toxic reactions This was encouraging, but **COE** and his colleagues[8] have since published a control series in which the effects of oral veratrum were compared with those of similar placebo tablets Of 25 patients to whom veratrum was administered, only 2 had a significant fall in blood-pressure, 16 noted symptomatic improvement, but similar benefit was reported by 14 out of 23 patients in the control group Nausea and vomiting proved troublesome, and some way of eliminating these toxic effects will have to be found before a fully effective dosage of veratrum in this form can be given by mouth In his survey Dr **KAUNTZE** has used a potent extract prepared by **STUTZMAN** et al[9] which has been given the proprietary name 'Veriloid.' **STUTZMAN** offers a new hypothesis to account for the hypotensive effect of veriloid. Moreover the experience of Dr **KAUNTZE** differs somewhat from that of the American workers, for he finds that the low pressures obtained with the extract were not maintained under atropinisation. On the other hand he agrees with the Americans in his observation that there was "no postural change in the blood-pressure comparable with that after the injections of hexamethonium" Moreover there was a sharp response to ephedrine

---

[1] Turner, R *Lancet* 1950, ii 353

[2] Douthwaite A H *Brit med. J* 1929 ii 844

[3] Goutier R *Brit. J Pharmacol* 1950 5 33

[4] Wilkins R W Freis E D Stanton, J R. *J Amer med. Ass* 1949 140 261

[5] Meilman E Krayer O *Circulation* 1950 1 187

[6] Krayer O Wood E. H Montes G *J Pharmacol* 1943 79, 215

If veratrum has an advantage over methonium it would seem to lie in the lesser risk of postural hypotension In potency, method of dosage, and variability of effect the two forms of treatment seem to have much in common Neither touches the cause of the disease Both, if they achieve their object, must threaten the patient with such risks as vascular thrombosis and extrarenal uræmia The side-effects, too, are evenly balanced. If veratrum is bad for peptic ulceration and can cause vomiting in its own right, at least it does not precipitate bromism, nor "methonium paralytic ileus" In short, both these types of preparation offer encouragement but as yet no fulfilment

Bacteriophage

THERE is now a tendency to discard the name "bacteriophage" and to refer collectively to these organisms as the bacterial viruses, for "bacteria-eating" is only one of the properties of the group, and one that occurs principally under experimental conditions in the laboratory To the microbiologist this group of viruses is at present important not so much because of their ability to destroy bacteria as because they provide a model system in which to study the relationship of a virus with its cell host

Using the technique described by **FISK**[10] it can be shown that many bacteria carry bacteriophage without undergoing lysis, so, unless we believe in spontaneous generation, or in some autocatalytic process in the bacterial cell, it is clear that these viruses are ordinarily in symbiosis with the bacteria Though itself apparently unaffected, the bacterial strain which carries phage is capable of causing lysis if mixed with a similar bacterial strain. To explain how a strain can carry phage without being attacked by it, two hypotheses are offered. The first is that the bacterial culture consists of two populations, one of which is resistant to the phage while the other is sensitive, and the phage is propagated by multiplication in the sensitive organisms which are derived by mutation from phage resistant bacteria The second possibility is that the phage-carrying strains are equivalent to an immune carrier, there being little multiplication until the phage meets a sensitive strain This second hypothesis finds support in the work of **GRATIA**[11] and others who have shown that phages can be carried by bacterial spores, and then have the same resistance to heat and other agents as the spore The immune bacterial carrier may have a chemical grouping at its surface to which the phage attaches itself and by which it is prevented from entering the bacterial cell

Electron-microscope studies have shown that the bacterial viruses vary as much in form as the animal viruses **RUSKA**,[12] in photographs of *Bacterium coli* bacteriophages, demonstrated variations from tadpole-shaped viruses to small round bodies, the tail, though resembling a flagellum, does not give motility to the virus Both **WYCKOFF**[13] and **MERLING**,[14] from electron-microscope studies of the reproduction of bacteriophage, have suggested that multiplication is by binary fission, but this has not been confirmed **DOERMANN**[15] has attacked the same problem by mechanically breaking up the bacterial cell after the bacteriophage particle has entered it Apparently, after the phage enters the cell it loses its identity, and it only reappears shortly before the cell would normally burst to liberate fresh phage particles (This finding fits in with **HOYLE**'s[16] observation of the appearance of the soluble antigen of influenza virus before the infectious particles appear in chick-embryo cultures) The lysis of the bacterial cell does not seem to be due to any enzymic action of the phage; nor apparently is it due to the cell becoming full of phage particles, since **COHEN**[17] has shown that in an oxygen-deficient cell a single phage particle causes immediate lysis—and thereby destroys itself

An understanding of virus metabolism might give a key to the preparation of compounds which would prevent the intracellular growth of viruses A step in the right direction is the work of **DELBRUCK**[18] and his colleagues in the development of the one-step growth-curve technique, which has shown that after the bacterium is infected there is a latent period before fresh virus is produced, and then, quite suddenly, virus is released from all cells infected at the same time The increase in phage numbers proceeds by a series of steps, the interval between steps being of the same duration, and characteristic for each bacteriophage, under constant conditions By using the growth-curve technique COHEN and ANDERSON[19] have determined the minimum nutritional requirements, in the medium in which the bacteria are grown, for multiplication of the bacteriophage Working with the T series of coliform bacteriophages, they and others have shown that the material for the synthesis of fresh virus comes not from the bacterial cell but from the medium in which the bacteria are growing, and that for such synthesis the virus depends on the bacterial host's enzyme systems This might explain KNIGHT's[20] claim to detect antigenic differences in influenza virus according to the host in which it is propagated It might also explain the specificity of the virus for a particular type of cell

---

[7] Freis E D Stanton J R. *Amer Heart J* 1948 36 723
[8] Coe W S Best, M. Kinsman J M. *J Amer med Ass.* 1950 143 5
[9] Stutzman, J W., Maison G L., Bauer R O *Proc New Engl cardiovasc. Soc.* February 1950
[10] Fisk, R. T *J inf. Dis* 1942 71 153.
[11] Gratia A. *Ann. Inst Pasteur* 1936 57 652
[12] Ruska, H *Naturwiss* 1941 29 367
[13] Wyckoff R. W G *Nature Lond.* 1948, 162 649
[14] Merling K. B E. *Brit J exp Path* 1949 30 139
[15] Doermann H. A *Carnegie Inst Wash. Year* 1948 47 176.
[16] Hoyle L. *Brit J exp Path* 1948 29 390
[17] Cohen S S *Bact Rev* 1949 13, 1
[18] Delbruck, M. *J gen Physiol* 1939 22, 365

Work on the genetics of the T series of *Bact coli* bacteriophages has shown that within this group a large number of recombinations can take place A notable experiment in this field is that of LURIA,[21] who treated two phages with ultraviolet light so that neither could reproduce itself These two phages were then introduced simultaneously into a single cell and were able to produce fresh phages with the mixed characters of the two parent strains To explain this successful rejuvenation, LURIA[22] has suggested that phage multiplication proceeds by a series of steps The particle entering the cell breaks up into a number of genetic units, which attach themselves to a host enzyme system and impose their own genetic pattern on it, so that each unit is reproduced a number of times These units then recombine to give the infective agent In his ultraviolet light-treated particles he supposes that the genetic units from one replace those destroyed by ultraviolet irradiation in the other The essential requirement for successful recombinations is that the cell shall be infected simultaneously with the two types of closely related virus Probably this condition is seldom fulfilled outside the laboratory, but if such recombination occurs naturally it may give birth to a new strain of virus with epidemic propensities Certainly in influenza there seems to be a periodic change of antigenic structure in the A strains prevalent throughout the world

---

[19] Cohen S S Anderson T F *J exp Med* 1946, **84**, 511

[20] Knight, C A *Ibid* 83 281

[21] Luria S E *Proc nat Acad Sci* 1947 **33**, 253

[22] Luria, S E *Science* 1950 **111**, 507

Annotations

PURE FOOD AND NUTRITION

THE more disreputable characters in *Candide* were killed off a number of times, but always turned up again as hale as ever, and it is so with abuses We can never say "That evil is gone for good," for sooner or later it will come sneaking back in some form or another Thomas Wakley's splendid campaign against the adulteration of food, which Mr Laurence Dopson recalls on another page, ultimately won for us the Sale of Food and Drugs Act of 1875, but Dr H E Magee, who presided at a conference on Nutrition and the Pure Food Laws held by the Nutrition Society on March 3, noted that chemical substances of increasing complexity are finding their way into food today Some are innocuous, some beneficial, and the action of some is open to doubt The preservative regulations are due for revision, and the word "preservative," in particular, as Mr G W Monier Williams, D SC, pointed out, needs defining afresh Mr C A Adams, of the Ministry of Food, remarked that food legislation for the protection of the consumer now provides that an article should not be deemed a food merely because it has medical value Moreover, the descriptive words "not of the nature, substance and quality" have now been changed to "not of the nature, not of the substance, not of the quality"—making three separate offences possible Under the Defence (Sale of Food) Regulations there are powers for dealing with misleading labels and advertisements, including those in which a true description of the foodstuff is given under a misleading title, and an advisory service to the Ministry has vetted 60,000 food labels since the regulations came into operation in 1943 Mr Adams mentioned that in the United States a manufacturer has to declare the vitamin content of a foodstuff by giving the proportion of the daily requirement of that vitamin which would be taken in average daily consumption of the food

The formulation of standards is never easy In Canada, said Mr Adams, though trade interests are consulted, recommendations come entirely from Civil Servants, in the U S A there is a public hearing, evidence is published—sometimes to the tune of 15,000 pages—and the standards are based on findings from the evidence Here, of course, we compromise A permanent Food Standards Committee, made up of representatives of Government departments, professional and technical experts, and trade advisors, meet in private and hear evidence from all who are likely to be affected by the proposed standard The committee then report to the Minister of Food, and if they recommend a standard the Minister publishes the report This gives opportunity for further comments which may lead the committee to amend the report, and finally the standard is adopted It is a sound procedure, but never takes less than a year A subcommittee of the Food Standards Committee, studying metallic contamination of foods, has already issued a report on arsenic, and is following it up with reports on lead and other metals, and another subcommittee, under Prof E C Dodds, F R S, is already examining the preservative regulations, so the public are much better off than they were in Wakley's day, when the likely adulterants in food included sawdust, lead, chalk and alum, with chicory in the coffee, water in the milk, and sulphuric acid in the vinegar

A small centenary exhibition in honour of Wakley's campaign was shown at the conference, and included the 1851 volume of this journal, in which the first report of the Lancet Analytical Sanitary Commission appeared, and photographs of pages of *Punch*, where the campaign was supported by Mr Punch in his "Lectures to Tradesmen"

PORPHYRINS

PORPHYRIN chemistry is one of a number of complicated biochemical subjects which are invading medicine, often to the discomfiture of the clinician Its importance, however, is fundamental, both in general biology—since it covers the biogenesis of haems, cytochrome, and chlorophyll—and in clinical practice The porphyria of lead poisoning is a useful diagnostic sign, while constitutional abnormalities of porphyrin metabolism, though rare, can simulate Addison's disease, Landry's paralysis, an acute abdominal emergency, or a confusional psychosis

An excellent short account of the porphyrins for clinicians was published by Chandler, Harrison, and Rimington[1] in 1939 Three types of substance are of medical significance, all being composed of four pyrrol units linked in a ring by methene bridges In proto porphyrin, which is present, united with ferrous iron, in haem, there are two peripheral carboxyl groups; in coproporphyrin there are four, and in uroporphyrin eight. There are four possible, and two naturally occurring, isomers of each of these; the protoporphyrin of haem belongs to type III, while the porphyrins excreted in disease normally belong to type I. Despite these complications, modern separation methods have made it possible to discover much about the synthesis of porphyrins in the body. By the use of labelled nitrogen one can trace their synthesis from glycine, and work is in progress to discover the relation between the abnormal porphyrins of porphyria and poisoning and the normal course of hæmopoiesis.

---

[1] Chandler F G Harrison G A, Rimington C *Brit med J* 1939 ii 1173

In the valuable lecture which we publish this week, Professor Watson, who is a pioneer of research on this subject, clinical as well as chemical, describes some clinical aspects of porphyrin chemistry. He detects significant differences between the porphyrins of alcoholic and non-alcoholic cirrhosis, and outlines the modern theory of porphyrin biogenesis. A measure of the complexity of this work is found in the fact that some of Watson's most interesting clinical findings depend on the separation of the two isomers of coproporphyrin.[2] This is technically very difficult. The fluorescence quenching method of Schwartz, on which these findings are based, has not proved very successful in this country, and search is in progress, so far without result, for a paper chromatographic technique. In this field the clinician must wait for the chemist, and he may hope for some fundamental information on cell metabolism; but, while waiting, he can greatly assist research by keeping his eyes open for cases of porphyria, and calling in the biochemist when he finds them. A full knowledge of hæmoglobin metabolism would be a big gain to medicine, and porphyrin chemistry is a department in which full-scale cooperation has already brought results. It is one more example of the extension of the scope of medicine to cover "pure" scientific subjects of which the doctor should be aware even when he does not attempt to memorise structural formulæ.

HEALTH CENTRES

NEWS of the likely establishment of the Manchester University Health Centre[3] is most welcome, even though it reminds us how few of the centres projected and promised so short a time ago are still on the stocks. Many local health authorities have secured sites and made plans, but money is no longer forthcoming for most of them. Moreover, all too often the prior development of alternative medical services in new communities, or the unwillingness of local practitioners to join in setting up a suggested centre, has compelled the health authority to withdraw from the plans it has made. In fact so many projects have come to nothing that everywhere enthusiasm for health centres is waning, and we are in danger of crying sour grapes, and of persuading ourselves, even before any have been tried, that health centres are things we never really wanted.

This would be a pity. When the promise of practice from health centres was first made it was received with favour both by the profession and by the public. Since then much thought has been given to the problems involved, and much valuable preparatory work has been done. While it is true to say that this work has revealed many difficulties to be overcome before the smooth running of health centres can be assured, no really insurmountable ones have been encountered, and those that remain are chiefly such as call for practical experiment. They provide in fact added reason for the early establishment of experimental centres rather than arguments against their development. A generation ago, Lord Dawson's committee gave us a detailed report on health centres; but the value of its work was largely lost because none of the suggestions were translated into action. The same will happen now, and the many recent studies will be wasted if their conclusions cannot be put to the test of daily practice in prototype centres. The more these prototypes can embrace different types of centre, and different types of community, the more valuable will the experiment prove when the time comes to create better health services than we can afford today.

The Manchester centre—if all goes well—is to develop under the auspices of Manchester University with assistance from the Nuffield Provincial Hospitals Trust and the Rockefeller Foundation. It is to be housed at Darbishire House, Chorlton-on-Medlock, which has latterly been a hostel for business women and students. The cost of its purchase and adaptation is being paid by the Nuffield Trust, and the building is being leased to the university at a nominal rent. The intention is that the centre shall be developed into a comprehensive health centre, with maternity and child-welfare and school health clinics, together with accommodation for five or six general practitioners and the necessary ancillaries. Within two years, as the scheme develops, it is hoped that each of the general practitioners in the centre will be putting in two weekly sessions at one of the clinics, and also two or three sessions as a clinical assistant at one of the local hospitals. The practitioners will also help to train students at the university medical school. These extra duties will necessarily take a good deal of time; so, though all their present lists exceed 3000, they have agreed with the university that they shall keep their lists in future below 2750. Financially they will not lose thereby, for with the extra remuneration they will receive for their hospital, clinic, and teaching work they should quickly be earning more than they could get from full lists of 4000. Moreover, during the first two years they are to pay nothing for the use of the health centre, and a fund provided by the Rockefeller Foundation guarantees them against any loss of income in the first seven years and assures them of pension rights equivalent to those accruing to a list of 4000 patients. Also they can still see private patients in their own home surgeries.

Altogether it seems that the doctors have made a good bargain. But the total money involved is not excessive, and it will be well spent if used to demonstrate the value of group practice in health centres and the wisdom of enabling suitable general practitioners to help in the training of medical students. The disadvantage of the financial arrangements has been that the Ministry of Health has not been able to agree that they really correspond with those it can sanction for health centres under the National Health Services Act. To bring the scheme within the terms of the Act the local health authority would have to have acquired or leased the centre and its equipment, from the university, and have accepted responsibility for its maintenance and for the payment of the non-medical staff. This would have meant an annual charge upon the Manchester City Council of close on £7000, of which half would have been reclaimable from the Ministry of Health. As the Ministry is unwilling to recognise the centre for purposes of grant, it is probable that the university will itself need to shoulder this expense, relying on the health authority to instal clinics and to make a voluntary contribution—without Government assistance—towards their maintenance.

In spite of these enforced variations from the expected usual procedure in health centre development, the Manchester experiment should be of real importance. But others are needed in addition, and we trust that doctors will henceforth refrain from saying, like those in Sheffield and more recently in Norwich, that it is an excellent idea to try health centres in almost any part of the country save their own A true pioneering spirit is needed in many more localities than one, if we are to learn how methods of general practice can be improved As the Collings report urged, there is immediate need for practitioners to form their own groups, without waiting for ideal buildings, and there are also other promising possibilities to be explored, such as the use of diagnostic centres We are very glad to print this week a letter from the secretary of the Nuffield Trust in which he describes the prototype diagnostic centre to be built at Corby

---

[2] Watson, C. J., Sutherland, D., Hawkinson, V. *J. Lab. clin. Med.* 1951, 37, 8.

[3] *Manchester Guardian*, Jan. 26, p. 4.

STANDARDISATION OF X-RAY FILMS

THE need for a high and uniform standard of X ray films in cases of suspected pulmonary disease has long been recognised Lack of agreement among observers as to what is the best type of radiograph, the use of sets of different capacity in different hospitals and clinics, and lack of standardisation of equipment made by different manufacturers, together with errors inherent in such apparatus as time switches and variations in mains supply, all make for difficulty in securing the standardisation needed for accurate diagnosis and assessment of progress The radiological subcommittee of the Industrial Pulmonary Diseases Committee of the Medical Research Council have been studying the problem and last year published their recommendations These cover size and identification of film, position of the patient, the control of variables in technique, darkroom procedure, and other points, and the committee also define what is in their opinion a satisfactory first radiograph

The committee say that much further research into the factors concerned with standardisation of chest films is evidently necessary, and they are planning further investigations But the recommendations they now make should go far to improve the standard and diminish the variation that exists not only between films taken on different sets but also between films taken on the same set and even of the same patient Meanwhile the collection of films which they used may be inspected, and sets of standard radiographs can be bought from Miss K C Clark, Tavistock House North (First Floor), Tavistock Square, London, W C 1

FAVISM

THIS curious hæmolytic disease is a serious hazard in the Mediterranean countries, especially Sardinia It is connected with broad beans, and is induced either by eating insufficiently cooked beans or, less often, by exposure to the pollen The anæmia may prove fatal, but, as we indicated three years ago,[1] pathological studies have been few Cadeddu,[2] however, has recorded 8 fatal cases on which he was able to carry out full post mortem examinations The clinical notes show that the red cells were grossly reduced to levels even below 1 million per c mm, and there was the usual accompanying leucocytosis, hæmoglobinuria and enlargement of the spleen were constant features The findings were those usual in hæmolytic anæmias whatever the cause, and do not help in determining the ætiology of the disease or in indicating treatment

The sensitivity to pollen of the broad bean flower has suggested that the condition may be allergic in origin Leone,[3] also working in Sardinia, has put this theory to the test by giving anti histamine drugs to 21 children, varying in age from 12 months to 12 years, who were suffering from favism They were severe cases, the initial red cell counts ranging from 770,000 to 2,470,000 per c mm Most of them were given pyribenzamine in a total dose of 150–300 mg, some had 'Antistin' or 'Fargan' Blood transfusions were needed in only 6 of the patients 16 of the children had hæmoglobinuria, which ceased after 1–3 days' treatment, the toxic symptoms—fever, vomiting, diarrhœa, and collapse—were rapidly and strikingly relieved Leone points out that she had previously recorded increased blood histamine levels in these cases From her experience she recommends immediate treatment with pyribenzamine or antistin, 50 mg daily for 3–6 days, these doses can probably be increased for adults

The biggest puzzle about favism—its distribution—still remains unsolved Favism is almost entirely restricted to the Mediterranean area Its chief focus is Sardinia, but it is also well known in Sicily, Crete, the Ionian isles, and a few small localities in Italy, Greece, and Turkey Sporadic cases have been reported from France, and 8 in Italians in the U S A Now Pedro Pons and Surinyach[4] report the first 8 cases found in Spain These were distributed among three families, and seventeen attacks of hæmolysis were recorded All the members of the first family were natives of Barcelona In the second family the mother, subject to favism, had a French father and a Catalan mother, the father, a native of Barcelona, did not have favism, but 2 of the 3 sons were affected The third family came from the Balearic Isles The geographical distribution of favism led to the theory of a peculiar toxicity of the soil or of certain stocks of vegetables This theory was disproved by the fact that the subjects of favism are sensitive to all kinds of broad beans from any country, and those who do not get favism are not susceptible to beans grown in Sardinia. The Sardinian workers therefore turned their attention to the condition of the blood in the apparently healthy parents and siblings of the affected children Boi[5] gives figures showing that increased serum bilirubin was common, the blood picture showed an excess of microcytic red cells, and the fragility of the red cells was often increased These findings support the view, consistently supported in Sardinia, that favism is based on a constitutional peculiarity that is not merely familial but also racial and may be linked with a racial peculiarity of hæmopoiesis

The Mediterranean area already has one constitutional "Mediterranean anæmia," also known as "thalassæmia" or Cooley's disease The Spanish report on favism suggests that the abnormality in favism is linked to Mediterranean anæmia But in fact the results quoted show that they are different In Mediterranean anæmia the blood picture is characterised by the appearance of "target cells" (unusually thin and resistant red cells), but Boi's pictures of the blood in patients with favism and their relatives show no target cells, and his figures show an increased fragility more like that seen in congenital spherocytic anæmia It is of course not improbable that some cases will be found with features of both favism and Cooley's disease Powell et al[6] have recently reported a remarkable family of Sicilian ancestry in which the father had sickle cells, the mother thalassæmia, and the children features of both Some anthropological studies have been made to see if traces of Cooley's disease, which causes typical skeletal changes, could be found in skeletons of ancient Mediterranean races Graziosi discovered generalised osteoporosis in a skeleton from the Upper Palæolithic age in Sicily, and interpreted it as due to disease during life Gatto claimed that the owner of the skeleton belonged to the Palæo Mediterranean race, in which had arisen the mutation responsible for thalassæmia or Cooley's disease Maxia and Cossu[7] have examined radiographically 95 skulls of various ages (including Neolithic, Bronze Age, Punico Roman, and medieval) in the anatomical museum at Cagliari In only 8 (3 of the Bronze Age and 5 medieval or modern) did they find any slight alterations referable to Cooley's disease They conclude that the suggestion that Cooley's disease was especially linked with ancient Mediterranean man is far from proved, and that it is not even certain that descendants of that race are to be found in Sicily and Sardinia In the latter country no skeletal remains or implements of the Upper Palæolithic period have yet been found

---

[1] *Lancet*, 1948, i, 480

[2] Cadeddu, G *Ann ital. Pediat* 1950, 3, 303

[3] Leone, A *Ibid* p 417

[4] Pedro Pons P Surinyach R *Med clin Barcelona*, 1950, 15, 220

[5] Boi G *Ann ital Pediat* 1950 3 447

[6] Powell, W N Rodarte, J G Neel, J V *Blood* 1950 5 887.

[7] Maxia C, Cossu, D *Ann. ital. Pediat.* 1950 3 416

SWIMMING-POOLS

SWIMMING BATHS in Britain date back to Roman times, and Dr Russell of Brighton first popularised the remedial effects of sea bathing around 1750, but it is only in the last hundred years that local authorities have begun to make provision for indoor bathing, and the modern type of swimming pool is less than 50 years old Today the demand greatly exceeds the supply, so that in the season overcrowding creates potentially dangerous conditions, the Ministry of Health have therefore revised their memorandum[1] indicating how these dangers may be obviated

The risk of infection from the water itself is often exaggerated Gastro intestinal infections are seldom traced to the swimming pool, and skin infections and conjunctivitis are more likely to be spread by contaminated towels and swimming suits than by contaminated water, though overdosage with chlorine or other chemicals may produce an irritative conjunctivitis and skin rashes. The swimming bath is sometimes blamed for otitis media, but it seems more probable that mechanical pressure from faulty breathing has helped to push infective material along the eustachian tube than that a hæmolytic streptococcal infection has been acquired from the water As for poliomyelitis, the main dangers associated with bathing are those of too close contact through overcrowding and of susceptibility being increased by over exertion, for the poliomyelitis virus is readily killed by efficiently chlorinated water Even during poliomyelitis epidemics the balance of evidence is against the closure of properly controlled public baths and swimming pools

Most of the Ministry's memorandum deals with the purification of bath water The old fashioned fill and empty system has given way to the continuous filtration method, fortified by sterilisation (usually with chlorine) and aeration, which, when properly done with modern plant, can keep the water clear and sparkling and its bacterial purity not far from drinking water standards For indoor baths the period of complete turnover of the water should not exceed 4 hours, and the rate of filtration through the sand filters should be about 200 gallons per square foot per hour The use of a coagulant, such as an aluminium salt, helps to clarify the water, which for this purpose should be kept slightly alkaline (pH 7 2–8 0), if necessary by adding soda ash or lime The sterilisation of swimming-pools by chlorination has advanced in the last few years Chlorine gas is the best form of chlorine to use, because the dosage can easily and accurately be controlled to meet varying demands, and instead of the older marginal chlorination method with a free residual chlorine concentration of 0 2–0 5 p p m, or the use of slower acting chloramines, breakpoint chlorination is now being widely adopted When chlorine is added to water containing ammonia, chloramines are formed, but in the presence of an excess of chlorine these break down to form hydrochloric acid and nitrogen During this process the addition of chlorine causes a fall in the total residual chlorine, but when the ' break point " has passed there is a rise in the free residual chlorine, which is much more rapidly bactericidal than chloramine Break point chlorination requires more chlorine and closer supervision than the older methods, but levels around 1–2 p p m are readily tolerated and give a wide margin of safety The memorandum describes the tests for free and combined residual chlorine with orthotolidine and other agents, and it suggests that, provided the chlorine concentration is tested at least three times a day, there is little need for bacteriological control, though occasional checks against the chemical tests seem useful

More attention should be paid to the risks of infection and contamination outside the actual swimming pool Hot showers and foot baths should be provided, to encourage bathers to wash before entering the pool The margins should be wide, sloping gently away from the pool, and the dressing boxes should if possible be placed so that the bathers need not walk on the margins before they undress Communal costumes and towels must be properly washed and sterilised The dressing boxes should be well lit and ventilated, and easily cleaned and disinfected, and the lavatory accommodation should be ample The bath superintendent, who is mainly responsible for maintaining hygienic conditions, should enter in a log book the number of bathers admitted every hour, the alkalinity, clarity, and chlorine content of the water, and the essential data about the performance of the filtration and sterilising plants —And now, let us pray for a warm summer!

TUBERCULOSIS A PRESCRIBED DISEASE

REGULATIONS have been made, under the Industrial Injuries Act of 1946, to prescribe tuberculosis as an industrial disease[1] for nurses and others who contract the disease as the result of close and frequent contact with the infection in the course of their occupations. It is interesting to reflect that, as far as nurses are concerned, this course would never have been necessary if all hospitals had been as thorough as the best in their care of their nurses' health, and of the welfare of those who, in spite of precautions, acquired tuberculosis in the course of their duties The scheme came into force on March 1, and a leaflet[2] explaining its provisions clearly and fully is now being distributed by the Ministry of National Insurance Those entitled to benefit by the new regulations must, at some time since July 4, 1948, have been in close and frequent contact with some source of tuberculosis infection, either when nursing or treating medically one or more people suffering from tuberculosis, or giving ancillary service as a ward maid, laundry worker, health visitor, or home help, or as a research worker engaged in research in connection with tuberculosis, or as a pathologist, laboratory worker, or post mortem attendant dealing with tuberculous material, or in an occupation ancillary to these To benefit, the worker must be suffering from tuberculosis, not necessarily of the lungs, and the infection must be due to the nature of her or his work in one of the occupations described The benefits are the same as for accidents at work, and the leaflet tells the patient how to claim for them

It is as well that this question is finally settled While it was still possible to argue over the degree of risk to which nurses and others are exposed, there were bound to be inequalities, both in the precautions taken to protect them, and in the amount of responsibility accepted for those who acquired a tuberculous infection Now it becomes a matter of duty for all hospitals to protect their nurses as far as possible, and to do all they can to ensure their recovery and reablement

THE INDEX and title page to Vol II, 1950, which was completed with THE LANCET of December 30, is now in preparation A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W C 2 Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now

---

[1] Purification of the Water of Swimming Baths H.M. Stationery Office 1951 Pp 36 1s 6d

[1] National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment Regulations 1951

[2] Leaflet N I 60

Special Articles

CURRENT ADVANCES IN THE STUDY OF *PHYSIQUE*

PHOTOGRAMMETRIC ANTHROPOMETRY AND AN ANDROGYNY SCALE *

J M TANNER
M B Lond , M D Penna, D P M
LECTURER IN PHYSIOLOGY, ST THOMAS'S HOSPITAL MEDICAL SCHOOL, LONDON

THAT some relations between physical build and behaviour exist in both normal and psychotic people is well known and requires little comment It is obvious enough to those who do not completely deny the validity of observations made in the field, but it is obvious only in its general, more anecdotal, aspect To particularise and clarify the relations demands many life times of careful, meticulous measurement, and the exact and understanding application of scientific method

In the last 10–15 years two new and more powerful techniques for the assessment of physique have been evolved and I wish to devote the first part of this paper to reviewing the more important results achieved by their use in relation to temperament, psychosis, and neurotic behaviour The latter two parts are concerned with the work of my own laboratory, first in developing the technique of *photogrammetric anthropometry*, as the measurement of individuals by means of photography is called, and secondly in constructing a new, and as I hope more powerful, measure of *androgyny*, or the degree of femininity of build in the male

I Physique, Psychosis, and Neurosis

The two recent classifications of physique I refer to are those of Sheldon (1940), known as *somatotyping*, and the *factor analysis* classification largely developed by Burt (1947) and Burt and Banks (1947) Both are by now too well known to warrant a long description here, and the situation has not materially changed since 1947, when on a similar occasion I discussed their relationships (Tanner 1947)

PHYSIQUE AND TEMPERAMENT IN THE NORMAL

Sheldon and Stevens in 1942 described a rating scale for assessment of temperament, and three components of temperament (viscerotonia, somatotonia, and cerebrotonia), which they alleged were closely related to the three components of physique—endomorphy, mesomorphy, and ectomorphy This caused a good deal of discussion, occasionally acrimonious, perhaps largely because the relationship was described as closer than previous workers had made out, and it was described in more detail and with considerably greater force There was, after all, nothing startlingly new in the idea, Kretschmer's work in particular had accustomed the present generation to it, and before him there were very many others In the face of this discussion, however, it was of first rate importance that some other investigator should try to confirm or repudiate the finding of Sheldon and Stevens, using the same methods for classifying physique and temperament Such a study was forthcoming (Seltzer et al 1948), along with much other highly important material, from the investigators associated with the Grant study of Harvard University, which is a continuing study of a group of healthy normal students during their time at college and in their subsequent careers (Heath et al 1946) A mass of data on the personality of these persons was available from the files of the staff psychiatrists, and 260 persons were classified temperamentally as evenly balanced or predominantly viscerotonic, somatotonic, or cerebrotonic by one of the investigators, McTernan, while another, Seltzer, somatotyped them, neither had any idea of the data of the other The report deals with only one aspect of the alleged physique temperament relationship, the association of dominant cerebrotonia with dominant ectomorphy in physique There were 50 persons whose dominant component of physique was ectomorphy, 42 of these were also predominantly cerebrotonic, and a further 6 showed evenly balanced components of temperament This well marked association between ectomorphy and cerebrotonia is highly significant statistically and, so far as it goes, bears out Sheldon's contention completely It is less quantitative than his investigation, however, and obviously this field could absorb the attention of large numbers of workers for a long time From the same material important studies have been published by Seltzer on the relationship of androgyny of physique to personality and the choice of career (Seltzer 1945) and of bodily disproportions to certain traits of behaviour (Seltzer 1946)

PHYSIQUE AND PSYCHOSIS

Little has yet been published on the relation of somatotype and psychosis Undoubtedly the most important event in this field is the publication of Sheldon's third volume in the Constitution Research Project series (Sheldon 1949) He concludes that manic depressives are, by and large, ectopenes—i e, people very low in ectomorphy (the other two components both being high but in varying proportions)—paranoid schizophrenics tend to be high in mesomorphy, and hebephrenic schizophrenics relatively high in ectomorphy These findings bear out exactly those of Kretschmer for the manic depressives and hebephrenes (Kretschmer's pyknic being an ectopene *in* Sheldon's terminology)

Kallman (1948) states that among schizophrenics the prognosis varies with the somatotype, the more ectomorphic the worse the prognosis, the more mesomorphic the better the prognosis, and endomorphy is irrelevant

There have been two reports on psychotics in which the factor analysis classification was used Cohen (1940) found differences, of the expected sort, between schizophrenics and manic depressives, and Moore and Hsu (1946) published a Thurstone type factor analysis of Connolly's measurements on 100 psychotics

An excellent bibliography of the pre 1940 literature on physique and schizophrenics will be found in Betz (1942), and the brilliant monograph of Wertheimer and Hesketh (1926) still remains a classic in the field Disappointingly little has yet been done on the two perhaps most fruitful aspects of physique in schizophrenia—androgyny and dysplasia—in both of which schizophrenics seem probably to be abnormally high Perhaps this is because both are difficult to measure, particularly dysplasia There are very few somatotypers skilled enough to obtain valid ratings of dysplasia by Sheldon's method, even if their over all somatotypes are accurate We badly need a metric technique for this

PHYSIQUE AND NEUROSIS

That there is a relation between physique and type of psychosis has been clear for a long time, whether this is also true of neurosis is perhaps more debatable but evidence is accumulating in favour of the idea Excepting Sheldon's (1949) work on delinquents there seems to have been little done in the somatotype field, apart from a study by Tanner and Jones (1948) on repatriated prisoners of war Rees and Eysenck (1945) carried out a factor analysis study of Army neurotics—i e , persons who had broken down under the stress of Army existence —and Rees (1945) has reported a difference in physique between neurotics who complain primarily of effort syndrome and a group of normal Army controls The situation regarding neurosis is not at all clear Hysterics seem to be lacking in ectomorphy, and persons with chronic effort syndrome are excessively androgynous Possibly neurotics as a whole tend to be more ectomorphic, more androgynous, and more dysplastic than the rest of the population, but none of these things has been shown to be certainly true We need more refined techniques both for classifying neurotic reactions and for studying these aspects of bodily build

---

* Abridged from an address delivered to the Royal Medico Psychological Association, May, 1950

II Photogrammetric Anthropometry

Each of the two modern methods of classifying physique starts from different fundamental observations on the person Somatotyping begins with a carefully and specially posed photograph The somatotype is rated *from protracted inspection of the picture and a comparison of it with a key file of pictures of known somatotypes* Sheldon s system fundamentally rests on anthroposcopy—i e , looking at the person Admittedly he later measured his pictures and thus produced a set of tables by which he claimed it was possible to somatotype quite objectively young men between the ages of 16 and 20 in a normal stage of nutrition and health (with the exception of an occasional tie between two somatotypes) Though ten years have elapsed since the publication of these tables there has been not a single report, so far as I know, of any attempt by other laboratories to use this anthropometric technique Perhaps this is because the technique is certainly arduous and time consuming , but it may also be that investigators have met unexpected difficulties Certainly we have , for several years in my laboratory we have been trying to use this metric technique and we have encountered considerable trouble

First, Sheldon gives insufficient details of the photographic technique he adopted for it to be repeated exactly A cardinal point is the exact distance of the camera from the person, and even more so the exact distance of the person's heels from the centre of rotation of the turn table on which he stands, since on rotation from front to back view he comes closer to the camera by an amount depending on this distance This is important because a measurement on the picture depends not only on the corresponding measurement of the man himself, but also on how close to the camera the particular dimension measured is This is called the parallax error , all dimensions have to be reduced to a standard camera centre of rotation of turn table distance

Personal communication dispelled these difficulties, but we then found others For example, the tables do not give unequivocal regional somatotypes when used objectively without a preliminary scopic estimate , thus, in the abdomen the regional somatotypes 263, 353, 433, 443, and 444 all have the same measurements , one cannot distinguish between them Also we consistently get lower readings for ankle diameters than the tables lead one to expect , either British students have slenderer ankles—though not wrists—than American students, or else some snag of turn table distances or, possibly, camera lens errors (the commonest of which tend to be of a type that spreads the image at the north and south poles) may be involved

I say all this not in criticism of somatotyping, which I believe to be the greatest single advance yet made in the study of human physique, but to indicate that in

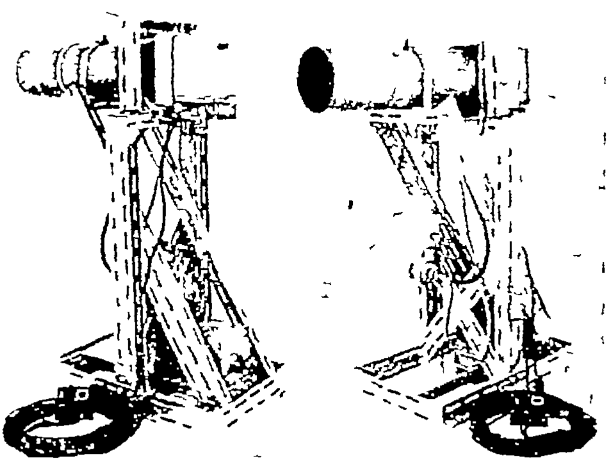


Fig 1—Aerial mapping camera adapted for photogrammetric anthropometry the camera is detachable from the stand and both are very easily portable.

Sheldon's *system measurement is a secondary considera*tion He has now made this very clear himself (Sheldon 1949)

For factor analysis, on the contrary, it is measurement that is all important Using, as a rule, the classical measurements of the physical anthropologist, the factorer can—indeed must—approach the classification of a person carefully blindfolded This, to my mind, is not very satisfactory Factor analysis has its own subjectivities, just as somatotyping has , they reside in the initial choice of measurements for use in the battery, and in the choice of the factor technique of rotation and so forth used after the measurements are intercorrelated Above all, one has the difficulty of reconstructing any kind of mental image of the subject from a set of, say, a dozen factor estimates This is an old difficulty well known to all physical anthropologists who have interested themselves in constitutional research , one has a mass of measurements on a man, but what on earth did he look like ? To answer some questions one may not need to know this, but to answer others and, above all, to think of new questions to ask, an image of the man is a very great help

It was thus perfectly obvious that what was needed was a combination of the two techniques, and it required only a tidying up of Sheldon's photographic technique to secure it The method known as *photogrammetric*

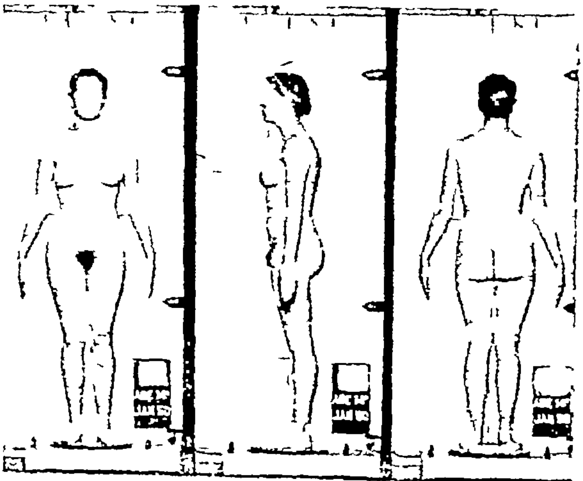


Fig 2—An almost perfectly posed picture. Note the metre and half metre markers in the plane of rotation of the turn-table.

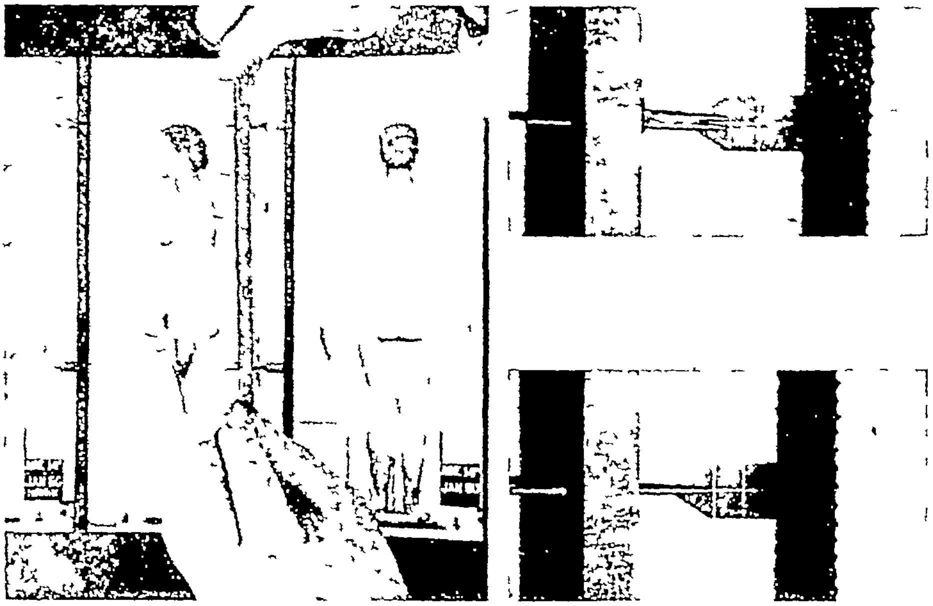


Fig 3—Testing the enlargement for accuracy The right hand picture shows enlargements of the pointers seen in the left hand picture

anthropometry involves taking pictures which not only meet all the requirements for somatotyping but also allow large numbers of measurements to be taken from the photographic image simply and expeditiously An associated desideratum was that large numbers of people should be handled in a short time, since a good deal of this type of work involves surveys where the persons' time for attendance is limited by industrial or educational considerations

The details of the technique have been discussed elsewhere (Tanner 1949a, Tanner and Weiner 1949, Dupertuis and Tanner 1950), we use a 10 metre distance from camera to centre of turn table, which reduces the parallax error to under 1% even in extreme cases, and a 10 cm heel centre of turn-table distance At first we used a 'Leica' camera with the 'Hektor' 13 5 cm lens, but we soon found that the only practicable way of getting accurate measurements was off fairly big enlargements, and those from the Leica had too much grain At the independent suggestion of Mr N M Richards, of the photographic and reproductions branch of the Air Ministry, and Dr Brian Stanford, we changed to the F or K 24 aerial mapping camera, which we have found far more satisfactory

The camera, fitted with a 20 in focal length lens, is illustrated in fig 1 It holds 50 ft of $5^1/_2$ in wide film and usually takes 5 in × 5 in square pictures, but we alter it to wind on only a half or a third of this amount, so that we can get front, side, and back photographs of up to 50 people before changing the magazine, which in any case takes only a minute Enlargements are made from these negatives to exact scale, as indicated by two sets of white crosses on the black pointers seen in fig 2—one 1 0 metre apart vertically the other 0 5 metre apart horizontally—which are brought up on the enlargement to 120 cm and 60 cm respectively, our allowable limits on the former being 119 6 to 120 4 cm and on the latter 59 8 and 60 2 cm, inclusive

The testing procedure is seen in fig 3 Waterproof base paper must be used, which does not shrink like ordinary material The pointers are fixed permanently to the turn-table in the vertical plane of its centre of rotation, so that no error in placing them can arise The background behind the person is illuminated fairly strongly to obviate all shadow, and a grid of horizontal and vertical wires, spaced as shown in fig 2, is put about 0 5 metre behind the turn table centre, we find it very useful when taking horizontal and vertical measurements and as a background for studies of growth in children The best lighting is by condenser discharge flash, using either a single central source, or, rather better, two sources angled at about 30° on either side of the person Everything is made automatic in these cameras, so that one merely presses a button and the light is flashed, the picture taken, and the film wound on ready for the next exposure.

The measurements, which are largely those of Sheldon, we take from the enlargements at the rate of 40-60 an hour by special pointed proportionately magnifying callipers (fig 4), the scale reads directly in 0 1 mm and is × 5, so that 0 1 mm on the print is 0 5 mm on the scale The reliability of

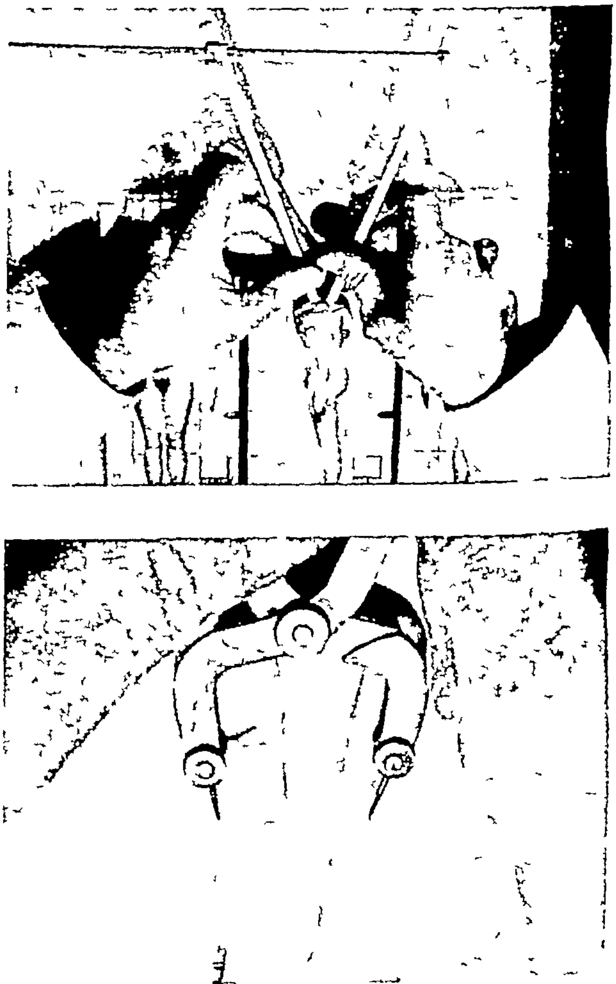


Fig 4—Measuring the photographs. The callipers give a × 5 enlargement.

this whole procedure has been extensively investigated (Tanner and Weiner 1949) and found to be as good as, or in some dimensions perhaps a trifle better than, that of the classical antropometric measurements By far the largest error comes in the exact posing of the person, and for this reason Dupertuis and Tanner (1950) have given a detailed description of a pose (fig 2) which we hope will be adopted as standard for all somatotyping and photogrammetric anthropometry

We do not eliminate from our routine all the classical measurements just because we want also a photograph and a lot of additional information the classical techniques cannot give us We routinely take stature, sitting height, weight, biacromial diameter, bicondylar diameters of humerus and femur, four subcutaneous tissue measurements, and others as circumstances dictate With two investigators and a recorder in the measuring team, the person's time of attendance is 5–10 minutes

Much valuable material could be collected by interested doctors who are not and do not intend to become expert somatotypers or physical anthropologists. Particularly in hospitals the labour involved would be small in relation to the knowledge resulting there from The technique described here was specifically evolved to meet such needs, once the camera and turn table have been placed in position, all is automatic Commercial firms will process and enlarge the pictures, and research-workers are eager and willing to help with somatotyping and measuring, if the investigator does not wish to do it himself All that the photographer need do is spend a day learning carefully how to pose his subjects—this is a necessary qualification If many outpatient departments and mental hospitals collaborated in such an enterprise, we would soon have a considerable body of knowledge on the physiques of patients with various diseases If the reader thinks this would be time wasted, let him look at the distribution of somatotypes of cancer patients (Sheldon 1949)

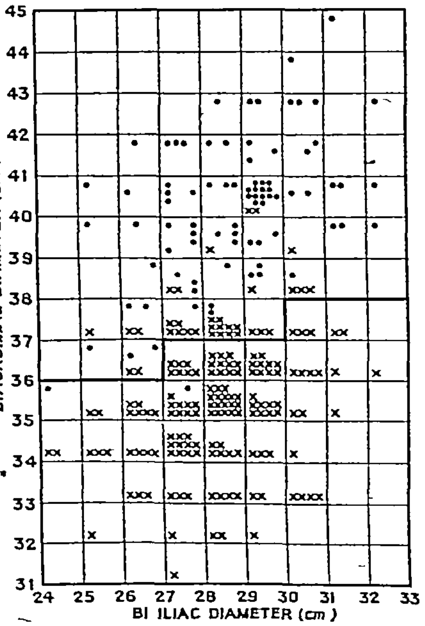


Fig 5—Discrimination of male and female students by hip and shoulder breadths: circles males crosses females; equation of heavy line $3 \text{ biacromial} - \text{bi iliac} - 82 = 0$.

III Discriminant Function Scale for Androgyny

For a long time physical anthropologists have used the ratio bi iliac diameter/biacromial diameter as a rough measure of androgyny, on the grounds that these are the two measurements which, relatively speaking, differentiate most the two sexes Granted the premises, however, it by no means follows that this ratio is the best method of combining the two measurements, in fact, it is certainly not so There is a statistical method available for finding the best combination, which is called a *discriminant function,* since it provides the best possible discrimination between males and females for any particular combination of measurements The discriminant function is a line—and in the case of the present data a straight line—which separates the sexes so that those individuals who are one side of it are males, those the other side females The line may not completely separate the sexes if the original measurements overlap in their distributions, but it separates them better than any other combination of the measurements would, that is, it misclassifies the minimum number of people Fig 5 shows the line which best separates a group of male and female Oxford students according to their biacromial and bi iliac diameters I am indebted to Dr R W Parnell for the data on which this figure was constructed, which comes from a study we are making together on students at the Institute of Social Medicine at Oxford It can be seen that a fair degree of separation has been achieved

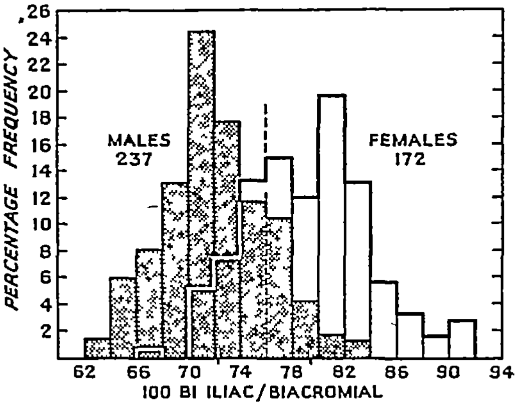


Fig 6—Distribution of bi iliac/biacromial ratio for male and female students Interrupted vertical line is line of separation; misclassification totals 21 %

This is a considerably better separation than that obtained by the use of the 100 bi iliac/biacromial ratio. The figure for the ratio which best separates the sexes in this group is 76, and this leaves 42 out of 237 males (18%) the wrong side and 46 out of 172 (27%) females, a total misclassified of 88 This is illustrated in fig 6.

The best straight line discriminant is approximately $3 \text{ biacromial} - \text{bi iliac} - 82 = 0$, and this misclassifies only 14 out of 237 (6%) males and 34 out of 172 (20%) females, a total of 48

This search for a metric distinction between males and females by a discriminating function may seem somewhat pointless, and peculiarly suited to the academic mind; the practical man tends to use other, to him more familiar, methods I would agree, were it not possible, perhaps,

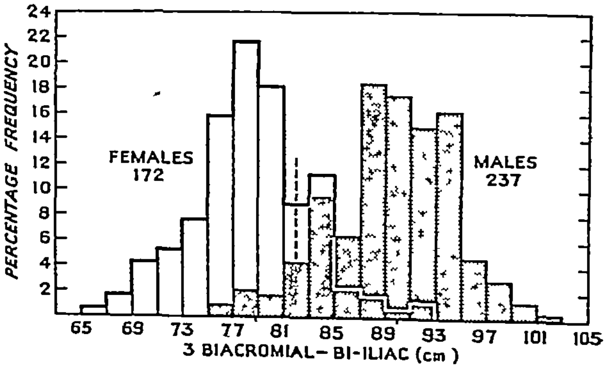


Fig 7—Distribution of androgyny score for male and female students: interrupted vertical line is discriminant line; misclassification totals 12%

to use this function as a basis for an androgyny scale It seems reasonable to suppose that the best measure of androgyny which uses these two measurements would be given by a person's distance away from the discriminating line, which would be simply his score on the equation *3 biacromial – bi iliac* diameter (the 82 being immaterial in this regard) The distribution of these scores for males and females with the discriminating line between is shown in fig 7, the means and standard deviations for males and females are 90 1 and 4 73, and 78 9 and 4 57 respectively It will be seen how much less overlap there is between the two distributions than in fig 6 The argument seems to be if a given person's score is 82—i e, falls on the dotted line—we cannot say at all whether the person is male or female If, however, the score is 95, the probability of the person's being a male is high, and if 75, relatively low A glance at the genitalia would tell us, but the point is that we are classifying as though the genitalia did not exist, or as though the genitalia were themselves misclassifying the individual, because what we are after is the degree of femininity of a male irrespective of the type of genitalia The last part of the argument is that, as the probability of being a biacromial bi iliac female increases in persons whose genitalia allege maleness, the degree of androgyny as we understand the word increases This last phrase contains an operational definition of androgyny, and, unless one granted that the method of measuring androgyny defines the concept, the argument stated above would, I think, be hard to sustain There is no doubt that this scale and the anthroposcopic estimate of androgyny or, as Sheldon calls it, gynandromorphy measure the same feature in human build, but it seems likely that the nature of the two scales will not be entirely similar On the discriminant function scale the distribution of males and females is approximately Gaussian, whereas on Sheldon's scale it is rather heavily skewed Possibly the discriminant has the biometrical advantage here, but I would hesitate to claim a biological one also Whatever the validity of the main argument, however, the discriminant androgyny score is a better scale than the bi iliac/biacromial ratio, which uses the same argument and is both biased and inefficient into the bargain

We could increase the efficiency of our discriminant function by including more measurements, at the same time bringing it to measure with more validity what the rater can so obviously see If leg length, in the form of subischial length (stature minus sitting height) is added, the best discriminatory straight line is then approximately

$$2\ \text{biacromial} + 0\ 53\ \text{subischial} - 1\ 25\ \text{bi iliac} - 81 = 0,$$

and it does improve our discrimination considerably Now only 10 men and 24 women remain misclassified, a total of 34 as opposed to 48 using biacromial and bi iliac only and 88 using the bi iliac/biacromial ratio The mean figures on this better androgyny scale (ignoring the constant 81) are 87 9 for men and 76 8 for women, with standard deviations of 4 07 and 3 95 respectively The best way to improve the scale further would undoubtedly be to use photogrammetric dimensions, because the next best discriminating part of the body is the pattern seen between the legs when the heels are together, or a fixed distance apart, and this is only easily measurable on the photograph However, we have not yet got enough photogrammetric pictures of women to complete such a study

The use of the scale may be illustrated by a single example Rees (1945), who measured 200 patients with effort syndrome and 100 normal soldiers as controls, concluded that patients with effort syndrome were more linear or leptosomic than the controls His data, however, make this conclusion somewhat questionable, he did not use a regular regression equation such as that of Burt and Banks (1947) for the estimate of leptosomic factor, but an index 100 stature/6 transverse chest diameter I have indicated at length elsewhere (Tanner 1949b) the sort of difficulties in which ratios like this sometimes involve one, I think they should be dropped from the anthropologist's armamentarium Though I cannot tell whether or not any of these difficulties arise in the present case, Burt's regression score for leptosomic factor does not differ significantly for Rees's two groups So the question of a difference in linearity had perhaps better be held sub judice for a while What is far more striking in Rees's data, however, are the large hips, narrow shoulders, and short legs of the patients with effort syndrome—the main indication seems to be of a difference in androgyny On the *3 biacromial – bi iliac* scale the 100 controls have a mean value of 89 8, which is indistinguishable from the mean for the 237 Oxford students, 90 1 The mean for 100 of Rees's patients with effort syndrome is, however, 84 1, and the difference of 5 7 units from the controls is undoubtedly very highly significant statistically, assuming any reasonable figure for the standard deviation of the patients with effort syndrome Indeed, fig 7 shows that only 15% of Oxford students are as androgynous as this mean figure for the patients with effort syndrome, and the difference between controls' and patients' means in relation to the standard error is almost certainly considerably higher than any one derived from Rees's single measurement or index comparisons The conception that these patients with effort syndrome were more androgynous than the normals also makes sense physiologically It is known that the higher the androgyny the worse is the exercise tolerance in normal men, both trained and untrained (Seltzer and Brouha 1943), and that women have a higher blood lactate level after a standard exercise than have men (Metheny et al 1942) Patients with chronic effort syndrome have been shown by Jones and Scarisbrick (1946) to resemble androgynous men in these physiological ways, having low effort tolerances and a high blood lactate level after standard exercise, their blood lactate level, indeed, lies somewhere between that of normal men and that of normal women

It remains to be seen finally, whether this androgyny scale will remain useful in relation to physiological investigations of physique and of the growth of children For it is from these directions that I believe the next major advances in the study of physique will come

Summary

Recent work relating physique and temperament in healthy young men, physique and type of psychosis in psychotics, and physique and types of neurosis is discussed briefly

The technique of measuring people photographically known as photogrammetric anthropometry is described

A new scale for measuring androgyny, or femininity of build in the male and masculinity of build in the female, is described It is founded on the use of a discriminant function obtained from measurements on male and female Oxford students, and the androgyny score is 3 biacromial diameter – bi iliac diameter when only these two measurements are used A better score is obtained using leg length in addition The discriminant line separates males and females much better than does the bi iliac/biacromial ratio, and an example of the use of the scale in medical work is given, showing patients with effort syndrome to be more androgynous than normal controls

Besides my debt to Dr Parnell for the measurements of Oxford students, I wish to acknowledge the continuous support

and encouragement of Prof Henry Barcroft, and the skilled and indispensable assistance of Mr R H Whitehouse, to whom I owe many points of technique I wish to acknowledge also the William Hyde Award of the Research Board for the Correlation of Medical Science and Physical Education, which helped defray expenses

REFERENCES

Betz, B J (1942) *Hum Biol* 14 21 192
Burt C (1947) *Psychometrika* 12 171
— Banks C (1947) *Ann Eugen* 13 238
Cohen J I (1940) *J ment Sci* 86 602
Dupertuis C W Tanner J M. (1950) *Amer J phys Anthrop* n.s 8 27
Heath C W Brouha, L Gregory L W Seltzer C C Wells F L Woods W L (1946) What People Are Cambridge Mass
Jones M. Scarisbrick R (1946) *Psychosom Med* 8 188
Kallman F J (1948) *J Hered.* 39 339
Metheny E Brouha L Johnson R. E, Forbes W H (1942) *Amer J Physiol* 137 318
Moore T V Hsu E H (1946) *Hum Biol* 18 133
Rees W L (1945) *J ment. Sci* 91 89
— Eysenck H J (1945) *Ibid* p 8
Seltzer C C (1945) *Amer J phys Anthrop* n.s 3 33
— (1946) *Psychosom Med* 8 75
— Brouha L (1943) *Amer J phys Anthrop* n.s 1 95
— Wells F L McTernan E B (1948) *J Personality* 16 431
Sheldon W H (1949) The Varieties of Delinquent Youth New York
— Stevens S S (1942) The Varieties of Temperament. New York.
— — Tucker W B (1940) The Varieties of Human Physique New York
Tanner J M. (1947) *Proc R Soc Med* 40 301
— (1949a) *Lancet* i 405
— (1949b) *J appl Physiol* 2 1
— Jones M. (1948) *J Neurol Neurosurg Psychiat* 11 61
— Weiner J S (1949) *Amer J phys Anthrop* n s 7, 145
Wertheimer F I Hesketh F E (1926) *Medicine Baltimore* 5 375

GENERAL MEDICAL COUNCIL

FEB 27 TO MARCH 2

THE General Medical Council held an extra session last week, when the new Medical Disciplinary Committee also met for the first time

Five new members were introduced to Prof David Campbell, the president, and took their seats Dr H Seaward Morley, Miss Florence Horsbrugh, C.B E, M P, and Mr J B Hynd, M.P, are Privy Council nominees, and Prof J H Biggart, C B E, and Prof. A P Thomson represent respectively the Queen's University, Belfast, and the University of Birmingham Miss Horsbrugh, who is an honorary fellow of the Royal College of Surgeons of Edinburgh, is the second woman to take her seat on the council.

DISCIPLINARY CASES

Frederic Syson registered as of 52, Station Road Horsforth, Leeds, M B Glasg (1925) appeared on a charge of having been convicted at Leeds in May, 1950, of incurring a debt of £3 15*s* so obtaining credit by fraud In May, 1949 the council had postponed judgment for one year after they had found him to have been convicted of two charges of drunkenness and two of embezzling in 1945 Dr Syson stated that at the time of the offence he had been in poor health and had taken phenobarbitone He now knew he had a chronic renal condition which interrupted elimination of the drug He was not aware of the offence until he was informed of it after he had been admitted to hospital The President announced that the council found the conviction proved, but to give Dr Syson further opportunity of regaining his position they had postponed judgment until their first session in 1952

Roger St Aubyn, registered as of 18, Redcliffe Square London, S.W 10 M.R C S (1946), was charged with having been convicted at West London magistrates court on June 16 1949, of driving a car while under the influence of drink, and of having been convicted of a similar offence on Sept 21, 1950 The council found the convictions proved but postponed judgment until their first session in 1952

The council directed the Registrar to remove from the Register the name of *Nigel Harold Maurice Russell Monro*, registered as of 442, Nell Gwynn House, Sloane Avenue, London, S W 3, M.R.C S (1936), who had been convicted on Jan 18, 1951, of two charges of procuring morphine when he was not authorised to do so

The President announced that the Registrar had been directed to erase from the Register the name of *Michal Mateusz Torpor Matuszewski*, M.B Polish School of Medicine (1949), provisionally registered, under the Medical Practitioners and Pharmacists Act, 1947, as of 40, Marchmont Crescent, Edinburgh, 9 The case was held in camera

Ram Kissoon Nandlal, registered as of 75, Green Lane, Small Heath, Birmingham L.M S.S.A (1930) appeared before the council charged with having committed adultery with a married woman patient The complainant was the woman's husband, who was represented by Mr E G A Beresford, instructed by Mr T S Walker, solicitor Dr Nandlal, who was represented by Mr Norman Richards, instructed by Messrs Le Brasseur and Oakley on behalf of the Medical Protection Society, denied the allegation After a hearing lasting three days, the council found the facts alleged against him proved to their satisfaction The Registrar was directed to erase his name from the Register

COMMITTEES

At the end of this case, the president said that this was the last penal case which the whole council would hear The council took their first penal case in the Royal College of Surgeons of England on August 11, 1859 "The end of the case of Nandlal," remarked Professor Campbell, "is the end of an era"

The council appointed the first Medical Disciplinary Committee, which held its first meeting in camera at the end of the session It did not consider any cases Because of the impending election the first committee will hold office only until April 28, 1951 The following were appointed

The president, ex officio *England and Wales* Prof R J Brocklehurst D M, Dr J A Brown, Dr O C Carter Sir Henry Cohen, F R C.P, Dr Guy Dain, Prof R B Green, F.R.C S Dr E A. Gregg, Dr J P Hedley, Lord Nathan, and Mr N E Waterfield, F.R C.S *Scotland* Dr R W Craig, Sir Andrew Davidson, M.D, Miss Florence Horsbrugh, M.P, Sir Sydney Smith, M.D Sir Henry Wade F R C S.E *Ireland* Dr James Boyd, Dr Frank Kane, Mr R A Stoney, F R C.S.E

The council approved alterations in the standing orders to give effect to its previous decision to abolish the public health, examination, and education committees

---

'. . . the immigration authorities regard successful migrants brought into this country from overseas as being equal to an asset to the country of £10 000 per head Judged by this basis for calculation it will be seen that the equivalent loss to the State as a result of deaths from causes which could and should be prevented will reach colossal proportions—for example road deaths alone in Australia account for a loss of 6400 multiplied by £10 000 or the equivalent of £64,000,000 for the five year period, or approximately £13,000 000 per annum In our own State measures to cope with this problem, serious as it is, have surely been started at the wrong end It is entirely the wrong approach when the Government through the Hospitals and Charities Commission has planned to build large accident blocks at two of the largest general hospitals in the city to cope with the increasing number of people injured in road accidents As I have often mentioned, almost all these casualties are preventible, and the enormous outlay for such hospital buildings and the staff to service them—even if available—could be very much better devoted to providing extra accommodation and nurses for the urgently sick, for whom at the present time the chances of obtaining a hospital bed at short notice are very remote . . .'—Dr ROBERT SOUTHBY, *Med J Aust* Feb 17, 1951, p. 245

Before Our Time

THE LANCET'S ANALYTICAL SANITARY COMMISSION OF 1851 AND ITS EFFECTS

LAURENCE DOPSON

ON May 23, 1850, Sir Charles Wood, the Chancellor of the Exchequer, stated in the House of Commons that neither by chemical nor by any other means could it be ascertained with accuracy whether a mixture contained chicory or not The cautious Civil Servant and the answers he drafts for his Minister change little down the years But this negative statement had memorable consequences, for Dr A H Hassall took up the parliamentary challenge and soon afterwards read to the Botanical Society of London a paper on the Adulteration of Coffee, which was widely reported in the daily press He followed it by a second paper on the detection, through the microscope, of impurities in sugar Hassall was already known to Thomas Wakley, the editor of *The Lancet*, for in 1850 he had described in *The Lancet* a microscopical examination of London water Wakley now arranged that Hassall should prepare a series of articles setting out the results of the analysis of samples of foods, beverages, and drugs bought at shops in and around London

Wakley had for many years contemplated running such a series, for in the days when he was an apprentice to an apothecary at Taunton he had seen something of the nefarious practices used in the adulteration of drugs At his suggestion the articles appeared under the title of Reports of the Lancet Analytical Sanitary Commission As editor of *The Lancet* he undertook to bear all the expenses and legal responsibility

DR. HASSALL

Crayon portrait drawn by J N Harland in 1853 (From the *Analyst*, 1929, **54**, 567)

AIMS OF THE COMMISSION

The forthcoming publication of the reports was announced in *The Lancet* in 1850, and the first report appeared by the first issue of 1851

In his introductory editorial Wakley showed his skill as a journalist by linking the inquiry with the 1851 exhibition

> "During the presence of the concourse drawn to the metropolis by the Great Exhibition of the Industry of All Nations, the temptation to adulterate articles of food and drink will be immense Against this evil our ANALYTICAL SANITARY COMMISSION will, we flatter ourselves, prove a powerful bar We enter upon the task, then, at an auspicious time, and though unaided, except in the support of the profession, we are determined to execute our self imposed labour for the protection of the public, the advantage of the fair trader, and the ultimate exposure and punishment of the fraudulent one That the duty shall be performed with the most strict and undeviating impartiality, we hope it is unnecessary to offer any pledge"

The editorial also contained this warning

> "Let not any tradesman, mechanic, or manufacturer, imagine for a moment that he can defeat our vigilance We bring the microscope and the test tube—those simple but mighty instruments of modern investigation—to bear with unerring truth upon things hidden and secret enough from the observation of the unaided senses A single glance of the practical microscopist, a single touch of the expert chemist, and the most intricate mystifications stand confessed and marked "[1]

Up to this time, Wakley held, the "mighty instruments of modern investigation" had not been used to defeat the adulteration of food Prout, Liebig, Dundas, and Thomson, he declared, "have devoted the aids and appliances of modern chemistry with the utmost success to the analyses of the ultimate elements of the solids and fluids which nourish the living body, but little or nothing has been done, or even attempted, in the systematic detection of adulterations of these great and universal agencies of health and diseases" In his enthusiasm for his new series Wakley was perhaps being unfair, for some writers had drawn attention to the subject—notably Friedrich Christian Accum who published in 1820,[2] *A Treatise on adulterations of food, And methods of detecting them* This had a dramatic woodcut on the title page showing a skull appearing out of the top of a stewing cauldron on which is written "There is DEATH in the Pot"[3] A second, enlarged edition of the book appeared the same year, in which Accum stated that the first printing of 1000 copies had sold within a month—an indication of the public interest The first section of the book dealt with the adulterations of drugs and medicines, and methods of detecting them, and there was a section on Frauds Practised in the Coal Trade

THE COMMISSION IN ACTION

The motto "Forewarned, forearmed" was printed at the head of every *Lancet* report as it appeared and in each the working principles laid down in the introduction were followed

> First, the reports were to contain the results of actual observation and experiment "we shall borrow but little from the writings of others"
>
> Secondly they were to be illustrated by "faithful engravings"
>
> "A third and highly important feature will be the *publication* of the *names* and *addresses* of the parties from whom the different articles, the analyses of which will be detailed, were purchased "
>
> This publication would not begin for three months, so that retailers and their suppliers would have time to put their house in order, meanwhile only the name of the street or the place would be published

Later Hassall described the care taken over the purchases

> "Two persons in whom confidence could be reposed, were sent out to purchase the articles Immediately on each purchase the name and address of the party was placed on the wrapper containing the article bought, with the date and the initials of the person purchasing I nearly always accompanied the purchasers of the articles, and saw that there could be no mistake or error committed "[4]

The main examinations were microscopical, and it is stated by Filby[5] that Hassall was "aided by several students who were keen microscopists, as well as artists," who produced the illustrations Where chemical analyses were required, Hassall was assisted by Dr Henry Letheby then lecturer in chemistry at the London Hospital Medical College A chemical laboratory was installed at the top of *The Lancet* offices, and investigations were made on the spot The scheme upon which the examinations were made was due to the joint invention of Wakley, Sir William O'Shaughnessy, who had published an article on Poisonous Confectionery in *The Lancet* in 1831, and Hassall. All the reports were written by Hassall, ' subject only to the first approval and revision of Mr Wakley "

---

[1] *Lancet*, 1851 i 18

[2] Accum F C A Treatise on Adulterations of Food and Culinary Poisons exhibiting sophistications of bread beer wine, spirituous liquors tea coffee cream and other articles employed in domestic economy And methods of detecting them London 1820 Accum was born at Bückeburg Westphalia in 1769 He came to London in 1793, and published a number of books in English on chemical subjects Later he left England and became professor of the Technical Institute Berlin His book on food adulteration was translated into German in 1822 Accum died in Berlin in 1838

[3] *2 Kings*, IV 40

[4] Hassall, A H First report from the Select Committee on the Adulteration of Food 1855

[5] Filby F A A History of Food Adulteration and Analysis London 1934

The introduction to the first report of the Lancet Sanitary Analytical Commission pointed the contrast of the fact that "the urchin who filches a bun, a penny-piece, or the value of one, breaks the law, and is liable to punishment and even imprisonment" Nor was adulteration merely a matter of honesty The physician, having prescribed a carefully planned diet, too often found his well grounded hopes frustrated, because the patient did not in fact obtain the food prescribed. "In one case he orders arrowroot and isinglass—the first is very commonly adulterated with potato, or some other farina, whilst for the second is substituted some ill-prepared form of gelatine." The doctor ordered strong coffee or strong tea, to counteract the effect of some narcotic *poison*. "The one is adulterated with a large quantity of chicory, and the other consists of exhausted tea leaves redried "

THE FIRST REPORT

Coffee and its Adulterations, the subject of Hassall's original paper, was chosen for the first investigation. Hassall pointed out that adulteration was indeed to be inferred from the fact that, while the consumption of other commodities had increased with the rise in numbers of the population, that of coffee had not, "although, as is well known, the use of a commodity, under the name of coffee, is now much greater than formerly, especially amongst the members of the different temperance and total abstinence societies." Secondly, more "coffee" was sold than passed through the Customs. Thirdly, ' chicory is cultivated in large quantities in various parts of this country, and it is even rumoured that *a minister of the Crown* is himself a large grower of this plant " Little or no chicory was retained as such, and it was in fact found that most of the samples were adulterated with chicory Other substances used were roasted corn, beans, potato, burnt sugar, and a combination of all four Unadulterated coffee was obtained from a shop in Oxford Street and another in Gracechurch Street, which were named, at 1*s* 4*d* per lb and 2*s* per lb respectively The report gave the following "Hints to Coffee Drinkers"—*buy the beans*, and never purchase coffee in a container, ' for he may be assured that it is even more adulterated than other coffee."

A GOOD PRESS

The reports obtained wide publicity in the lay press From the start the *Times* supported *The Lancet* in its campaign. The editor of the 'Lancet' is entitled to the thanks of the profession and the public for his noble and patriotic scheme,' wrote the *Manchester Guardian* Support came too from the *Commercial Daily List* the *Illustrated London News* and the *Lady's Newspaper* *Punch* wrote

> ' Our contemporary the Lancet has conferred a great boon on the public by establishing a new order of constabulary which may be called the Scientific Detective Police If any of the knaves thus pilloried in the Lancet, abetted by a disreputable attorney and dishonest barrister, endeavour to avenge themselves through the technicalities of the law Punch hopes they will meet with twelve true men in the jury box who will scout both them and their legal accomplices out of court '

Without support from the popular press *The Lancet* could not have reached such a wide circle of readers and influenced public opinion as surely as it did The pages of the *Family Herald*[7] shows the impression made by the commission

> ' In consequence of the recent exposures in the Lancet the grocers are in a state of perturbation, and have divided themselves into an *anti*-chicory and a *pro* chicory party
>
> The journal also took up *The Lancet's* argument, and employing the reductio ad absurdum principle asked
>
> If we are doomed to suffer adulteration, let us have no monopoly of it. . If it is right to adulterate coffee, why wrong to adulterate the silver spoon with which we sip it '

A correspondent from Bristol wrote that almost immediately after the number of *The Lancet* containing a report on canister coffee reached the city, ' one of the most dashing establishments here suddenly withdrew their canistered coffees from the windows, and substituted bags of roasted, unground. '

The second report on coffee,[8] stated " It appears, that while the prevalence of the adulteration of coffee with *chicory has not undergone any diminution, that* with roasted corn, beans, &c has This satisfactory result we believe to be mainly attributable to the exposures which we have made, and which have done more to check the adulteration of food than has the whole very costly machinery employed for that purpose by the Excise authorities "

Letters to the editor also showed how widespread was the effect of the reports A grocer wrote giving his name and saying that immediately he read the report and realised that adulterated coffee had been bought in his shop, he got in touch with his suppliers, who took the consignment back, explaining that they had not known of the adulteration either, as they were only importers. The grocer was complimented, and others were advised to follow his example A discordant note was sometimes struck, and in the "replies to correspondence" appeared the defiant entry "One who does not Fear the Analytical Commission. We only laugh at such threats . "

The story of the commission's work spread abroad, and later in the same year *The Lancet* quoted a report in the *Ceylon Overland Observer* that a public meeting at Kandy had passed a vote of thanks to "the valuable and unremitting efforts of their friends at home, and especially the talented editor of *The Lancet*, in exposing the numerous and abominable adulterations of coffee and chicory '

FURTHER WORK OF THE COMMISSION

The Analytical Sanitary Commission was concerned not only with sophistication, but with all types of impurities Thus an early report gave truly frightening pictures of the types of organisms drunk by Londoners with their water The first description of the meal mite appeared in the report on bread, this same report also described the development of the yeast fungus The fourth report of the Analytical Sanitary Commission was on pepper This was found to be less adulterated than formerly, because it had been supervised by the Excise authorities. This finding Wakley held to be convincing proof that adulteration could be prevented by inspection, and he made short work of arguments which the Civil Service put up in opposition to the idea. Other reports dealt with sugar and arrowroot

At the end of the three months—in April, 1851—the names of shops where the samples were bought were published Protests there were, of course, though perhaps not so many as might be expected. *The Lancet* published all the replies, but stuck to the validity of its findings. It is perhaps remarkable that there was not a single prosecution against *The Lancet* in this campaign But the following excerpt from the evidence given before the Select Committee on the Adulteration of Food suggests why many traders who would have liked to take proceedings thought better of it

---

[6] *Punch* 1851 20 16

[7] *Family Herald*, 1851, April 15

[8] *Lancet* 1851, I, 465

VISCOUNT GOODRICH You said that in the case of these persons who brought matter to you to analyse, with a view to proceedings against the Lancet, you were obliged to inform them that the articles were adulterated ?

Prof J QUECKETT Yes

Throughout 1851 and subsequently the reports appeared relentlessly In a parliamentary inquiry into the quality of provisions for the troops at the Crimea mention was made of their revelations, and Lord Tennyson wrote

> Chalk and alum and plaster are sold to the poor for bread
> And the spirit of murder works in the very means of life

Poisonous coloured confectionery was dealt with in articles which appeared in 1854 (At least the names of the sweets sound pleasantly nostalgic—especially "rasher of bacon," "mutton chop on plate," and "oyster fish") But even after *The Lancet* Commission had achieved the passing of an Act of Parliament to control the manufacturer of poisoned sweets, Charles Kingsley was saying in *The Water Babies* "Dr Letheby and Dr Hassall cannot catch them, though they are setting traps for them all day long"

The last of the first series of reports appeared on Dec 23, 1854 [9] In 1855 Hassall undertook the responsibility of republishing all the reports in a single volume [10]

THE PROVINCES JOIN IN

All the reports which had appeared in *The Lancet* up to this time dealt with food bought in London It was, however, in the provinces that the question of the reform which was shown to be needed was first taken up, and in 1854 *The Lancet* carried this significant report "A new local official—viz, a public analyzer, charged with the examination and suppression of adulterations in all articles of consumption, has been appointed by the Town Council of Birmingham" [11]

Mr John Postgate, surgeon and lecturer in anatomy at Sydenham College, Birmingham, led a campaign for national action He had begun work at the age of 11 as a grocer's boy, and so, like Wakley, had early learnt at first hand the facts of adulteration Also he had had a patient who developed purging and vomiting after drinking adulterated coffee In *The Lancet* of 1854 a letter signed jointly by him and Dr A H Browne of Wolverhampton appealed for support from fellow practitioners It further stated that "acting in concert with the movement thus commenced, Mr Scholefield, M P, has already given notice of his intention, early in the next session, to bring the matter before the House of Commons" [12] This led to the establishment of a Select Committee which, under the chairmanship of Mr Scholefield, heard evidence on the question

"Towards the end of the summer of 1855," runs the preface to *Is Killing Murder ?*, one of the books which later gave in popular form the evidence before this committee, 'while the good people of England were anxiously awaiting the news of the fall of Sebastopol from the *feu d enfer* of the allied armies, they were themselves bombarded from a room in the House of Commons, where a Committee of members was sitting daily, examining witnesses and investigating evidence as to the truth of the allegations set afloat by the eminent members of *The Lancet* Commission, that the three kingdoms were emeshed in a network of secret poisonings and covert frauds, less tangible, but of deeper dye, than those of the poisoner Palmer, because not only were they more difficult of detection, but, when detected, not amenable to the law of the land Killing was found to be going on, but could not be recognised as murder by law [13]

Wakley, Hassall, Letheby, Dr A Normandy, and Sir John Simon were among those who appeared before this committee, which continued its sittings in 1855 The testimony of Mr Thomas Blackwell, of Crosse & Blackwell, showed how *The Lancet's* work had brought reform He said that his company abandoned the use of copper to colour preserved vegetables "after the articles which appeared in *The Lancet*" At first this prejudiced the sale of his wares, but later favoured it, as the public became educated to the dangers of copper

In 1857 *The Lancet* Commission extended its investigations to the provinces, adulteration was commoner in the provincial cities than in the villages but less common than in London By 1858 the incidence of food adulteration was scarcely 10% of that revealed in the original investigations

It was not until 1860 that the first legislation arising out of *The Lancet's* campaign was passed The Act for Preventing the Adulteration of Articles of Food and Drink provided that parochial chemical analysts could be appointed But the measure was permissive, not mandatory, and, as *The Lancet* pointed out, parish vestries were often composed of the tradesmen who profited by adulteration An amending Act was passed in 1872, strengthening the provisions of the earlier one, and in 1875 came the Sale of Food and Drugs Act, which repealed all the previous anti adulteration legislation Four years later the appointment of analysts was at last imposed as a duty on local authorities

So in the end, helped considerably by *The Lancet's* campaign launched 100 years ago, Britain obtained unadulterated food and drink, showing that even an overcautious parliamentary answer may have an unexpected value

Medicine and the Law

What Makes a Nerve Tonic ?

Liverpool magistrates on Feb 23 dismissed summonses which alleged that a proprietary preparation was being offered for sale under a label which falsely described it or which was calculated to deceive According to the report of the case in the *Manchester Guardian* (Feb 24), the prosecution stated that a sampling officer had bought a bottle of 'Nervone' "brain and nerve regenerator tablets", the label bore the words "For vim, vigour, and vitality It puts courage into you because it contains one of the most potent nerve nutrients known to modern science" Nervone, said the prosecution, was found to contain 99 7% lactose and 0 3% inorganic matter, of which 0 1% contained five ingredients A Home Office pathologist gave evidence that the words "brain and nerve regenerator" conveyed practically nothing to him, that there was no reason to call lactose a nerve regenerator, and that the amounts of the other ingredients were too small to be of any consequence On the other hand, a medical witness called by the defence stated that he had been practising homœopathic medicine for thirty nine years and that all the ingredients mentioned on the label were recognised homœopathic medicines and were usually prescribed for nervous disorders Another medical witness testified that he had analysed nervone and found the ingredients to be stated on the label with complete accuracy

Counsel for the manufacturers had an easy task in emphasising that, if the prosecution witness did not know what a brain and nerve rejuvenator was, the description could hardly be proved to have been false He could not resist adding the comment that the medical profession would like to drive proprietary medicines out of existence If the proceedings failed, the *Manchester Guardian's* account has at least given readers the choice between the alternative opinions

---

[9] *Lancet* 1854 ii 536

[10] Hassall A H Food and its Adulterations London 1855

[11] *Lancet* 1854 i 293

[12] *Ibid* p 492

[13] Dalton W Is Killing Murder ? A key to the adulteration of our daily food Compiled from the evidence given before the Committee of the House of Commons in the years 1855–56 London 1857

In England Now

A Running Commentary by Peripatetic Correspondents

ALMOST every paper written on any branch of medicine or surgery ends with a list of references to previous work in the same field Such is the custom, and few articles would be accepted for publication if they did not respect it But do these references serve any useful purpose, and does the reader ever look them up? The general medical reader whose interests lie elsewhere will never have the time, and the specialist in the same field already knows about them The references are easy enough to obtain A request to the Royal Society of Medicine will bring by return of post a list as long as your arm It seems to me that references are often a form of academic snobbery The longer the list at the end the better the paper appears to be, and many a minor potboiler can be made to look impressive by a skilled librarian with a well-kept card-index Is it not time that Klumpferdinck X (1895) *Munch kleine Nachtmusik*, 79, 5674 was swept away? Mr Klumpferdinck must by now have exceeded his quota of glory

* * *

I was convalescing from influenza X My wife brought me on a tray a glass of water, two capsules of Goddamfiendicol, and the new *Lancet* for March 7, 1952 The *Lancet's* opening paper, by Professor Lilo, should be read and re read by every doctor in the land, and I am quoting the opening paragraphs here, so that doctors going abroad can change their plans

In the course of nutrition experiments on the ruminant skewbald monotesticular rat of Rodriguez (R.S M T R.R) we (Lilo et al 1939, 1946a, 1947b) have noted, on the one hand, an increase of weight that constantly followed the exhibition of brown bread in one colony, and we (Lilo 1948c) have contrasted this with the loss of weight that occurred some time after the withdrawal (forced non availability or F.N.A) of brown bread from other colonies of the same species

'Dr and Mrs Statiks (Statiks and Statiks 1949) have analysed our results and report an obesity rate of 7 015 ± 0 53% They reassure us (Statiks and Statiks, personal communication over a cocktail) that the exact significance of our work can never be established This encouraged us to neglect further, for the moment, the starved (F.N A) rat (Lilo 1949c) in order to give our full attention to the brown bread fed skewbald ruminants (B.B.F S R) As a result of the rush at feeding times certain injuries have become frequent, and the subjects of these strains (Sans Humo s 'loads) walk now with a characteristic sideways scurry The resemblance of their gait to that of people (*Homo sapiens occidentalis*) with alleged herniation of a slipped lumbar disc struck us from the first (Lilo 1950 and 1951b) and excellent results have followed operation in certain selected cases (Lilo 1952 in press) It is much regretted that the opportunity thus offered of comparing the results of manipulation (Kenon 1950) with those of operation (Burnhem Yung 1951) could not be taken, accurate handling having been persistently opposed by the strained B B F S.R 's "

The references to Professor Lilo's previous articles are not given in detail because they have been worn threadbare by keen reading and are no longer legible I was glad to see, however, that, in response to the widespread demand, Professor Lilo has arranged for his experimental work, with all the relevant literature, to be published in quarterly instalments, panoramic diagrams in brilliant colours being included as a free-gift supplement with each issue Postcards, with cheques attached, will receive his personal attention

Note—The Institute of Interpreters of Medical Literature (INSINTERMEDDLE) informs me that its Fellows are always available to help would-be readers and that a 24-hour service is being maintained for the duration of the Festival of Britain

* * *

Four years ago, when I had the temerity to write in these columns some (illustrated) hints to brides on answering a doctor s telephone, I thought I knew all about the G.P 's evil genie But I didn't, not by a long chalk In all humility I now cry for aid

A woman at the far end of the town has a telephone number almost identical with ours Just a single numeral misdialled and the public get her instead of us One evening when she was playing bridge she was disturbed by a call from someone wanting my husband She lost no time before complaining to me "You must do something about it," she demanded, "when one has friends in for bridge one cannot be disturbed " I obediently notified the Post Office They turned up trumps, as usual, and did various tests Their sympathy was with us and they rang her several times from our house. When she lifted her receiver she heard "Post Office testing," and then the line went dead That kept her quiet for about six weeks, but now she's at it again "You *MUST* tell your patients your number clearly," she told me, "can't you put it up somewhere?" With mounting hysteria I told her it was on my husband's plate, on his prescription pads, on our note-paper, and in Mr Marquand's lists at the post offices "Then people must be very stupid," she said As cuttingly as I could I replied, "They are " But there must be a snappier retort than that, can any fellow sufferer recommend a really flattening one?

What with the smallpox and then the flu, my husband has taken to picking up the phone when it rings, listening to the gist of the message, and if it isn't urgent saying "I'm sorry he's engaged with a patient, ring later " Then, patting himself on the back, he sets off to do another score or so of calls, leaving me to cope with the "rings back." This morning the long line of flu, constipation, wind-round-the heart, and depression was at last broken by a cheery call from our normal and healthy curate about his jumble-sale I could have kissed him on both cheeks What a relief to speak to someone who hasn't been ill, isn't ill, and doesn't intend to be ill if he can help it!

* * *

Be good, G.P , and let who will be clever
Stitch up those cuts , don't send them all along
To hospital, where patients wait for ever
And later make
A fearful song

* * *

With most of us in a state of postinfluenzal depression, tea in the laboratory was a dreary affair The talk ranged gloomily from atomic warfare to the class-Z call up, from the cost of living to the 8*d* meat ration, and ended, aptly enough, with Death and the Manner of Dying We recalled memories of student days when every pain in the knee betokened osteogenic sarcoma, when the slightest cough foreshadowed a carcinoma of the lung or sarcomatous metastases, and when tummy-ache was an almost certain sign of inoperable gastric cancer In those days, of course, we all knew in our secret hearts that we had T B , and felt sure that in the end, if our tumours did not kill us first, we would be found in the digs coughing our last over Price's *Textbook of Medicine* With brave sad smiles playing about our pallid lips we pressed on regardless Eventually, to our own surprise and our teachers' amazement, we qualified The crutches were flung away, the sarcomas and carcinomas regressed, and the lungs became as new From that day on we were far too busy to worry about our health But today brought back all the old fears and we were a glum crew as we discussed how and when the last curtain might fall We envied the one colleague who knows how and roughly when he is going to die, if (so to speak) he is spared until then For generations all the men in his family have died suddenly in their fifties As he himself said ruefully, "In our family unless you make something of your life before you're fifty, chum, you've had it " Apparently their coronary vessels just don't or won't anastomose, so his relations go out like lights at regular intervals He is convinced that if any of them did reach the sixties his body would fall victim to all sorts of diseases, and he would die, "Riddled, my boy, absolutely riddled " With these gay words ringing in our ears we crept back to the lab and thence home to read Schopenhauer's *Studies on Pessimism*

* * *

Aphorism of the Week

The nearer the bone the safer the surgeon

Letters to the Editor

SPECIALISATION

SIR,—Though there were many other and important suggestions in Dr Todd's article of Feb 24, I would like to pursue further one particular argument about the general practitioners' need of facilities for diagnosis which too often at present they lack Dr Todd argues the need for "health centres where general practitioners could have the more important investigations done For no doctor can be efficient without the aid of certain X-ray films, blood counts, urinary examinations, and a few other tests" And he rightly attributes the overcrowding of medical outpatient departments of hospitals, in part, "to the attendance of patients whose general practitioners desire, not a second opinion, but an investigation which they cannot get done themselves"

Lest general practitioners should be once more and still further discouraged by having dangled before them, as the chimerical solution of all their ills, "health centres" which they (and all of us) know cannot now be built—at any rate to the scale originally envisaged—it may be opportune to discuss rather simpler, certainly less expensive, and perhaps more acceptable alternatives

The Nuffield Provincial Hospitals Trust is hoping to be able presently to put to practical test a "diagnostic centre" for general practitioners in the town of Corby The idea is not that the practitioners of Corby and the surrounding villages should transfer the whole of their practices to a central building, but rather that they should refer to the "diagnostic centre" such of their patients (estimated by the general practitioners themselves at about a quarter) as require detailed diagnosis and special diagnostic tests—whether by the general practitioner unaided or in consultation with specialists The centre would be equipped with X ray facilities and a pathological laboratory, to be provided by the Regional Hospital Board, and specialists would attend on specified days to see patients and consult with the general practitioners (In addition, the Regional Hospital Board intends also to provide, on the site, a maternity block for uncomplicated midwifery, and, in the more distant future, perhaps general practitioner beds Ultimately it is hoped that the local authority clinics would be erected on part of the same site)

The need for such a centre arises in Corby from considerations at least as much of the patients' as of the practitioners' convenience the nearest hospital, at Kettering, is 7 miles away What, in effect, it is hoped to attempt is a combination of (*a*) general practitioner consulting rooms, with diagnostic aids (and simple treatment rooms), and (*b*) an outstation, in Corby, of the Kettering outpatient departments—so that general practitioner, patient, and specialist may meet where the facilities for full diagnosis are centrally and conveniently provided That the specialist can consult personally with the general practitioner, on the general practitioner's own ground, rather than correspond impersonally from a hospital outpatient department, may be a significant step towards the development of something nearer to domiciliary consultation

Whether this "diagnostic centre" at Corby will be realised depends on many factors outside the Trust's control But at least we have thought it right to attempt to throw this bridge across the gulf which at present divides the services provided under Parts II and IV of the National Health Service Act The enthusiastic reception of the proposal by the local general practitioners has been of the greatest encouragement to the Trust

L FARRER BROWN

Secretary Nuffield Provincial Hospitals Trust

12, Mecklenburgh Square
London W C 1

SIR,—Dr Todd suggests (Feb 24) that clinical registrars should be selected from the ranks of general practitioners, and that the minimum period spent in general practice should be three years

It has become the fashion to set up committees to inquire into the ways of improving the standards and working conditions of general practice Dr Todd now draws attention to the shortcomings of the specialists

There are four groups of cases which are referred to the hospital specialist

1 *Cases for outpatient treatment*—For example, a case of obvious arthritis in which physiotherapy is the only suitable treatment—but the patient must first be seen at the medical outpatients department

2 *Cases for laboratory investigation*—For example, a case of anæmia where a blood picture is required in order to decide on appropriate treatment, or a case of glycosuria where a blood sugar estimation is required in order finally to establish a diagnosis

3 *Cases for inpatient treatment*—For example, where domiciliary treatment is difficult, impossible, or undesirable

4 *Cases for diagnosis*—Where the general practitioner is completely unable to arrive at a diagnosis, and a second opinion is necessary

As a general practitioner, I have discussed with colleagues both in this area and in other parts of the country the often grave deficiencies of the younger school of specialists and consultants Perhaps I am cynical or unfortunate, but out of every ten Group 4 cases referred to consultants of the younger school, the diagnosis evades the consultant's clinical examination in nine instances, and after full laboratory investigation he is still in the dark in six out of the nine Where a confident diagnosis is made, he is ultimately proved wrong, in whole or in part, in 50% of cases

Specialists will, no doubt, hotly contest my figures, but I would refer them to the paragraph headed "Diagnosis in the Broad Sense," in Dr Todd's article

In his second paragraph, Dr Todd appears to suggest that the following four factors go to make a specialist brains, luck, money, or influence Since we all have brains, of sorts, it might be more accurate to substitute for the word "brains," "flair for academic examinations" There are, of course, other influences which rightly contribute to a man's success—e g, pertinacity and thoroughness But there is one great factor which cannot be acquired quickly, and that is *experience* It is on this count that the young consultant or specialist falls lamentably short, and it is for this reason that he so often fails in what I have termed the Group 4 cases On extremely rare occasions, however, clinical brilliance may make good this deficiency

What can the profession do about it? Obviously, it is impossible to present the younger specialist with a period of "twenty years' experience" as though it were a pound of cheese Similarly, we cannot bestow brilliance of intellect upon a body of men whose mental calibre is no different from that of their general practitioner colleagues

I would suggest that no one should attain the rank of consultant before the age of 45 at the earliest The intervening years would be spent as "general practitioner–hospital registrar" At least half of the working day and night would be in general practice, and the other half in hospital practice As to remuneration, this would be based solely on his general practitioner work His list would be half the current maximum, but the scale of remuneration would be double the prevailing rate

This "general practitioner–registrar" would then be competent to deal with all cases in Groups 1, 2, and 3, with a consequent saving in registrars' and specialists' salaries The true consultant would once more regain that prestige and respect from his colleagues, which, alas, is fast dying out

J S WOOD

Bootle Liverpool

SELF-IMPROVEMENT DISCOURAGED

Sir,—One of your recent leaders stated that Disraeli's Two Nations had virtually disappeared. Whether or no this is so, there is no doubt that Two Nations are rapidly developing inside the profession.

There is a widespread feeling that the general practitioner, often referred to as the salt of the earth but apparently regarded as the soul of incompetence, should improve himself or be improved. Now if the elderly general practitioner tries to improve himself by reading in his scanty leisure for a diploma of some kind, say in obstetrics, he will find himself thwarted at every turn unless he has held, or is able and willing to take up, a whole-time resident appointment at an approved hospital for six months. Failing this he is simply not allowed to sit for such examinations. No credit whatsoever is given for knowledge and experience acquired in 20 years or more of private practice.

Surely the acid test of admission to an examination should be *whether or no* the candidate possesses the requisite knowledge and experience, not *how* he has acquired them. The present situation is not only manifestly unfair to the general practitioner who wants to be a better general practitioner, but, what is more important, unfair to his patients and trainee assistants (if any). What is to be feared from admitting to these examinations general practitioners of experience? If they are not good enough to pass it is easy enough to plough them. If, having worked for them in their spare time, they are good enough to pass, who is worse off? Is there an apprehension lest some of them might wish to leave general practice and attempt to become consultants? Not a very real danger, I fancy, from those of riper years.

Crediton. L. N. Jackson.

NURSING INFECTIOUS DISEASES

Sir,—Twenty-five years' fairly close study, as a layman, of nursing recruitment, and of the channels of tuition and experience by which the general body of qualified nurses is fed, convince me that the best nurse is made on a basis of fever training. So much of the material of nursing (in and out of hospital) comes from the very large group of diseases based on infection, and so much of infection accompanies many others, that it is difficult to see how the General Nursing Council can do other, if it is at all forward looking now, than use the infections as the core of nurse training, rather than as a casual extra.

Granted that there is no longer a case for the continuance of hospitals specialising wholly in "fevers," there is a solid case for the one-time sizable London fever hospitals (500–600 beds) keeping infectious disease units of, say, 200 beds and building up special units (tuberculosis, non-surgical children, &c.) on this most valuable basis, and using their nurse-training resources to provide the tuition in the infections which they can so brilliantly give.

The smaller outlying ex-fever hospitals can, if they are not too ancient—and they modernise easily—play their part also. (They are, incidentally, the hospitals which, properly handled, can take the tuberculosis challenge in their stride.) Any group fortunate enough to have an ex-fever hospital not only has the answer to the development of group nursing, but, in applying it, can straight away smash the evils outlined by Dr. Stanley Banks.

There is room for the thought that, in London, the severe lesson of 1938 and the Sonne bacillus has been too easily forgotten if ever really learned; that there is altogether too much regard for the possibilities of using fever hospitals as decanters for unwanted clinical material elsewhere; too little for their potential value in their own field and in the production of the complete nurse.

The reasoning, logical in the conditions of the mid-19th century, which separated the handling of fevers from day to day general-hospital work has now become an unpardonable habit of thought.

St. Mary Abbots Hospital,
London, W.8. W. J. Crabb.

METHONIUM COMPOUNDS IN HYPERTENSION

Sir,—Recent reports have described encouraging results with the methonium compounds in the treatment of hypertension. As these drugs are now freely available and are, to our knowledge, in use in general practice, we believe that those who experience unfavourable results should make the facts known. We therefore wish to record the following fatal case.

A married woman, aged 47, was admitted to hospital on Jan. 3, 1951. She had a long history of migraine and of hypertension, with severe generalised headache for two years. One month before admission she had a violent headache followed by transient dysarthria and dyslexia. The family history was strongly positive for both migraine and hypertension.

The patient was obese. There was a small non-toxic thyroid adenoma. The heart was moderately enlarged, with a thrusting impulse; there were no murmurs; triple rhythm was absent; and no evidence of cardiac failure was found. The retinæ showed arterial hypertensive changes only. Neurological examination was negative except for trivial hesitancy in reading and writing. The blood-count was normal; the urine showed no abnormal constituents or deposit; the blood-urea was 31 mg. per 100 ml.; and the electrocardiogram showed the pattern of left ventricular hypertrophy.

On admission the blood-pressure (B.P.) was 236/160 mm. Hg; this settled overnight to 180/120, and it fell to 136/90 after three doses of 'Sodium amytal' gr. 3 at hourly intervals.

Treatment with hexamethonium bromide was initiated in view of the high diastolic pressure, persistent and incapacitating headaches, and the history of a resolved cerebrovascular incident. An initial intramuscular test dose of 50 mg. reduced the B.P. only to 160/110 mm. Hg. Single daily oral doses were then begun, with hourly B.P. recordings, the dosage being increased until an adequate hypotensive effect was obtained. This practice has been followed by us in order to obtain a record of the degree, duration, and variability of response to single doses before increasing the frequency of administration. The B.P. did not fall below 140/90 mm. Hg until a dose of 2·5 g. was reached; this produced a reading of 120/90 mm. Hg six hours after administration. Vision was blurred and there was some nausea. The next morning the patient vomited and the B.P. was only 115/75 mm. Hg; but it had risen to 165/115 mm. Hg by the afternoon. Investigations into the possibility of a coronary thrombosis gave negative results. The patient developed diarrhœa, and it was thought that the condition was possibly a coincidental infection—a conclusion which in retrospect we doubt.

Hexamethonium bromide was withheld for six days and resumed at the same dosage for nine days with relief of symptoms, side-effects being slight and variable. The lowest B.P. readings were noted between one and eight hours after administration of the drug and ranged from 110/80 to 170/124 mm. Hg. The responses showed no progressive pattern and there was no significant variation in the preliminary B.P. readings before each day's dose. On the tenth day the dosage was decreased to 2 g. on account of side-effects. The initial B.P. was 190/120 mm. Hg, and three hours later the B.P. was 120/90 mm. Hg; at that stage the patient fainted on standing up. Thereafter the B.P. fell still further and by the next morning it was 80/50 mm. Hg, the patient meanwhile having started to vomit large amounts of clear green fluid. Intramuscular methedrine produced only a small and temporary rise in B.P.; and though dehydration was prevented by saline infusion the B.P. remained in the region of 80/60 mm. Hg. Intravenous adrenaline was then used; and as there was an immediate response in the B.P. an intravenous saline drip containing adrenaline was set up and the dosage, using "booster" doses when necessary, was adjusted in an attempt to maintain the systolic pressure over 140/mm Hg on the basis of recordings every fifteen minutes or less A steady increase in dosage was necessary and the patient died after twenty one hours, having had a total of approximately 70 mg of adrenaline For almost the whole of that period the required B.P level was maintained, but the pressure always dropped precipitately during the brief periods when the drip was discontinued

Autopsy showed no cardiac infarction and no unusual or severe renal lesions A small cerebral cyst, filled with altered blood, was present in the parietal region on each side

Through the kindness of the research department of Messrs May and Baker Ltd, the hexamothonium bromide content of the last three urine specimens collected was examined In the last twenty four hours of life only two catheter specimens, totalling 13 ml, were obtained, together containing 7 5 mg of the drug, previous specimen twenty seven hours before death contained 55 2 mg There was no methonium in the vomitus, which had a chloride content of 352 mg per 100 ml

We wish to stress that this patient, under careful supervision in hospital, entered an irreversible, progressive, and fatal hypotensive state after an oral dose of hexamothonium bromide smaller than those which she had previously taken without alarming or consistent reduction in the B P Further, no progressive fall in the initial morning B P had occurred to suggest a cumulative effect Indeed, the high chloride content of the copious vomitus (260 oz) makes it questionable whether death was due simply to sympathetic blockade Earlier use of adrenaline might have averted the fatal outcome, but continuous therapy for twenty one hours was unavailing

We have reason to believe that this is not the only tragedy which has occurred with the methonium compounds, and we doubt whether it is justifiable for these substances to be used at all outside a hospital Disasters are probably inevitable in the early stages of experience with any new and potent drug, but the course of hypertension is so unpredictable, particularly in women, and the response to hexamanthonium bromide has been so unreliable in our experience, that we do not propose to use these drugs again except for patients in whom a relatively early death appears inevitable with any other form of medical treatment

West Herts Hospital
Hemel Hempstead

C HIRSON
A R KELSALL

SPINAL ANÆSTHESIA

SIR,—The arguments of your annotation last week justify disuse of spinal anæsthesia for merely securing abdominal relaxation Unfortunately the considerable prejudice against it, especially in obstetrics, has prevented its use in conditions where there is increasing reason to think it valuable Evidence of its efficacy in eclampsia and anuria is being sporadically reported, and Hingson has provided a long list of successes In interpreting his method of Pavex caudal analgesia it becomes clear that he aims at a "denervation" of the kidney and at avoiding a fall of blood pressure meanwhile In eclampsia low spinal block is equally effective The meagre fall of blood pressure herein ensuing cannot be held responsible for the improvement It is reasonable to assume that these two almost similar procedures have a common target In the Hingson technique it is the kidney directly In the other the same organ is indirectly involved by interruption of a uterorenal reflex No other explanation comes to mind Shorr's work on V E M and V D M would explain postoperative shock through the mediation of the kidney, and should be an incentive to the anæsthetist to devise methods of insulating that organ from stimulation during major surgical procedures Here again caudal anæsthesia is the goal The decline in the practice of spinal anæsthesia will blur a new horizon needlessly

London W 1

J SOPHIAN

PROPHYLAXIS AGAINST TETANUS IN BURNS

SIR,—In his review of burns and their management (Feb 24, p 460), Mr Clarkson advises that "Anti tetanus serum should certainly be given in all cases," and he suggests that active immunisation of the whole population should be seriously considered He bases this advice on the fact that Dupuytren mentioned the risk of tetanus in burns over 100 years ago, and on Dr Altemeier's report to the recent Washington Conference of "an incidence of contamination by tetanus organisms of 3% in routine smears from primary burns" I have looked up Dr Altemeier's published work on the bacteriology of traumatic wounds (two papers, one of which mentions 13 burns) but I have found nothing to support the idea that true tetanus bacilli frequently contaminate these latter injuries I did not hear Dr Altemeier's statement in Washington, but I think it unlikely that he would rely on "routine smears" for the positive identification of tetanus bacilli

However, quite apart from this evidence, I wonder how often Mr Clarkson has encountered, or heard of, tetanus as a complication of burns in this country? I have no doubt it may occur occasionally but in the course of 8 years' contact with burned people (about 6000 cases) I have not experienced it I realise that there are likely to be other injuries in the event of an atomic "incident" over this country, and active immunisation of the population might well be worthy of consideration in connection with them, but I question whether we should inflict yet another injection, and the risk of serum sickness, on those who have only burns

Farnham Royal

LEONARD COLEBROOK

EXPERIMENTAL GLOMERULONEPHRITIS

SIR,—Heymann and Lund,[1] Solomon et al,[2] and Pressman et al,[3] using improved methods, have confirmed the glomerular origin of the antigen that gives rise to nephrotoxic serum In consequence the observation by us of the nephrotoxic effect of anti rabbit stomach serum was unexpected

We immunised ducks by intraperitoneal administration of antigen prepared from rabbit stomach, and injected intravenously into the rabbit the serum thus obtained A pathological process ensued which clinically and histologically resembled closely acute and subacute glomerulonephritis in man

The manifestations of nephritis, which appeared after a latent period averaging six days, were albuminuria, microscopic hæmaturia, cylindruria, hypertension, water retention, and occasionally anuria These manifestations developed in the course of a few days and this sudden onset reminds us of anaphylactic reactions The animals either recovered or died of uræmia It seems remarkable that experimentally, as in man, uræmia is preceded by hyposthenuric polyuria

Necropsy usually revealed a large white kidney, among 12 animals we found only 1 granular kidney In 3 cases we found multiple bleeding gastric erosions, but peptic ulceration had not developed

Histological examination showed that in some cases virtually all the glomeruli were affected, and the pathological changes were diffuse In the glomeruli could be discerned the specific capillary reaction accompanied by local anæmia that characterises the disease in man The loops, despite occasional extreme dilatation, did not contain red blood cells These peculiar empty loops recalled Froehlich's *Plasmalücke*,[4] which is a local anaphylactic phenomenon In the exudative phase the dilated cavity of the glomerular capsules was filled with albumin, in the proliferative phase the size of glomeruli was almost doubled, owing to endothelial

---

1 Heymann W Lund H Z *Science* 1948 108 448
2 Solomon D H, Gardella J W Fanger H Dethier F M Ferrebee J W *J exp Med* 1949 90 267
3 Pressman D Hill R F, Foote F W *Science* 1949 109 65
4 Froehlich A. *Z ImmunForsch* 1914 20 476

proliferation In certain places the loops and capsule adhered, elsewhere half moon formation appeared.

As a control two rabbits were given two intravenous injections of 20 ml. of normal duck serum. The animals have been observed for eight weeks, during which no abnormality has become evident

From these findings we conclude that the glomerulo nephritis described is a specific process, the pathogenesis of which is to be found in an antigen antibody reaction, and that the rabbit stomach contains what may be called "heterotopic antigens," identical with those in the glomeruli. In the duck these heterotopic antigens evoke specific nephrotoxic antibodies

Our experience does not refute Masugi's[5] theory of the specific origin of nephrotoxic nephritis, and it provides additional evidence of the allergic origin of the disease in man Our findings do, however, show that not only kidney antigens but also heterotopic antigens can give rise, by an immunological process, to glomerulonephritis

Further details of this work are to be published in *Acta medica hungarica*

Medical Department,
Szeged University
Hungary

ARTUR HAMORI
FERENC OLAH

CORONARY DISEASE AND MODERN STRESS

SIR,—Dr Stewart (Dec 23) gives the following comparison of occupational groups with regard to death from coronary disease

Agricultural workers	32
Coalminers below ground	40
Banking and insurance officials	153
Anglican clergy	218
Physicians and surgeons	368

He says that these figures are remarkable and significant No doubt they are, but what is their significance? He suggests that the differences are proportional to the degree of mental stress in the classes mentioned. Are they not just as likely to be inversely proportional to the amount of physical work done by the classes concerned? At the present time agricultural workers do more work than any of the other classes mentioned Physicians and surgeons do the least They rarely even walk. Some clergy and some banking and insurance officials do If one postulates that physical work is a preventive of coronary artery disease, then the figures quoted by Dr Stewart fit in perfectly This hypothesis would also agree well with Dr Stewart's statement that members of primitive races are immune but lose their immunity when subjected to civilised life He says that two main influences are brought to them by civilisation, unfamiliar stress and increased richness of diet But as Dr Percy Stocks points out (Feb 10) there is also a third factor—a decrease in physical effort

It is also in favour of this hypothesis that the differences in physical work are a known factor, whereas the differences in mental stress are merely a suggestion put forward by Dr Stewart I wonder whether the manual workers have as little mental stress as he imagines When we start weighing other people's mental stress we are apt to fall into error Does the manual worker as he feverishly turns over the evening paper to see if the second leg of his double has come up in the 4 30 experience more or less stress than the doctor who lies awake at night wondering if he can afford to send his son to his old school? Who knows?

I have put forward one hypothesis which I think fits the facts given us by Dr Stewart as well or better than his modern stress theory There are of course other hypotheses which would fit his facts just as well, but it is not necessary to elaborate them, for my purpose has been to show that the identification of sufferers from coronary disease as the selected victims of modern stress may not be as reasonable as Dr Stewart suggests

In an effort to prevent this letter from being entirely destructive, I put forward rather hesitantly some personal speculations

I think that long periods of hard physical labour continued over a long time are bad for the cardiovascular system, and if carried to the extreme degree will cause serious cardiovascular degeneration In these cases the coronary arteries tend to be calcified On the other hand, absence of physical activity tends, I think, to produce degenerative changes in the coronary arteries, and this degeneration shows itself in the formation of atheromatous patches

It seems to me that hard physical work for relatively short periods may have a protective effect on the coronary arteries We know that hard physical exercise greatly increases the flow of blood through the coronary arteries, and it may be that this increased flow benefits the condition of the arteries We know also that hard physical exercise produces considerable movement of the diaphragm, and this seems bound to affect the coronary circulation

I know well the dangers of putting forward unsubstantiated hypotheses to solve medical problems, and in this case I have taken the risk for two reasons—(1) because we have had little help from the scientific investigators, and (2) in the hope that further investigations may be made There are two simple investigations which might throw some light on this problem a comparison of the incidence of coronary artery disease in scholastic teachers and physical instructors, and a careful investigation of the condition of the coronary arteries in racehorses, particularly a comparison between those which continued in training till they were aged and those which were retired to stud as three year olds

Houston Renfrewshire EDGAR RENTOUL

BACTERIAL VARIANTS PRODUCED WITH CHLORAMPHENICOL

SIR,—In the interesting articles by Dr Voureka in your issue of Jan 6 there are three points on which I should like to comment

(*a*) The only mention Dr Voureka makes of the type of urine specimen she examined is in connection with case 2, in which "samples of mid stream urine were plated" She does not say how the other specimens of urine were obtained, or whether her patients were men or women and one wonders whether this intricate and detailed work may not have been carried out on organisms not representative of those causing the initial infections in the patients' urine, for non catheter specimens are notoriously misleading

(*b*) Dr Voureka stated that, when *Bact coli* D433 was exposed to chloramphenicol alone no stable atypical colonies were obtained throughout the experiment "It was then thought that special conditions in the body might have influenced the production of these forms " She draws an analogy between the effect in vitro on *Bact coli* D433 exposed to both chloramphenicol and a specific antiserum and the effect obtained when she carried out her painstaking cultural investigation on urines of patients with *Pseudomonas pyocyanea* and coliform infection This might be an unfortunate analogy, for another worker in the same laboratory, W H Hughes,[1] has emphasised that cases with urinary infections develop no agglutinins he made use of this observation in recommending that vaccine therapy should be followed by chemotherapeutic agents, when a chemotherapeutic agent by itself would not produce a cure Therefore I assume that Dr Voureka's cases probably had no agglutinins in their serum to produce an effect analogous to her in vitro experiments on *Bact coli* D433 Except for some unconfirmed work by Giles, no one investigating cases of gastro enteritis associated with *Bact coli* D433 has demonstrated the production of antibodies by the patient harbouring these organisms , so it would seem that on two critical points the analogy Dr Voureka draws is an unfortunate one

---

[5] Masugi M. *Beitr path Anat* 1933 91 82 *Ibid* 1934 92 429

[1] Hughes, W H *Proc. R Soc. Med* 1943 36 477 Paper (unpublished) read at Summer meeting 1948 of the Pathologica Society of Great Britain and Ireland

(c) For those who work with the specific strains of *Bact coli* it is a problem to know what names should be given to the strains so far identified We have Bray's original name of "var *neapolitanum*,"[2] Giles and Sangster's "alpha,"[3] and Joan Taylor's "D433,"[4] all referring to the same specific strain of *Bact coli* I and my colleagues[5] may have also confused the issue, when we were only working with this strain, by referring to it as "B G T," the initials of these first three workers Smith[6] isolated a second specific type of *Bact coli* and this has been labelled "beta"

Now that there are other specific types of *Bact coli* which are found intimately associated with infantile gastro enteritis in different epidemics, it is more than unfortunate that Dr Voureka has allowed *Bact coli* D433 to have these three children—the variants alpha, beta, and gamma—particularly as the alpha antigen of Stamp and Stone[7] (for which priority must be claimed) is a surface antigen which may be found on some strains of *Bact coli* A study of the literature reveals the confusion that has arisen in the use of such names as those employed by Dr Voureka

Children's Hospital,
Birmingham, 16

K B ROGERS
Clinical Pathologist

KWASHIORKOR

SIR,—Dr MacPherson (Jan 6) believes that *Kwashiorkor* is the native name for a form of "ju-ju" or devil possession, and not the name of a disease, as previously stated by Dr Cicely Williams

Infantile pellagra, or nutritional œdema, is recognised by all the peoples of the Gold Coast, under various names *Kwashiorkor* is used by the Ga (Accra) tribe, while other names are *Akwosi* (Ashanti), *Abusamba* (Fanti), *Kpagyavi* (Ewe), *Tari* (Busanga), and *Jeredi* (Low Hausa) Of these, only *Kwashi* or *Kwasi-orkor* appears to be a descriptive name, the others being specific titles of no known derivation *Kwashi* or *Kwasi* is the name given, not only by the Ga and Akwapim peoples but by most of the Akan tribes, to a male child born on Sunday It is also used, much as "Tommy" or "Jock," to attract the attention of a boy whose correct name is not known *Orkor* means "red" The disease is characterised by pellagrinous patches on the skin, which appear reddish in colour against the normal black brown of the African skin , but, more evidently, the hair is thin, brittle, and rusty in colour The restoration of the hair to its normal curly glossy black is the final criterion of cure

I have asked lay people of the various tribes, who are knowledgeable in native lore, for descriptions of the disease With only minor variations I have been told that "when a woman, who is suckling her infant, becomes pregnant again, she must put the child away from the breast in order that her strength may go to the fœtus" (One or two tribes say that her milk becomes poisonous to the child) "When the parents are poor the infant cannot get any proper substitute for its mother's milk, and so gets the sickness" (This is, of course, a free translation from the vernacular) Normally, breast-feeding continues, with or without supplementary feeding, until pregnancy again supervenes Intercourse is forbidden for a period varying from twelve to twenty four months after parturition , hence deficiency disease is most common among children in the second and third years It is interesting to find that, among the Northern peoples, the care of the child, newly weaned, devolves on the father, who presumably shares with it the more digestible portions of his own food, which is rich in proteins

Where native opinion, everywhere, expresses the correct ætiology of the disease, it is unlikely that the Ga name derives, as Dr MacPherson considers, from possession by evil spirits Indeed, since reading his letter, I have questioned, specifically, Africans who are usually pleased to discuss with me "ju ju" and allied subjects I have met with denial of knowledge of any such belief, and kindly, though pitying smiles, which are my portion whenever I make a gaffe about native customs However, I must agree with Dr MacPherson in one thing The "casting out of devils" is an essential part of the treatment The "exorcism" is performed with santonin and calomel

Bogosu,
Gold Coast

J M DONNELLY

MUNCHAUSEN'S SYNDROME

SIR,—Dr Asher's first case uses his "Buckinghamshire" name when he visits us I wonder if any enthusiastic surgeons have noticed the ileotransverse colostomy which we performed in 1944 for fæcal fistula One month later he was in for a few hours after which we heard that in Liverpool His Majesty had some interest in his welfare By 1948 he was chief officer, Australian Merchant Navy, and had been blown up at sea His story and his abdomen were embroidered with steel wire (not confirmed by X rays) While he was obviously perfectly well, his abdomen was enormously distended Letters to addresses in Dalkeith and Bristol elicit replies from a wife who has disowned him for years and a lady who is "tired of getting wires about him" The letter suggests two other names he may be using Having been "shot down in Germany" he looked us up in June, 1949, was recognised, and discharged himself at 6 A M next day

Dr Stretton's case (Feb 24) is also well known at this hospital

Mile End Hospital,
London, E 1

S WILLSON HOLMES
Surgeon

TRAINING OF INVALID CHILDREN

SIR,—In your issue of Feb 24 Dr Field asks "What is the best way of looking after lame ducklings ?" Her letter is not easy to follow The Invalid Children's Aid Association's appeal for funds for a new home, despite an overdraft on current account, clearly disturbs her The Association's executive and finance committees, while sharing her concern about the overdraft (all contributions thankfully received !), are not one whit disturbed at the prospect of increasing their capital in the form of a new Home Their task here is to help any family burdened with the care of a chronically sick or handicapped child by giving the child a holiday and the parents a break

Dr Field wonders how far time and money should be spent on children who may never become useful citizens Perhaps the lessons learned by the I C A.A in England may help her in Malaya The Association, some sixty years ago, took over from the squire, the parson, and the kindly neighbour some of the growing work of the care of invalid children It mobilised the charitable impulses of those with time and energy as well as money to spare It found what work needed doing and devised methods of doing it The aftercare and rehabilitation of hospital patients, including convalescent treatment and the follow up of cases after their return home, came first Then came the establishment of Schools of Recovery for long term cases, such as the well known Heart Home at West Wickham, and, at Dr Field's own suggestion, the Meath Home for children with bronchiectasis The Association's work in these fields has become a common place in pædiatrics This is not the place for a full account of all its activities, but the Association still regards it as a duty to find, and to seek to fill by voluntary effort, gaps in the social service to invalid and crippled

---

2 Bray J *J Path Bact* 1945, 57 230
3 Giles C Sangster G *J Hyg Camb* 1948 46 1
4 Taylor J Powell, B W Wright J *Brit med J* 1949, ii, 117
5 Rogers K B Koegler S J Gerrard J *Ibid*, p 1501
6 Smith, J *J Hyg Camb* 1949 47 221
7 Stamp, Lord Stone D M *Ibid* 1944 43 266

children This does not prevent coöperation over such statutory work as is delegated to the Association by regional hospital boards and local authorities

Now with the growth of the Welfare State two things happen First, voluntary societies become more concerned with the gaps and with the difficult and the expensive problems Secondly, the cost of a State service, trying to be comprehensive, soon becomes prohibitive Already there are signs of rationing and a loss of amenities hitherto enjoyed—unless voluntary endeavour comes to the rescue The Association firmly believes that a great part of social work among children can only be carried on by voluntary societies

Dr Field will not expect to apply in one plan all the methods that have grown slowly and solidly in England in the last hundred years She should find and tackle whatever are the most urgent social problems of Malaya's invalid and crippled children She must build on whatever foundation has been laid by missionary and other philanthropic societies in her community In time and with experience of doing what lies closest at hand she will become less interested in "priorities" and "best methods" and more content just to do as much as can be done for as many children as possible, and Malaya's progress in civilisation will, in Professor Moncrieff's terms which she quotes in her letter, be judged by how much the community cares for its lame ducklings

Invalid Children's Aid
Association 4 Palace Gate
London W 8

ALFRED WHITE FRANKLIN
Chairman

DEFINITION AND NOTIFICATION OF TUBERCULOSIS

SIR,—The letters of Dr Stewart (Feb 24) and Dr Barran (Feb 10) are timely and important, because the Ministry of Health is considering new regulations for the notification of tuberculosis Notification may be a dry "subject," but all will agree that progress in public health has depended and will depend on knowledge obtained from compulsory notification

The Minister of Health's Standing Advisory Committee on Tuberculosis has wrestled recently with a definition of tuberculosis and sent a draft for consideration to the Joint Tuberculosis Council. The definition of tuberculosis should not be considered in isolation but in connection with other possible or desirable alterations to the present regulations for notification, including intimation (provisional notification) Intimation has I understand, been a useful and successful part of notification in Northern Ireland under the Public Health (Tuberculosis) Northern Ireland Act

The Ministry have not incorporated, so far, in their proposed new regulations, any recommendation that notification should be in two stages (*a*) intimation (provisional notification) and (*b*) registration (full notification) A general practitioner under the National Health Service Act, by his terms of service, must refer any patient whose condition is beyond his competence to the appropriate branch of the hospital service to get the required treatment But no special reference is made to tuberculosis, all cases beyond the competence of the practitioner service being lumped together for reference to the specialist branches

In many perhaps most tuberculosis schemes before the National Health Service Act came into force, general practitioners were invited to refer suspicious or doubtful cases of tuberculosis to the tuberculosis dispensary before making notification The tuberculosis officer (now chest physician—a stupid title when tuberculosis is a systemic disease) after examining a suspect gave in his written report to the general practitioner, advice as to the need to notify to the medical officer of health By this procedure, in some parts of England, for example Lancashire, over 90% of new cases were examined and "screened" by the tuberculosis officers *before* notification This step in practice corresponded in part to "intimation" Has anything like this figure of 90% become general in England, Wales, and Scotland? The answer to this question would appear to govern the urgency or importance of making "intimation" a statutory procedure

Would medical practitioners find it a convenience to have provision on the all purpose notification form for an intimation to be sent? This could be introduced on the notification form as an alternative to and alongside the Form of Certificate of Notification as is shown below (In Northern Ireland there are two sheets A and B which I understand led to some confusion at first)

FIRST SCHEDULE

Form of Certificate	*Alternatively* *Form of Intimation*
To the Medical Officer of Health of ______	To the area Tuberculosis Physician Dr ______
I hereby certify and declare that in my opinion	I have examined ______ of ______
(1) ______ of (2) ______ is suffering from tuberculosis	and suspect the patient may be suffering from Respiratory/Non-respiratory Tuberculosis
Age ______ Sex ______ Occupation or description ______	Age ______ Sex ______ Occupation ______
Organ or part affected ______	Medical condition ______
Place of ordinary residence if different from that at (2) above ______	I would like this patient to be specially examined for tuberculosis and a confidential report sent to me Attendance at the Clinic can/cannot be arranged
Signed ______	Signed ______
Address ______	Address ______
Dated the ______ day of ______ 19__	Date ______ 19__
	If the suspicion of tuberculosis is confirmed a fee will be paid.

(1) Insert full name
(2) Insert full address of place where person is living at the time

Church Stretton Salop

G LISSANT COX

CELLOPHANE ENVELOPES FOR A SYRINGE SERVICE

SIR,—The specially stout 'Cellophane' envelopes devised by Dr J E McCartney (March 3, p 509) provide, as he says, "a simple, cheap, and disposable container for the syringe"

There are two disadvantages in the use of such envelopes The wrapper provides for the reasonably safe outward transit of these sterile syringes, but on the return journey to the laboratory the syringes lack the protection afforded by test tubes or aluminium tubes, and the saving under all heads, is more than offset by the increased breakage rate in syringes.

The other disadvantage is that Messrs Clear View Ltd can only guarantee supplies of these envelopes in thinner quality there is no hope (meantime, we presume) of them stocking the thicker film We have tried the thinner envelopes and find them quite suitable, but more liable to be cracked on handling even after being allowed to become pliable

From our experience of running a syringe service, for a few years, we are of opinion that the most suitable containers are aluminium screw-capped tubes, with smaller aluminium tubes to take the needle and act as a distance-piece to support the syringe assembly in these screw capped tubes Unfortunately, aluminium too is in short supply at present—but we are well served by stout 'Pyrex' test tubes (with rims on which the syringe rests) which, although dearer than ordinary test tubes, are of long life and are easily cleaned

North Middlesex Hospital London N 18

J F HEGGIE

VACCINATION AGAINST SMALLPOX

SIR,—In his article entitled "Does Vaccination help to spread Smallpox?" (Jan 13), Dr Millard is asking a question based on some observations which have apparently led him to believe that the answer is in the affirmative But if this is so, it is not the fault of the vaccination itself but of the lax way in which vaccination has been regarded and enforced in the United Kingdom The recent abolition of compulsory vaccination has only served to make the public even more complacent This would perhaps be justifiable if there were no risk of the introduction of the disease from outside the country, but almost every epidemic in recent years has been started in this way, and the increasing use of air travel has increased the risk, not diminished it The examples given by Dr Millard himself bear this out "a seaman" (1912, Newhaven), "a de mobbed soldier" (1918, Croydon), "a seaman" (1921, New Forest), "an Asian seaman" (the recent outbreak in Glasgow) In this last case, the man was said to be "well vaccinated" If this was so, one must admit failure No one has claimed 100% protection for vaccination, but one failure is not sufficient to condemn the whole system

It would seem that there are two courses open to the health authorities in the U K Either they must see that the public is properly vaccinated, or else they must see that all persons entering the country have been recently vaccinated This latter provision is obviously the simpler, and is only what is already required by most other countries of the world

Traditional British policy has always been against any sort of "quarantine laws," on the assumption that if a country sees to its own internal hygiene it need not fear the introduction of disease from without This is no doubt true of many of the international diseases, particularly cholera and yellow fever, but it is dangerous to generalise and apply this line of thought to smallpox, which is quite unaffected by "hygiene" of the ordinary sort The only "hygiene" which would protect the country from the introduction of smallpox from outside is wholesale compulsory and repeated vaccination

In any case what is the objection to vaccination? If done in infancy it is perfectly harmless, within the limits of human fallibility The only way to enforce vaccination is to see that the person has something to lose if he is not vaccinated Travellers can be made to comply by being refused admission to the country Parents can be made to comply by refusing their children admission to school unless vaccinated, as is done in America In this way the objectionable and "un British" prosecution of offenders would be done away with

It would be a great pity if opinions such as Dr Millard's were allowed to hamper the already difficult work of those health authorities who appreciate the value of vaccination as a well tried and tested method of protection

South African Native College
Fort Hare Cape Province

W NORMAN TAYLOR
Professor of Hygiene

SIR,—Dr Millard desires a revision of the present status of vaccination against smallpox on the following grounds

1 Vaccination is responsible for mild and modified cases which escape detection and thus spread smallpox amongst the unvaccinated

2 Infant vaccination may lead to an increase in virulence of the strain of the disease

Smallpox in vaccinated persons is almost always mild and modified and may ordinarily be mistaken for varicella However, correct diagnosis, even in cases which arouse only the slightest suspicion, should present no difficulty, particularly in the United Kingdom with its highly organised Public Health Laboratory Service Van Rooyen and Illingworth have pointed out that elementary bodies of variola virus can be demonstrated in less than half an hour from stained tissue scrapings obtained even from the "bathing drawers" rash which appears as early as the 2nd day of the disease I quite realise that Dr Millard may have in mind those ambulant patients who scarcely feel ill and spread infection during their perambulations, but such a contingency only strengthens the plea for the regular and systematic protection of the whole population at risk It does not appear to be a sound proposition to have the whole community highly susceptible, so that cases of smallpox when they do occur will be severe and thus easily detected The occurrence of such mild and missed cases can obviously never be ruled out, particularly at ports, and the only way of limiting mischief from them is to maintain a high level of herd immunity at places which are possibly at risk

Dr Millard states that while vaccination benefits the individual it is detrimental to the community This antagonism will not arise when the whole community enjoys the same level of protection, by mass vaccination That mass vaccination effects a diminution in the incidence of smallpox in addition to a striking reduction in mortality is supported by statistical data from Palestine, China, and India Perhaps the best evidence in this respect is furnished by the striking relation that can be observed between the incidence of smallpox and the different vaccination laws that prevail in the various States in the U S A

Dr Millard advances the theory that infant vaccination may tend to increase the severity of the strain of the disease He implies thereby, that the present indigenous disease "alastrim" may be permanently displaced by smallpox as a result of a continuous process of transmission of infection from mild cases of smallpox amongst the vaccinated to the unvaccinated Vaccination has been prevalent in the United Kingdom for the last so many years, and for several decades its practice has been concurrent with the process of displacement of smallpox by alastrim It is hard to see how vaccination can now be considered to lead to a reversal of the process On the other hand one should rather be alert for possible repercussions of the recent relaxation of vaccination laws

His observation that smallpox has not been eradicated from India is quite correct That, as he rightly recognises, is due to the high virulence of the virus, protection against which demands a very high level of immunity The belief among a very large section of the population that vaccination in infancy protects for life hampers revaccination work, which requires a large measure of public cooperation The result is that there is always a large proportion of susceptible population which contributes among other factors to the periodic epidemics of smallpox in this country

Dr Millard's suggestion for the implantation of alastrim in India with the idea of its elbowing out smallpox is indeed a fascinating one He thinks that for a start inoculation with alastrim virus instead of vaccinia (vaccination) may be undertaken in a town or district and that even more heroic measures would be justified The situation in the United Kingdom has no doubt prompted this suggestion The gradual and striking reduction in the incidence of smallpox in the U S A from 42,679 in 1930 to 1346 in 1934 without any nationwide vaccination efforts has also led to the speculation that a mild strain of smallpox which often goes undetected is rapidly immunising large numbers of persons It is however a moot point whether such substitution is possible or desirable except through purely natural forces Alastrim is after all a disease whose symptoms, though mild, are not unlike those of smallpox—e g, fever with generalised eruption and constitutional disturbance Mass inoculation, in however small an area, with a virus which makes itself felt so appreciably, is certainly not a measure one can take with equanimity

Further the difficulty of maintaining a sufficient stock of alastrim virus is too apparent, for it can with certainty be transmitted only to monkeys, and there is no guarantee that with continued passage in embryonated eggs it will breed true.

I feel I should conclude by quoting Dr Frederick F. Russell's contribution to a symposium held at the Harvard School of Public Health in 1929:

> "A community is not a stationary group; its age composition may have a certain stability but it is maintained by constant accessions and constant deaths; and it should be looked upon not as fixed group but as a parade, steadily and regularly marching past. To maintain a constant level of immunity against smallpox in such a group, vaccination must be done regularly on all newcomers, if possible in the first year of life; and revaccination must be carried out on all school children. To this activity there should never be an end until the whole world is vaccinated, and smallpox completely eradicated; so long as this disease lurks in some backward region, it may reappear in epidemic form unless all civilized countries continue to vaccinate each new generation."

Vaccine Institute,
Belgaum, India. R. S. RAO.

WILL WE NEVER LEARN?

SIR,—Much heart searching must follow Sir Heneage Ogilvie's letter in your last issue. I refer more particularly to the first part of his mixed grill. Every young doctor nowadays is a potential soldier, and if he is surgically inclined, and war provides the opportunity, he will be used in one part of the chain that stretches from the regimental aid post, across continents and seas, to the home hospital. Appointing a consulting surgeon to a group in the field is not the answer, be he even a marathon runner. Reading the surgical history of past wars is not a practical proposition. Many factors go to the making of a successful surgical set up in any campaign, and the terrain will always modify the pattern. Medical directives and surgical pocket books are a boon, and an O. i/c division who gives his teams regular surgical anatomy talks is a treasure, &c. "Will we never learn?" The answer is "Yes, if we are taught." In every medical teaching centre there should be a chair of military surgery, and for choice it should be filled by one who has actually operated in the field.

Sir Heneage Ogilvie is in the highest regard in the highest of places, and is the very man to initiate the implementation of such a project.

Longtown, Cumberland. R. RUTHERFORD
Hon. Colonel T.A.

SIR,—Having had the honour of serving with Sir Heneage Ogilvie in the first world war, I would welcome the opportunity of condemning with him the "have a go" mentality. As a radiologist one has had unique opportunities for watching most of the game. A problem has faced the master surgeon; he has studied it carefully in the light of his past experience and that of his colleagues; and, as a senior, after much patience, he has devised a method of attack and with great skill has carried it through successfully. So successfully that he has tried to repeat it with other cases; but whether because no two cases are the same, or because subsequent ones have not been subjected to the same critical inquiry, the results have sometimes been so disappointing that he has abandoned it. Long after this, men who have heard of the success of the original case, but do not possess the same knowledge or have not even acquired the necessary skill continue to use the method, apparently hoping that one day they will be rewarded.

No more glaring instance of the lack of thought for the patient has been witnessed than in the removal of foreign bodies. We established in the first war that with care radiological localisation could be so accurate that surgical removal of the foreign body could be done with little more time than was required to make the necessary incision. It was so accurate, and the actual removal required so little skill, that the sister of one department I serve received a notice from the surgeon: "Please do not put any localising mark on the skin—it spoils our fun."

I much regret that radiography is responsible for much of this "have a go" activity; without it more attention would have to be paid to the patient and much incitement would be missing.

But this type of activity is not only applicable to surgeons. Sir James Paget described his case of osteitis deformans only after careful clinical observations throughout more than 20 years; and his description was so complete that no important contribution has been made since, though many thousands of cases of Paget's disease have been subjected to multiple investigations, employing surgery, biochemistry, physiotherapy, and radiology merely because various workers had described tests, of no value to the treatment, which yielded positive and negative results. The fact that a writer of repute has described a particular finding—something which one need but remember—seems to lead every man who has such a case to apply the test described, no matter how inferior his means for applying it, or how able he is in its interpretation; and should he obtain a different result he records it and incites others to check.

The answer to Sir Heneage's question appears to be "No" since a number of our leading teachers in all spheres of medicine have written similar criticism. Perhaps none more forcibly than Sir James Walton[1] in the words: "Perhaps in the lifetime of many of you these marvellously skilled operations will cease to be performed, and will be regarded as curiosities of the past."

With apologies to the memory of Ruskin I would say that in former days men used their art to remove the cause of pain, but more recently they have used the cause of pain to show off their art—unfortunately not always to the benefit of the patient but at great expense to the community.

Birmingham. JAMES F. BRAILSFORD.

SIR,—Sir Heneage Ogilvie has come charging down from Mount Olympus, over which he appears to enjoy the sole shooting rights, in an attempt to drive me from the small holding I have tried to establish in one of the foot hills.

His attack is also directed at a young naval surgeon doing his unattractive duty off the coast of Korea. The Senior Service may remain silent, but not I.

We two unmentionable men are accused of writing articles on subjects about which we know little and have thought less. We are lamentably lacking in experience and totally unfamiliar with what is known as the literature.

How does a surgeon gain his experience? By obtaining surgical registrarships and working hard under the direction of men who are older and wiser than he. During my early years I held five such registrarships, two of them in teaching hospitals other than my own. I assisted at hundreds of gastrectomies and I had access to the records of hundreds more. It was this very experience that sent me in search of a safer way of dealing with the duodenal ulcer.

The search took me to France, Switzerland, Germany, Austria, and the United States of America, not as an honoured guest or in an official capacity but as a private person paying my own expenses and spending my own spare time. Sir Heneage underestimates my diligence if he imagines that I could miss Manchester. After enjoying the stimulating and cordial hospitality of Mr Wilson Hey I returned to London more eager than ever to employ the operation which in his hands and in mine gave such promising results

---

[1] *Brit. med. J.* 1950, i, 306.

Am I so ignorant of the literature ? I fear I may be, but I do try to keep myself informed about a number of things For many years I have read surgical journals in three foreign languages as well as a carefully selected series from both sides of the Atlantic, many of which are written in English Before the war I made translations from the foreign publications and condensed them for publication in one of our well known weekly medical journals But I must admit that I completely missed the series of one unsatisfactory case mentioned in the *British Medical Journal* in 1947 and I have not read of the Madras disasters But then I am handicapped by having no Telegu

Sir Heneage does not like my article, and he has a perfect right to say so , but to suggest that it is a casual contribution or an exhibition of flippant ignorance is just a little discourteous Now that I have gained my majority as a fellow of the college I rather dislike being rated as an irresponsible adolescent by the house master

My article is an interim report If in another ten years another tale must be told, be sure that I shall tell it If, in the meantime, I am in a minority, I shall not mind The kindly earth of Kirkcudbright has for centuries concealed the broken bones of men who dared to disagree with their powerful neighbours, and they all bore the name of your humble contributor,

London, W 1 EDWARD MACLELLAN

THE INVESTIGATION OF SUGAR TOLERANCE

SIR,—I was most interested to read Dr Lawrence's letter of Feb 24 It is true that the isolated 2 hour blood-sugar level will not give a precise diagnosis in all cases of symptomless glycosuria , but it will show whether or not the glycosuria results from reduced sugar tolerance The differentiation of renal glycosuria from lag storage as the cause of glycosuria will demand additional blood sugar determinations if it is considered necessary to distinguish between them Starvation and thyrotoxicosis both cause reduced sugar tolerance, with elevation of the 2 hour blood sugar level The fasting blood sugar may be normal or raised in such cases, and thus may not assist in making a diagnosis from diabetes mellitus

It will be generally agreed that the results of any method of testing for sugar tolerance must be interpreted in the light of the information obtained from interrogating and examining the patient

Department of Medicine
Middlesex Hospital London, W 1 JOHN FRIEND

FOOD AND ENERGY

SIR,—The following *quotation*[1] *appears to need no* comment

"DIET AND ENERGY"

"There is no doubt that diet plays an important part in enabling the American worker to work faster and to keep up the effort The question was discussed with several operators and it was estimated that the American worker had in the course of a week

Meat	3 lb to 4 lb
Eggs	12 to 18
Milk	5 to 6 pints
Fats	Four times as much as the English worker with a good supply of fruit juices either in concentrated form or as fresh fruit

Here we might mention that members of the Team enjoyed much greater energy as the weeks went by and were able to do their arduous job of walking round factories all day without fatigue In addition they were able to follow without difficulty the American way of life and carry on with the minimum of sleep "

London W 1 FRANKLIN BICKNELL

---

[1] Report of a Visit to the U.S A. in 1950 of a Productivity Team Representing the Rigid Boxes and Cartons Industry Published by the Anglo American Council on Productivity London, February 1951

Parliament

QUESTION TIME

New R A F "T A B T" Vaccine

Mr P L WELLS asked the Secretary of State for Air what was the nature of the new kind of inoculation proposed to be used at certain Royal Air Force camps.—Mr ARTHUR HENDERSON replied The "new" inoculation introduced by the R.A.F is a combination of two well tried immunising agents, T A B vaccine and anti tetanus toxoid , it is named T A B T Two injections are given initially, at a few weeks' *interval, and one injection annually thereafter or* on first arrival in an overseas command No further proof has been sought of the proven efficacy of T A B vaccine or tetanus *toxoid, and the medical authorities are satisfied that they* can be given together without harm or loss of effect No bad results have been reported from the use of this substance. All ranks are reminded periodically that vaccination and all inoculations are voluntary

Influenza and Sickness Benefit Claims

Replying to Mr SOMERVILLE HASTINGS Dr EDITH SUMMERSKILL, Minister of National Insurance, said that *her department had had the heaviest load of sickness benefit* claims in its short history in respect of the influenza epidemic. The local offices and the central office, Newcastle, had stood *up to the test well* During the first six weeks of the year the number of new claims to sickness benefit was almost double the figure for the same period last year—just over *2,100,000, compared with about 1,100,000* At one time some 1,500,000 persons—1 in 15 of the insured population —were claiming sickness benefit

Tuberculosis Beds in Switzerland

Mr HENDERSON STEWART asked the Secretary of State for Scotland if he would make a further statement on the provision of beds in Swiss sanatoria for Scottish tuberculous patients —Miss MARGARET HERBISON replied *Exploratory discussions are now proceeding with the authorities* of certain Swiss sanatoria as to the charges they would make for the treatment of patients from this country These discussions will *be concluded shortly and I hope it will then be* possible for the Government to reach a final decision

Hospital Costs

Colonel LEONARD ROPNER asked the Minister of Health if, with a view to stimulating efficiency and economy in the *hospital services,* he was preparing a detailed analysis of hospital costs under the National Health Service —Mr ARTHUR BLENKINSOP replied that a uniform system for analysing hospital costs in some detail had been introduced for the first time this year and would relate to the year 1950–51 as a whole Broadly the return would be in a similar form to that issued by the Department of Health in Scotland The Ministry were still discussing with the Treasury the best way in which this information could be made available to Parliament and the public at a suitable time

Corporal Punishment in Approved Schools

Mr R W SORENSEN asked the Home Secretary what consultation with psychologists, specialists in juvenile delinquency, and other authorities had taken place in his department during recent years in respect of appropriate discipline and punishment in remand homes and approved schools ; whether particular attention had been given to the incidence of corporal punishment both as a deterrent and with regard to its alleged remedial effect on individual *characters* , and to what extent the experience and example of other countries in regard to this problem and the fact that corporal punishment was not administered in *similar* institutions in many countries had been examined in relationship to modifications of our own practice —Mr CHUTER EDE replied Methods *of discipline and punishment,* including corporal punishment, in remand homes and approved schools are kept under constant review, as regards their suitability and the extent of their use, by the inspectorate of the Home Office children's department, which includes psychiatrists, in consultation as necessary with the managers and staff of the homes and schools, who have extensive knowledge and experience of the problems presented by young offenders A *psychiatrist, and* persons with wide experience of dealing with delinquents, are among the members of the committee which I appointed in November 1948, to review punishments in prisons, Borstal institutions, approved schools and remand homes. The committee's report dealing with approved schools and remand homes is expected to be available shortly

Mr SORENSEN Are there not numbers of psychiatrists and others who deprecate excessive corporal punishment ?—Mr EDE The committee appointed as a result of an undertaking given during the passing of the Criminal Justice Act, 1948 has been fully investigating this matter Psychiatrists differ even more than doctors

Births in Prisons

In answer to a question, Mr EDE said that since the Order relating to births in prisons came into force on Dec 27 15 children had been born in His Majesty's prisons and borstals in England and Wales, and 92 women had been confined in outside hospitals It was the practice for every woman to be asked, well before her confinement, whether she preferred to be removed to an outside hospital for the confinement, and if she did, suitable arrangements were made In a few cases, for instance, where labour was precipitate, it had not been possible to effect the removal in time

Public Health

Prescribed Diseases

UNDER the National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment (no 2) Regulations, 1951, the Minister of National Insurance extends insurance under the National Insurance (Industrial Injuries) Act, 1946, against byssinosis to people employed in certain rooms in waste-cotton factories. The regulations also provide for payment of disablement and death benefit from the date when the regulations came into operation (March 1) in the case of people covered by the regulations who suffered or died from the disease before this date

New regulations extending insurance under the same Act to tuberculosis in nurses and certain others insurably employed in occupations involving close and frequent contact with tuberculous infection are discussed on p 573

Influenza

During the week ended Feb 24 deaths from influenza in the great towns of England and Wales decreased to 15 3 per million population from 23 7 per million in the previous week. For the great towns grouped regionally the influenza death-rate decreased everywhere except in the northern and eastern regions, where slight increases were recorded The proportion of influenza deaths in patients aged 55 or over was 89 3%, compared with 88 8% in the previous week. In the whole of England and Wales new claims to sickness benefit in the week ended Feb 20 numbered 161,600, compared with 200,300 in the previous week

Infectious Diseases in England and Wales

Disease	Week ended Feb.			
	3	10	17	24*
Diphtheria	51	44	40	43
Dysentery	967	956	972	1366
Encephalitis				
Infective	2	6	2	2
Postinfectious	1	3	8	6
Food poisoning	139	82	99	119
Measles excluding rubella	16 329	21 634	24 587	27 776
Meningococcal infection	73	52	59	45
Ophthalmia neonatorum	36	42	24	33
Paratyphoid fever	3	6	11	13
Pneumonia primary or influenzal	3514	3031	2117	1656
Poliomyelitis				
Paralytic	21	12	15	16
Non paralytic	11	7	6	5
Puerperal pyrexia and fever	87	90	67	31
Scarlet fever	575	692	904	828
Smallpox			1†	
Typhoid fever	3	5	4	5
Whooping-cough	4916	5114	5662	5925

* Not including late returns
† Imported case

Births, Marriages, and Deaths

BIRTHS

ANDREWS—On Feb 25 in London the wife of Dr Peter Andrews—a daughter

BROWN—On Feb 26 at Colac Victoria, Australia, the wife of Dr A G Brown—a daughter

HOSKYN—On Feb 26 in London the wife of Dr C H. Hoskyn, O.B.E.—a daughter

MCVICKER.—On Feb 17 the wife of Colonel Daniel McVicker O.B.E., M.C. R.A.M C. retd—a daughter

STARKS—On Feb 23 at Wolverhampton to Dr Isobel Starks (née Morrison)' wife of Dr J M. Starks—a son

TUCKER.—On Feb 26 in London the wife of Dr H. M. Tucker—a son

VINCENT—On Feb 27 in London the wife of Dr Charles Vincent—a daughter

WYNYARD—On Feb 24 in London the wife of Dr Martin Wynyard—a son.

YARROW—On Feb. 27 at Sevenoaks the wife of Dr Dudley Yarrow—a son

MARRIAGES

THOMAS—CLARK.—On March 1 at South Weald Essex Stanley Thomas, M.B. to Madge Clark

DEATHS

ALTON—On March 2 in Birmingham, Edgar Hepworth Alton L.R.C.P E. aged 81

BROWNE.—On Feb 27 at Rapallo, Italy Cuthbert Garrard Browne, C.M G D.S O, M.R.C.S. lieut.-colonel R.A.M C retd

DOBSON—On Feb. 22 Josiah Rowland Benjamin Dobson M.B. Lond. B.SC. Wales

FALCONAR.—On March 2 William Ernest Falconar M.B Durh., aged 79

MAUNDER.—On March 3 at Erith, Harold Arthur Maunder D.S O M B. Melb

SHAW—On Feb 27 Kenneth Rodas Devaignes Shaw L.R.C.P.E.

WATERS—On Feb. 16 at St. Aubin Jersey Walter James Waters O B.E. M.R.C.S aged 74

WILLIAMS—On Feb 25 at Milford Haven Hugh Owen Williams M.B. Lond D.P.H.

Appointments

BROUGH M. C M.D Dubl consultant chest physician Leicester area.

BROWNRIGG E. K. M.B. Lond D.A consultant anæsthetist, Winchester group of hospitals.

CAYLEY F E. DE W M B.E M.D Lond M.R.C.P consultant in diseases of chest Brighton hospital group

CLIFFORD JONES EDWARD M B Lond. consultant chest physician Wrexham Powys, and Mawddach hospital group

CROWLEY NORA M B. N U.I. D C.H asst M-O maternity and child welfare and school medical inspection Northants

DAVIES T C H M.B Wales F R.C.S consultant orthopædic surgeon Newport and East Monmouthshire and North Monmouthshire hospital groups

EDWARDS K. C S M.R.C.S. D.P.M asst. psychiatrist (S H.M.O grade) North Wales Hospital Denbigh

EGERTON B H M.B. anæsthetic registrar Norfolk and Norwich Hospital

ELTON ARNOLD M.S Lond F.R C.S consultant general surgeon Harrow Hospital

GIBSON M. O J M.B Camb M.R.C.P consultant in diseases of chest Dartford hospital group.

GUNTER G S M.S F.R.C.S. F R.A C.S senior registrar in plastic surgery Frenchay Hospital Bristol

HOLDEN W S., M B. Manc. M.R.C P D.M.R D radiologist United Oxford Hospitals

JARDINE PHILIP L.R.C.P.E F.R.C.S.E. D O.M.S. consultant ophthalmic surgeon Southmead Hospital Bristol

LEWIS BARBARA M.D consultant dermatologist Brighton hospital group

LOANE R C R M.B. Belf F.R.C.S consultant surgeon South Tyrone Hospital

LUCAS H K. M.B.E M.B. M.CH ORTH Lpool F R.C.S E consultant orthopædic surgeon Bristol clinical area

MCCORMACK M P M.B. Edin F R.C.S.E consultant orthopædic surgeon Bristol clinical area

MCKENDRICK G D W M.A. B.M Oxfd M R.C.P deputy resident physician Ham Green Hospital Bristol

MANN T P, M.D Lond M.R.C.P D C.H consultant pædiatrician Brighton hospital group

MONTGOMERY D A D., M B.E. M D Belf M.R.C.P physician Royal Victoria Hospital Belfast

PANTRIDGE J F M.C M.D Belf. M.R.C P I physician Royal Victoria Hospital Belfast

PHILP L D M.B. Edin D.M.R.D asst radiologist Wigan and Leigh area.

RAWLINGS E E., M.D Leeds M.R.C O G consultant asst obstetrician and gynæcologist Hope Hospital Salford

ROBERTON T P M.B Lpool D.P.H M O H and school M O Bootle Lancs

ROSS H A M.B. Glasg D P.H physician superintendent (consultant) South Wales Sanatorium Talgarth.

SKOTTOWE, J S I., M D Glasg D.P.M psychiatrist Warneford and Park Hospitals Oxford

SWERDLOW MARK M.B. Manc D A consultant anæsthetist Salford Hospital Centre

WATSON JOHN M.B Belf. M.R.C O.G consultant obstetrician and gynæcologist Mid Ulster Hospital

WHALLEY NORMAN M.B. Manc. F.R.C S E consultant neuro surgeon Glantawe Hospital

WHITTET M. M. M B. Glasg M.R.C.P.E F R.F.P.S D.P.M. physician superintendent and consultant psychiatrist Craig Dunain Hospital Inverness

Notes and News

NEGOTIATIONS WITH THE MINISTER

ON Feb 28 a deputation appointed by the General Medical Services Committee met the Minister of Health to discuss the Ministry's latest proposals on the remuneration of general practitioners No statement was issued after the meeting The members of the deputation were Dr S Wand, Dr W Jope, Dr E A Gregg, Dr H H D Sutherland, Dr A Campbell, Dr H G Dain, Dr A B Davies, Dr F Gray, and Dr W M Knox, with the actuary, Mr R C Simmonds, F I A An emergency meeting of the committee was held on March 6, and a special conference of representatives of medical committees will take place on March 29

"Z" RESERVISTS

THE Central Medical War Committee and the Scottish Central Medical War Committee have been informed that they may consider appeals from doctors who, as members of "Z" Reserve, receive a warning notice of recall for 15 days' training and consider that their withdrawal for this period would jeopardise the civil medical services in their areas Appeals should be addressed to the secretary of the Central Medical War Committee at B M A House, Tavistock Square, London, W C 1, or, in Scotland, to the secretary of the Scottish Central Medical War Committee, at 7, Drumsheugh Gardens, Edinburgh These committees cannot deal with any question of personal hardship, which is a matter for the Service department

REBIRTH OF THE MIDDLESEX ARCHIVES

THE *Archives of the Middlesex Hospital* died in 1916, at the age of twelve, killed by the first world war It has now been restored to life under the editorship of Dr Douglas McAlpine, and we wish it long life and prosperity Mr Victor Bonney, in the introduction, reminds us of the achievements of its first years, when it carried Sampson Handley's classical papers on parietal dissemination of mammary carcinoma, William Pasteur's original observations on massive collapse of the lung after abdominal operations, and Bonney's own study of the connective tissue in carcinoma, as well as many other notable contributions The hope of the new editor and his committee is to encourage the younger members of the Middlesex staff and the registrars to write up interesting cases and make original observations At the same time, every number will contain one or two articles of direct interest to the general practitioner

The first number of the new *Archives* lives up to these intentions The six articles in it deal with arteriography of the abdominal aorta, atypical abdominal tuberculosis simulating myeloid leukæmia, toxoplasmosis, disorders of the cervical intervertebral discs reconstitution of the vas deferens after a sterilising operation, and "chronic mastitis—a non existent disease" The lively text, the splendid illustrations, and the fine glossy paper combine to lure the reader on

GUY'S HOSPITAL DENTAL SCHOOL

THE annual clinical meeting of Guy's Hospital Dental School was held on March 3 Although this year there was nothing comparable to the colour television of the last meeting, all departments combined to present an excellent programme of demonstrations and clinical cases The endeavour was to show the many and divers aspects of the present dental curriculum and to emphasise the close relation between dentistry and general medicine

From the many demonstrations it is only possible to single out a few that have medical as well as dental interest An exhibit by Mr A Bulleid and Mr C W T Shuttleworth, of the department of preventive dentistry was concerned with the use of the various antibiotics in the treatment of apical infections Penicillin has so far proved the most effective although there has been an unfortunate increase in the number of penicillin resistant strains of bacteria found in the mouth It is now a routine practice to administer a massive parenteral dose of procaine penicillin before extracting impacted wisdom teeth Mr Bulleid emphasised the importance of determining the erythrocyte sedimentation rate before condemning teeth with chronic apical infection or those surrounded by chronic pyorrhœa, the E S R is never increased in chronic dental conditions but only in those which are acute A further point mentioned was the necessity of controlling the treatment of gum lesions with penicillin by means of gum smears, since clinical abnormality disappears long before the bacterial picture returns to normal Work is still in progress on the various methods of caries control—topical applications of sodium fluoride, ammonium urea toothpowders, and Gottlieb's enamel impregnation method—and though most of the methods show moderately good results, it is still too soon for definite statistical appraisal of their value Slides and specimens of some of the rarer oral diseases were on view in the department of dental medicine, and this department also demonstrated the determination of the organic content of enamel by paper chromatography—a method of importance now that caries is generally held to begin as a process of proteolysis rather than of decalcification Orthodontic treatment is now being used more and more in the postoperative treatment of cleft palate and hare lip, and the children's department arranged a demonstration to show what can be achieved in the way of cosmetic and functional improvement During the morning session Mr N L Eckhoff performed an epithelial inlay operation for the improvement of a deformity after a hare lip repair Some examples of the work of the upper respiratory tract unit were also shown, during the treatment of malocclusion and oral deformities this unit investigates the whole medical history and the social background of the patient One of the dental advances of the year has been the introduction of self polymerising acrylic resins for restorations in anterior teeth, the technique was demonstrated by Mr J W McLean

University of Oxford

On Feb 24 the degree of D M was conferred on R W Parnell and Sheila R Tangye

University of Cambridge

At a recent examination for the degree of M CHIR the following were successful

T G E Loosemore, G M Lunn J R Thompson, J F R Withycombe

University of London

The William Julius Mickle fellowship for 1950-51 has been awarded to Mr R C Brock surgeon to Guy's Hospital and the Brompton Hospital, London

University of Glasgow

In connection with its 500th anniversary celebrations the university is conferring over 50 honorary degrees The medical graduands from this country are Prof E D Adrian, O M, Prof H F Humphreys, F D S, Prof Dorothy Russell, and Sir John Parkinson Those from overseas are Prof Evarts Graham (Washington University), Prof J M Holst (Oslo University), Prof B A Houssay (formerly of Buenos Aires University) Prof René Sand (Brussels University), and Prof G H Whipple (Rochester University)

Royal College of Obstetricians and Gynæcologists

A Leverhulme research scholarship (£250) is offered for research into problems connected with obstetrics and/or gynæcology It may be held simultaneously with another appointment Forms of application may be had from the secretary of the college 58, Queen Anne Street, London, W 1, and should be returned by July 1

A prize (£50) will be awarded by the council of the college in 1952 for the best original work on the Improvement of Forceps Deliveries Further particulars may be had from the secretary of the college

International Congress of Physical Medicine

This congress will be held in London from July 14 to 19, 1952, under the presidency of Lord Horder Further particulars may be had from Dr A C Boyle, hon secretary, 45, Lincoln's Inn Fields, W C 2

Use of Radioactive Materials

The Ministry of Supply has set up an atomic energy school to teach workers in industrial and medical laboratories how to use radioactive materials The first course, lasting six weeks, begins at the Atomic Energy Research Establishment at Harwell on April 2 Twelve students will be accepted on each course, which after the first, will last for four weeks The second and third courses are expected to begin on May 15 and June 18 Further particulars are available from Dr J E Johnston Isotope Division A E R E, Harwell, Berks

Central Council for Health Education

Dr Robert Sutherland, for the past eight years medical adviser and secretary to the council, has resigned to take up an appointment as senior lecturer in preventive medicine and public health at the University of Leeds

Postgraduate Work in Plastic Surgery

Mr R J V Battle will be at the Royal College of Surgeons on April 5 and on following Thursdays from 2 30 P.M. to 3 P M to advise graduates from this country and overseas on postgraduate studies in plastic surgery He will try as far as possible to find suitable clinical vacancies Further details may be had from Mr. W F Davis, secretary of the postgraduate bureau Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2,

Courses in Hospital Administration

A course which will last about two years, will start in October at the Hospital Administrative Staff College of King Edward s Hospital Fund. Candidates, who must hold an appointment in the hospital service, will be selected by a special panel set up by the Fund, and the Ministry of Health has agreed that study leave with pay may be granted to the candidates selected Although no strict age limit will be imposed it is expected that candidates will be over 25 and under 35 Application forms may be had from the principal of the college, 2, Palace Court, Bayswater, London W 2

Royal Sanitary Institute

Lord Hesketh will preside over the health congress of the institute, which is to be held at Southport from April 23 to 27 Medical speakers will include Sir Henry Cohen and Dr E T Conybeare (The Rheumatic Diseases), Dr A. Torrie (Placement of Children for Adoption), Prof A. V Neale Dr Winifred Kane, and Dr R W Eldridge (Relationship of the Child Welfare Officer and the School Medical Officer to the National Health Service), Dr D W Horn (Cerebrospinal Fever), Dr H N Davies (Tuberculosis), Prof G P Crowden (Coöperation Between Medical Science and Engineering in Industrial Hygiene) Dr J N Morris (Industrial Health What is it we are Trying to Do ?)

Colonial Appointment

Dr Samuel Layinka Ayodeji Manuwa, whose appointment as director of medical services, Nigeria, was lately announced, has been a member of the West African Medical Service since 1927

Dr Manuwa was born in 1903 at Porogun Ljubu Ode Nigeria, and he was educated at the C.M.S grammar school Lagos King's College Lagos and Edinburgh University He graduated M.B at Edinburgh in 1926 The same year he also took the D T.M at Liverpool and the L.M at Dublin In 1927 he joined the Colonial Medical Service as junior medical officer in Nigeria He proceeded to his M D in 1934 also taking the D T.H. at Liverpool. Two years later he obtained the F R.C.S.E In 1944 he was appointed a surgical specialist in the Colonial Medical Service and in 1947 senior specialist In 1948 he was promoted to be deputy director of medical services (regional) He has published papers on Hernia in the West African Negro and Chronic Splenomegaly in West Africa. He was appointed O B E in 1948

Anti-tuberculosis Centre at Istanbul

The new W H.O anti tuberculosis centre, built by the Turkish government at a cost of $130 000 was opened in Istanbul on Feb 17 The centre has been working in temporary premises since its foundation last June, and at the opening of the new headquarters several speakers stressed the value of the work done by W H O in Turkey, where tuberculosis causes 40 000 deaths annually Dr Etienne Berthet director of the centre, recalled that its primary function was to train medical and health workers in modern anti tuberculosis methods and to create a unified organisation against the disease which would serve as a model for similar services elsewhere Dr J B McDougall chief of the tuberculosis section of W.H.O explained that the staff of the centre, consisting of a French tuberculosis specialist an English X ray technician, and a French nurse, had in eight months given instruction to nearly 300 Turkish doctors and nurses In addition 10 000 X ray examinations had been made, 8000 people tested with tuberculin and 3000 vaccinated against tuberculosis A second W.H.O anti tuberculosis centre has already been established in New Delhi and others are in course of preparation for Thailand, El Salvador, Burma, Ceylon, and Pakistan

International Hæmophilia Society

The annual general meeting of this society will be held at the Society for Visiting Scientists, 5, Old Burlington Street London, W 1, on Sunday, March 11, at 2 30 P.M.

Ophthalmological Society of the United Kingdom

The annual congress of this society will be held at 1 Wimpole Street, London, W 1, on Thursday, Friday and Saturday March 29 30, and 31, under the presidency of Mr M H Whiting who will give an address on Surgical Treatment of Rodent Ulcers near the Eye Further particulars may be had from the hon secretary, 45, Lincoln s Inn Fields, W C 2

The Minister on Joint Consultation

Speaking at Darlington on Feb 25, Mr H A Marquand, Minister of Health, remarked 'I am a profound believer in joint consultation in industry, and I want to encourage and develop joint consultation to the maximum extent in the health service I want everyone in the service—doctor nurse, physiotherapist, welfare officer, clerk, or whatever they may be—to feel that they are partners in this great national enterprise, that their ideas and suggestions are welcomed and considered, that their coöperation is highly valued"

Dinner to Sir William Kelsey Fry

The Duke of Gloucester was present at a dinner held at the Royal College of Surgeons of England on Feb 21, to give friends and colleagues the opportunity of congratulating Sir William Kelsey Fry on his knighthood Sir William s health coupled with that of Lady Fry, was proposed by Mr Arthur Bulleid, Air Commodore G A. Ballantyne, and Mr C W Roberts Sir Cecil Wakeley, P.R C S who had been in the chair, presented Sir William with an album containing the signatures of those present

Proposal for Normal Confinements at Home

The London Local Medical Committee has resolved that steps to remedy the shortage of hospital beds ' should include an instruction to hospitals in the London area to see that normal maternity cases are not admitted to hospital except where a responsible person certifies that home conditions make hospital confinement essential Dr Frank Gray, secretary of the committee, said ' Three quarters of all births in the London area are now taking place in hospitals and other institutions A very large number of these could just as well take place at home There is no doubt that a considerable number of people would still be alive today if only beds could have been found for them in hospitals '

Kingston Victoria Hospital

Mr H A Marquand, Minister of Health in a letter to Mr J A. Boyd Carpenter, M.P for Kingston, Surrey, upholds the decision of the South west Metropolitan Regional Hospital Board to convert Kingston Victoria Hospital from a general practitioner hospital into a gynæcological unit " I am quite clear, writes Mr Marquand, that the balance of advantage very definitely lies with the regional board s decision. It is made, I need hardly remind you, after receiving expert medical as well as lay advice ' Mr Marquand goes on to remark that he is alive to the importance of general practitioners in the area having proper alternative hospital resources for their ordinary work, and also every possible facility for following up their own patients when these come under the care of specialists in hospital The proposed arrangements at the Surbiton annexe should he thinks, give reasonable alternative beds for ordinary general practitioner work, particularly if the doctors themselves will coöperate with the board in settling and carrying out some of the details of the arrangement of the new accommodation at their hospital " Mr Marquand has been assured by the chairman of the regional board that the board intends to see that clinical assistantships are offered to the general practitioners and also that the practitioners are given every encouragement to keep in contact with their patients and their treatment when these patients are in the hands of specialists in the hospitals

A statement issued after a meeting on March 5, of the combined medical board and lay committee of Kingston Victoria Hospital contended that this letter ignored the main issue—the provision of equivalent facilities for both patients and doctors—which had been put by a deputation seen by the Minister The committee once again pressed for an impartial public inquiry

Prospect of War

A meeting, sponsored by the writers of the letter on this subject in our issue of Jan 20 (p 170) and other colleagues, will be held at 45, Russell Square, London, W C 1, on Friday, March 16, at 8 P M All doctors interested in the preservation of peace are invited to attend and take part in the discussion

British Medical Association

Dr A W S Sichel, president of the Medical Association of South Africa since 1945, has been elected president of the British Medical Association for 1951–52 Dr Sichel, who is a graduate of Edinburgh University, has been a member of the B.M.A since 1920 The annual meeting of the B M A, which is to be held in London this year, was at one time to have taken place in Johannesburg

Uncertificated Almoners

The Institute of Almoners has opened a supplementary register for some of the almoners employed in the National Health Service who do not hold the institute's own certificate of qualification.

The supplementary register will be open from March 1 to Dec 31 1951 Those applying for admission must be over 30 years of age engaged in medicosocial work in hospital, and known as almoner both at the time of application and continuously for 3 years before July 5 1948 Those admitted to the supplementary register will be entitled to apply for a special category of membership of the institute which will bring them under the ægis of the institute in all professional matters including negotiations for salaries and conditions of service

Foot Health Educational Bureau

This bureau has now formed an advisory panel which includes representatives from medicine, surgery, chiropody, and physical education, and members from the technical and educational sections of the shoe and leather trades Brigadier G S Parkinson is chairman of the panel, and other medical members are Mr S L Higgs, Mr S A S Malkin, Dr R Piper, Mr T T Stamm

Medical Congress at Turin

An international health exhibition with international medical surgical meetings will be held in Turin from May 30 to June 12 These events have been arranged by staff of the *Minerva Medica* and they are sponsored by the Italian Medical Association Prof A M Dogliotti, director of the Turin Surgical Clinic, is chairman of the general committee Further information may be had from the general secretary Prof S Teneff, Palazzo delle Esposizioni al Valentino, Turin, Italy

---

Prof G F Marrian, F R S, is visiting France, under the auspices of the British Council, to lecture to the medical faculties of Paris, Lyons, and Lille on the Metabolism of Progesterone

Prof Jimenez Dias director of the Institute of Medical Research Madrid, and professor of internal medicine in the University of Madrid, is visiting the United Kingdom, under the auspices of the British Council

---

CORRIGENDA

Micromanipulators —In our annotation of March 3 (p 516) the sentence (line 11) describing de Fonbrune's micromanipulator should read This apparatus has micropipettes controlled pneumatically by a ' joystick ' operating three syringes containing air

The New Chambers's Encyclopædia —In our article last week (p 521) there were two major errors of omission We should have stated that the advisory editor responsible for the medical contributions was Dr Hugh Clegg, editor of the *British Medical Journal* And we should also have mentioned that subscription terms on which the new encyclopædia may be purchased will be forwarded on application to Messrs George Newnes, Tower House, Southampton Street, London W C 2

In announcing Dr Karl Bremer's appointment as South African minister of health and social welfare we attributed to him the qualifications of his son The new minister is a graduate of the University of London where he obtained the M B in 1909

Diary of the Week

MARCH 11 TO 17

Monday, 12th

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square W C 1
5 P M Prof F Bremer (Brussels) Cerebellar Mechanisms.

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P.M Mr A G Cross Anti histamine Drugs in Ophthalmology

MEDICAL SOCIETY OF LONDON 11 Chandos Street W 1
8 30 P M Dr A H Douthwaite Dr C B Heald Nature and Treatment of Fibrositis

Tuesday, 13th

ROYAL COLLEGE OF PHYSICIANS Pall Mall East S W 1
5 P M Prof K J Franklin Aspects of the Circulation's Economy (First Oliver Sharpey lecture)

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Mr J C Goligher Functional Results following Sphincter-saving Excisions of the Rectum (Hunterian lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene, Keppel Street W C 1) Prof A Bradford Hill D.SC Statistics in Medical Research

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Street, W C 2
5 P M Dr I Muende Lipoid Affections of the Skin

CHELSEA CLINICAL SOCIETY
7 P M (South Kensington Hotel 47, Queen's Gate Terrace S W 7) Dr Russell Brain P R C P Some Literary Diagnoses Mr Edward Shanks and Mr Lionel Hale will also speak

EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly, W 1) Mr H J Eysenck, D.SC Neuroticism in Twins

Wednesday, 14th

ROYAL COLLEGE OF SURGEONS
3 45 P M Mr C E Shattock Tumours of the Breast (Erasmus Wilson demonstration)
5 P M *Faculty of Anæsthetists* Dr R J Minnitt Reassessment of Ether as an Anæsthetic Agent (Joseph Clover lecture)

INSTITUTE OF DERMATOLOGY
5 P.M Dr C W McKenny X ray Technique

LONDON COUNTY MEDICAL SOCIETY
3 P M (Colindale Hospital The Hyde Hendon, N W 3) Clinical meeting

NORTH EAST LONDON CLINICAL SOCIETY Prince of Wales's General Hospital Tottenham, N 15
8 P M Mr W S McKenzie The Surgery of Deafness—Fenestration Operation

Thursday, 15th

ROYAL COLLEGE OF PHYSICIANS
5 P M Professor Franklin Aspects of the Circulation's Economy (Last Oliver Sharpey lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M Dr E E Pochin Application of Radioactive Isotopes to Medical Research Problems

BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1
8 15 P M Dr L F Lamerton Radiobiological Progress in the United States

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mrs A Pirie Structural Biochemistry of Eye Tissues

HARVEIAN SOCIETY OF LONDON
8 15 P.M (Royal College of Surgeons) Sir James Learmonth Surgery of the Spleen (Harveian lecture)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
7 30 P M (Royal Army Medical College Millbank S W 1) Laboratory meeting

LIVERPOOL MEDICAL INSTITUTION
3 30 P M (Royal Infirmary Chester) Joint meeting with Chester and North Wales Medical Society

Friday, 16th

ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S W 1
5 30 P M Prof A W Downie, Jenner's Cowpox Inoculation (Jenner lecture)

BRITISH INSTITUTE OF RADIOLOGY
6 30 P M Mr J N Barron and Mr N Veall Use of Radioactive Isotopes in Problems Connected with Plastic Surgery

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr S P Meadows Optic Nerve Compression

FACULTY OF RADIOLOGISTS
2 15 P M *Therapy Section.* (Royal College of Surgeons) Prof T Crawford Dr J W D Bull Mr Wylie McKissock Dr J Jackson Richmond Primary Tumours Involving the Spinal Cord

BIOCHEMICAL SOCIETY
2 P M (Department of Biochemistry University College Gower Street W C 1) Scientific papers

---

Messrs Vitamins Ltd have available a few tickets for doctors who may wish to watch the Boat Race on March 24 from their premises Application should be made to Dept B.R 1, Vitamins Ltd , Upper Mall, London, W 6

INFECTION OF "CLEAN" SURGICAL WOUNDS BY THE SURGEON AND FROM THE AIR

THE WORK AND VENTILATION OF AN OPERATING-THEATRE

G R GIRDLESTONE*
D M. Oxfd F.R C.S
SURGEON TO THE WINGFIELD MORRIS ORTHOPÆDIC HOSPITAL AND THE RADCLIFFE INFIRMARY, OXFORD

R B BOURDILLON
C.B.E , D.M. Oxfd
MEMBER OF THE SCIENTIFIC STAFF OF THE MEDICAL RESEARCH COUNCIL

With an Appendix by

ALLAN M. MCFARLAN
M.A., M.B Camb
READER IN HUMAN ECOLOGY UNIVERSITY OF CAMBRIDGE

I —The Surgeon's Activities
(G R G)

BOTH the scope and the length of surgical operations tend to increase with the progressive reduction in the risk to life from shock and loss of blood Advances in anæsthesia, surgical technique, and hæmostasis and a wiser use of blood-transfusion have combined to give surgeons a confidence which is dangerous unless equally progressive precautions are taken against infection for the risk of infection increases with the length and severity of an operation.

Advances in chemotherapy have provided new and most welcome antiseptic agents. Local and general chemotherapy is advisable as a precaution where there is special reason to fear infection, and general chemotherapy is imperative when clinical symptoms and signs indicate postoperative inflammation But for many reasons we should not permit any relaxation of effort to attain asepsis.[1]

The desire for safety is particularly strong in orthopædic work because grafts of autogenous tissues and the insertion of foreign substances increase the danger of uncontrolled infection, and make its outcome more than ordinarily disastrous These are convincing arguments for impeccable asepsis but the need for the highest possible standard of safety is even more pressing when it is remembered that many of the biggest orthopædic operations are not life saving measures but are undertaken with the limited aim of relieving discomfort or improving function It is greatly to the credit of Arbuthnot Lane, a pioneer in the adventure of operating for the betterment of function, that he was acutely aware of this responsibility, and not only adopted a meticulously careful technique but also emphasised its vital necessity He knew that greater initiative in surgical interference must be matched by greater vigilance.

Such prophylaxis includes the care of the patient as a whole and of the tissues of the wound in particular, and the prevention of infection by many procedures, including the good design and ventilation of the theatre Infection by pyogenic organisms does not necessarily cause appreciable inflammation , indeed pyogenic organisms are probably introduced, or fall, into clean wounds many times for every case in which suppuration appears

The care of the patient as a whole is not considered here , though it should be mentioned that his comfort, reassurance, and sleep during the days and nights before and after operation lessen shock and favour the vitality and recuperation of every part of his body So too do the steps taken to maintain the pressure and composition of his blood within normal limits during operation and thereafter

Suppuration of surgical wounds can be prevented

1 By *taking* the utmost care of the tissues so that they may retain their powers of resistance as fully as possible With this must be remembered accurate hæmostasis and temporary drainage of the wound whenever the subsequent formation of a hæmatoma is at all possible
2. By avoiding infection from the patient s own skin, from the hands of the surgeon and his assistants from instruments, gloves, gowns, mackintoshes, swabs sutures, and fluids, from the air and through soaked dressings or plaster-of paris

CARE OF THE TISSUES

The care of the tissues is of primary importance, for healthy vascular tissues are not easily infected, and their resistance to infection is favoured by good circulation and physical rest On the other hand, they are in danger if they have been bruised or dried by long exposure at operation, especially if they are subsequently devascularised from compression or disturbed by repeated movement

Unnecessary bruising can be avoided by thoughtful and sensitive technique Skill and delicacy of touch, clean sharp dissection without a single avoidable movement, swabbing by momentary pressure without a rub, exposure by design of incision rather than by powerful retraction , all these, with accurate hæmostasis, contribute to the safety and comfort of a wound. It is better to operate without a tourniquet when the operation can be carried out with equal accuracy , and when a tourniquet is used it should with few exceptions be removed for hæmostasis before the wound is closed, for long-continued compression is an undesirable and often ineffectual means of controlling subsequent bleeding , and a hæmatoma favours suppuration

Every stitch should be tied gently Deep skin stitches which include underlying tissues should not be tied tight enough to bring the skin together , the exact approximation of the skin is better achieved by the way the superficial stitches are inserted than by pulling them tight Finally in applying a bandage or plaster-of paris over the dressings great care should be given to the avoidance of undue compression Provision should always be made for subsequent swelling, and exact instructions given about the signs and symptoms of compression and the prompt action that should be taken for its relief. Postoperative plasters are better split vertically from top to bottom, and then held by a few bow ties of bandage, which can easily be untied and retied after the plaster case has been adjusted to give complete relief to the patient and to restore free circulation to the part

THE PATIENT'S SKIN

About a third of the population of this country carry *Staphylococcus aureus* in nose or skin, and the proportion

---

* Mr Girdlestone died on Dec. 30 1950

[1] In an address (unpublished) to the Association of Surgeons in 1949 Sir Hugh Cairns gave some personal experiences of operative infection In the first period (192‾–38), when I was operating in two nursing homes as well as at a hospital where the theatre opened off the main corridor the incidence of fatal infection in operations for brain tumour was 2·7% In the second period (1938–44) when I worked in one air-conditioned theatre the incidence of fatal infection was 1% and the over all incidence of operative infection, including superficial wound infection and mild meningeal reactions was 4·4% In 1944 conditions otherwise being unchanged, we began insufflating penicillin sulphamethazine powder into all clean wounds as a routine prophylactic measure, and in the third period (1944–47) the incidence of operative infection fell from 4·4% to under 1% That there were no deaths from infection in this period cannot be attributed solely to prophylaxis, because when infections arose they were energetically treated with antibiotics.

Prospect of War

A meeting, sponsored by the writers of the letter on this subject in our issue of Jan 20 (p 170) and other colleagues, will be held at 45, Russell Square, London, W C 1, on Friday, March 16, at 8 P M All doctors interested in the preservation of peace are invited to attend and take part in the discussion

British Medical Association

Dr A W S Sichel, president of the Medical Association of South Africa since 1945, has been elected president of the British Medical Association for 1951–52 Dr Sichel, who is a graduate of Edinburgh University, has been a member of the B.M A since 1920 The annual meeting of the B M A , which is to be held in London this year, was at one time to have taken place in Johannesburg

Uncertificated Almoners

The Institute of Almoners has opened a supplementary register for some of the almoners employed in the National Health Service who do not hold the institute's own certificate of qualification.

The supplementary register will be open from March 1 to Dec 31 1951 Those applying for admission must be over 30 years of age engaged in medicosocial work in hospital and known as almoner both at the time of application and continuously for 3 years before July 5 1948 Those admitted to the supplementary register will be entitled to apply for a special category of membership of the institute which will bring them under the ægis of the institute in all professional matters including negotiations for salaries and conditions of service

Foot Health Educational Bureau

This bureau has now formed an advisory panel which includes representatives from medicine, surgery, chiropody, and physical education, and members from the technical and educational sections of the shoe and leather trades Brigadier G S Parkinson is chairman of the panel, and other medical members are Mr S L Higgs, Mr S A S Malkin, Dr R Piper, Mr T T Stamm

Medical Congress at Turin

An international health exhibition with international medical surgical meetings will be held in Turin from May 30 to June 12 These events have been arranged by staff of the *Minerva Medica* and they are sponsored by the Italian Medical Association Prof A M Dogliotti, director of the Turin Surgical Clinic, is chairman of the general committee Further information may be had from the general secretary Prof S Teneff, Palazzo delle Esposizioni al Valentino, Turin, Italy

---

Prof G F Marrian, F R S , is visiting France, under the auspices of the British Council, to lecture to the medical faculties of Paris, Lyons and Lille on the Metabolism of Progesterone

Prof Jimenez Dias director of the Institute of Medical Research, Madrid, and professor of internal medicine in the University of Madrid is visiting the United Kingdom, under the auspices of the British Council

---

CORRIGENDA

Micromanipulators —In our annotation of March 3 (p 516) the sentence (line 11) describing de Fonbrune s micromanipulator should read ' This apparatus has micropipettes controlled pneumatically by a ' joystick ' operating three syringes containing air '

The New Chambers s Encyclopædia —In our article last week (p 521) there were two major errors of omission We should have stated that the advisory editor responsible for the medical contributions was Dr Hugh Clegg, editor of the *British Medical Journal* And we should also have mentioned that subscription terms on which the new encyclopædia may be purchased will be forwarded on application to Messrs George Newnes, Tower House, Southampton Street, London, W C 2

In announcing Dr Karl Bremer s appointment as South African minister of health and social welfare we attributed to him the qualifications of his son The new minister is a graduate of the University of London where he obtained the M B in 1909

Diary of the Week

MARCH 11 TO 17

Monday, 12th

INSTITUTE OF NEUROLOGY, National Hospital Queen Square, W C 1
5 P M Prof F Bremer (Brussels) Cerebellar Mechanisms.

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Mr A G Cross Anti histamine Drugs in Ophthalmology

MEDICAL SOCIETY OF LONDON 11 Chandos Street W 1
8 30 P M Dr A H Douthwaite, Dr C B Heald Nature and Treatment of Fibrositis

Tuesday, 13th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East S W 1
5 P M Prof K J Franklin Aspects of the Circulation's Economy (First Oliver Sharpey lecture)

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
5 P M Mr J C Goligher Functional Results following Sphincter saving Excisions of the Rectum (Hunterian lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene Keppel Street, W C 1) Prof A Bradford Hill D SC Statistics in Medical Research

INSTITUTE OF DERMATOLOGY, St John s Hospital Lisle Street W C 2
5 P M Dr I Muende Lipoid Affections of the Skin

CHELSEA CLINICAL SOCIETY
7 P M (South Kensington Hotel 47, Queen s Gate Terrace S W 7) Dr Russell Brain P R C P Some Literary Diagnoses Mr Edward Shanks and Mr Lionel Hale will also speak

EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly, W 1) Mr H J Eysenck D.SC Neuroticism in Twins

Wednesday, 14th

ROYAL COLLEGE OF SURGEONS
3 45 P M Mr C E Shattock Tumours of the Breast. (Erasmus Wilson demonstration)
5 P M *Faculty of Anæsthetists* Dr R J Minnitt Reassessment of Ether as an Anæsthetic Agent (Joseph Clover lecture)

INSTITUTE OF DERMATOLOGY
5 P M Dr C W McKenny X ray Technique

LONDON COUNTY MEDICAL SOCIETY
3 P M (Colindale Hospital, The Hyde Hendon, N W 3) Clinical meeting

NORTH EAST LONDON CLINICAL SOCIETY Prince of Wales s General Hospital Tottenham, N 15
8 P M Mr W S McKenzie The Surgery of Deafness—Fenestration Operation

Thursday, 15th

ROYAL COLLEGE OF PHYSICIANS
5 P M Professor Franklin Aspects of the Circulation s Economy (Last Oliver Sharpey lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M Dr E E Pochin Application of Radioactive Isotopes to Medical Research Problems

BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1
8 15 P M Dr L F Lamerton Radiobiological Progress in the United States

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mrs A Pirie Structural Biochemistry of Eye Tissues

HARVEIAN SOCIETY OF LONDON
8 15 P M (Royal College of Surgeons) Sir James Learmonth Surgery of the Spleen (Harveian lecture)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
7 30 P M (Royal Army Medical College Millbank, S W 1) Laboratory meeting

LIVERPOOL MEDICAL INSTITUTION
3 30 P M (Royal Infirmary Chester) Joint meeting with Chester and North Wales Medical Society

Friday, 16th

ST GEORGE S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner S W 1
5 30 P M Prof A W Downie, Jenner's Cowpox Inoculation (Jenner lecture)

BRITISH INSTITUTE OF RADIOLOGY
6 30 P M Mr J N Barron and Mr N Veall Use of Radioactive Isotopes in Problems Connected with Plastic Surgery

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr S P Meadows Optic Nerve Compression

FACULTY OF RADIOLOGISTS
2 15 P M *Therapy Section* (Royal College of Surgeons) Prof T Crawford Dr J W D Bull Mr Wylie McKissock, Dr J Jackson Richmond Primary Tumours Involving the Spinal Cord

BIOCHEMICAL SOCIETY
2 P M (Department of Biochemistry University College Gower Street W C 1) Scientific papers

---

Messrs Vitamins Ltd have available a few tickets for doctors who may wish to watch the Boat Race on March 24 from their premises Application should be made to Dept B.R 1, Vitamins Ltd , Upper Mall London, W 6

INFECTION OF "CLEAN" SURGICAL WOUNDS BY THE SURGEON AND FROM THE AIR

THE WORK AND VENTILATION OF AN OPERATING-THEATRE

G R GIRDLESTONE*
D M Oxfd , F.R C S
SURGEON TO THE WINGFIELD MORRIS ORTHOPÆDIC HOSPITAL AND THE RADCLIFFE INFIRMARY, OXFORD

R B BOURDILLON
O.B.E , D.M Oxfd
MEMBER OF THE SCIENTIFIC STAFF OF THE MEDICAL RESEARCH COUNCIL

With an Appendix by
ALLAN M MCFARLAN
M A., M B Camb
READER IN HUMAN ECOLOGY, UNIVERSITY OF CAMBRIDGE

I —The Surgeon's Activities

(G R G)

BOTH the scope and the length of surgical operations tend to increase with the progressive reduction in the risk to life from shock and loss of blood Advances in anæsthesia, surgical technique, and hæmostasis and a wiser use of blood transfusion have combined to give surgeons a confidence which is dangerous unless equally progressive precautions are taken against infection, for the risk of infection increases with the length and severity of an operation

Advances in chemotherapy have provided new and most welcome antiseptic agents Local and general chemotherapy is advisable as a precaution where there is special reason to fear infection, and general chemotherapy is imperative when clinical symptoms and signs indicate postoperative inflammation But for many reasons we should not permit any relaxation of effort to attain asepsis[1]

The desire for safety is particularly strong in orthopædic work because grafts of autogenous tissues and the insertion of foreign substances increase the danger of uncontrolled infection, and make its outcome more than ordinarily disastrous These are convincing arguments for impeccable asepsis, but the need for the highest possible standard of safety is even more pressing when it is remembered that many of the biggest orthopædic operations are not life saving measures but are undertaken with the limited aim of relieving discomfort or improving function It is greatly to the credit of Arbuthnot Lane, a pioneer in the adventure of operating for the betterment of function, that he was acutely aware of this responsibility, and not only adopted a meticulously careful technique but also emphasised its vital necessity He knew that greater initiative in surgical interference must be matched by greater vigilance

Such prophylaxis includes the care of the patient as a whole and of the tissues of the wound in particular, and the prevention of infection by many procedures, including the good design and ventilation of the theatre Infection by pyogenic organisms does not necessarily cause appreciable inflammation, indeed pyogenic organisms are probably introduced, or fall, into clean wounds many times for every case in which suppuration appears

The care of the patient as a whole is not considered here, though it should be mentioned that his comfort, reassurance, and sleep during the days and nights before and after operation lessen shock and favour the vitality and recuperation of every part of his body So too do the steps taken to maintain the pressure and composition of his blood within normal limits during operation and thereafter

Suppuration of surgical wounds can be prevented

1 By taking the utmost care of the tissues so that they may retain their powers of resistance as fully as possible With this must be remembered accurate hæmostasis and temporary drainage of the wound whenever the subsequent formation of a hæmatoma is at all possible
2 By avoiding infection from the patient's own skin, from the hands of the surgeon and his assistants, from instruments, gloves, gowns, mackintoshes, swabs, sutures, and fluids, from the air and through soaked dressings or plaster of paris

CARE OF THE TISSUES

The care of the tissues is of primary importance, for healthy vascular tissues are not easily infected, and their resistance to infection is favoured by good circulation and physical rest On the other hand, they are in danger if they have been bruised or dried by long exposure at operation, especially if they are subsequently devascularised from compression or disturbed by repeated movement

Unnecessary bruising can be avoided by thoughtful and sensitive technique Skill and delicacy of touch, clean sharp dissection without a single avoidable movement, swabbing by momentary pressure without a rub, exposure by design of incision rather than by powerful retraction, all these, with accurate hæmostasis, contribute to the safety and comfort of a wound It is better to operate without a tourniquet when the operation can be carried out with equal accuracy, and when a tourniquet is used it should with few exceptions be removed for hæmostasis before the wound is closed, for long continued compression is an undesirable and often ineffectual means of controlling subsequent bleeding, and a hæmatoma favours suppuration

Every stitch should be tied gently Deep skin stitches which include underlying tissues should not be tied tight enough to bring the skin together, the exact approximation of the skin is better achieved by the way the superficial stitches are inserted than by pulling them tight Finally, in applying a bandage or plaster of paris over the dressings great care should be given to the avoidance of undue compression. Provision should always be made for subsequent swelling, and exact instructions given about the signs and symptoms of compression and the prompt action that should be taken for its relief. Postoperative plasters are better split vertically from top to bottom, and then held by a few bow ties of bandage, which can easily be untied and retied after the plaster case has been adjusted to give complete relief to the patient and to restore free circulation to the part

THE PATIENT'S SKIN

About a third of the population of this country carry *Staphylococcus aureus* in nose or skin, and the proportion is probably considerably higher in hospital staff (Vollum 1950). By no method of preparation has it proved possible to achieve sterility right through the skin, but tests have shown that the painting of dry skin with various liquids, of which iodine 2% in 70% alcohol seems the most effective (Gardner and Seddon 1946), produces a surface which is sterile and will remain sterile for an hour or more unless the sweat glands become active. Up to now it has been thought right to prepare the skin the day before operation. The area of operation, together with a large margin of safety, after being thoroughly washed and dried, is painted with the antiseptic of choice and wrapped and bandaged in a light sterile towel (heavy coverings are to be avoided lest they promote perspiration). In the theatre the coverings are carefully removed in such a way as to leave the prepared area of skin untouched. But the surface is no longer aseptic and must be repainted. Professor Gardner, however, writes regarding the use of 2% iodine in 70% spirit: "It seems that for surgical incisions also a single painting just before the operation is all that is necessary, and that elaborate washings and other preparation of the skin could be omitted, for we know that no amount of washing removes all the 'resident' bacteria."

---

* Mr Girdlestone died on Dec. 30 1950

[1] In an address (unpublished) to the Association of Surgeons in 1949 Sir Hugh Cairns gave some personal experiences of operative infection "In the first period (1927–38), when I was operating in two nursing homes as well as at a hospital where the theatre opened off the main corridor, the incidence of fatal infection in operations for brain tumour was 2 7% In the second period (1938–44), when I worked in one air-conditioned theatre, the incidence of fatal infection was 1%, and the over all incidence of operative infection, including superficial wound infection and mild meningeal reactions, was 4 4% In 1944, conditions otherwise being unchanged, we began insufflating penicillin sulphamethazine powder into all clean wounds as a routine prophylactic measure, and in the third period (1944–47) the incidence of operative infection fell from 4 4% to under 1% That there were no deaths from infection in this period cannot be attributed solely to prophylaxis, because when infections arose they were energetically treated with antibiotics"

In my own view the part should be thoroughly washed and inspected on the previous day, then left uncovered. The skin is less likely to sweat, and the patient is more comfortable during the night without extensive coverings to disturb his sleep and remind him of the morrow. In any case it would seem wise for the surgeon to cleanse the skin over the area of the incision with several "ether-meth" swabs before painting it with iodine in spirit.

When, however, the incision is made, sweat glands and hair follicles are laid open, and at once the edges of the cut become a possible source of infection.

As part of an investigation made at the Wingfield-Morris Orthopædic Hospital (O'Brien 1947) swabs were taken from the cut edges of the skin immediately after incision. These grew normal skin flora in about a third of the cases, and further swabbing at the end of the operation revealed a higher proportion of positives. From one of two heavy skin carriers of *Staph. aureus* identified before operation the organism recovered from the cut edge was of the same phage type (healing was uneventful).

No good purpose is served by pasting fabric on the skin with mastic before making an incision. This is one more rite; the mastic is one more material to sterilise and keep sterile; and the appearance of safety is an illusion, for the cut edges of the skin remain exposed.

Skin Towels

How best can the wound be protected from infection from the skin? Experience of nearly forty years' operating since I adopted the iodine spirit preparation leaves me doubtful whether the covering of the cut edges of the skin and the skin surrounding the area of operation by skin towels is beneficial, neutral, or harmful. My operating experience can be divided into three parts—about twenty years before I clipped skin towels round the wound, followed by about twelve years of the routine use of skin edge towels for all large or long operations, and, finally, a period in which I have abandoned them (except for operations through windows in plaster of paris). During the towelled skin edge period suppuration developed several times after operations which I had previously done with complete impunity. For this experience other factors may be responsible. Indeed the period includes the worst war years, when patients' skins were dirtier, and when hospital staff were experiencing repeated nasal contamination from the dressing of heavily infected gunshot wounds (for however effective good masks may be in preventing infection of the air *from* nose and mouth they have little value in the other direction, from air to nose).

Nevertheless it is perhaps worth while to consider the state of affairs round the wound with its edges towelled and not towelled. The towels are commonly fastened round the edge with some form of clamp or Michel clip with claws that grip or penetrate the skin. These clamps are left in place throughout the operation, however long; they lead to local trauma and ischæmia of the skin, and tend to squeeze out material from the glands. The exudation mixes with blood and soaks through the towel along the edge of the wound. There must be some danger of staphylococcal infection in both cases, but there is this difference: in the towelled wound the margins look safe, whereas in the untowelled wound they look dangerous. Therefore the surgeon is ready to allow suture materials, swabs, and so on to brush against the towelled skin edge but is careful to avoid anything of the kind with the uncovered skin edge.

The skin towels also cover the surface of skin round the wound. But adequate preparation keeps the surface of the skin safe until there is gradual reinfection from its depths. Furthermore the surface and edges can be gently wiped after the incision, and every 30 minutes thereafter, with swabs soaked in acriflavine 1/1000 in water, 1% tetrachlorxylol in 70% spirit, or some other relatively non-toxic antiseptic. If iodine in spirit has been repeatedly applied to the surface of the skin, it is well to wipe the skin well with 70% spirit after closure of the wound.

In the hope of getting some further information by experiment on this point, an investigation was undertaken at the Wingfield Morris Orthopædic Hospital in 1949–50. Unfortunately this not only entailed repeated disturbance of major operations but also threw a good deal of extra strain on an overworked laboratory. Therefore it was not considered justifiable to continue it very long, and the numbers are relatively small. The investigation was made at my request by Mr. G. Mitchell, the resident surgical officer, who was solely responsible for an investigation covering 98 cases. From these he selected a series of 50 comparable operations, 25 with towels and 25 without. The remaining 48 operations did not satisfy the criteria as regards severity and length, which were (1) a major operation requiring protracted retraction, and (2) exposure of the wound for over 40 minutes.

Material for culture was obtained as follows:

No skin towels used.—By rubbing the cut edges of the skin (1) immediately after incision, (2) after 30 minutes, and (3) after 60 minutes.

Skin towels used.—(1) By rubbing the newly cut skin edges before the application of towels; (2) from the surface of the towels where they covered the skin edges 10 minutes after skin towels had been applied; (3) after 30 minutes; and (4) after 60 minutes.

When no towels were used, *Staph. aureus* was recovered from swabs at both 30 minutes and 60 minutes after the incision in one case and at 60 minutes only in a second case. When towels were used, *Staph. aureus* was recovered immediately after incision in one case, and the later swabs over the towels were all negative.

To discover whether there was any relation between these findings and postoperative wound sepsis the results of culture and the evolution of the wound in the whole 98 cases were investigated. There were 5 patients with positive skin swabs, and of these 1 had an infected hæmatoma, and 1 a superficial stitch infection. Of the 93 with negative swabs 1 had an infected hæmatoma, and 2 had a superficial stitch infection.

There is a great difference between the finding of "normal skin flora" in rather more than a third of the swabs rubbed along the edges of the incision by Dr. O'Brien, and of *Staph. aureus* in particular in only 5 out of 98 cases by Mr. Mitchell in the later series.

It is clear that the number of cases is not sufficient to allow of any conclusion as to the relative advantages of towelling the edges and of leaving them exposed Furthermore, in the investigation any antiseptic wiping of the surfaces and edges of the skin was avoided, so as to favour the collection and culture of bacteria, whereas in my practice this is a periodic precaution

Further bacteriological investigations were made by O'Brien (1947) to discover (1) how far one strain, or a few strains, of staphylococci were responsible for the infection of the 19 cases of surgical infection which were under review , and (2) whether the strain in the pus was the same as that of any *Staph. aureus* recovered from the patient's skin

The organism was a coagulase-positive *Staph. aureus* in 18 cases and *Pseudomonas pyocyanea* in 1 Of the cultures of *Staph aureus*, 16 were sent to Dr V D Allison, who phage typed 12, reporting the other 4 as untypable The strains from 3 patients operated on within six weeks of each other showed the same type, but for the others at least 10 different strains were responsible

The skin of 12 of the infected patients was swabbed some time after infection had become obvious (hence there was the possibility of infection from the wound) In 6 cases skin and nasal swabs did not grow *Staph aureus* , in 1 case the phage type of a staphylococcus recovered from the skin was different from that in the wound, and in 5 the phage type was identical

This evidence supports but does not prove the suggestion that some patients become infected by the staphylococci on their own skin

It is also clear from an investigation carried out by McFarlan (see below) into one case and those of O'Brien (1947) that it is by no means easy to be sure of the source of an infection leading to suppuration Indeed it is noteworthy that, in a case in which a surgeon carrying *Staph aureus* had a punctured glove, the *Staph aureus* recovered from the pus was not of the same phage type as that of the surgeon's hand , in another case, where *Staph aureus* was found on the patient's skin, the suppuration was due to *Staph aureus* of another type , and in a third case, where a heavy carrier of *Staph aureus* (nose and skin) took part in the operation, a similar difference was found. These results make the investigation appear inconclusive , but at the same time they indicate the multiplicity of sources of infection, and suggest that staphylococci of several different groups—e g , from a nurse's nose, a surgeon's hands, or the patient's skin—may simultaneously infect our wounds, and that suppuration may develop only when a cluster of staphylococci (of whatever group) reaches favourable soil ,, bruised devascularised tissue or a hæmatoma

Deep infection seems to be closely related to the length of incision, and the duration of exposure of the deep tissues, for the operations in which such infection has taken place have been operations with long incisions and long exposure, particularly operations on the hip with a Smith Petersen incision, and not operations with relatively short incisions on knee, hand, or foot

Now this is the more remarkable when one remembers that in the big hip operations everything can be done gently and there is very little bruising of the tissues, whereas at the other end of the scale, in subcutaneous tenotomy followed by manipulation, considerable bruising and stretching of structures is entailed and yet infection is almost unknown I have never seen an infected subcutaneous tenotomy though I have done very many, and McCrae Aitken (1935) quotes Robert Jones as saying that his uncle, H O Thomas (in practice between 1859 and 1891), and he had done over two thousand subcutaneous tenotomies without any case of inflammation

Lymphatic Infection

The possibility of the area of operation being infected during or after the operation from a peripheral skin lesion via the lymphatics passing through it must always be remembered for this reason the hand or foot distal to the site of operation on a limb should be carefully examined on the patient's admission.

THE SURGEON'S HANDS

One can do something to avoid becoming a carrier of pyogenic organisms by using instruments for septic dressings, and gloves for palpation near purulent discharge The hands of surgeons and nurses, gloved or not, which have been contaminated by pus, should never be used for turning on a tap or handing a towel. And experiments have shown that it is best to wash with plenty of soap and friction, and with few rather than frequent douches under running water [2]

Living organisms can be left on the surface of the gloves by defective sterilisation, and can be placed there by faulty technique in gloving, but are very much more often transferred from within through a puncture or a tear Infection from within the gloves may be due to incomplete sterilisation of their inner surface, inadequate washing of the hands or their deep infection, or to the escape of talcum powder, which may itself be infected (see below) or add to the danger of the establishment of infection by its foreign body effect

The drying, powdering, and gloving of the hands need considerable care to avoid any risk of contamination,[2] but danger is not over when the gloves are on Care will keep their outer surface as safe as the swabs and instruments *except for the risk of puncture* That this risk is by no means negligible is shown by a recent investigation

Of gloves used in major orthopædic operations in the Wingfield-Morris Orthopædic Hospital in 1947 a puncture or a tear was discovered in 202 out of 816 (24 7%) This figure is remarkably similar to that reported by Devenish and Miles (1939) in their comparable series, in which 1593 out of 6585 (24 2%) were punctured

These figures suggest a very frequent danger of infection from the surgeon's hands The matter was followed up as follows

On 36 occasions, after the surgeon had finished operating, his gloves and those of all assistants were turned inside out and inflated, and three of the fingers were extensively rubbed on blood-agar plates Three of the surgeons and one nurse were found regularly to have *Staph aureus* on the inside of their gloves

All the surgeons and the theatre staff who assisted at operations were frequently tested by nasal swabs and a moistened swab rubbed on the back of each hand and, for a time, throat swabs also These were cultured on blood-agar and Chapman plates, and later the swabs were also immersed in broth and incubated and then subinoculated on to blood-agar plates. *Staph aureus* was isolated regularly from five of the sixteen surgeons and nurses, and occasionally from a further six

The phage type of the organisms recovered from the regular carriers was determined, and the findings compared with the analysis of the twelve strains recovered from the infected patients It is remarkable that in this group, covering the only patients (18) to which this test could be applied, in no instance were the staphylococci grown from the pus of a patient of the same phage type as those grown from the hands of the surgeon who had operated or his assistants

The numbers are small, and suppuration of surgical wounds may well be at present more often due to infection from the surface of the hands through punctured gloves than to any other cause, and it seems well worth while that frequent periodic investigations should be made in all hospitals on the lines of those described by Devenish and Miles (1939)

It is possible for the surgeon to develop a standard of discipline of himself and his team which will ensure that is probably considerably higher in hospital staff (Vollum 1950) By no method of preparation has it proved possible to achieve sterility right through the skin , but tests have shown that the painting of dry skin with various liquids, of which iodine 2% in 70% alcohol seems the most effective (Gardner and Seddon 1946), produces a surface which is sterile and will remain sterile for an hour or more unless the sweat glands become active Up to now it has been thought right to prepare the skin the day before operation The area of operation, together with a large margin of safety, after being thoroughly washed and dried, is painted with the antiseptic of choice and wrapped and bandaged in a light sterile towel (heavy coverings are to be avoided lest they promote perspiration) In the theatre the coverings are carefully removed in such a way as to leave the prepared area of skin untouched But the surface is no longer aseptic and must be repainted Professor Gardner, however, writes regarding the use of 2% iodine in 70% spirit "It seems that for surgical incisions also a single painting just before the operation is all that is necessary, and that elaborate washings and other preparation of the skin could be omitted, for we know that no amount of washing removes all the 'resident' bacteria"

---

[2] The details and order of these processes differ widely in different places , perhaps some standardisation of washing, masking, gowning and gloving is desirable

In my own view the part should be thoroughly washed and inspected on the previous day, then left uncovered The skin is less likely to sweat, and the patient is more comfortable during the night without extensive coverings to disturb his sleep and remind him of the morrow In any case it would seem wise for the surgeon to cleanse the skin over the area of the incision with several "ether-meth" swabs before painting it with iodine in spirit

When, however, the incision is made, sweat glands and hair follicles are laid open, and at once the edges of the cut become a possible source of infection

As part of an investigation made at the Wingfield-Morris Orthopædic Hospital (O'Brien 1947) swabs were taken from the cut edges of the skin immediately after incision These grew normal skin flora in about a third of the cases, and further swabbing at the end of the operation revealed a higher proportion of positives From one of two heavy skin carriers of *Staph aureus* identified before operation the organism recovered from the cut edge was of the same phage type (healing was uneventful)

No good purpose is served by pasting fabric on the skin with mastic before making an incision This is one more rite , the mastic is one more material to sterilise and keep sterile , and the appearance of safety is an illusion, for the cut edges of the skin remain exposed

Skin Towels

How best can the wound be protected from infection from the skin ? Experience of nearly forty years' operating since I adopted the iodine spirit preparation leaves me doubtful whether the covering of the cut edges of the skin and the skin surrounding the area of operation by skin towels is beneficial, neutral, or harmful My operating experience can be divided into three parts—about twenty years before I clipped skin towels round the wound, followed by about twelve years of the routine use of skin edge towels for all large or long operations, and, finally, a period in which I have abandoned them (except for operations through windows in plaster of paris) During the towelled skin edge period suppuration developed several times after operations which I had previously done with complete impunity For this experience other factors may be responsible Indeed the period includes the worst war years, when patients' skins were dirtier, and when hospital staff were experiencing repeated nasal contamination from the dressing of heavily infected gunshot wounds (for however effective good masks may be in preventing infection of the air *from* nose and mouth they have little value in the other direction, from air to nose)

Nevertheless it is perhaps worth while to consider the state of affairs round the wound with its edges towelled and not towelled The towels are commonly fastened round the edge with some form of clamp or Michel clip with claws that grip or penetrate the skin These clamps are left in place throughout the operation, however long , they lead to local trauma and ischæmia of the skin, and tend to squeeze out material from the glands The exudation mixes with blood and soaks through the towel along the edge of the wound There must be some danger of staphylococcal infection in both cases, but there is this difference in the towelled wound the margins look safe, whereas in the untowelled wound they look dangerous Therefore the surgeon is ready to allow suture materials, swabs, and so on to brush against the towelled skin edge but is careful to avoid anything of the kind with the uncovered skin edge

The skin towels also cover the surface of skin round the wound But adequate preparation keeps the surface of the skin safe until there is gradual reinfection from its depths Furthermore the surface and edges can be gently wiped after the incision, and every 30 minutes thereafter, with swabs soaked in acriflavine 1/1000 in water, 1% tetrachlorxylol in 70% spirit, or some other relatively non toxic antiseptic If iodine in spirit has been repeatedly applied to the surface of the skin, it is well to wipe the skin well with 70% spirit after closure of the wound

In the hope of getting some further information by experiment on this point, an investigation was undertaken at the Wingfield Morris Orthopædic Hospital in 1949–50 Unfortunately this not only entailed repeated disturbance of major operations but also threw a good deal of extra strain on an overworked laboratory Therefore it was not considered justifiable to continue it very long, and the numbers are relatively small The investigation was made at my request by Mr G Mitchell, the resident surgical officer, who was solely responsible for an investigation covering 98 cases From these he selected a series of 50 comparable operations, 25 with towels and 25 without The remaining 48 operations did not satisfy the criteria as regards severity and length, which were (1) a major operation requiring protracted retraction, and (2) exposure of the wound for over 40 minutes

Material for culture was obtained as follows

No skin towels used —By rubbing the cut edges of the skin (1) immediately after incision , (2) after 30 minutes , and (3) after 60 minutes

Skin towels used —(1) By rubbing the newly cut skin edges before the application of towels , (2) from the surface of the towels where they covered the skin edges 10 minutes after skin towels had been applied , (3) after 30 minutes , and (4) after 60 minutes

When no towels were used, *Staph aureus* was recovered from swabs at both 30 minutes and 60 minutes after the incision in one case and at 60 minutes only in a second case When towels were used, *Staph aureus* was recovered immediately after incision in one case, and the later swabs over the towels were all negative

To discover whether there was any relation between these findings and postoperative wound sepsis the results of culture and the evolution of the wound in the whole 98 cases were investigated There were 5 patients with positive skin swabs, and of these 1 had an infected hæmatoma, and 1 a superficial stitch infection Of the 93 with negative swabs 1 had an infected hæmatoma, and 2 had a superficial stitch infection

There is a great difference between the finding of "normal skin flora" in rather more than a third of the swabs rubbed along the edges of the incision by Dr O'Brien, and of *Staph aureus* in particular in only 5 out of 98 cases by Mr Mitchell in the later series

It is clear that the number of cases is not sufficient to allow of any conclusion as to the relative advantages of

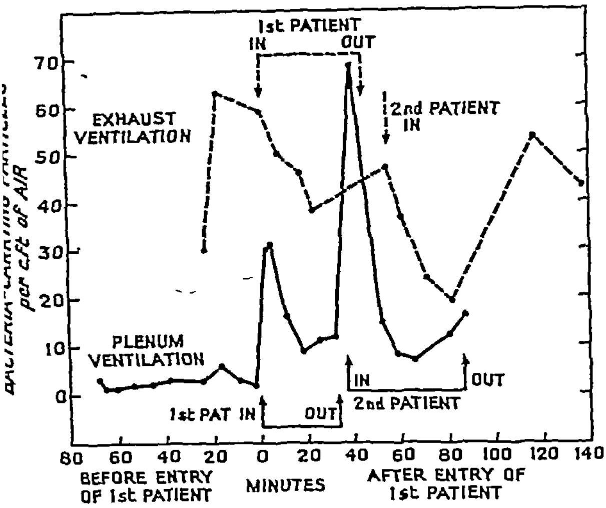


Fig. 1—Airborne bacteria in Wingfield Morris theatre

This process is illustrated by the series of tests shown n figs 1–3 Fig 1 gives the total counts of bacteria-carrying particles per c ft. of air found with a slit sampler (Bourdillon et al. 1948) in the Wingfield orthopædic theatre before and during operations The sampler was placed about 2 ft 6 in from the patient's head in the position shown at S_1 in fig 2 The interrupted line shows the counts obtained during part of a typical session of operations with exhaust ventilation only After starting at 30 infected particles per c ft of air the count rose to 63 about a quarter of an hour before the entry of the first patient It then fell slowly, and showed irregular variations for the rest of the morning For most of the time it remained at over 30 per c ft, and only fell below 20 for a brief period

The cause of the strikingly high figures found before the entry of the first patient was then studied as follows It was evident that these figures might be due either to very fine particles that had remained suspended for a long time, or to some special source of infection arising in the preoperative period Samples taken at intervals during the night and the early morning showed counts of only 2 or 3 per c ft, thus proving that the trouble was not due to the long-continued suspension of very fine particles It was also found that switching on the exhaust fan and sweeping the floors of the theatre and corridor during the night caused only a moderate rise in the contamination of the theatre air (to about 25 per c ft), in contrast to the higher figures shown in the preoperative periods A detailed study was therefore made of the events occurring before a morning's session of operating Three observers, each using a slit sampler, recorded the bacterial air counts and the movements of personnel, blankets, &c, in the theatre, corridor, and anæsthetic room from 6 45 to 9 20 A M A plan of the theatre and adjacent rooms, &c, with the position of the samplers, is shown in fig 2 The theatre sampler was always used in about the same position in relation to the operating-table

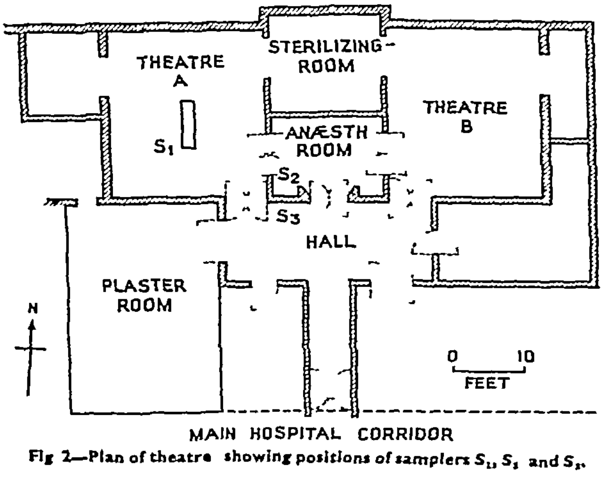


Fig 2—Plan of theatre showing positions of samplers S_1, S_2 and S_3.

This study showed that a rise in bacterial counts in all three samplers began as the first patients entered the hall outside the theatre, and increased rapidly when the ward blankets were changed for the theatre coverings before the patient entered the anæsthetic room The greatest rises took place just after the change of the second patient's blankets The order in which the highest counts were reached at the three sampling points was the same as would be expected from the direction of the air flow as shown by smoke tests Thus air flowed from the hall both directly under the theatre doors and through the anæsthetic room into the theatre (also under the doors) The maximal counts appeared first in the hall, next in the anæsthetic room, and last in the theatre These results seemed conclusive evidence that the chief cause of high contamination of the theatre air during the preoperative period was the sucking-under the doors of air from the hall and anæsthetic room floors, contaminated by dust from the ward blankets, the porters' feet, and so on

The further question was considered how far the theatre air might be infected by air from the plaster room, which opened on to one side of the hall, and in which infected wounds were often handled at that period The results of tests on this point are shown in fig 3 This gives the counts obtained in two tests taken at night, with the rooms empty except for the experimenters In each test the theatre air was sampled for bacteria with the exhaust fan running and all doors closed, and half way through the test the air in the plaster room was contaminated by sweeping the floor Test *a* was done in a light north easterly breeze, and test *b* in a south west wind The difference is striking, and shows the importance, in studies of this type, of taking observations in at least two different states of wind and weather, instead of relying on a single day's tests

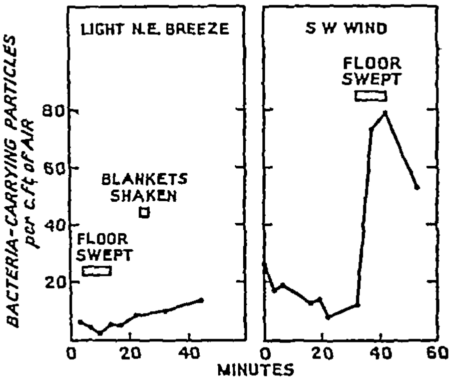


Fig 3—Effect of stirring up dust in plaster room with all doors shut on bacterial count in theatre air

It was thus clear that the exhaust fan in the theatre unit caused the introduction of large quantities of dirty dust laden air, which might at any moment be dangerous if it included active pathogens The hospital authorities decided promptly that conditions must be improved, in spite of war time shortages, and a 'Plenum' (positive pressure) system of ventilation was installed In this plant a 2 h p motor in the basement drew clean air from above the roof of the hospital and forced it through oiled metal filters to remove insects and coarse particles, and then into the theatre through two openings (each 42 × 15 in) controlled by adjustable louvres above the theatre doors The old exhaust fan above the sterilisers was retained, but, since it was of much lower output than the input no swab, needle, ligature, or part of an instrument which has been touched by the gloved hand enters the wound. But for some operations and some operators the gain in touch, delicacy, and speed justify the direct use of gloved hands (except by carriers of staphylococci or streptococci).

INSTRUMENTS, EQUIPMENT, AND MATERIALS

The procedure described below is based on accepted practice which has been modified in certain directions in the Wingfield Morris Orthopædic Hospital as a result of tests of sterility. It is essential to test periodically the efficacy of drum sterilisation of various awkward articles such as mackintoshes and bandages.

Drum Sterilisation

To ensure the sterilisation of the inner surface of *rubber gloves* it is necessary to facilitate the entry of steam. The following procedure has proved effective.

The rubber gloves are packed loosely with the wrist reflected and the palm held open with a pad of gamgee tissue. Each pair of gloves is put in a loose double folder of lint, in one of the pockets of this folder is placed a very small quantity of talcum powder in a flat muslin packet. To ensure the sterilisation of the talcum powder the additional precaution has been taken of previously exposing it in thin layers (less than $^1/_4$ in. deep) on flat trays for two hours to a temperature of 160–180°C. For the gloves 5–10 lb. pressure for 20 minutes is adequate.

Gowns, towels, mackintoshes,[3] *&c.*, are sterilised at 20 lb. for 30 minutes, or 15 lb. for 45 minutes.

Sterilisation tests are carried out every three weeks in the following manner.

Living spores of an unnamed aerobic bacillus isolated from the soil, relatively heat-resistant and proved satisfactory for the purpose, are obtained from the bacteriological laboratory on a piece of string in a screw top bottle. The screw is loosened and the bottle placed in the centre of the drum, or the place least accessible to the steam. This method of testing is applied to all drums whatever their contents.

Instruments, and Suture and Ligature Materials

Ordinary instruments are boiled in 1% sodium bicarbonate for five minutes. *Knives* are boiled for three minutes, and then kept in 90% spirit. *Chisels* and *nibblers* are sterilised in oil at 250°F (121°C) for 10 minutes. *Needles* are kept in equal parts of lysol and 70% methylated spirit. After dirty cases the needles are boiled in 1% sodium bicarbonate for 10 minutes, and then kept in the lysol spirit solution. After clean cases the needles are put into pure lysol for half an hour, and then kept in the lysol spirit solution.

Suture and ligature materials have been subjected to much study. They fall into two classes: (1) those that can be sterilised by boiling but remain undissolved in the body, constituting a potential source of trouble if infection arises, and (2) catgut, desirable for its solubility within the body but requiring a high standard of sterilisation by its "manufacturers." Further, the handling of these materials within the theatre, whether on reels or in sealed tubes, calls for a safe ritual. *Silk* and *linen thread* are steam sterilised at 10 lb. for 30 minutes, wound rather loosely and in fairly short lengths on glass reels; after use the reels are boiled for 3 minutes in 1% sodium bicarbonate, then kept in 1–60 phenol. *Silkworm gut* and '*Nylon*' are boiled for 10 minutes, and after use the hanks are boiled again for 3 minutes, then stored in 1–60 phenol. The sterile tubes of *catgut* are kept *under* 1–60 phenol until they are taken out for use.

Beef bone pegs are boiled for 15 minutes, then stored in equal parts of 'Dettol' and 70% spirit.

Specimens from all these materials are examined for sterility every six months.

Bandages

Wool bandages for use under plaster are unrolled and rolled again loosely before sterilisation, to avoid the risk of their proving impermeable to the steam. All felt, gamgee, lint, wool, &c., used in the theatre is sterilised before it is brought in.

Wherever *plaster of paris* is applied over the wound it is first covered with several layers of sterile gauze and plaster wool. It is possible for pathogenic organisms in the plaster to be carried through the sterile dressings during the application of the plaster, or to infiltrate a subsequent exudation of bloody fluid from the wound.

Twenty-seven plaster bandages taken from stock at different times grew no organisms of the species commonly recognised as pathogenic. The home-made plaster bandages occasionally grew *Staph. albus*, hence presumably they could be infected during manufacture by a heavy *Staph. aureus* carrier.

The felt used under plaster is autoclaved against spore bearing organisms before it is brought into theatre or plaster room.

THE OPERATING THEATRE

Where the theatres are large there is little danger of direct contamination of the walls. At the Wingfield these are washed down with a weak solution of dettol in water once a week. The floors are swabbed and squeegeed with 2% lysol at the end of the day's operating, using a stirrup pump spray, and are subsequently washed with ordinary soap and water. Overhead lamps are wiped and oiled every day to avoid the risk of falling particles. Tables and anæsthetic machines are washed with 2% dettol. If the portable X ray machine is taken into the theatre it is wiped over, including the wheels, with 2% dettol, and the machine and cassettes are draped with sterile towels.

II.—Airborne Infection

(R. B. B.)

There should be little need to justify the desirability of avoiding airborne infection as far as is practicable. That air contamination in theatres is a real danger is suggested by personal experiences published by Cairns (1939), Robinson et al. (1946), and Sevitt (1949) in this country and by the studies of Hart (1938) and others in the U.S.A.

It is true that in many theatres the dangers of contact infection are probably greater than those of airborne infection, but this does not afford proper grounds for neglecting simple measures such as improved ventilation, which will often do much to reduce air contamination.

The chief sources of air contamination are the air supply to the theatre and infection of the air in the theatre by the surgeon and his staff and by the patient and his coverings.

AIR-SUPPLY TO THEATRE

It is a remarkable fact that it has been the usual practice in this country to ventilate theatres solely by exhaust fans, without any serious consideration of the routes by which the air enters the theatres. These exhaust fans are installed with the primary purpose of removing steam from sterilisers. Though they do this efficiently, they often have the serious drawback of sucking air and dust at high velocity under the theatre doors. Even when special inlets are provided for the air, these often, if fitted with a filter, have sufficient resistance to air flow to cause an appreciable reduction of air-pressure in the theatre, and, not infrequently, are blocked up altogether to avoid draughts. As a result of this reduced pressure, if the air in the corridor outside the theatre is contaminated with dust (from ward blankets or other source), large numbers of bacteria will be sucked in under the doors and distributed throughout the theatre air.

---

[3] For the importance of adequate cleansing of mackintosh aprons see Corry (1950).

standards for theatre air have been suggested recently by Bourdillon and Colebrook (1946) For the total number of airborne particles carrying organisms which grow to visible colonies after twenty four hours on blood-agar at 37°C, after sampling during periods of quiet operation, the figures suggested were as follows (1) for rooms used for dressing small wounds or for minor operations only, 20 per c ft , (2) for theatres used for ordinary major operations, 10 per c ft , and (3) for theatres used for long operations on easily infected tissues, 2 0–0 1 per c ft The lower counts can only be maintained by taking pains and spending money on ventilation plant

We wish to thank Prof A D Gardner, Dr A T Robb Smith, Mr R L Vollum, D.PHIL., Dr A. M McFarlan, Dr J R O'Brien, Dr J. Cairns, and Dr M Pickles for assistance in the bacteriology , surgical colleagues for their coöperation, and Dr McFarlan for taking and studying samples of airborne bacteria

Appendix

INVESTIGATION OF WOUND INFECTION

(A. M McF)

On Jan 26, 1942, a request was made for investigation of a case of wound infection following operation A visit was paid to the hospital, and it was learnt that the patient, a woman aged 44, admitted on Jan 19, 1942, had undergone next day a subtaloid arthrodesis and had a plaster case applied On the evening of Jan 23 the patient's temperature rose to 104 2°F On Jan 24, a window was cut in the plaster and the dressing was inspected , it appeared clean and was not disturbed On Jan 25, the dressing was foul smelling It was removed, and a fresh plaster was applied The patient's temperature was swinging between 101° and 104°F On Jan 26, sulphapyridine was given by mouth 2 g initially and 1 g four-hourly thereafter On Jan 27, the wound was dressed with soft-paraffin gauze On Jan 29, eusol dressings were applied, and the plaster was changed The wound subsequently improved satisfactorily

Cultures of swabs taken from the wound on Jan 25, yielded *Strep pyogenes* group A, type 27 , *Staph. aureus* coagulase positive , *Bacillus mesentericus*, and *Bact aerogenes*

Cultures of swabs taken on Jan. 27, yielded *Strep pyogenes* group A, type 27 , *Staph aureus* coagulase-positive , and *Bact aerogenes*

Probably the serious infection of the wound was due to the hæmolytic streptococcus, but the staphylococcus may have played some part The presence of *B mesentericus* and *Bact aerogenes* suggested the possibility of an infection by dust

Possible Sources of Infection

The Patient —Neither the patient nor anyone in the house where she had been living had recently had a respiratory infection. Previous operations on her ankle had not been followed by infection

Those Present at the Operation —Nose and throat swabs were taken of the surgeon who assisted and of the theatre staff, but none was found to be a carrier of hæmolytic streptococci The theatre nurses had all had colds recently but had been wearing thicker masks than usual The nurse who took the operation on Jan 20 went off duty on Jan. 23 with an upper respiratory tract infection. On Jan 26 she was carrying considerable numbers of coagulase-positive *Staph aureus* in her nose Thus no evidence was obtained that there was a carrier of hæmolytic streptococci in the theatre

Several visitors were present at the operation, and there was a considerable amount of coughing Some of the masks provided for visitors were small and thin, and the visitors may have contributed some organisms to the air

Dressings and Plaster —The arrangements for sterilisation in the autoclave were excellent and controlled by Browne tubes The patient operated on before the present patient had plasters applied, and no infection had arisen Two patients had had skin-grafts done later in the morning and had shown no signs of superinfection Thus there was no evidence of a gross failure of sterilisation on the day in question

Possibly, however, the plaster-wool which was put in the autoclave in tight rolls was not always sterilised completely Still more worthy of consideration was the unsterilised plaster-wool, which lay on the plaster-room trolley exposed to the air, and the outer exposed part was applied next to the skin Possibly moisture from the plaster and exudate from the wound might have permeated both unsterile and sterile plaster-wool and the sterile dressings, and organisms present in the unsterile wool thus passed to the wound

Samples of plaster-wool were examined, and *B mesentericus* and *Bact aerogenes* were isolated from an unsterilised roll taken from the theatre store cupboard These strains showed the same morphological, colonial, and biochemical reactions as those isolated from the wound This suggested that organisms might pass to the wound from unsterile plaster-wool. Many of the organisms in cotton-wool may be harmless, but it has been shown that tetanus spores may be present , hence thorough sterilisation is necessary

Air of Theatre and Plaster Room.—During observations on the bacterial content of the air in the theatre and plaster room aerobic spore bearers appeared on the plates, sometimes in considerable numbers, after a patient had been moved in Some strains showed a peculiar spreading growth with greening of the blood-agar plate A similar growth was obtained when cultures were made of a roll of plaster-wool taken from the plaster-room trolley This is evidence that organisms present in the air settle on the materials exposed on a plaster trolley Coagulase-positive staphylococci and hæmolytic streptococci have been found in the air, but only occasionally and in small numbers Possibly, however, sufficient numbers of a virulent strain to initiate infection might settle on plaster-wool and so gain access to wounds

Summary and Recommendations

After a clean operation a wound became infected with a type-27 hæmolytic streptococcus, a coagulase-positive staphylococcus, *Bact aerogenes*, and *B mesentericus*

No evidence of the source of the streptococcus was obtained

The theatre nurse who took the operation was later found to be carrying a coagulase-positive staphylococcus in her nose This cannot be considered to incriminate her, for no investigation was made of many possible reservoirs of staphylococci in the noses of the visitors and on the skin of those taking part in the operation

Bact aerogenes and *B mesentericus* were isolated from an unsterilised roll of plaster wool. The application of a plaster over unsterilised materials may allow organisms to penetrate the sterile dressings

Plaster-wool exposed on a trolley in the plaster room may be contaminated by organisms present in the air

It is suggested that (1) efficient masks should be provided for all those present at operations , (2) all plaster wool used under a plaster should be autoclaved, and before autoclaving the rolls should be unwound and rolled loosely to ensure their penetration by steam , and (3) plaster-wool should not be exposed on the plaster-room trolleys either before or after sterilisation

REFERENCES

Aitken D M (1935) Hugh Owen Thomas His Principles and Practice London

Bourdillon R B Colebrook L (1946) *Lancet* i 561 601

— Lidwell O M. Lovelock J E (1948 *Spec Rep Ser med Res Coun Lond* no 262

Cairns H (1939) *Lancet*, i 1196

Corry D C (1950) *Ibid* i 909

Devenish E A , Miles A A (1939) *Ibid* i 1088

Gardner, A D Seddon H J (1946) *Ibid*, i 683

Hart, D (1938) *Arch Surg Chicago* 37, 521

Harwood F C Powney J Edwards, C W (1944) *Brit med J* i 615

O Brien J R (1947) Personal communication

Robinson D T McLeod J W , Downie A W (1946) *Lancet* i 152

Sevitt S (1949) *Ibid* ii 1075

Vollum R. L (1950) Personal communication

fan, the net result was a slight positive pressure in the theatre, so that air always flowed outwards under the doors to the hall and anæsthetic room This system proved most satisfactory The continuous line in fig 1 shows typical bacterial counts obtained during a session of operations with the new ventilation It is noteworthy that, until the arrival of the first patient, all counts were less than 10 per c ft, and that, although much higher counts were produced at the time of the entry and arrangement of each patient at the beginning of an operation, these counts fell rapidly during the quiet operation to a point below 10 per c ft This was in striking contrast to the results obtained previously with the exhaust ventilation, when the continued entry of dirty air from outside had often prevented the counts from falling below 20–30 per c ft (cf the interrupted line in fig 1)

In addition to its effect on airborne bacteria, the new ventilation system gave increased comfort to the surgeons and nurses This was obtained by directing the adjustable louvres through which the air entered the theatre so that a gentle stream of air flowed towards the heads of the staff without causing any appreciable draught at the level of the patient Though thermostatic control of the steam grille would have given a more uniform temperature, manual control was much cheaper, and proved satisfactory under the control of a capable theatre sister The input fan was designed to deliver up to 3000 c ft per min into the total theatre volume of about 15,000 c ft—i e, to give about twelve air changes an hour With the inlets provided, this was found slightly draughty, and the fan speed was adjusted to give a rather lower figure With more inlets the larger flow would have been preferable

Effect of Temperature on Inflow of Corridor Air

It is worth remembering that, although a good plenum system will cause a uniform outflow of air from a theatre while the doors are shut, it cannot prevent some entry of air from the corridor when the doors are open, since the mean pressures in the two spaces become practically equal almost immediately after the door has been opened The amount of air then entering depends chiefly on the temperature differences between theatre and corridor If the corridor air is much cooler than the theatre air, a brisk exchange will begin, the cool corridor air flowing into the theatre through the lower half of the door and displacing warmer theatre air through the upper half. This is easily demonstrated by a smoke test—e g, by holding a cigarette at different heights near the edge of the door If the air temperatures in theatre and corridor are nearly equal, little air movement will take place

Though such air exchange is undesirable, and indicates a need for keeping the corridor air tolerably clean, it is much less dangerous than the sucking of air under the theatre door, since the thermal air currents move relatively slowly and do not pick up bacterial particles from the floor

INFECTION OF AIR IN THEATRE BY SURGEONS AND NURSES

Infection from the respiratory tracts of the staff should always be regarded as a potential danger, even when the utmost care is taken with masks I have not yet seen a mask capable of retaining all the infectious particles emitted during a vigorous sneeze, and tests made with a slit sampler during a quiet operation in the presence of an assistant surgeon with a cold have shown a sudden emergence of α hæmolytic organisms into the theatre air just after a coughing fit There can be no doubt that the rigorous exclusion from operating-theatres of all persons carrying an active infection is highly desirable, even though it may be very difficult at times

Infection from particles scattered from the hair of the staff, including their eyebrows and eyelashes, should also be guarded against Though the hair of everyone in the theatre should be fully covered, it is desirable that those taking direct part in the operation, who are liable to place their heads above the wound, should have applied oil or a cosmetic cream to their hair, face, eyebrows, &c Without this precaution slight movements causing friction between the edges of the cap, the tapes of the mask, and so on, may cause a shower of bacteria to fall into the wound This danger is increased if two persons' heads accidentally touch over the wound

The clothing of assistant staff is often a possible source of contamination, especially when gowns left partly open at the back rub to and fro over woollen jerseys It should be a rule that no unsterilised woollen clothes should be visible in the theatre, at least at any level above 1 ft from the floor

INFECTION OF AIR IN THEATRE BY PATIENT AND HIS COVERINGS

The patient's nasopharynx can be an appreciable source of infective particles, especially if he is coughing, or has coughed during the induction of anæsthesia When practicable, it is desirable that the direction of air flow in the theatre should be from wound to anæsthetist rather than the reverse The logical development of such considerations is the use of a duct carrying a stream of sterile air, of controlled temperature and humidity, playing directly on to the wound at a low velocity, and so excluding the possibility of contamination from the surrounding air This is, however, only worth considering when standards of asepsis are already high and specialised operations make the avoidance of airborne infection of especial importance

The patient's skin and coverings are potent sources of bacterial clouds, and it is usual to find when sampling theatre air during operations that the turning over of a heavy patient, or the movements attendant on the arrival of a fresh patient, cause a considerable increase in the number of airborne bacteria (see continuous line in fig 1) It is now recognised that unoiled blankets, sheets, pillow cases, and patients' nightgowns or pyjamas readily liberate bacterial clouds, unless recently sterilised Although ward blankets are now rigorously excluded from most theatres, very questionable things are still done For instance, I have seen a patient walk into the theatre in a woollen dressing gown and even climb on to the table with it, thus liberating thick clouds of bacteria just before the operation Again, although ward blankets are excluded before an operation they are sometimes admitted at the end of it, without regard to the effect on the air for the next patient

A good method of dealing with the problem of bacteria from textiles is to arrange for instruction in the technique of oiling these fabrics to be given to the hospital laundry (Harwood et al 1944), and to have all the patient's coverings oiled, except those which are sterilised immediately before use Tests have shown that the use of a theatre blanket kept solely in the theatre, and always used in a sterilised cotton cover which is renewed each morning, is a reasonably clean procedure There is, however, little doubt that it becomes safer if the blanket is oiled during laundering so as to reduce the number of fine particles shed inside the cover

STANDARDS OF AIR PURITY

It is now common practice to insist on certain standards of purity before water is considered fit for drinking Although similar standards for the purity of air have not yet been widely accepted, it does seem reasonable to suggest that hospitals and surgeons should pay some attention to the cleanliness of the air in operating theatres, and should insist on the attainment of at least a moderate standard of cleanliness Provisional

When the effect of previous relapses on the efficacy of treatment was investigated, no correlation could be made out between them The number of relapses before treatment was begun did not influence the subsequent chances of relapse, whatever treatment was used Some workers have maintained that several relapses before treatment render it more effective, others that the reverse is true Treatment made no difference to the duration of subsequent relapses.

VALUE OF NEOARSPHENAMINE

Opinions on the value of neoarsphenamine in relapsing fever vary remarkably widely There is no doubt that some enthusiastic reports have been misleading, and there is little good evidence in its favour In reports such as those of Wright and Harold (1920), Briggs (1935), Ordman (1939), and Magee (1942), where claims are made for organic arsenicals, numbers of cases are admitted where relapses occurred On the whole, good effects were noted more often in the earlier papers on the subject

Dissatisfaction has been voiced by many workers—e g, Nicolle (1932), Adler et al (1937), Bulmer (1943), Marques (1944), and Quin and Perkins (1946) In fact most workers report poor effects with neoarsphenamine in this form of relapsing fever

This resistance to treatment has been variously explained Increasing resistance to arsenic has been postulated by Hindle (1931), but this seems unlikely to be the explanation in Cyprus, where tick-borne relapsing fever, only recently recognised and never before treated there, was found at once to be relatively refractory to neoarsphenamine

Several factors have probably caused the present uncertainty (1) it is clear that many patients have not been followed up for the necessary month or six weeks after treatment to ensure that relapses were not missed, (2) some workers' criteria of cure seem to include the possibility of relapses, and (3) there is evidence that different strains of spirochætes differ in their susceptibility to the drug

Charters (1942), Magee (1942), and Stuart (1945) favour large doses of neoarsphenamine rather than small ones, especially if given early The present series offers no evidence for or against this method Suggestions that full doses are dangerous in tick-borne relapsing fever are for the most part unconvincing No fears need be entertained, provided the patient is otherwise in good health

In louse borne relapsing fever it has long been held that neoarsphenamine is effective Here also doubts are beginning to arise (Chung and Chang 1939, Wolman 1944) but probably the drug is of greater value in louse borne than in the tick borne form In assessing the results of treatment it must not be forgotten that the former usually causes a much shorter illness

OTHER DRUGS

Most of the other drugs that have been tried are not superior to neoarsphenamine, and many are without any effect (Hindle 1931, 1935) The more recent of them that merit notice are sodium potassium bismuth tartrate (Todd 1930, Kammer 1943), 'Stovarsol' (Van Nitzen 1927, Bulmer 1944, Stuart 1945) tryparsamide (Hawking 1941), oxophenarsine ('Mapharsen') (Stuart 1945), gold compounds (Wolman et al 1945 Dubois 1932), and antibiotics.

Of these, oxophenarsine deserves more extended use

Hopes that penicillin would cure relapsing fever (McAlpine 1946, Lourie and Collier 1943, Heilman and Herrell 1943, Eagle and Magnuson 1944, Augustine et al. 1944, Schuhardt and O'Bryan 1944) are unfortunately not likely to be fulfilled (Tucker 1946, Muwazi 1946, Pospelova-Strom and Tiburskaya 1946, Anderson 1946)

Heilman (1945) who tried the effect of streptomycin in experimental relapsing fever, did not think the results were so good as with penicillin, but Levaditi and Vaisman (1947) thought streptomycin was better, especially at eradicating brain infections in mice infected with *Sp duttoni*

Aureomycin was tested by Heilman (1948), who found it more effective than penicillin at sterilising the bloodstream Its effect on brain infections is not yet known

SUMMARY

The effect of neoarsphenamine in the treatment of 82 cases of tick-borne relapsing fever in Cyprus in 1942–43 has been studied On the whole the response to treatment was unsatisfactory

A course of three or four injections given at intervals of 5–7 days brought the relapse-rate down to 17 4% (23 cases) One injection, usually given during the fever, produced a relapse rate of 53% (34 cases), or, if the 12 cases of Wood and Dixon (1945) are included, of 50% (46 cases) Two injections brought the relapse rate down to 38 5% (13 cases) The advantages of multiple doses are discussed

When multiple intravenous doses of neoarsphenamine are used, the first should be 0 45–0 6 g and subsequent doses 0 6 g given at intervals of not more than seven days No evidence of any toxic effects with this dosage was found among Indians, who formed the majority of the patients

Alternative forms of therapy are briefly described From the work of others penicillin seems to be about as efficacious as organic arsenicals. Other drugs with interesting possibilities are tryparsamide (for neurological complications), oxophenarsine, gold compounds, and several antibiotics, or several remedies can be used together

I wish to thank Majors R C Wood and K C Dixon, R.A.M.C., and Major B J Doran, I.A.M.C., for allowing me to refer to cases under their care and for giving me details of treatment used, Captain B Brown I.A.M.C., for his coöperation and help, and Captain D Pietroni R.A.M.C and Captain S Bose, I.A.M.C., for their help.

REFERENCES

Adler S Theodor O Schieber H (1937) *Ann. trop Med. Parasit* 31 25
Anderson E S (1946) *Trans. R Soc trop Med Hyg* 40 93.
Augustine D L. Weinman D McAllister J (1944) *Science* 99 19
Briggs L H (1935) *Calif West Med* 42 350
Bulmer E (1943) *Brit med J* i 374
— (1944) *Trans. R Soc trop Med Hyg* 37 225
Charters A D (1942) *Ibid* 35 271
Chung H L Chang F C (1939) *Chin med J* 55 6
Coghill N F (1949) *J R Army med Cps* 93 2
Dubois, A (1932) *Ann Soc belge Med trop* 12 429
Eagle H Magnuson H J (1944) *Publ Hlth Rep Wash* 59 583
Gambles, R. M Coghill N F (1948) *Ann trop Med Parasit* 42 288
Garland H (1946) *Lancet* ii 809
Hawking F (1941) *J trop Med (Hyg)* 44 104
Heilman F R (1945) *Proc Mayo Clin* 20 169 183
— (1948) *Ibid*, 23 569
— Herrell W E (1943) *Ibid*, 18 457
Hindle E (1931) in Medical Research Council's System of Bacteriology in Relation to Medicine. London vol VIII
— (1935) *Trop Dis. Bull.* 32 309
Johnson W B (1925) *Trans R. Soc trop Med Hyg* 19 177
Kammer V M. (1943) *E Afr med. J* 20 55
Kassirsky J A. (1933) *Arch Schiffs u. Tropenhyg* 37 350 abstr in *Trop Dis Bull.* 1934 31 36.
Katz D I (1930) *Pensée méd. Usbéquist* no 11–12 p 5 abstr in *Trop Dis Bull* 1931 28 298
Levaditi C Vaisman A (1947) *C.R. Acad. Sci Paris* 225 709
Lourie E M. Collier H O J (1943) *Ann trop Med Parasit* 37, 200
McAlpine D (1946) *Proc. R. Soc. Med.* 39 169
Magee G R. (1942) *Publ Amer Ass. Adv Sci* no 18 106
Manson J K. Thornton L H D (1919) *J R Army med Cps* 33 97 193
Marques, A. (1944) *S Afr med J* 18 36
Muwazi E. M K. (1946) *E Afr med J* 23 55
Nicolle C (1932) *Bull Inst Pasteur* 30 961
Ordman D (1939) *S Afr med. J* 13 491
— Jones F R (1940) *Ibid* 14 81
Pospelova-Strom M V Tiburskaya N A (1946) *Med Parasitol Moscow* 15 54 abstr in *Trop Dis Bull.* 1947 44 213
Quin C E Perkins E S (1946) *J trop Med* 49 30
Schuhardt V T O'Bryan B. E (1944) *Science* 100 550
Sergent A. Manceaux A Balliste R (1933) *Bull. Soc. Path. exot* 26 906
Stuart G (1945) *Epidem. Inform. Bull UNRRA Hlth Div Wash* 1 453
Todd J (1930) *Brit med J* i 312
Tucker W A L (1946) *E Afr med. J* 23 13
Van Nitzen R. (1927) *Ann Soc belge Med trop* 7 147
Wolman M (1944) *E Afr med J* 21 336
— Omar M. Abu Taleb M. (1945) *Lancet* ii 775
Wood R C Dixon K C (1945) *Brit med J* ii 526
Wright H D Harold, C H H (1920) *J R Army med Cps*, 35, 203

TREATMENT OF TICK-BORNE RELAPSING FEVER

NEOARSPHENAMINE AND OTHER REMEDIES

N F COGHILL
M A, M B Camb, M R C P,
PHYSICIAN, WEST MIDDLESEX HOSPITAL, LATE MAJOR R A M C, MEDICAL SPECIALIST

THE therapy of tick-borne relapsing fever has always been unsatisfactory No apology is needed for further consideration of neoarsphenamine, for penicillin and the later antibiotics have not proved more effective

MATERIAL

Tick borne relapsing fever occurred among military personnel in Cyprus in 1942–43 (Wood and Dixon 1945, Gambles and Coghill 1948) Records of the treatment of 82 cases are available, including the 12 cases of Wood and Dixon (1945), the 35 reported by Coghill (1949), and 35 from different hospitals on the island Among these 82 there were 7 in which the diagnosis was not confirmed by the finding of spirochætes in the peripheral blood, but clinically they were undoubted cases of relapsing fever

METHOD

The preparations of neoarsphenamine used were 'Sulphostab' and 'Novostab,' both intravenously Tryparsamide, bismuth, and potassium iodide were used in 1 case with facial palsy

There is a general opinion that neoarsphenamine should be given as the temperature is rising at the beginning of an attack of fever For various reasons it often proved impossible to do this, but most of the patients received their initial injection when febrile Although on theoretical grounds there is not a great deal to favour this practice, it is probably true that in single dose methods of treatment neoarsphenamine is best given early in the febrile phase

After relapsing fever had been dealt with for some months, investigation showed that different methods of treatment were used at different centres in the island Since a single dose of neoarsphenamine often failed to prevent relapses, some medical officers had begun to give two or more injections of the drug in the form of a short course This system of treatment was first suggested to me by Captain B Brown, I A M C, but previous attempts had been made to show that multiple doses of neoarsphenamine are better than single ones (Kassirsky 1933, Ordman and Jones 1940, Stuart 1945) Katz (1930) suggested that the injections need not necessarily be given with strict regard to the stage of the disease

Various considerations finally led us to believe that three doses at intervals of about a week might be the best form of treatment It is commonly supposed that neoarsphenamine acts better on the spirochætes when they are in the blood stream (i e, during fever), but there must always be some remaining in the internal organs These are more likely to be affected by neoarsphenamine given over a period than by one injection, no matter when it is given Unfortunately little is known about the action of neoarsphenamine in relapsing fever Doubts naturally arise as to its efficacy when patients contract relapsing fever after a large dose of neoarsphenamine (Johnson 1925, Magee 1942) or relapse within a few hours of a third or fourth dose (Sergent et al 1933, Coghill 1949)

In the earlier cases the patients tended to receive only one injection of neoarsphenamine, whereas in the later cases they more commonly received two, three, or even four injections as initial treatment The treatments used in the 82 cases were as follows

Treatment	*Organic arsenical*
A	0 45 or 0 6 g, usually during fever
B	0 6 g usually during fever 0 6 g eight days lat
C	0 3 or 0 45 g, usually during fever, 0 45 or 0 6 from five to eight days later
D	0 3 g, usually during fever, 0 45 g five days later 0 6 g seven days later
E	0 6 g usually during fever, 0 6 g seven days late 0 6 g seven days later
F	0 3 g, usually during fever 0 6 g five days later 0 6 g seven days later
G	0 6 g, usually during fever, 0 6 g five or six day later, 0 45 g five or six days later, 0 45 g five or six days later

The chief reason why many patients received low doses, at least at the first injection, was that the medical officers feared toxic effects in Indians, who comprised 63 of the 82 patients It was supposed that they were peculiarly intolerant of arsenic The basis for this belief was not clear, but it might be justified by the fact that many Indian soldiers weighed relatively little (Garland 1946) There was no evidence that any patient sustained hepatic or other damage from the doses of neoarsphenamine used in this series

A single injection of neoarsphenamine was given in 46 cases, and multiple doses in 36

RESULTS

The results of the different treatments are shown in the accompanying table It has been assumed, probably with good reason, that if a patient relapsed at his unit after treatment he was readmitted to one of the hospitals on the island, so the records of all were scrutinised Many of our own cases were retained in hospital for three or four weeks after the last relapse Others were followed in a local convalescent depot It is therefore unlikely that many relapses were missed Since follow up measures were more stringent in the later cases, relapses are most likely to have been missed in the earlier ones, which mostly received treatment A The table shows that multiple doses—those after the first being given without special regard to the clinical state—were better than a single injection given usually during the fever The relapse rate was 50% when only one dose was given (treatment A), came down to 25% when two or more doses were given (treatments B–G), and to 17% when three or more were given (treatments D–G) Although the results with neoarsphenamine were on the whole unsatisfactory, the figures indicate a relative improvement with multiple doses

RESULTS WITH THE DIFFERENT METHODS OF TREATMENT

Treatment	A	B	C	Total of B and C	D	E	F	G	Total of D–G	Total of B–G	Total of A–G
No of patients treated	46 (12)*	1	12	13	14	2	4	3	23	36	82
No of patients who relapsed after treatment	23 (5)*	1	4	5	1	0	3	0	4	9	32
Relapse rate (%)	50			38 5					17 4	25	39

* Figures in parentheses are those of Wood and Dixon (1945) and are included in the totals

In the cases which relapsed the only effect of treatment, apart possibly from the shortening of the attack in which it was given, was to delay the appearance of the next relapse, sometimes considerably The longest interval was 39 days from the end of an attack to the appearance of a relapse Afebrile periods in treated patients were not often so long, and were usually no more than double those of untreated patients This phenomenon has been described before, by Manson and Thornton (1919), Marques (1944), and Wolman (1944) Intervals between attacks in untreated cases in Cyprus were usually 3–6 days and seldom more than 8

Quick and Stefanini (1948a) A modification of this method is described below All these determinations were made with a human brain thromboplastin prepared by dehydration with acetone according to the method of Quick (1945) and capable of clotting an equal volume of oxalated fresh human plasma in twelve seconds in an optimal concentration of $CaCl_2$

Quantitative One-stage Assay of Concentration of Labile Factor in Plasma

The prothrombin time of oxalated human plasma stored at 4°C for about fifteen days is much prolonged owing to the striking and prompt depletion of the labile factor When 1 volume of fresh oxalated human plasma is added to 9 volumes of stored plasma, the prothrombin-time of the mixture is reduced to twenty seconds (Stefanini and Quick 1948) When a given plasma is deficient in labile factor, the prothrombin-time of the mixture is directly proportional to the extent of this deficiency

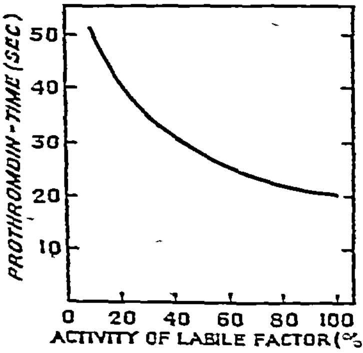


Fig 1—Curve for calculation of activity of labile factor in human plasma from prothrombin-time. Decreasing volumes of fresh normal oxalated plasma were mixed with increasing volumes of saline solution to obtain known concentrations of the labile factor from 100 to 10%. To 0·09 ml. of stored human oxalated plasma 0·01 ml. of each different dilution was added and the prothrombin-time of the mixture was determined. An optimal concentration of prothrombin was present in each mixture.

Reagents.—(1) Stored oxalated human plasma. Blood is collected by venepuncture from a normal person, mixed with 1/10 volume of sodium oxalate 0·1 M, and centrifuged for 10 min. at 2000 r.p.m. The supernatant plasma is transferred to open glass test-tubes kept at 4°C for a minimum of 15 and a maximum of 25 days. This period is specified because there is a negligible depletion of the labile factor during the first 2 weeks of storage and after 25 days prothrombin begins to be inactivated and fibrinogen denatured. Citrated human plasma should not be used, because it maintains a high concentration of labile factor for a long time.

(2) Human or rabbit brain thromboplastin, prepared according to Quick (1945)

(3) Calcium chloride, 0·02 M

(4) Sodium oxalate 0·1 M

Method.—By venepuncture 4·5 ml. of the blood to be examined is collected and added to 0·5 ml. of sodium oxalate 0·1 M The plasma is obtained by centrifugation at 2000 r.p.m. for 10 min. With a pipette graduated to 0·01 ml. 0·09 ml. of the stored plasma is added to 0·01 ml of the plasma under examination in a 'Pyrex' test-tube (130 mm. × 10 mm.) and the prothrombin time of the mixture determined. It is advisable to use plasma from a healthy subject as a control and run the test within one hour of collection of the plasma.

Calculation.—The percentage of labile factor present in the plasma under examination is calculated directly from the prothrombin time obtained, by means of a dilution curve (fig 1) The dilution curve is constructed as follows decreasing volumes of fresh normal oxalated plasma are mixed with increasing volumes of saline solution to obtain known concentrations of labile factor from 100 to 10%, 0·1 ml. of each dilution is added to 0·09 ml. of stored plasma, and the prothrombin time of the mixture determined. The average analytical values obtained are as follows

Concentration of labile factor (%)	100	90	80	70	60	50	40	30	20	10
Prothrombin time (sec.)	20·2	21·6	22·1	23·5	25·6	28·3	31·4	35·2	40·7	50·2

Definition of labile factor activity, prothrombin activity, and prothrombin concentration, and meaning of their values as expressed in percentage have been discussed at length in a previous paper (Stefanini 1950a)

RESULTS

In Liver Dysfunction and Obstructive Jaundice

The 32 patients in this group included 4 with obstructive jaundice, 14 with Laennec's cirrhosis, 6 with chronic hepatitis, 5 with infective hepatitis, 2 with cardiac cirrhosis, and 1 with pigmentary cirrhosis. The degree of liver dysfunction was determined in each case on the basis of the clinical findings and the result of liver function tests (total serum-protein and A G ratio, serum-cholesterol and cholesterol esters level, bromsulphthalein retention, cephalin-cholesterol flocculation test, thymol turbidity test, serum-alkaline phosphatase, &c.)

The activity of the labile factor was normal in obstructive jaundice and always strikingly depleted in patients with impaired liver function The depletion of labile-factor activity did not parallel the behaviour of any of the liver-function tests but seemed to parallel roughly the serum-protein level. The importance of the level of labile-factor activity as a criterion of differentiation between obstructive and parenchymatous jaundice has been emphasised by Owren (1949), Harrington et al (1950), and Stefanini and Crosby (at the International Congress of Hæmatology in 1950), and is confirmed by the present findings. Owren also considers the activity of labile factor as an important prognostic sign and although more observations of this type are required, we also feel that in extremely severe liver dysfunction the progressive depletion of the labile factor more or less parallels the progressive functional failure of the hepatic parenchyma.

Little information is available at present on the site and the mechanism of synthesis of the labile factor in the body It was therefore decided to study the effect of vitamin K (material essential for the building of the prothrombin molecule) on the synthesis of the labile factor Of 28 cases of liver dysfunction 18 were selected for this study in whom the intravenous administration of synthetic vitamin K ('Hykinone,' Abbott, 70 mg) was followed by a significant increase in the plasma-prothrombin activity within twenty-four hours. The plasma labile-factor activity remained practically unmodified in all, as shown in fig 2, which illustrates a typical experiment. These results could be criticised on the ground that they were obtained in patients whose ability to synthesise prothrombin in the liver was impaired in part (the greatest effect of vitamin K occurred usually after twenty-four instead of four hours, as in cases of obstructive jaundice with preserved liver function) They indicate, however, that in all probability the synthesis of the labile factor takes place in the liver but does not require vitamin K

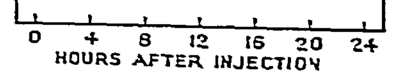


Fig 2—Typical increase in prothrombin activity with almost unaltered activity of labile factor of plasma after a large intravenous dose of vitamin K in cirrhosis of the liver with moderately affected liver function. Interrupted line represents response of level of prothrombin activity in a patient with obstructive jaundice, given for comparison. The patient received a dose of 70 mg of water-soluble vitamin K (Hykinone Abbott) intravenously

ACTIVITY OF PLASMA LABILE FACTOR IN DISEASE *

Mario Stefanini †
M D Rome, M Sc Marqueth
INSTRUCTOR IN MEDICINE, TUFTS COLLEGE MEDICAL SCHOOL, BOSTON, ASSISTANT PHYSICIAN, NEW ENGLAND CENTER HOSPITAL, BOSTON, MASS , U S A

That the formation of thrombin requires another plasma factor besides the three postulated in the classical theory of Morawitz (prothrombin, thromboplastin, and calcium) was first suggested by Nolf (1908) Quick (1943) gave the first convincing evidence of the existence of this factor, which he called at first " component A " and later " labile factor " (Quick 1947) Independently, Owren (1944) described a similar factor, which he called " factor V," and a hæmorrhagic condition due to its deficiency Fantl and Nance (1946) described an " accelerator factor " and Ware et al (1947) a " plasma Ac globulin " Owren (1948), Fantl and Nance (1948), and Ware and Seegers (1949) think that these last three factors are probably identical with the labile factor of Quick (1947)

The properties of the labile factor have been summarised as follows by Quick and Stefanini (1949a)

1 It is a normal globulin constituent of plasma and serum, and disappears fairly rapidly from human oxalated plasma stored at 4°C in oxygen or in atmospheric air The depletion of the factor during storage is much less in citrated or in native plasma (Stefanini 1948), being usually related to the concentration of calcium left in the plasma (Quick and Stefanini 1948b)

2 It is inactivated by heating at 58°C and is not adsorbed from oxalated plasma by various adsorbent gels thus making its separation from prothrombin relatively easy (Quick and Stefanini 1948b)

3 Its concentration varies from species to species, being very high in the rabbit, high in the dog, and comparatively low in man (Quick and Stefanini 1948a) Its concentration is not decreased in the hypoprothrombinæmia induced by dicoumarol or by vitamin K deficiency

4 Deficiency of the labile factor is indicated by a prolonged plasma prothrombin time and may be responsible for a severe hæmorrhagic diathesis (Owren 1947b) which can be controlled only by the transfusion of *fresh* blood or plasma

The labile factor is obviously a key substance in the formation of thrombin Ware and Seegers (1948) believe that it is strictly catalytic, whereas Quick and Stefanini (1950) suggest that it takes part in the formation of thrombin in stoichiometric relationship with prothrombin, calcium, and thromboplastin, since the concentration of labile factor in the plasma seems to determine the amount of prothrombin utilised during coagulation In further support of this view Stefanini and Crosby (1950b) have shown that the amounts of prothrombin and labile factor utilised during the coagulation of blood in normal and abnormal conditions are in close quantitative relation Owren (1947a) has found that thrombin cannot be formed in the absence of " factor V " It is admittedly difficult to analyse a reaction (the formation of thrombin from prothrombin) which intervenes between two enzymatic reactions—the activation of thromboplastin and the formation of fibrin

Other work suggests another possible action of the labile factor in the coagulation of blood Ware and Seegers (1948) have postulated that their " plasma Ac globulin " is activated by thrombin to a " serum Ac globulin," a much more powerful accelerator of the formation of thrombin This finding has been extended to man by Stefanini and Crosby (1950a), who also reviewed the importance of these results and their interpretation in the light of our present knowledge of blood coagulation at the International Congress of Hæmatology at Cambridge in 1950

In view of the obvious importance of the labile factor in the formation of thrombin it is somewhat surprising that only fragmentary and isolated studies have appeared on the variations of the labile factor in diseases characterised by bleeding and/or a prolonged prothrombin time. Perhaps one of the reasons for the lack of such studies is the difficulty of determining the activity of the labile factor accurately I have introduced a quantitative technique for determining its activity in plasma (Stefanini 1950a) and in serum (Stefanini and Crosby 1950b) By this method the activity of the labile factor has been determined in a large number of patients and the results are reported here The values so obtained have been compared with the activity and concentration of prothrombin in the plasma, to investigate the importance of the depletion of the labile factor in determining the prolonged prothrombin time in various diseases

MATERIALS AND METHODS

The present series (see table I) included 187 persons who had active bleeding or a prolonged prothrombin time and 15 cases of hypoprothrombinæmia induced by dicoumarol treatment Labile factor and prothrombin activity as well as concentration of prothrombin in plasma were determined in each case The values obtained were correlated with other clinical laboratory data

The activity of prothrombin was determined from the prothrombin time, both on undiluted and 10% diluted plasma, by the methods of Quick (1945) and of Tuft and Rosenfield (1947) respectively The purpose of the latter determination was to avoid errors due to possible changes in the concentration and reactivity of fibrinogen. The method of Tuft and Rosenfield was slightly modified by using as a diluent plasma deprothrombinised with $Ca_3(PO_4)_2$ gel (Quick and Stefanini 1948a) Concentration of prothrombin was determined quantitatively (Stefanini 1950a) by a method based on observations previously reported (Quick and Stefanini 1949a) The activity of the labile factor was determined by the method of

TABLE I—ACTIVITY OF PROTHROMBIN, CONCENTRATION OF PROTHROMBIN, AND ACTIVITY OF LABILE FACTOR IN PLASMA OF 187 HEALTHY SUBJECTS AND PATIENTS WITH DIFFERENT CONDITIONS

Conditions present	No of cases	Prothrombin activity (%)	Prothrombin concentration (%)	Labile factor activity (%)
Healthy people	20	98 00	97 5	96 8
Liver dysfunction	28	47 4	53 7	52 8
Obstructive jaundice	4	25 5	28 0	97 5
Polycythæmia vera	12	100 0	100 0	100 0
Pseudohæmophilia	5	100 0	100 0	100 0
Anaphylactoid purpura	2	100 0	100 0	100 0
Vascular purpura	38	95 4	95 0	98 2
Hereditary hæmorrhagic telangiectasia	3	98 0	95 0	98 0
Hæmophilia	5	77 0	75 5	93 7
Idiopathic thrombocytopenic purpura	9	60 8	68 4	96 3
Symptomatic thrombocytopenia	35	74 0	77 3	59 1
Thrombo asthenia	1	95 0	95 0	98 5
Hypoprothrombinæmia of the newborn	7	31 8	61 7	90 4
Sprue	2	84 0	85 5	73 5
Pernicious anæmia	4	77 5	74 0	90 5
Terminal carcinoma	12	42 8	48 7	56 2

---

* Labile factor has been recently called plasma prothrombin conversion factor (P P C F)' by the author of this article His reasons for this change in terminology and the selection of the new word have been given in *Blood* (January 1951 p 84) Throughout this paper however the definition of 'labile factor ' will be maintained to avoid confusion and indicate clearly the method of assay used for the quantitative determination of the factor

† This work was completed during the tenure of a Damon Runyon senior clinical research fellowship administered by the American Cancer Society and was aided by grants from the Charlton Fund and the American Cancer Society *Massachusetts Division* It was done in the Ziskind Laboratories (hematology section) Joseph H Pratt and New England Center Hospitals and the Department of Medicine *Tufts College* Medical School

After Major Operations

15 patients were studied in the fourteen days following major surgical operations: splenectomy for various causes in 7, neurosurgical procedures in 3, cholecystectomy in 2, total hysterectomy in 1, nephrectomy in 2. Only patients with good postoperative liver function were studied. The results presented here were somewhat influenced by the administration of fresh bank blood which, because of the presence of sodium citrate in the approximate concentration of 0·18 *M* in the anticoagulant fluid, exhibited good labile factor activity (Quick and Stefanini 1948b). As indicated in fig. 4, which presents the average results obtained in the 15 cases, while the activity of prothrombin remained substantially unmodified and normal, that of labile factor much decreased immediately after the operation, reaching its lowest level on the third day and slowly returning to normal on the ninth day. The behaviour of the labile factor appeared largely independent of that of total protein and its different fractions and that of fibrinogen. The level of fibrinogen reached the highest peak on the third postoperative day, the time at which the labile factor activity of plasma was at its lowest level.

DISCUSSION

Little is known at present about the mechanism of production of labile factor in the body. Sykes et al. (1948) have observed depletion of "plasma Ac globulin" after liver injury in dogs. The decrease of plasma labile factor activity observed by Owren (1949) and Harrington et al. (1950) and reported by me (Stefanini 1950a) also confirms the important rôle of the liver in the synthesis of labile factor. Further proof comes from the rough relation repeatedly found between depletion of labile factor activity and fall in serum protein level. It is, however, a moot question whether the liver is the only organ in which labile factor is produced, for we have shown that this factor can be depleted in those cases of acute leukæmia, pernicious anæmia, and sprue, in which no liver dysfunction can be demonstrated. Though the solution of this and other questions will have to await further investigation, the most significant information obtained from the clinical observations presented here is probably that no vitamin K is required for the synthesis of the labile factor in the body.

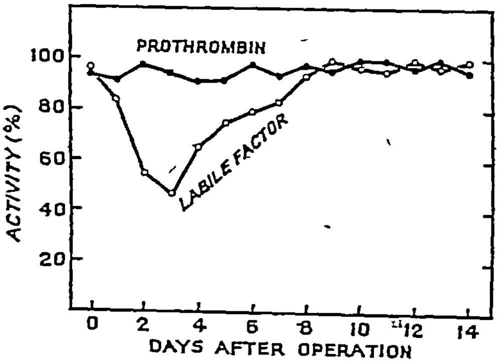


Fig. 4—Comparative behaviour of prothrombin and labile-factor activity in immediate postoperative period. Curves represent average of results in 15 cases.

The present findings also confirm previous conclusions (Stefanini 1950a) that an isolated depletion of plasma labile factor activity without associated depletion of prothrombin activity is seldom found. According to our studies this situation occurs only in rare congenital cases, like the one described by Owren (1947b) under the debatable term of "parahæmophilia," and after operation. More often the deficiency of labile factor is associated with that of prothrombin. This observation emphasises the need for separate assay of prothrombin concentration and labile factor activity in every case of hypoprothrombinæmia (Stefanini 1950a). It also raises a number of practical points, the most important of which is obviously the choice of blood to be used in case of hæmorrhage in patients with hypoprothrombinæmia. It is evident that only fresh blood should be used to render normal the clotting-mechanism of patients when plasma labile factor activity is depleted. The use of fresh blood is even more imperative in patients with associated platelet and labile factor deficiency (acute leukæmias), where only blood freshly drawn (2–4 hours) will temporarily render the hæmostatic mechanism normal.

The observation that labile factor activity is not depleted during dicoumarol treatment is of considerable importance. Ever since the importance of the labile factor in the formation of thrombin has been recognised, the one-stage procedure for determining the prothrombin-time of Quick has been criticised as inaccurate technique of control of dicoumarol therapy. It is argued that the method would not distinguish between changes in the concentration of prothrombin and activity of labile factor.

It must be admitted that, theoretically at least, the most accurate test for the control of dicoumarol therapy is one which will accurately indicate the changes of prothrombin only. Our results indicate that no changes in the activity of plasma labile factor can be demonstrated during dicoumarol therapy; Fahey et al. (1948) and Olwin (1949) also agree that changes in concentration of "plasma Ac globulin" revealed by two stage methods in the course of dicoumarol therapy are limited in extent and quite transitory. The obvious conclusion is that the one-stage procedure of Quick is a safe and accurate method of controlling anticoagulant therapy. It may be added here that, in the course of dicoumarol treatment, the results of the Quick one-stage method for the determination of prothrombin activity of plasma and those of the test recently introduced (Stefanini 1950a) for the direct calculation of concentration of plasma prothrombin have thus far agreed within ± 5%.

The significance and importance of the depletion of plasma labile factor in the immediate postoperative period remain to be assessed. Observations are in progress to establish whether this is a constant finding and what relationship it has, if any, to the thrombotic tendency known to occur after operation. It is quite possible that the depletion of plasma labile factor might be due to the loss of blood during operation and its substitution with bank blood, which contains a suboptimal concentration of labile factor. A contemporary transitory liver dysfunction, due to the stress of undergoing operation, would explain the slow regeneration of the factor by the liver. It is common clinical observation that thrombosis appears late in the postoperative course, always after the second or third postoperation day. It might be interesting to speculate at this time whether thrombosis in the early postoperative period is prevented by the existing depletion of plasma labile-factor activity.

SUMMARY

By a simple method the labile factor activity of plasma was determined and compared with plasma-prothrombin activity and concentration in a large number of patients, including cases with active bleeding or a delayed prothrombin time.

A significantly depleted activity of plasma labile factor was consistently found in liver dysfunction, thrombocytopenia of acute leukæmia and other hæmatological disorders, hypoprothrombinæmia of terminal carcinoma, and the immediate postoperative period.

In liver dysfunction large doses of vitamin K did not restore to normal levels the plasma labile-factor activity

Hæmorrhagic Conditions

Plasma prothrombin and labile factor activity were determined in 117 cases of different hæmorrhagic conditions Labile factor activity was normal in all cases in which dysfunction of the vascular factor of hæmostasis is known, or assumed, to be responsible for the hæmorrhagic manifestations Vascular purpuras of various types, hereditary hæmorrhagic telangiectasia, and anaphylactoid purpura belong to the first group, polycythæmia vera to the second In pseudohæmophilia, a familial condition characterised by a prolonged bleeding-time in the absence of other abnormalities of the hæmostatic mechanism (Estren et al 1946), plasma labile factor activity was also normal

No substantial depletion of labile factor activity was found in 9 cases of thrombocytopenic purpura, idiopathic and allergic, and in 1 case of thrombo asthenia These results agree with the experimental observation that decrease in the number of platelets brought about in normal plasma by centrifugation does not affect the determination of labile factor activity In the experiment shown in table II normal plasma aliquots were centrifuged for various periods at different speeds to produce various diminutions of the number of platelets Since all the experiments were conducted in silicone coated containers, it is highly improbable that liberation of platelet products influenced the results 36 cases of symptomatic thrombocytopenia were examined, most of the patients having acute leukæmia of the lymphocytic, myelocytic, and monomyelocytic variety Only 1 presented evidence of a heparin like circulating anticoagulant (Allen et al 1947) and was therefore excluded from the series The remaining 35 presented a striking depletion of labile factor activity When compared with the results obtained in our cases of idiopathic thrombocytopenic purpura, this finding suggests that the depletion of labile factor activity in these cases is not due to platelet deficiency but rather to something else, such as impaired synthesis of the factor by an inefficient liver Against this conclusion, however, is the depletion of prothrombin in both idiopathic and symptomatic thrombocytopenic purpura Further studies are now in progress

Labile factor activity was normal in hæmophilia, even immediately before and during spontaneous bleeding episodes On the other hand, an interesting observation was made in this disease, which might be of some importance in explaining the mechanism of bleeding The clotting time of whole blood was prolonged and the prothrombin activity significantly decreased for about a week preceding and a week following the episode of active bleeding (fig 3) This observation was made in only 2 cases being followed routinely and requires further confirmation

TABLE II—INFLUENCE OF NUMBER OF PLATELETS ON PROTHROMBIN AND LABILE FACTOR ACTIVITY AND CONCENTRATION OF PROTHROMBIN IN HUMAN PLASMA * IN A TYPICAL EXPERIMENT

No of sample	Platelets per c mm	Labile factor activity (%)	Prothrombin activity (%)	Prothrombin concentration (%)
I	4000	100	100	95
II	55 000	95	96	90
III	115 000	95	92	92
IV	474 000	90	100	96

* All samples were collected by a two-syringe method (Stefanini 1950b) in syringes coated with silicone and transferred to chilled test tubes also coated with silicone Depletion of platelets in plasma was determined by centrifuging the different samples of blood at different speeds for various times sample I for 20 minutes at 3000 r p.m sample II for 5 minutes at 1500 r p m and sample III for 2 minutes at 1500 r p.m Sample IV was allowed to sediment spontaneously for 30 minutes in the cold

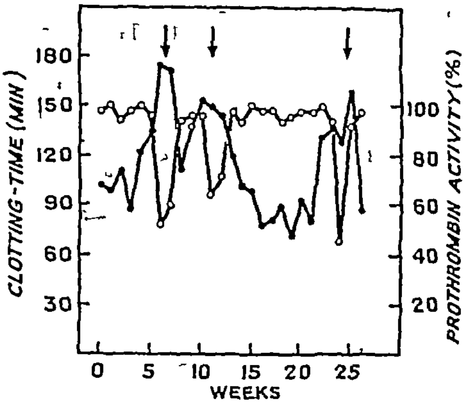


Fig 3—Behaviour of clotting-time (black dots) and plasma-prothrombin activity (white dots) in a hæmophiliac, determined at weekly intervals for six months. Three episodes of spontaneous bleeding (indicated by arrows) were preceded by prolongation of clotting-time and depletion of prothrombin activity Both changes were temporary

In Hypoprothrombinæmia of the Newborn

In disagreement with observations of previous workers, Randall and Randall (1949) gave evidence that no deficiency of known "accelerators" of the conversion of prothrombin to thrombin could be substantiated in hypoprothrombinæmia of the newborn From indirect findings they concluded that hypoprothrombinæmia of the newborn was due to depletion not only of prothrombin but also of an accessory unknown factor favouring the formation of thrombin In our 7 cases of hypoprothrombinæmia of the newborn the labile factor activity of plasma was only slightly depleted, whereas plasma prothrombin activity was much reduced during the third day after birth However, the percentage of concentration of plasma prothrombin, determined by the method recently described (Stefanini 1950a), was significantly higher than that of plasma prothrombin activity The difference consistently observed between the values of the two constants, being the labile factor activity normal, suggests that the deficiency of another probably plasmatic factor besides prothrombin is responsible for the prolonged prothrombin time of the newborn. More work is in progress

In Dicoumarol Hypoprothrombinæmia

Quick and Stefanini (1949b) could not detect any change in labile factor activity of plasma in rabbits and dogs treated with dicoumarol Fahey et al (1948), however, found that a decreased concentration of "plasma Ac globulin" could be found in the early stages of dicoumarol treatment in laboratory animals The level quickly returned to normal even when the treatment was continued Essentially similar results were obtained in man by Olwin (1949) Olwin and Fahey et al used a two stage method of assay whereas Quick and Stefanini used a one stage method, hence the discrepancy of results among the various investigations is very likely due to the different methods Our finding, obtained with the one stage method described here, confirms that no appreciable changes in labile factor activity estimated daily can be observed in man during dicoumarol therapy Of our 15 cases, in 12 the labile factor activity of plasma was determined on the fourth day of therapy, and in the remaining 3 was followed daily for thirty days.

In Terminal Carcinoma

In 12 cases of terminal carcinoma the labile factor activity was consistently reduced, along with the activity and concentration of prothrombin in plasma. The decrease of plasma labile factor activity was roughly parallel to the depletion of serum protein of these patients when initially seen forty eight hours before death this child seemed to have pneumonia, its respirations being rapid, inverted, and associated with working alæ nasi, but at necropsy no lesions in the lung were found

The fatal cases (1, 2, and 4) all developed a spinal block

Necropsy Findings

At necropsy cases 1, 2, and 4 all presented a similar picture in the central nervous system Both cerebral hemispheres were almost covered, and the spinal cord was encased, in tenacious yellow green pus In case 1 the exudate was bacteriologically sterile

Laboratory Findings

In all the cases the strains of *H influenzæ* isolated were type b The sensitivities for streptomycin was 2–10 units per ml. and for penicillin 1–10 units per ml. In cases 1, 3, 6, and 7 the cerebrospinal fluid (C.S.F) became sterile in twenty four hours No streptomycin resistant strains developed in any of the cases The C S.F streptomycin levels twenty-four hours after an intrathecal injection of 25–50 mg of streptomycin were 4–64 units per ml.

Sibling Relationship

Ounsted (1950) found that the 13 children with influenzal meningitis he had treated all had two or more older sibs under the age of 12 years He concluded ‘ It seems possible that the *H influenzæ* organisms require one or two bacterial passages through partially immune contacts before a strain is evolved that can pass the meningeal barriers ” In our cases the ages of the children in the family were as follows, sibs under the age of 12 years being shown in italics

TABLE III—AGE INCIDENCE OF INFLUENZAL MENINGITIS IN 104 CASES REPORTED IN GREAT BRITAIN IN TEN YEARS

Age	No recovered	No died	Total no
6 mos or less	3	2	5
7–12 mos	14	6	20
1 yr –1 yr 6 mos	19	15	34
1 yr 7 mos.–2 yr	10	2	12
2 yr	9	8	17
3 yr	3	1	4
4 yr	2	—	2
5 yr	5	1	6
6 yr	2	1	3
7 yr	1	—	1
Total	68	36	104

CASE NO	AGE OF PATIENT (MOS)	AGES OF SIBS
1	4	17 12 yr *9 yr 5 yr*
2	13	*8 weeks*
3	12	*2 yr 12 mos (twin of patient)*
4	22	*6 yr*
5	12	13 12 yr *9 yr 6 yr 5 yr*
6	8	21 18 15 *5 yr*
7	15	*10 yr 9 yr 6 yr*
8	18	*11 yr 4 yr 3 yr*
9	6	*5 yr*
10	15	—
11	19	*3 yr*

TABLE IV—RELATION OF MORTALITY TO TIME OF APPEARANCE OF MENINGEAL SYMPTOMS AS DETERMINED BY DATE OF LUMBAR PUNCTURE

Length of symptoms before lumbar puncture (days)	No of cases	No recovered	No died
1	22	16	6
2	9	7	2
3	19	13	6
4–5	8	5	3
6–7	18	12	6
8–14	15	9*	6
15–21	9	4	5
22–35	4	2	2
Total	104	68	36

* Two patients became demented.

Thus in 4 of our 11 cases there were two or more sibs under 12 years Ounsted (1950) compared his figures with those for cases of meningococcal meningitis and found a significant difference In the 21 cases of meningococcal meningitis in children below the age of 2 years treated in Leeds General Infirmary during the same period as our series the number with two or more sibs under 12 years was 3

DISCUSSION

The diagnosis of *H influenzæ* meningitis is made particularly difficult by the age of the patients Of 104 cases in the British Isles in the past ten years 88 were under the age of 3 years (table III) This age group is characterised not only by a paucity of comprehensible expression but also by an uncoöperativeness compounded of fear and negativism In this country cases of *H influenzæ* meningitis are rare in one physician's experience, since there never has been an epidemic of the condition Smythe (1948) drew attention to two types of severe case (1) a short fulminating illness, and (2) a subacute type which tended to deteriorate into a critical state Of the 104 cases mentioned, 28 (about a quarter) had their first lumbar puncture on or after the eighth day of illness (table IV) There were 13 deaths in this group and 2 children became demented, giving a recovery-rate of 47% The only way of improving the outlook in this group is by earlier diagnosis

In some cases the symptoms did not suggest meningitis 5 children presented with a gastro intestinal syndrome and 16 others with symptoms of upper respiratory infection When upper respiratory infections are prevalent it is not easy to detect that a feverish cold is due to a more serious infection Still more difficult is it to revise an established diagnosis On the other hand, meningism and convulsive phenomena should be accorded the respect that their possible ætiology warrants A diagnosis of teething as a cause of fits is likely to be

TABLE II—TOTAL DOSAGE OF DRUGS GIVEN

Case no	Sulphonamides (g)	Penicillin (units)		Streptomycin (mg)		Other treatment
		I.M	I T	I.M	I T	
1	—	—	—	720	75	—
2	—	—	—	720	75	—
3	—	—	—	3200	450	—
4	—	256 000	50 000	600	25	—
5	—	33 520 000	1 500 000	35 400	1150	Heparin 90 000 units
6	Sulphadimidine 15 5 Sulphadiazine 7 5	2 880 000	180 000	2400	350	—
7	Sulphadiazine 25 5	3 970 000	120 000	2880	600	—
8		15 600 000	440 000	20 800	1100	Intrathecal streptokinase 96 units
9	Sulphamerazine 21 0	10 300 000	80 000	6800	80	—
10	Sulphamerazine 38 0	6 000 000	—	5040	—	Chloromycetin 14 5 g
11	Sulphadimidine 30·0	16 000 000	480 000	7600	450	—

I.M = intramuscular　I T = intrathecal

in those cases in which the prothrombin activity was restored to normal, indicating that, though the labile factor is probably produced in the liver, vitamin K is not requred for its synthesis

No changes in labile factor activity were noticed during dicoumarol therapy

Two additional findings of importance were made in the course of this investigation (1) suggestive evidence that the deficiency of an additional unknown plasma factor plays a definite part in the pathogenesis of the hypoprothrombinæmia of the newborn, and (2) a constant exaggerated delay of the clotting time and depletion of prothrombin activity in the week immediately preceding and that following spontaneous bleeding episodes in hæmophilia Labile factor activity of plasma was normal in both conditions

REFERENCES

Allen J G Bogardus G , Jacobson, L O , Spurr, C L (1947) *Ann intern Med.* **27**, 382
Estren, S , Sanchez Medal, L , Dameshek W (1946) *Blood*, **1**, 504
Fahey, J L , Olwin, J N , Ware, A G (1948) *Proc Soc exp Biol., N Y* **69**, 491
Fantl, P Nance, M (1946) *Nature Lond* **158**, 708
— — (1948) *Med J Aust* 1, 128
Harrington, W J , Manheimer, R H Desforges, J F Minkel, H P , Crow, C B , Stohlman, F (1950) *Bull. New Eng med Center*, **12**, 121
Nolf P (1908) *Arch intern Physiol* **6**, 1
Olwin, J H (1949) *J Lab clin Med* **34**, 806
Owren, P A (1944) *Proc Norwegian Acad. Sci.* **1**, 21
— (1947a) *Acta med scand* suppl no 194
— (1947b) *Lancet*, i 446
— (1948) *Biochem J* **43**, 136
— (1949) *Scand. J clin Lab Invest* **1**, 131
Quick, A J (1943) *Amer J Physiol* **140**, 212
— (1945) *Amer J clin Path* **15** 560
— (1947) *Amer J Physiol.* **151** 63
— Stefanini, M (1948a) *J Lab clin Med* **33**, 819
— — (1948b) *J gen Physiol* **32** 191
— — (1949a) *J Lab clin Med* **34**, 973
— — (1949b) *Proc Soc exp Biol N Y* **72** 232
— — (1950) *Amer J Physiol* **160**, 572
Randall A., Randall, J P (1949) *Proc Soc exp Biol , N Y* **70**, 215
Stefanini M. (1948) *Amer J clin. Path* **18**, 537
— (1950a) *Ibid*, **20**, 233
— (1950b) *Bull New Eng med Center* **12**, 102
— Crosby, W H (1950a) *Fed Proc* **9** 233
— — (1950b) *Proc Soc exp Biol N Y* **74**, 370
— Quick, A J (1948) *Fed Proc* **7**, 191
Sykes E M jun , Seegers W H , Ware, A G (1948) *Proc Soc exp Biol , N Y* **67** 506
Tuft H S Rosenfield R E (1947) *Amer J clin Path* **17**, 704
Ware, A G Guest M M Seegers W H (1947) *Science* **106**, 41
— Seegers W H (1948) *Amer J Physiol* **152**, 567
— — (1949) *Amer J clin Path.* **19** 471

HÆMOPHILUS INFLUENZÆ MENINGITIS TREATED WITH STREPTOMYCIN

DIFFICULTIES IN DIAGNOSIS

E C Allibone
M D Leeds, M R C.P , D P M
PHYSICIAN TO CHILDREN'S DEPARTMENT, LEEDS GENERAL INFIRMARY

J D Pickup
M.D Leeds, D C H
LECTURER IN PÆDIATRICS

K Zinnemann
M D Frankfort
LECTURER IN BACTERIOLOGY

UNIVERSITY OF LEEDS

Most reports on the streptomycin treatment of *H influenzæ* meningitis published in this country (Wilson 1948, Smythe 1948, Roscoe and Gleeson-White 1948) have emphasised that failure is usually due to the rapid development of streptomycin resistance in the infecting organism This feature was not encountered in our series, where failures of treatment were due to other causes Ounsted (1949), in his 10 cases, did not observe drug fastness either, nor did he have to deal with more than one case of the subacute type (Zinnemann 1946, Smythe 1948) The generally poor prognosis in the subacute type of case is only mentioned in passing in one of the reports cited (Smythe 1948) Alexander et al (1946) emphasised that intensive treatment of subacute cases with streptomycin might lead to survival, but with serious and permanent cerebral damage These cases seem worthy of particular attention because if efforts were intensified to diagnose them earlier the prognosis would be considerably brightened (Alexander 1943, Jones 1947)

TABLE I—CLINICAL DETAILS OF 11 CASES OF *H Influenzæ* MENINGITIS

Case no	Age (mos)	Presenting symptoms	Clinical severity	Duration of illness before admission (days)	Period between admission and 1st lumbar puncture (days)	Total period before meningitis suspected (days)	Duration of treatment (days)	Result
1	4	Meningismus	Severe	7	0	7	7	Death
2	13	Gastro enteritis	Severe	1	6	7	9	Death
3	12	Gastro enteritis	Moderate	7	6	13	7	Cure
4	22	Vomiting	Severe	5	0	5	1	Death
5	12	Upper respiratory infection	Severe	7	2	9	60	Dementia, blindness, hydrocephalus
6	8	Meningismus	Moderate	6	0	6	15	Cure
7	15	Convulsion	Severe	2	0	2	12	Cure
8	18	Vomiting	Severe	5	0	5	22	Cure
9	6	Upper respiratory infection meningismus	Moderate	4	2	6	17	Cure
10	15	Meningismus	Severe	3	0	3	12	Cure
11	19	Listlessness, upper respiratory infection	Moderate	21	9	30	20	Cure

The following 11 cases (tables I and II), treated at the Leeds Streptomycin Clinical Trials Centre in the last two years, illustrate some of the difficulties of early diagnosis

Presenting Symptoms

Only 5 of the 11 cases showed presenting symptoms suggesting involvement of the central nervous system Cases 2, 3, and 4 were thought to have gastro enteritis, and cases 5 and 11 an upper respiratory infection As a result, diagnostic lumbar puncture in these cases was delayed for 5–30 days after the onset of the illness

Antecedent Manifestations

In 4 of the histories there were antecedent manifestations, the significance of which is problematical but which may have some bearing on the subsequent development of the disease Case 1 had a persistent cough for a month before admission Case 5 was admitted to hospital fifteen days before the final admission, was treated for an upper respiratory infection, and was discharged the day before the onset of what was at first considered to be a relapse Cases 2 and 6 had a head injury—in case 2 the fall was on the forehead six days before the onset and the child subsequently continued to rub its head up to the start of gastro enteritic symptoms , and case 6 fell out of bed twelve hours before the start of symptoms

Complications

On admission case 1 had a fluctuant swelling 2 cm in diameter at the right lateral angle of the anterior fontanelle , at necropsy this was found to be a herniation from the subarachnoid space full of tenacious yellow green pus On the day of admission case 4 developed a painful swelling of the left elbow joint and left knee joint , necropsy confirmed a purulent arthritis In case 10 a swollen left knee was detected on the second day in hospital Cases 3 and 7 had congestion of the tympanic membranes Case 4 had bilateral purulent otitis media , of a drip glucose transfusion, which was maintained for some time after the nitrogen mustard had been given

URETHANE

Paterson et al. (1946) first reported the use of urethane in the treatment of leukæmia and, at the end of this report, stated that urethane had also been given to a few patients with advanced carcinoma without any degree of success The dosage used was 3–5 g daily by mouth

Haddow and Sexton (1946), working with the Walker rat carcinoma, found that urethane, given intraperitoneally in a dosage of 0 25–0 5 g per kg of body weight, produced very pronounced cytological changes in implanted tumours and pronounced inhibition of tumour growth

Urethane was also shown to be capable of inducing tumour growth, and Henshaw (1945) and Larsen (1946) showed that urethane could produce pulmonary adenomata in mice Orr (1947) has shown that the first effect of urethane is to set up inflammation in the lungs of mice, and that the adenomata seem to come as a result of further changes in the inflammatory lesions

My work with urethane began in 1946 in the department of surgery in the University of Liverpool, when, because of the apparent affinity of urethane for bronchial epithelium, I treated patients with inoperable carcinoma of the bronchus with large doses of urethane Two patients with this condition and two patients with inoperable carcinoma of the breast were treated. The results were very unsatisfactory Acute hæmolysis developed in two cases, jaundice occurred in all, and in biopsy specimens in three cases before and after treatment no change was seen in the cell picture In the first case (carcinoma of bronchus) urethane was given intravenously in doses of 28 g daily, and, although the patient died from pyæmia seven days after treatment had begun, at necropsy both primary and secondary growths were found to be completely necrotic This case and the third case, which came to necropsy also, showed subacute necrosis of the liver

The further use of urethane was therefore postponed for an indefinite period, and not until I came to Hong-Kong did I resume this work All patients with nasopharyngeal carcinoma were regarded as beyond hope of other treatment, and consequently high and potentially dangerous dosage of this toxic drug was considered justifiable For administrative convenience the daily dose was standardised at 10 g dissolved in 20 ml. of water, which in the average patient weighing about 40 kg approximated to Haddow and Sexton's (1946) minimal dosage in rats—i.e , 0 25 g per kg of body-weight

An intravenous drip transfusion of 5% glucose in water was set up , and, after it had been running for a few minutes, the whole dose of urethane was injected into the tube The urethane was then washed through the vein quickly and the drip continued until 1000 ml. of 5% glucose had been given The immediate results of treatment are given in the accompanying table, and are summarised as follows

Died in hospital	5	
Refused adequate treatment	5	
No improvement	4	
Slight improvement	4	(2 untraced after 4 and 6 months 1 recurred after 4 months 1 died within 3 months)
Great improvement	5	(1 recurred after 6 months 1 died after 4 months cause unknown 1 large recurrence after 2 months 3 too recent to follow up)

"Great improvement" means disappearance of the primary or the secondary mass, or both "Slight improvement" means diminution in size of the mass and usually increased mobility

The follow-up period is very short, and the difficulties of following up patients in a shifting and overcrowded community like that of Hong-Kong are considerable It is felt, however, that the initial results of this investigation are of considerable significance, because this tumour does not regress spontaneously Apart from those five cases in which treatment was hopelessly inadequate, a noticeable improvement occurred in nine out of eighteen cases, and very great improvement—i e , disappearance of the tumour—in five out of eighteen

We do not yet know how long the remission will last , but, since the earliest cases in the series already show signs of recurrence, urethane seems to give temporary benefit only Possibly a combination of urethane and radiotherapy may hold out greater hopes of permanent relief, but this has not yet been tried here

Urethane given in this way is far from pleasant, and there is evidence of considerable toxicity Anorexia, nausea, and vomiting invariably develop, and patients vary a good deal in the way in which they react to this A soft or fluid diet with glucose drinks will usually be tolerated. In this series jaundice occurred only three times In two patients this was just before death, and in these two patients there was no evidence of subacute necrosis of the liver In the third patient (case 23) the dosage of urethane was increased, after six doses of 10 g daily, to 15 g daily for the next six doses The white cell count fell sharply, and jaundice followed three days after the end of treatment Jaundice persisted, and at peritoneoscopy on July 29, 1950, the liver was seen to be finely granular Biopsy was not done, and the patient's condition was deteriorating rapidly The effect in the white cell count is very variable Often in the first few days the total count rises to about 12,000 cells per c mm and thereafter falls slowly, but this change is not constant , and, when a patient receives two courses of urethane—e g , case 22,—the white cell count may fall on the first occasion, recover in the interval, and not fall at all in the second course In other cases there is no initial rise but a steady and progressive fall in the total count, polymorphs, and lymphocytes being equally attacked

SUMMARY

Haddow and Sexton (1946) have shown that urethane in large doses partially inhibits the growth of implanted tumours in animals, slowing down the growth but not completely stopping it

A similar effect has now been demonstrated in man with nasopharyngeal carcinoma, when on certain occasions very great diminution in size has been noted as a result of high dosage of urethane intravenously

So far as can be foreseen at present, the effect is only temporary, for in most cases where some benefit has been shown the tumour has recurred fairly rapidly

REFERENCES

Digby K. H Fook W L Che Y T (1941) *Brit J Surg* 28 517
Haddow A Sexton, W A (1946) *Nature Lond* 157, 500
Henshaw P S (1945) *J nat Cancer Inst* 5 419
Larsen C D (1946) *Ibid* 7 5
Mekie E C Ransome G (1950) *Brit J Surg* 37, 344
Orr J W (1947) *Brit J Cancer* 1 311.
Paterson E , Haddow A. Ap Thomas I Watkinson J M. (1946) *Lancet* i 677

"I think that the next thing that the public expects the medical profession to do is to recognise that the subject of medical care is not the exclusive domain of the medical profession It is the primary concern of every citizen. All too often the medical profession leaves the impression that it regards the discussion of a medical problem by a non-medical speaker or writer as an unwarranted interference with the practice of medicine "—L B SELTZER, *J Amer med Ass* 1950, 114, 1573 wishful thinking We endorse the plea of Alexander (1943) for earlier and more frequent lumbar puncture in any case of fever accompanied by meningeal irritation

Our figures for sibling relationship do not bear out the hypothesis of Ounsted (1950), but it was interesting to find that only 5 of the 104 British cases collected in the last ten years were in children under the age of 6 months

SUMMARY

Eleven cases of *H influenzæ* meningitis treated with streptomycin are reported to illustrate the difficulties of diagnosis in young children and the poor prognosis in cases where treatment is started in the advanced stages

The causes of therapeutic failure are discussed

Earlier diagnosis by lumbar puncture is essential if the results are to be improved

REFERENCES

Alexander H E (1943) *Amer J Dis Child* 66, 172
— Leidy, G , Rake, G , Donovick, R (1946) *J Amer med Ass* 132, 434
Jones H E (1947) *Lancet* ii 368
Ounsted C (1949) *Ibid* ii 639
— (1950) *Ibid*, i 161
Roscoe, J D , Gleeson White, M H (1948) *Ibid* ii 885
Smythe, P M (1948) *Ibid* p 485
Wilson C (1948) *Ibid*, p 445
Zinnemann, K (1946) *Brit med J* ii 931

NITROGEN MUSTARD AND URETHANE IN THE TREATMENT OF NASOPHARYNGEAL CARCINOMA

FRANCIS E STOCK
M B Lond , F.R C S , D T.M & H
PROFESSOR OF SURGERY IN THE UNIVERSITY OF HONG KONG

ADEQUATE clinical descriptions of nasopharyngeal carcinoma have been published from time to time, and an excellent and profusely illustrated description of the condition as seen in Hong-Kong was published by Digby et al (1941) Virtually nothing, however, is known of its ætiology, despite the fact that it is the most common type of carcinoma encountered in Hong-Kong and South China

The age incidence is very wide In the short series recorded here the average age was 37, seven patients being aged 30 or less, and nine being aged 40 or more

Treatment of the condition is extremely unsatisfactory Radical surgery is impracticable because of the primary site of the tumour and because in most cases large fixed glands are present when the patient first appears. Mekie and Ransome (1950) have treated patients with advanced disease by prefrontal leucotomy with the idea of relieving pain, and this method is also being adopted here in selected cases Radiotherapy is in most cases only palliative, if indeed it has any effect at all, and with the present shortage of staff and equipment in the main government hospital in Hong Kong patients with nasopharyngeal tumour are not accepted for radiotherapy

Our interest in the treatment of this apparently hopeless condition has turned in other directions, and I report here the first attempts made in this department to combat this condition with specific carcinolytic drugs. Two drugs have been used in this series and they will be considered separately

NITROGEN MUSTARD

A series of 25 cases was started in May, 1949 The cases were entirely unselected but represented all the late stages of nasopharyngeal carcinoma In all the cases glands were available for section, and usually biopsy was done before treatment began and again at the end of treatment

This series is not reported in detail because, though in a few cases there was a very slight diminution in size of the glands, and in advanced cases with bone involvement a temporary decrease in the amount of pain experienced, in no case did this temporary remission last for more than four weeks, and in most cases no effect at all was seen in the tumour mass and there was no amelioration of symptoms The biopsies done before and after treatment showed no significant change in the cell picture The dosage of nitrogen mustard used was 0 1 mg per kg of body weight daily for six doses administered by direct injection into the tube

RESULTS OF TREATMENT OF NASOPHARYNGEAL CARCINOMA WITH URETHANE

Case no	Age (yr)	Sex	Daily dose (g)	Total dose (g)	Length of treatment (days)	Treatment ended	Immediate result	Follow up
1	34	M	10	150	48	Dec 14 1949	Great improvement	July 11, 1950, mass larger again
2	33	F	10	200	47	Dec 9 1949	No improvement	
3	30	F	10	160	60	Jan 24, 1950	Toxic reaction, slight improvement	June, 1950 untraced (returned to village)
4	36	F	10	150	35	Jan 12, 1950	No improvement	
5	49	M	10	100	16	Jan 3 1950	Died Jan 11, 1950	
6	25	M	10	60	22	Jan 23, 1950	Refused further treatment, nausea and vomiting considerable	
7	51	M	10	150	46	March 9, 1950	No improvement	
8	42	F	10	200	48	March 9, 1950	Slight improvement	July 11, 1950, mass much larger
9	55	F	10	130	34	Feb 25 1950	Developed toxic nephritis great local improvement	June 1950, died recently, cause unknown
10	33	M	10	10	1	Jan 23 1950	Severe vomiting, refused further treatment	
11	34	M	10	50	12	Feb 7 1950	Severe vomiting, refused further treatment	
12	45	M	10	20	3	Feb 6 1950	Severe vomiting refused further treatment	
13	19	M	10	200	64	April 28 1950	Severe reaction great improvement	June 1950 large recurrence
14	19	M	10	150	29	Feb 24, 1950	Slight improvement	June 1950 died recently
15	40	F	10	170	35	April 6 1950	Slight improvement	June 1950 untraced (returned to village)
16	51	F	10	150	25	April 24 1950	Died April 25 1950	
17	27	M	10	40	5	April 7 1950	Refused further treatment	
18	30	F	10	100	23	April 24 1950	Died April 27 1950	
19	47	F	10	130	15	April 30 1950	Died May 4 1950	
20	27	F	10	80	11	June 10 1950	Great improvement treatment discontinued when white cell count fell to 1000 per c.mm	
21	44	F	10	30	6	June 7 1950	Died after refusing further treatment	
22	38	F	10	170	17	May 3 1950	Great improvement	
			10	100	9	June 8 1950		
23	36	M	10	150	12	June 7 1950	No improvement	
			15			June 13, 1950	Jaundice and ascites	

fever, the patient was given an intravenous injection of cardophylin 0·48 g with no effect

In an attempt to obtain diuresis without the reactions the patient was given tablets of mersalyl by mouth, in 80 mg 160 mg and 320 mg doses a day for 1, 4, and 5 days respectively, with no fever or diuresis

Dimercaprol was tried in the hope that it might abolish the reactions and leave some diuretic effect The patient was given three intramuscular injections of 100 mg at 6 and 10 A.M. and 2 P.M. At 10 15 A.M. he was given neptal 0·25 ml intramuscularly At 1 30 P.M. he was very miserable, complaining of pain in his limbs and back, irritation of his skin, and a sensation of heat on the top of his head He was shivering and cyanosed but developed no fever A few days later he was given a similar injection of neptal without the dimercaprol, and the reaction was indistinguishable from the previous one

In view of the gross subjective disturbance it was not thought justifiable to pursue the question of sensitivity further

COMMENTS

These two cases illustrate a pyrexial reaction to mercurial diuretics after 6–10 days The fever and subjective symptoms increased daily Different brands of mercurial drugs with slightly different molecular structure produced identical responses, and oral administration caused fever in one case but no effect on temperature or diuresis in the second. Dimercaprol (B.A.L.) was tried and had no effect, but an insufficient amount seems to have been given before the neptal (Sussman and Schack 1947)

Both of the present patients showed a heightened reaction to intradermal injections of these drugs compared with controls

We wish to thank Prof E P Sharpey-Schafer for permission to publish these two cases

REFERENCE

Sussman R. M. Schack, J A (1947) *Proc Soc exp Biol. N Y* 66 247

URTICARIA FOLLOWING ADRENALINE BUT NOT NORADRENALINE

H. Herxheimer
L.R.C.P.E

CLINICAL AND RESEARCH ASSISTANT UNIVERSITY COLLEGE HOSPITAL, LONDON

URTICARIA is usually suppressed by adrenaline There seems to be only one case on record of urticaria produced by an injection of adrenaline (Dumm 1941), this patient reacted only to natural adrenaline, and the rash could not be provoked by synthetic adrenaline An intriguing feature of the case described below was the strikingly different effect of adrenaline and noradrenaline

A man, aged 33 had suffered from asthma and urticaria since 1944 when he served with the R.A.F in Egypt In 1945 he was given an adrenaline injection for his asthma, a short time later he had severe palpitations followed by an urticarial rash all over his body while the asthma subsided The same occurred after a second injection of adrenaline and again when he was given ephedrine tablets He had since avoided these drugs

In December 1949 when the patient came under observation at University College Hospital his asthma was mild and the urticaria appeared only occasionally An asthmatic attack could be induced by letting him inhale mould extract or pollen extract whereas the urticaria was precipitated by the emotions such as fear or vexation.

The patient was given 1 minim of synthetic adrenaline 1 1000 subcutaneously after 5 minutes he noted mild palpitations and after 30 minutes an urticarial rash appeared on his arms trunk, and legs This reaction could be prevented by giving 150 mg of the anti histamine drug 'Chlorcyclizine by mouth one hour before the adrenaline injection. A subcutaneous injection of 3 minims of adrenaline produced a similar rash but this could not be completely prevented by chlorcyclizine When the man received 200 mg of chlorcycline by mouth, and then, after an interval of an hour, 5 minims of adrenaline subcutaneously, the rash appeared 15 minutes later Subcutaneous injections of either 1 or 3 minims of noradrenaline did not produce any rash. An injection of sodium metabisulphite solution, which is usually added to commercial adrenaline solutions as a "stabiliser," did not cause any urticaria, whereas adrenaline containing none of this substance still produced the rash. When the man inhaled 2% isopropylnoradrenaline aerosol tachycardia and palpitations developed, but no rash appeared.

No further investigations could be carried out in this case because the patient left London

I am indebted to Dr Norman Whittaker and Dr V Davies for referring this case to me

REFERENCE

Dumm J F (1941) *Prensa med argent* 28 303

LICHEN STRIATUS

Harold Lee
M.D Leeds

SENIOR REGISTRAR DERMATOLOGICAL CLINIC, NOTTINGHAM

LICHEN striatus is a relatively rare condition which usually occurs in children in the form of a linear lichenoid papular eruption (Ormsby and Montgomery 1948) Generally the arms are involved, and the condition commonly is unilateral. The onset is sudden, and the extension of the eruption to form linear bands is rapid. These bands are composed of small lichenoid papules, which often coalesce to form regions of lichenified dermatitis As a rule there are no subjective symptoms.

Senear and Caro (1941) drew attention to the condition and reviewed the literature Since then a few cases have been reported in America, but hitherto none in Great Britain

CASE RECORD

A girl aged 8 years was first seen on July 15 1949 with a history that some eight weeks previously she had developed german measles (rash on face and body with cervical adenitis), and when this cleared she had become aware of a rash on the left mid-calf This rash had spread quickly in the form of a line up and down the limb

On examination there was a continuous line of lichenoid papules extending from the topmost part of the left thigh downwards to behind the internal malleolus (fig 1) The band, which was about 1/4 in. wide and about 1 in. medial to the midline of the limb was slightly scaly behind the malleolus. No other lesions were present on the skin or the mucosal surfaces The band was completely asymptomatic. A biopsy specimen was taken from just above the knee flexure

Progress —The patient was next seen on Aug 11, 1949, when the eruption was beginning to fade Her mother reported that it had been even better at one stage, but had seemed to return again. On the next visit Nov 4, 1949 the eruption had faded completely, leaving no trace except a very little superficial scaling behind the malleolus

Histology

The histological report (Dr E A. Horne) was in keeping with the clinical diagnosis of lichen striatus

Epidermis (figs 2 and 3) —The epidermis showed some loose hyperkeratosis In some places possibly in association with follicular openings there was slight dipping of this layer The stratum granulosum was present throughout, but was considerably thinned—in some places not more than one

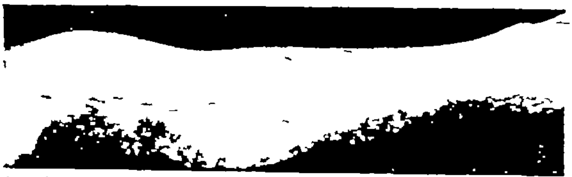


Fig 1—Lichen striatus on dorsum and medial aspect of left leg

SENSITIVITY TO MERCURIAL DIURETICS

REPORT OF TWO CASES

C A FOSTER
M B Lond

P F D NAYLOR
M A , M B Camb

HOUSE PHYSICIANS, ST THOMAS'S HOSPITAL, LONDON

REACTIONS to mercurial diuretics given intramuscularly are rarely reported, and their diagnosis is not always easy, as the following cases show

CASE 1

A man, aged 21, was admitted to a surgical ward on Jan 21, 1949, with twelve hours' history of abdominal pain and vomiting He said he had had rheumatic heart disease since the age of 14, and was receiving digitalis, physical examination showed the presence of mitral stenosis with auricular fibrillation Mesenteric embolism was diagnosed and was confirmed at operation, but the collateral circulation seeming adequate, no resection was done After the operation the patient showed signs of overdosing with digitalis, so this drug was withheld The abdominal wound became infected, and on Feb 3, 1949, a secondary skin suture was done

On Feb 9, 1949, the patient began to have evening pyrexia up to 100 2°F Examination showed œdema of both legs, crepitations at the bases of both lungs, and probably an effusion at the base of the right lung There were no embolic phenomena, and blood cultures were sterile Small doses of digitalis were started again

On Feb 21, 1949, the patient was transferred to a medical ward because his cardiac failure was increasing and because it was thought that his pyrexia could not be due to the infected abdominal wound alone

Examination showed his jugular venous pressure raised to the angle of the jaw, bilateral œdema of the ankle but no sacral œdema, a right sided pleural effusion, the liver palpable three finger breadths below the right costal margin, and a moderate degree of ascites There were no embolic phenomena A swab from the wound yielded *Staph aureus* insensitive to penicillin, blood cultures were sterile, and a differential white cell count was normal The patient's temperature began to settle during the next week

On March 4, 1949, injections of 'Neptal' were started (fig 1), 1 ml intramuscularly every day at about 9 A M A fairly good diuresis was produced

On March 12, 1949, the eighth day after the start of the daily injections, the patient had shivering and bouts of coughing at 11 30 A M—i e, about three hours after the injection His temperature rose to 100°F He began to perspire at 3 P M, and his temperature quickly returned to normal On March 13, 1949, exactly the same sequence of events recurred, except that in addition to the coughing and shivering the patient became much cyanosed and his extremities were very cold His temperature rose to 103°F, in the afternoon he perspired freely, and his temperature fell during the late evening The same thing happened on March 14, when his temperature rose to 104°F, and on March 15 when his temperature rose to 105°F The neptal was still being given every morning There were no changes in the physical signs in the cardiovascular system or the abdomen No embolic phenomena were observed, the spleen was impalpable, there was no clubbing, blood cultures were sterile, and a differenti white cell count and radiography of the chest revealed nothin abnormal

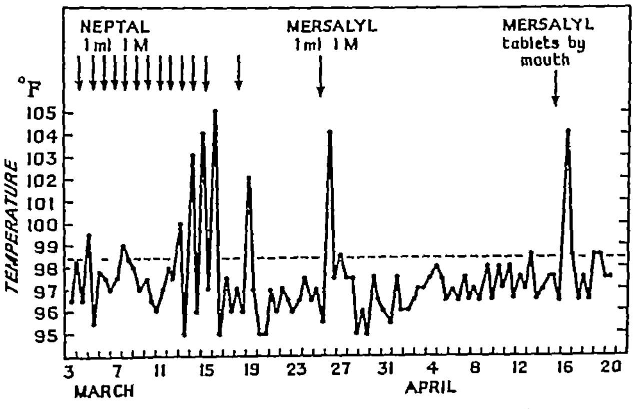


Fig 1—Treatment and temperature chart of case 1

On March 16, no neptal was given and the patient remaine afebrile throughout the day

On March 18 the patient was given neptal 1 ml. and had further rigor and his temperature rose to 103°F

On March 25 the patient was given an injection of mersaly 1 ml and had a rigor exactly similar to the ones apparentl provoked by neptal He still had the signs of cardiac failur with a raised venous pressure, peripheral œdema, a palpabl liver, and ascites

On March 29 at 3 P M, 0 1 ml of 1 84% neptal was injecte intradermally into the left forearm At 6 P M there was circular area of slight œdema 1 cm in diameter and erythem 3 cm in diameter There was also extremely well marke lymphangitis running up the medial aspect of the arm the axillary lymph glands were neither palpable nor tender A similar injection given to another patient as a contro produced an area of erythema 1 cm in diameter with no lymphangitis

It was thought that possibly the effects might have been due to the theophylline in the neptal, but no sensitivity was demonstrated when 'Cardophylin' was given intravenously or intradermally

On April 15, 1949, it was decided to try mercurial diuretics by mouth, and two tablets of mersalyl, each containing 0 08 g of mersalyl and 0 04 g of theophylline, were given. These produced cyanosis, coughing, and a rigor, and the patient's temperature rose to 104°F

The patient was given methyl thiouracil and digitalis, and with rest his cardiac failure improved sufficiently to warrant his being discharged to a convalescent home

CASE 2

An Irish labourer, aged 73, was admitted to hospital complaining of breathlessness on exertion, swelling of the legs for six months, and an irritative rash for about a month For two months he had been taking digitalis pills On examination he had congestive cardiac failure due to ischæmic heart-disease with auricular fibrillation and gross cardiac enlargement His rash was a patchy erythema *Treatment* consisted of rest in bed, a low salt diet, and, from his fourth day in hospital, a daily intramuscular injection of neptal 1 ml His rash was successfully treated with 'Antistin' He lost two stone in weight in the first seventeen days and was much improved

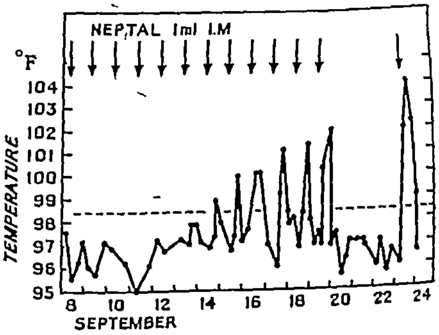


Fig 2—Treatment and temperature chart of case 2.

In the afternoon of the seventh day of his daily injections of neptal his temperature rose to 99°F, and on the next two afternoons it rose to 100° and 100 2°F, it was down to normal in the evenings (fig 2) The fever was associated with malaise and skin irritation

The patient was found to have a small pleural effusion, and it was thought that he might be developing an empyema He was treated with penicillin, in spite of which his temperature rose to 102°F, with a rigor, in the afternoon after his twelfth morning dose of neptal It was thought that, since the fever was so similar to that in case 1, it might also be due to neptal, so the injections were stopped The temperature remained normal in the next three days

To find out if the pyrexia was due to the diuretic, the patient was given 1 ml of mersalyl intramuscularly Five hours later his temperature rose to 104°F with the most severe rigor that he had had, much cyanosis, and skin irritation

To ascertain his sensitivity to neptal, an intradermal injection of 0 1 ml of a 0 46% solution of neptal was given which caused a patch of erythema 2 in in diameter in a control a similar injection caused a patch $^1/_2$ in in diameter To exclude the theophylline as being the cause of the

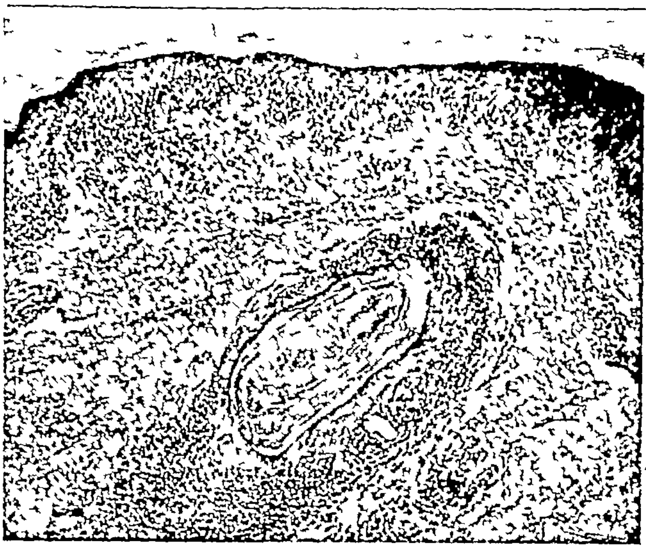


Fig 2—Epidermis affected by lichen striatus and showing irregular acanthosis, œdema, invasion by cells infiltration of papillæ, and perivascular and perifollicular reaction

cell thick. The prickle cell layer showed an irregular acanthosis (fig 2). There was broadening of the rete pegs, with lateral fusion. The basal cell layer was broken in places, especially in relation to the papillæ which were most infiltrated. The prickle cell layer showed both intercellular and intracellular œdema (fig 3). This was most marked in the lower half of the epidermis and especially in relation to the papillary infiltration. In these areas also the epidermis was infiltrated by the cells through the papillæ. Patchy pigmentation was present. There was some thinning of the epidermis in this region where the papillary infiltrate was very marked.

Dermis.—A considerable amount of cellular reaction was present and was mainly perivascular. Lymphocytes and histiocytes were seen, together with melanophores. No polymorphs or eosinophils were noted. The cellular infiltrate was most marked in the papillæ and in the superficial part of the dermis but could be seen at deeper levels. The capillaries were congested, and there was some œdema of the papillæ. A hair follicle in the sections examined was surrounded by a heavy pleiomorphic infiltrate. The outer sheaths of the hair follicle showed much intracellular œdema, and there was some vagueness in the line of demarcation between epidermal cells and infiltrate. The collagen appeared unchanged. The sweat-glands appeared normal, as did the sebaceous glands. A nerve was seen in the section and appeared normal, but was associated with cellular infiltration, thus showing the depth to which the infiltration penetrated.

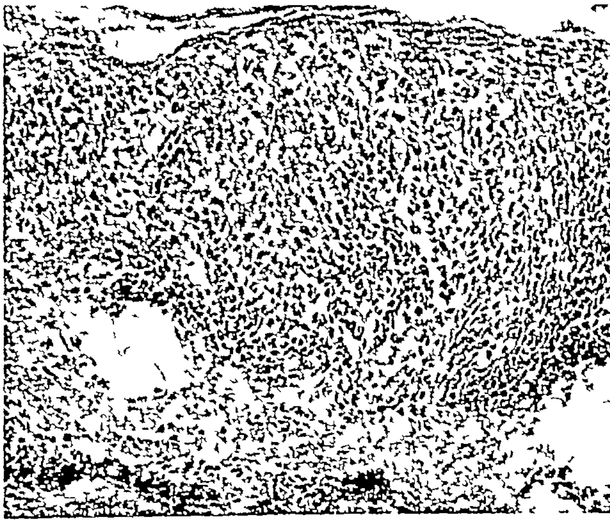


Fig 3—Epidermis affected by lichen striatus and showing intercellular and intracellular œdema of epidermis and cellular infiltration of epidermis and papillæ.

Elastic Tissue.—Special stains showed that the elastic tissue of the corium was absent or much diminished in the papillæ, where there were areas of infiltration. Elsewhere the elastic tissue appeared normal.

DISCUSSION

Lichen striatus has a distinct clinical picture with definite clinical and histological characteristics. According to Senear and Caro (1941) the most striking feature is the course: there is a sudden onset, followed by a rapid extension to form a linear band. The lesions disappear in a few weeks or several months, either spontaneously or after the application of bland medicaments. The eruption consists of lichenoid papules which primarily are small and discrete. They may be flattened, glistening, and angular, but the angularity is produced by the normal markings of the skin. The papules are not those of lichen planus; there is no umbilication or Wickham's striæ. They coalesce to form an erythematosquamous dermatitis. The bands, which may be homogeneous, consist of narrow parallel streaks, may be continuous or interrupted, and vary in length and width. No preceding history of injury, local pressure, or contact with external irritants has been noted, and subsequent involution takes place without atrophy. The condition is relatively asymptomatic.

Senear and Caro (1941) described 10 cases in each of which there was a linear lichenoid papular eruption. With one exception this eruption involved the arms and was unilateral. Of the patients, 7 were children. In all instances the onset was sudden, the extension to form lichenoid bands rapid, and the eruption of short duration and self limited. As a rule the disease was asymptomatic. The eruption was composed of primary small lichenoid papules which often coalesced to form patches of lichenified dermatitis.

Lewis (1942) reported a similar eruption on the left arm of a girl aged 13. The eruption consisted of lichenified discrete confluent scaly lesions grouped in a line. Lichen planus was considered, but no typical papules were seen, and there were no buccal lesions. Schmidt (1942) reported a case on the left arm of a five year old negro child. Netherton (1944) reported a case in a woman of 44 with a five weeks' history, the eruption this time occurring on the right leg and extending from the right buttock downwards over the posterior surface of the thigh, calf of the leg, and forwards to involve the whole lateral surface of the right foot. There was some itching. Rothman (1946) reported a case in a child aged sixteen months, the eruption being along the line of the sciatic nerve. Pinkus (1948) reported a case associated with lichen planus; the diagnosis was established with the help of the biopsy, and, whereas subsequently the lesions of lichen striatus disappeared, those of lichen planus persisted and recurred.

Ætiology

Little is known about the ætiology of this condition, but Senear and Caro (1941) tried to explain the linear distribution by the concept of the existence in the skin of zones of increased irritability (fragile zones), which were determined congenitally by various factors. In the case reported here the condition was preceded by rubella.

Differential Diagnosis

The four conditions to be considered are linear psoriasis, linear lichen planus, linear nævus, and lichen striatus.

It is characteristic of lichen striatus that the lesions are self limited and disappear spontaneously in a few weeks or months. The other conditions usually display typical morphology, clinical characteristics, and histology, but the differentiation from lichen planus may be in table II There is no significant difference in the effectiveness of the two vaccines (level of significance P = 30% approx) It is important to note also that no allowance was made in the preparation of the Ty2 suspension for the added advantage of the A, B, and C components of the Lister vaccine

Finally, the sera from each group of rabbits immunised in the present series of experiments were pooled and filtered Passive protection tests in mice were carried out, using as controls sera prepared in 1939 against acetone dried suspensions of Ty2 and T6S In addition, we included a sample of the "provisional standard antityphoid serum" described by Felix (1938) and held at the Department of Biological Standards, National Institute for Medical Research Table III summarises the results of one passive protection test in mice The mucin technique was used in this experiment (Henderson 1939) The results show clearly that the protective value of the various sera are fully in accord with their agglutinin titres, and there is no suggestion of alteration in the efficiency of the antibody produced against the long stored antigen preparations

COMMENT

These simple experiments are of interest not only from the historical point of view, but also because they may provide a basis for research on the stability of typhoid and perhaps other vaccines It may prove that the acetone method of drying is not the most suitable Nevertheless, the evidence is that some form of dried vaccine is worthy of trial

Acknowledgment is made to the Chief Scientist, Ministry of Supply for permission to publish

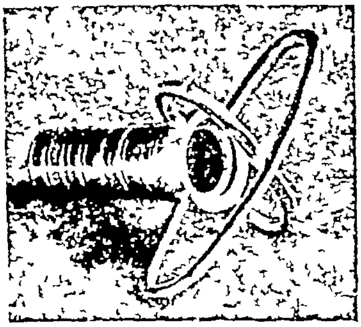
REFERENCES

Felix, A (1938) *J Hyg Camb* 38 750
— (1941) *Brit med J* i, 391
— Petrie G F (1938) *J Hyg Camb* 38 673
— Pitt M. (1934) *Lancet* ii 186
Henderson D W (1939) *Brit J exp Path* 20, 1
— Morgan W T J (1938) *Ibid* 19 82

New Inventions

SAFETY ENDOTRACHEAL CONNECTION

THE under-mask method of endotracheal anæsthesia is probably the simplest technique and has a wide range of usefulness There must however be some arrangement to prevent the tube from slipping down the trachea, and to ensure that the open end of the endotracheal airway is not obstructed when in position under the mask The devices now used include a safety pin, one of the standard endotracheal connections, and the flange described by Gordon [1] All these are effective in preventing the tube slipping downwards but they do not guarantee a patent orifice A partial obstruction is commonly caused by the open end of the tube or its connection abutting against the inside of the mask.



I have recently been using the safety endotracheal connection shown in the figure, and have found the wire frame entirely successful in keeping the orifice free

The connection was made for me by the Medical and Industrial Equipment Co Ltd , of 12, New Cavendish Street, London, W 1

Edinburgh HENRY E BELL, M.B N U.I., D A.

---

[1] Gordon J *Brit med. J* 1947 ii 785

Reviews of Books

Psychological Factors of Peace and War

Editor Prof T H PEAR London Hutchinson 1950 Pp 262 16*s*

THIS is a book of outstanding importance, even though it contains little that is new to psychologists The scientific and medical professions have been slow to apply the findings of social science to their own thinking Not unnaturally they tend to continue to accept the face-value view of political processes which is accepted by the majority of their fellow citizens In this book Professor Pear has collected a series of essays on the socio-psychological, psychopathological, and demographic forces which produce international tension or operate in war time The underlying assumptions of the book are revolutionary, and despite its defects it marks a movement in scientific thought which may well have extensive repercussions on the attitude of scientists to the society in which they work Dr H J Eysenck's essay on war and aggressiveness, Prof J C Flugel on aspects of integration, and Dr H V Dicks on the German character, would be hard to better, and the essays achieve a level of objectivity which is a major feat in itself

In this book we see the translation into terms of practical political psychopathology of the pioneer work of Ruth Benedict, Lasswell, and many others It represents a tendency which no informed scientist can afford to ignore

Cancer Where We Stand

SIDNEY RUSS, O B E , D SC F INST.P , professor emeritus, University of London With a foreword by Lord HORDER London Oxford University Press 1950 Pp 192 10*s* 6*d*

MOST doctors would agree with Lord Horder's view, set out in a foreword to this book, that cancer is decidedly a subject which should be presented to lay readers , and in many ways Professor Russ is the right man to do it He explains the principles of modern X-ray and radium treatment clearly, and tells the history of their discovery with warm enthusiasm Other aspects of research are dealt with less fully, which may disappoint some readers Rightly or wrongly the layman believes that discovery of the cause could not but hasten discovery of a cure , and he likes to know how we are getting on

To show how much our present methods of treatment can accomplish, especially with the early case, Professor Russ publishes several tables showing 5 year survival figures To doctors these will appear encouraging enough, but laymen are less used to the cold blooded study of statistics They will notice, for example, that of 6380 patients treated by radiation only 2295 were alive five years , and this will leave them little heart to notice that of the 1727 early cases in this series no less than 1181 were alive five years later The same information could probably have been given more tellingly in the text

Nevertheless Professor Russ has put a good deal of information together on a subject of universal importance to mankind, and his book is welcome

Bacterial Toxins

W E VAN HEYNINGEN, M A M SC PH D , senior research officer, Sir William Dunn School of Pathology, Oxford Oxford Blackwell Scientific Publications 1950 Pp 133 15*s*

FOR some time past those interested in the biochemical activities of bacteria have spoken among themselves a language often barely intelligible to their colleagues It is therefore a pleasant task to call attention to a book, at once authoritative and readable, on bacterial toxins and their chemistry which should be easily understood by the workaday bacteriologist A subject to which chemists, pharmacologists, and pathologists have all made contributions in a great variety of journals is especially suited to publication in monograph Dr van Heyningen has himself made valuable additions to our knowledge, and his book succeeds in being more than a compilation. In particular he has abandoned the

PRESERVATION OF TYPHOID VACCINE

D W HENDERSON
D Sc , Ph D

S PEACOCK J RICHLEY

From the Microbiological Research Department, Porton, Wilts

THE storage of vaccines in liquid suspension is often unsatisfactory owing to serious loss in immunogenic value The loss is greatest if the materials have to be stored, transported, and used in warm climates In recent discussion on this subject we were reminded of materials one of us (D W H) had prepared in 1939 at the Lister Institute, Elstree There was reason to believe that they might still be in existence, and eventually they were unearthed Their history of "rough usage" could hardly have been more severe For some time they had been in a laboratory at Elstree (not to be described as cool in summer), then they were in a cellar for several years, thereafter they were "lost", and eventually they were found in a store which in summer weather gets well into the 80s One of us (S P) around 1948 was mindful of them and they were placed in a refrigerator It was here they were located a few months ago

TABLE II—ACTIVE PROTECTION TEST IN MICE

Antigen			Test dose (Ty2 intraperitoneally in 0 5 ml Ringer solution)	Mice		
Type	Doses (subcut)	Days between doses		Tested	Died	% survival
Acetone dried Ty2 (stored ten years)	(a) 2 × 10^8* (b) 4 × 10^8	10	2 × 10^8	60	8	86 7
	(a) 2 × 10^8 (b) 4 × 10^8	3		60	11	81 7
Lister Alcoholised TABC vaccine (current)	(a) 2 × 10^8† (b) 4 × 10^8	10		56	4	92 8
	(a) 2 × 10^8 (b) 4 × 10^8	3		58	5	91 4
Control mice			2 × 10^8 1 × 10^8 5 × 10^7	20 20 20	20 18 12	0 10 40

Mice challenged 20 days after second dose of vaccine All animals from one stock Weight at commencement 18–20 g average weight at time of challenge about 28 g (0 5% non specific deaths during course of immunisation)

* Dose estimated on basis of opacity

† The preparation was stated to contain (per ml) 1000 million *S typhi* and 500 million each of *S paratyphi* A B, and C

Among them were acetone dried suspensions of *Salmonella typhi*, including the classical strains Ty2 and "O" 901, as well as a sample of the "pure" Vi strain T6S (Felix and Petrie 1938) The method for their preparation was as described by Henderson and Morgan (1938), and they were in 1 oz McCartney screw capped bottles with no special sealing By good fortune the preparation of the Ty2 strain had been used for the immunisation of rabbits (and horses) in 1939, and on close search some of the original rabbit immune serum was also located We decided, therefore, to examine the properties of some of these long stored antigens

Samples of each were re suspended in water, and groups of rabbits were injected intravenously, using the dose and time interval between doses that had been standard practice a decade earlier (Henderson 1939) The response was exactly as would be expected from using freshly prepared suspensions Table I shows the Vi and "O" agglutinin response of the rabbits to the Ty2 suspension, and includes for comparison an original pooled rabbit immune serum prepared in 1939 from the same material.

TABLE III—PASSIVE PROTECTION TEST IN MICE

Rabbit serum				Challenge dose (Ty2)	Intravenous dose serum (ml)	Mice	
Antigen used for immunisation		Agglutinin titre					
Type	Age	Vi (T6S)	O ('O" 901)			Tested	Survived
Vi + O	10 yrs	1/600	1/10,000	5 × 10^4	0 005 0 002 0 001 0 0005	10 10 10 10	10 8 9 4
(Ty2)	1 month	1/1000	1/2000		0 002 0 001 0 0005 0 0002	10 10 10 10	10 10 8 7
Vi	10 yrs	1/600	1/100		0 005 0 002 0 001 0 0005	10 10 10 10	10 8 9 1
(T6S)	1 month	1/1000	1/200		0 002 0 001 0 0005 0 0002	10 10 10 10	10 9 8 5
Provisional standard antityphoid serum (Vi + O) horse serum, dried		1/400	1/20,000		0 005 0 002 0 001 0 0005	10 10 10 10	8 6 6 3
Normal rabbit serum				5 × 10^4 5 × 10^3 5 × 10^2 50	0 005	10 10 10 10	0 0 1 1
Mucin controls						10	10

This encouraging result led to an active immunisation test in mice, using the same Ty2 material After consultation with Dr Felix, F.R.S., we included a group of mice, using as vaccine for them a current TABC alcoholised preparation made according to his method at the Lister Institute, Elstree (Felix 1941) The technique used for the experiment was that of Felix and Pitt (1934) Interestingly enough, the Ty2 stock used for the preparation of the challenge dose had also been laid down as "dried" culture in 1939, the technique used being that then in common use by the National Collection of Type Cultures The results are summarised

TABLE I—"O" AND Vi AGGLUTININ RESPONSE IN RABBITS FOLLOWING IMMUNISATION WITH TEN-YEAR OLD ACETONE-DRIED TYPHOID ANTIGEN

Rabbit	Vi (T6S suspension)								('O' 901 suspension)				
	1/100	1/200	1/300	1/400	1/500	1/600	1/800	1/1000	1/500	1/1000	1/2000	1/5000	1/10 000
1	+ + + +*	+ + ±	+ +	±	(±)	−	−	−	+ + + +	+ + + +	+ ±	(±)	−
2	+ + + +	+ + +	+ +	±	(±)	((±))	−	−	+ + + +	+ + +	+ + +	+	−
3	+ + + +	+ + + +	+ + +	+ +	+	±	(±)	((±))	+ + + +	+ + + +	+ +	±	−
4	+ + + +	+ + + ±	+ + +	+ + ±	+ +	±	(±)	−	+ + + +	+ + + +	+ + +	+ ±	(±)
Original pooled serum (stored 10 years)	+ + + +	+ + + ±	+ + ±	+ +	+	±	(±)	((±))	+ ±	(±)	((+))	−	−

* + + + + to ((±)) varying degrees of agglutination from complete clearing to faint traces observed with hand lens.

Folinic Acid: the “Citrovorum Factor”

The discovery that folic acid, an essential growth factor for *Lactobacillus casei*, was also needed for the proper maintenance of erythropoiesis and granulopoiesis in rats and pigs, and that in man it would cause the pathological megaloblastic erythropoiesis to return to normoblastic, revealed a hitherto unsuspected link between bacterial growth factors and factors of hæmatological importance. This link has been fully exploited both in the search for new factors and in devising methods for the microbiological assay of known hæmopoietic factors, such as vitamin B_{12}. The latter is a growth factor for another member of the lactobacillus family. The latest growth factor that promises to be of hæmatological interest is, however, necessary for quite a different organism—*Leuconostoc citrovorum*.

Sauberlich and Baumann[1] proposed to utilise *Leuconostoc citrovorum* for the microbiological assay of alanine. They were surprised to find that for satisfactory growth a factor had to be added to the medium that was not present in the usual “vitamin-B complex.” The best source of this growth factor was found to be the refined liver extracts prepared for treating pernicious anæmia. These refined extracts usually contain little folic acid, and tests with folic acid showed that, though it would assist the growth of *L. citrovorum*, the growth was not so good and the growth curve different. Later these workers[2] succeeded in preparing a concentrate of this “citrovorum factor” that was much more active, weight for weight, than folic acid. But it soon became clear that the citrovorum factor (C.F.) was closely related to folic acid. Sauberlich[3] had observed that rats fed on a diet deficient in folic acid excreted little C.F. in the urine; when folic acid was added to the diet there was a large increase of C.F. excretion. In man, too, administration of folic acid caused an increased excretion of C.F. in the urine. Sauberlich[4] further showed that aminopterin, a folic-acid antagonist, would inhibit the growth of *L. citrovorum*, and that C.F. would overcome this inhibition.

Nichol and Welch[5] provided more evidence. They found that when rats were fed on a diet deficient in folic acid, and had reached the stage of wasting with severe diarrhœa, their livers contained about twenty times *less* C.F. than a normal rat liver. When they incubated liver slices with folic acid, the C.F. content rose to the same high level with livers from both deficient and normal rats, the increase being much greater in the livers from animals on the diet deficient in folic acid. Ascorbic acid evidently played some part in this reaction, for it could double the C.F. content of incubated liver slices from either deficient or normal rats, and the greatest increase of C.F. content was obtained when the slices were incubated with folic acid and ascorbic acid together. Nichol and Welch therefore suggested that some at least of the added folic acid is converted enzymatically to citrovorum factor, and that ascorbic acid aids the conversion. Meanwhile, Bond, Bardos, Shive, and their collaborators at the University of Texas had been examining substances that they found to be effective in countering the action of folic acid antagonists, and they had discovered one that was considerably more effective than folic acid itself in neutralising the inhibiting action of methylfolic acid; they named this substance “folinic acid.”[6] They showed that folinic acid would support the growth of *Lactobacillus casei* in the absence of folic acid, and that it would act as a growth factor for *Leuconostoc citrovorum* in the same way as Sauberlich and Baumann's citrovorum factor. Later they reported[7] that by converting folic acid to formylfolic acid and then reducing the formylfolic acid in the presence of ascorbic acid they had produced a reaction mixture that was a million times more active, weight for weight, than folic acid in stimulating the growth of *L. citrovorum*. They were not sure whether this preparation was a single substance or a mixture, but they suggested that folinic acid contains a modified pteridine ring attached to the same groupings that are found in folic acid.

There seems to be little doubt that citrovorum factor and folinic acid, if not actually identical, are very closely related. Their relation to folic acid naturally suggests that they may have hæmatological actions. May, Sundberg, and Schaar[8] used crude folinic acid for the treatment of a megaloblastic type of anæmia produced in monkeys by dietary deficiency; the animals were also scorbutic. A dose of 50 *micro-grammes* of folinic acid caused a prompt response; the megaloblast-like cells disappeared from the marrow within 48 hours and the marrow was more or less normal within 10 days; there was a convincing increase of reticulocytes, red cells, and hæmoglobin. To get a similar effect with folic acid, a dose of 15 *milligrammes* had to be used. It is interesting to note that ascorbic acid did not have to be added to the diet for folinic acid to exert its action. Clinically, Schoenbach, Greenspan, and Colsky[9] gave synthetic citrovorum factor, presumably prepared from folic acid, to two patients who were receiving large doses of folic-acid antagonists for the treatment of malignant disease. One had received 10 mg. of ‘Amethopterin’ daily for 18 days and had developed a large ulcer on his hard palate. Citrovorum factor, 40 million units daily intramuscularly, was now given and the amethopterin continued. The ulcer healed on the 5th day, and new ulcers appeared when the citrovorum factor was stopped. The other patient was receiving 2 mg. daily of ‘Aminopterin’ and had developed stomatitis and ulceration of the mouth and palate; folic acid, up to 75 mg. daily, failed to heal the ulcers while the aminopterin was continued, and 20 million units of C.F. also failed; but when the dose was doubled the ulcers healed in 5 days.

It is clear then that citrovorum factor, or folinic acid, is yet another factor of much interest to hæmatologists. Reports on its action in human megaloblastic anæmias should soon be to hand, and we may speculate capillaries before the secondary results of their obliteration are well established. The main effect of obstruction in the pulmonary circulation is to increase the load on the right ventricle, so any chronic obstruction leads typically to pulmonary hypertension and hypertrophy of the right ventricle, which may or may not end in right-sided heart-failure. The term "cor pulmonale" is applied when some pulmonary disease directly or indirectly produces right ventricular strain, for various extra-pulmonary diseases can cause identical circulatory changes, and both groups will raise the blood-pressure in the pulmonary circulation. GELFAND[1] classifies the main causes of chronic pulmonary hypertension as follows:

---

[1] Sauberlich H E Baumann C A *J biol Chem.* 1948 176, 165

[2] Sauberlich H E Baumann C. A. *Ibid* 1949, 181 871

[3] Sauberlich H E *Ibid* p 467

[4] Sauberlich H E *Arch Biochem.* 1949 24 224

[5] Nichol C A Welch A D *Proc Soc exp Biol, N Y* 1950 74 52

[6] Bond T J Bardos T J, Sibley M. Shive W *J Amer chem. Soc* 1949 71 3852

[7] Shive W Bardos, T J Bond T J, Rogers, L L *Ibid* 1950 72 2817

[8] May C D Sundberg D Schaar F *J Lab clin. Med* 1950, 36, 963

[9] Schoenbach E B Greenspan E M., Colsky, C J *J Amer med Ass* 1950 144 1558

1. *Cardiac group.*—Left-sided heart-failure from systemic hypertension, coronary sclerosis, or mitral stenosis—the condition lately discussed by BAYLISS et al.[2] in these columns. Congenital defects.

2. *Pulmonary group.*—Changes in the thoracic cage, such as kyphoscoliosis and those following thoracoplasty. Vascular changes, including arteritis and external pressure obstructing the pulmonary artery, and endarteritis obliterans of the pulmonary arterioles (Ayerza's disease). Changes in the lung parenchyma—either primary emphysema with or without fibrosis, or emphysema and fibrosis secondary to such chronic lung diseases as asthma, phthisis, pneumoconiosis, and bronchiectasis.

Why do some cases of long standing asthma with emphysema develop cor pulmonale whereas others do not? This is one of the many questions being tackled by research-workers from occupational, constitutional, endocrine, and neurological standpoints. Modern techniques of investigation, and catheter studies in particular, by confirming the existence of pulmonary hypertension and making it measurable, are now focusing more and more attention on this condition. Clinically, as Dr EVAN BEDFORD pointed out at the Royal Society of Medicine on Feb. 27, it can be recognised by well defined physical signs—a diffuse apex beat, triple rhythm, a systolic murmur, and a loud pulmonary second sound, followed sometimes by the soft diastolic Graham Steell murmur in the pulmonary area. Some of his cases had hypercyanotic angina. In chronic asthmatics the development of cor pulmonale may be hard to detect, but GELFAND has adopted these criteria: (1) asthma and emphysema of at least 5 years' duration with no other heart disease; (2) an increase in the existing dyspnœa and cyanosis; (3) orthopnœa in a patient who has hitherto breathed better lying flat; (4) raised pressure in the pulmonary circuit (deduced or measured by catheter); (5) X-ray evidence of cardiac enlargement; and (6) electrocardiographic signs of right ventricular hypertrophy. Radiologically the pulmonary artery and its main branches are prominent; right ventricular enlargement makes the cardiac apex look abnormally square, and fullness of the right auricle produces some enlargement to the right. Usually both the heart rhythm and the systemic blood pressure are normal.

When the heart failure is secondary to chronic lung disease, such as bronchitis and emphysema, the prognosis is bad. Treatment is directed not at the heart but at the lungs, for these patients die a pulmonary death of anoxia, usually from a terminal bronchopneumonia. At the Royal Society of Medicine Dr J. P. D. MOUNSEY demonstrated that when such patients get a pulmonary reinfection there is always a rise in their pulmonary arterial and venous pressures and a fall in their vital capacity. Prof. E. P. SHARPEY SCHAFER sets great store on the oxygen tent, but in some cases, he said, it causes a rise in cerebrospinal fluid pressure, which may explain the mental confusion that sometimes occurs in spite of the relief of cyanosis. He strongly favours determinations of arterial oxygen saturation for estimating cardiac function and as a guide to treatment. In some emphysematous subjects, well enough to sit up in bed and read a newspaper, he has been surprised to find arterial oxygen saturation values below 40%. This suggests that such cases have an effective compensatory adaptive mechanism, which may prove to be the high pulmonary arterial pressure. He has tried to reduce the cardiac output therapeutically with large doses of thiouracil (up to 2 g. daily) with a beneficial raising of oxygen saturation. However, the bigger fall in cardiac output which occurs in the terminal stages of pulmonary heart-failure is accompanied by a compensatory peripheral vascular constriction, and the heart then reaches a stage of fixed output from which recovery is impossible.

Uniform histological changes in the pulmonary capillaries in pulmonary heart-disease were regarded by Dr WILLIAM EVANS as responsible for the variability of its clinical course. He showed examples of pulmonary arteriolar medial endarteritis fibrosa and correlated its degree with the clinical findings in different conditions. For example, in a case of patent ductus arteriosus, electrocardiographic evidence of right ventricular predominance was in his opinion proof that endarteritis was present, causing pulmonary hypertension by involving the lesser branches. In some instances the Gibson murmur might even be absent when a high pulmonary arterial pressure obliterated the fistula effect, and these cases could be mistaken for atrial septal defect. Pulmonary heart-failure of whatever cause, he said, is usually related to pulmonary endarteritis, and this can be demonstrated post mortem. By injecting the pulmonary arterial tree with a radiopaque substance he had obtained pictures which showed a pruning effect of the terminal branches when endarteritis was present. With characteristic simile he described how the lungs differed in pulmonary heart-disease and in pure emphysema "as a denuded shrub in autumn differs from a leafy bush in spring." Though he argued that this pathological change is always the primary cause of pulmonary hypertension, analogy with the histological findings in systemic hypertension suggests that it may represent the end result. Much still remains to be explained before Dr EVANS's ingenious hypothesis is proved.

Recently interest has again turned to the bronchial vascular system[3] and future work may disclose further evidence of the function of a bronchopulmonary precapillary anastomosis, playing an important part in pulmonary heart disease by redistributing the flow of blood within the lungs.

---

[1] Gelfand, M. L. *Amer. J. Med.* 1951, 10, 27.

[2] Bayliss, R. I. S., Etheridge, M. J., Hyman, A. L. *Lancet*, 1950, ii, 889.

[3] Marchand, P., Gilroy, J. C., Wilson, V. H. *Thorax*, 1950, 5, 207.

Sweden has staffing difficulties like the rest of us Nurses are scarce, but, on the other hand, if they take up the profession they seem to stick to it wastage is said to be only 3% This may be partly because nearly all the trained staff live outside the hospital, and appreciate the opportunity, but it may also be because the Swedish nurse has a very interesting training, with experience of laboratory work and radiology When she is qualified, moreover, she is entrusted with important technical duties for example, blood-transfusions are almost everywhere given by nurses The British visitors were inclined to shake their heads over the time spent by Swedish nurses in the X ray department and the various laboratories, taking this into account, they thought 3 years and 5 months was not long enough to train a nurse Canadian experience, however, has shown that an intelligent girl can become proficient in nursing in 2 years are the Swedes perhaps right in using the remaining 17 months to stretch her mind ? Evidently girls who are capable of managing responsible procedures, are entering the Swedish nursing service, and a wastage of only 3% from such a class of entrants means that the training has captured their enthusiasm We might well aim to do as much ourselves

CARDIAC ARREST UNDER ANÆSTHESIA

No more dramatic event takes place in an operating-theatre than cardiac arrest under general anæsthesia, for everything may hang on early recognition of this complication and on swift and decisive action The fact that full recovery is possible even after the heart has stopped for a considerable time is shown by a case studied by Turner[1] The patient was anæsthetised by thiopentone and cyclopropane, and after seven minutes' stoppage the heart was made to beat again by cardiac massage through a subcostal incision During the next twenty four hours it stopped beating four times and breathing stopped several times, but on the second day deepening coma was replaced by gradual return of consciousness, and by the tenth day the patient was fully orientated He had a permanent retrograde amnesia of twelve hours and a postoperative amnesia of about four days, and a year after the accident he had symptoms suggestive of a mild frontal lobe syndrome But after a further twelve months recovery seemed complete

Anderson and her colleagues[2] keep in the theatre a "cardiac resuscitation kit" consisting of 2 small retractors, 6 curved and 6 straight hæmostats, 2 toothed forceps, and 2 scalpels, together with a syringe containing 9 5 ml. of 1% procaine and 0 5 ml of 1 in 1000 adrenaline When warned of cardiac inhibition, the surgeon's first duty, if he is operating on the abdomen or chest, is to confirm that the great vessels are pulseless, and his next task is to reach the heart by whatever route seems best, not hesitating, if need be, to enter the left side of the chest through the fourth or fifth intercostal space[3] "All surgical residents early in their training should be shown at the autopsy table how best to approach the heart for massage through the chest and through the diaphragm" With the anæsthetist maintaining artificial respiration by intermittent compression of the breathing bag, the surgeon compresses the heart at a rate of 60–80 per minute (120 is the most efficient rate, but it is too tiring for a single surgeon) Further action, if spontaneous rhythm is not soon resumed, depends on whether the heart is found to be fibrillating or at a standstill. If fibrillation is found, and if the electrical apparatus for serial defibrillation is not at hand, 40–60 mg procaine in a 1% solution is injected intravenously This may restore normal rhythm or bring the heart to a standstill, in the latter event (and when the heart is found in the first place at a standstill) manual massage will often suffice to bring about normal rhythm, but the heart beat will be strengthened by injecting up to 0 5 ml. of 1 in 1000 adrenaline into a vein or into the right auricle or ventricle Anderson et al defend their combination of procaine and adrenaline in a single injection on the ground that when circulatory arrest develops it is rarely possible to be sure whether the cause is cardiac standstill or ventricular fibrillation

The mechanism of cardiac arrest under general anæsthesia has been studied by Johnstone,[4] who concludes that probably the anæsthetic stimulates sensory nerve endings in the lungs with resulting inhibition through the pulmocardiac reflexes The arrhythmias to which the inhibition gives rise include sinus bradycardia, auriculoventricular nodal rhythm, partial and complete auriculoventricular block, ventricular standstill, and complete cardiac arrest He judges that before operation atropine gr $^{1}/_{100}$ intravenously probably protects against cardiac inhibition for about thirty minutes, and gr $^{1}/_{50}$ intramuscularly for ninety minutes, but special care to avoid high concentrations of anæsthetic vapours should be taken where vagal tone is increased (as with jaundice, simple sinus bradycardia, and peptic ulceration) Johnstone emphasises that simultaneous intravenous administration of atropine and neostigmine to anæsthetised patients is dangerous, for in combination they may precipitate fatal ventricular fibrillation, and the only way to eliminate this danger is to give minimal doses of curare, thereby eliminating the need for neostigmine Johnstone maintains that in cases of myocardial disease or where anæsthesia is protracted, electrocardiographic records should be taken during the operation

OUR ELDERS

VOLUNTARY and statutory bodies have formed many notable alliances in the cause of social welfare In the last few years their joint endeavours have made a remarkable difference to those old people whose lot has fallen to them in unpleasant places, and their projects have owed much, both in counsel and cash, to the National Corporation for the Care of Old People[5] In the past year the governors have had in mind the difficulties voluntary bodies nowadays meet in attempting to raise money, and have therefore increased the average amount of grants above the sums given in previous years, especially to homes for the infirm A condition is that the voluntary bodies applying for grants should apply to the appropriate local authority for help with the maintenance costs of individual residents, and nearly every authority approached has responded—without, moreover, attempting to make strict conditions Two county boroughs, only, have refused The governors point out that such refusals are shortsighted, for all the homes that can be provided are needed urgently, and an authority can only benefit by having a home provided and run by a responsible organisation If authorities would go even further and agree to pay the whole cost of maintaining old people in such homes, the voluntary bodies could, of course, do much more, but so far only a few authorities have agreed to this course.

Towards the end of the year the governors arranged that Mr Howell E James should visit the homes to which grants had been made, partly to see how the funds were being used but mainly to help in planning future policy Some homes have solved problems with which others are still wrestling, and the governors hope to pool such experience for the benefit of all One problem presented by the old is that they grow older, and whether folinic, rather than folic, acid is the important factor in the treatment of these diseases, and whether folic acid really acts only when converted to folinic acid It should not be hard to get the facts, but we hope that a sufficiency of reliable clinical tests will be assembled before any new theories about the ætiology of megaloblastic anæmias are proposed

---

[1] Turner H J Neurol Neurosurg Psychiat 1950 13 153

[2] Anderson R M Schoch W G Faxon H H New Engl J Med 1950 243 905

[3] Lampson R S Lincoln J R Schaffer W C J Amer med Ass 1948 137 1575

[4] Johnstone M Brit Heart J 1951 13 47

[5] Third Annual Report, for the year ended Sept 30, 1950 Pp 26 The corporation's address is 33 Doughty Street London W C 1

Annotations

SYMPTOMS OF PUBERTY

" JUVENILE delinquency is what the law says it is " , and the law draws the line in different places in different countries Dr Lucien Bovet, who quotes this saying in a new W H O monograph,[1] notes that in many European countries a minor is a delinquent only if his behaviour is an offence to the whole population, whereas in parts of the United States he may be brought into court for a number of other things, including truancy from school, consistent disobedience to parents, consumption of alcohol, and smoking in public In England a boy is legally incapable of sexual intercourse before the age of 14 , and though he may have raped another child and caused her death, if he is less than 14 he must be declared " not guilty " A country with an efficient police force has a higher delinquency rate than a country where the police are slack , and in any country the social position and influence of the parents may decide whether a child is charged or not Even the severity with which an offence is punished varies from one magistrate or judge to another Indeed, our response to the whole idea of juvenile delinquency is illogical We can never outgrow, it seems, our astonishment that those so young should be so bad , yet statistics make it quite clear that the peak age for crime is in the teens and early twenties In other words, if criminal behaviour is ever to be expected, it is to be expected then, along with neurotic or schizoid episodes, erotic fantasies, physical ebullience, a taste for brilliant garments, and all the other signs of adolescent instability and stress

Moral indignation is no more relevant to the aberrant conduct of the adolescent than it would be to the depression, hot flushes, and giddiness of the menopausal woman both are expressions of hormonal disequilibrium of which the subject is only obscurely conscious The social difficulty is that in the adolescent such expression may range from giggling inconsequence to seemingly wanton destructiveness or brutal outrage What decides the form it takes ? That is for research to discover, as Dr Bovet insists Mr Joyce Carey, in *Charley is my Darling*, gives an intuitive answer as far as destructiveness goes The need to boast, the need to make the boast good, the need to get excited and break things, are not forces the boy can reason about , they befall him, and so do the consequences Probably no living adult has made the curious and difficult adjustment perfectly at every step , who, then, is qualified to advise the growing child ? Dr Bovet's monograph is studded with reports of our ignorance, but he outlines the growing body of knowledge and opinion and directs attention to whatever is sure

Treatment may vary—and indeed it should vary, if it is to be adapted to the needs of individual children —but the aim of even the most diverse methods is the same to help the child to build up safe and stable relationships with the people round him, and to achieve that inner security on which are founded his own moral independence and that consideration for others which lies behind good social behaviour In time we shall know better how to do this difficult thing

---

[1] Psychiatric Aspects of Juvenile Delinquence World Health Organisation, Palais des Nations Geneva 1951 Pp 90 5s

SWEDISH HOSPITALS

SWEDEN, with its lakes and forests, clean air, and bracing climate, is a fine place for hospitals , and indeed it has some of the most up to date hospitals in the world Nevertheless, the members of the International Hospital Federation [1] who made a study tour of Swedish hospitals last September were more taken with the older, smaller, more homely, hospitals than with the great Södersjukhus at Stockholm,[2] with its 9 floors, 40 wards, 50 lifts, and vast central kitchen, perched at the top of the main block and connected to its 11 branch kitchens by a 400 ft corridor, along which the staff dash to and fro on scooters Scooters, indeed, are a good idea, and might well be introduced into some of our own long hutted hospitals (Stoke Mandeville, for instance) But the mere notion of anything so large as the Södersjukhus shocks our new British thrift, concerned as never before with the cost of upkeep The expense of maintaining the great place is, in fact, already beginning to weigh heavily on the authorities of this hospital

We have plenty to learn, however, from other aspects of the Swedish hospitals They seem to pay more attention to the comfort of the patient and his relatives than is usual here These hospitals are quieter than ours, for instance walls and ceilings are made of sound absorbing material, and lift doors of wood with no clanging inner gates , trolleys are often electric and are all well made and easy to move , doors are fitted with door checks, and many of them are designed to push open so that noisy handles are unnecessary Relatives are received in a large and pleasant entrance hall which usually contains a florist's shop, a tobacco and news paper stall, a cafeteria, and sometimes a post office, and a hairdressing salon for the use of ambulant patients There is nearly always an information bureau as well, and a large model of the hospital on which a visitor can learn his way about The beds, it is true, were thought to fall short of British models They measure 2 ft 6 in across, and have their bottom legs set back some way from the foot, which gives them rather a makeshift look Actually they are rather ingenious, for they are fitted with a wheeling device, and when the foot is lifted they can be pushed easily about like a wheelbarrow Screens are not used in the wards, since treatments, dressings, and blanket baths are given in a separate annexe and patients are usually wheeled to the water closet either in their beds or in a lavatory chair This must reduce greatly the traffic in bedpans, though these are of course provided The pans are all made of stainless steel, and are well maintained, though the cleaning equipment is not of that latest type which cleans and sterilises They are washed in a deep metal sink, usually in cold water, sometimes under pressure , but they are only sterilised in maternity and gynæcological wards The pans are numbered, however, and each patient retains his own throughout his stay in hospital

The medical equipment is of a very high standard indeed, and extremely lavish and well cared for Theatres in the newer hospitals are spacious and well planned, and many operations are done by daylight—another advantage of clean bright air In the wards lights are conveniently placed over the beds, and are often fitted with a revolving shutter which allows the patient to adjust the amount of light given out The night light is never overhead, but usually placed in a recess in the wall, near the door, about a foot from the floor In one hospital the night light was sunk flush in the centre of the floor of the ward, which must give a specially restful effect

---

[1] Report of Study Tour of Hospitals in Sweden International Hospital Federation at King Edward's Hospital Fund for London 10 Old Jewry London E C 2 1951 Pp 60 7s 6d

[2] See *Lancet* 1945 ii, 571

Sweden has staffing difficulties like the rest of us Nurses are scarce, but, on the other hand, if they take up the profession they seem to stick to it wastage is said to be only 3% This may be partly because nearly all the trained staff live outside the hospital, and appreciate the opportunity, but it may also be because the Swedish nurse has a very interesting training, with experience of laboratory work and radiology When she is qualified, moreover, she is entrusted with important technical duties for example, blood transfusions are almost everywhere given by nurses The British visitors were inclined to shake their heads over the time spent by Swedish nurses in the X ray department and the various laboratories, taking this into account, they thought 3 years and 5 months was not long enough to train a nurse Canadian experience, however, has shown that an intelligent girl can become proficient in nursing in 2 years are the Swedes perhaps right in using the remaining 17 months to stretch her mind ? Evidently girls who are capable of managing responsible procedures, are entering the Swedish nursing service, and a wastage of only 3% from such a class of entrants means that the training has captured their enthusiasm We might well aim to do as much ourselves

CARDIAC ARREST UNDER ANÆSTHESIA

No more dramatic event takes place in an operating-theatre than cardiac arrest under general anæsthesia, for everything may hang on early recognition of this complication and on swift and decisive action The fact that full recovery is possible even after the heart has stopped for a considerable time is shown by a case studied by Turner[1] The patient was anæsthetised by thiopentone and cyclopropane, and after seven minutes' stoppage the heart was made to beat again by cardiac massage through a subcostal incision During the next twenty four hours it stopped beating four times and breathing stopped several times, but on the second day deepening coma was replaced by gradual return of consciousness, and by the tenth day the patient was fully orientated He had a permanent retrograde amnesia of twelve hours and a postoperative amnesia of about four days, and a year after the accident he had symptoms suggestive of a mild frontal lobe syndrome But after a further twelve months recovery seemed complete

Anderson and her colleagues[2] keep in the theatre a "cardiac resuscitation kit" consisting of 2 small retractors, 6 curved and 6 straight hæmostats, 2 toothed forceps, and 2 scalpels, together with a syringe containing 9 5 ml. of 1% procaine and 0 5 ml of 1 in 1000 adrenaline When warned of cardiac inhibition, the surgeon's first duty, if he is operating on the abdomen or chest, is to confirm that the great vessels are pulseless, and his next task is to reach the heart by whatever route seems best, not hesitating, if need be, to enter the left side of the chest through the fourth or fifth intercostal space[3] "All surgical residents early in their training should be shown at the autopsy table how best to approach the heart for massage through the chest and through the diaphragm" With the anæsthetist maintaining artificial respiration by intermittent compression of the breathing bag, the surgeon compresses the heart at a rate of 60–80 per minute (120 is the most efficient rate, but it is too tiring for a single surgeon) Further action, if spontaneous rhythm is not soon resumed, depends on whether the heart is found to be fibrillating or at a standstill. If fibrillation is found, and if the electrical apparatus for serial defibrillation is not at hand, 40–60 mg procaine in a 1% solution is injected intravenously This may restore normal rhythm or bring the heart to a standstill, in the latter event (and when the heart is found in the first place at a standstill) manual massage will often suffice to bring about normal rhythm, but the heart beat will be strengthened by injecting up to 0 5 ml of 1 in 1000 adrenaline into a vein or into the right auricle or ventricle Anderson et al defend their combination of procaine and adrenaline in a single injection on the ground that when circulatory arrest develops it is rarely possible to be sure whether the cause is cardiac standstill or ventricular fibrillation

The mechanism of cardiac arrest under general anæsthesia has been studied by Johnstone,[4] who concludes that probably the anæsthetic stimulates sensory nerve endings in the lungs with resulting inhibition through the pulmo cardiac reflexes The arrhythmias to which the inhibition gives rise include sinus bradycardia, auriculoventricular nodal rhythm, partial and complete auriculoventricular block, ventricular standstill, and complete cardiac arrest He judges that before operation atropine gr $^1/_{100}$ intravenously probably protects against cardiac inhibition for about thirty minutes, and gr $^1/_{50}$ intramuscularly for ninety minutes, but special care to avoid high concentrations of anæsthetic vapours should be taken where vagal tone is increased (as with jaundice, simple sinus bradycardia, and peptic ulceration) Johnstone emphasises that simultaneous intravenous administration of atropine and neostigmine to anæsthetised patients is dangerous, for in combination they may precipitate fatal ventricular fibrillation, and the only way to eliminate this danger is to give minimal doses of curare, thereby eliminating the need for neostigmine Johnstone maintains that in cases of myocardial disease or where anæsthesia is protracted, electrocardiographic records should be taken during the operation

OUR ELDERS

VOLUNTARY and statutory bodies have formed many notable alliances in the cause of social welfare In the last few years their joint endeavours have made a remarkable difference to those old people whose lot has fallen to them in unpleasant places, and their projects have owed much, both in counsel and cash, to the National Corporation for the Care of Old People[5] In the past year the governors have had in mind the difficulties voluntary bodies nowadays meet in attempting to raise money, and have therefore increased the average amount of grants above the sums given in previous years, especially to homes for the infirm A condition is that the voluntary bodies applying for grants should apply to the appropriate local authority for help with the maintenance costs of individual residents, and nearly every authority approached has responded—without, moreover, attempting to make strict conditions. Two county boroughs, only, have refused The governors point out that such refusals are shortsighted, for all the homes that can be provided are needed urgently, and an authority can only benefit by having a home provided and run by a responsible organisation If authorities would go even further and agree to pay the whole cost of maintaining old people in such homes, the voluntary bodies could, of course, do much more, but so far only a few authorities have agreed to this course.

Towards the end of the year the governors arranged that Mr Howell E James should visit the homes to which grants had been made, partly to see how the funds were being used but mainly to help in planning future policy Some homes have solved problems with which others are still wrestling, and the governors hope to pool such experience for the benefit of all One problem presented by the old is that they grow older, and some who were hale enough when admitted have later become infirm Most homes have been planned and staffed to take residents who are fit, and they cannot easily cope with illness One way of overcoming the difficulty is to appoint more staff this adds to the cost of maintenance, but the governors point out that there is a real need for enough staff to manage these inevitable episodes in the lives of the old It would of course be wrong for a home to keep any resident who needed hospital treatment, but then a hospital bed cannot always be found

---

[1] Turner H J *Neurol Neurosurg Psychiat* 1950 13 153
[2] Anderson R M Schoch W G Faxon H H *New Engl J Med* 1950 243 905
[3] Lampson R S Lincoln J R Schaffer W C *J Amer med Ass* 1948 137 1575
[4] Johnstone M *Brit Heart J* 1951 13 47
[5] Third Annual Report for the year ended Sept 30 1950 Pp 26 The corporation s address is 33 Doughty Street London W C 1

As everyone now knows, many hospital beds are occupied by old people who could be sent out—at all events for a time—if they had somewhere suitable to go, and the governors have for some time been planning to pay the capital cost of rest-homes which would receive them, and so free beds for others Unfortunately there are administrative difficulties Sick old people come under the National Health Service, while those who need care and protection come under the local authorities, and the suggestion of the governors is that the maintenance costs of patients in the home —who would belong to both categories—should be shared between the hospitals and the local authorities in proportions to be agreed upon from time to time So far it has not proved possible to proceed on this basis However, the governors have at their disposal a large fund generously given by the people of South Africa, which they intend to spend on experimental work for old people They have therefore bought Warren House, at Stanmore, which they hope to run in conjunction with the West Middlesex Hospital, where Dr Marjory Warren has charge of the geriatric unit, as a rest home of the kind described This should show whether the administrative difficulties are insuperable or not Those who believe in the value of a fait accompli will be greatly astonished if they are

SOCIAL CONSEQUENCES OF PNEUMOCONIOSIS

BETWEEN January, 1931, and July, 1948, over 19,000 cases of pneumoconiosis were certified in South Wales Some 16,000 of these men are now living, and about a quarter of them are capable of useful work but cannot find it The problem is a residue of the Workmen's Compensation Act which, on certification, suspended men automatically from further mining Under the National Insurance (Industrial Injuries) Act, 1946, this no longer holds, and some men can and do continue to work in the pits The end of pneumoconiosis, however, is not yet to be, and for various reasons several thousand men with this disease are likely to be unemployed for some years to come The Medical Research Council's pneumoconiosis unit[1] are anxious that better provision should be made for them Provided it is not with "pick and shovel," the men with lesser disability can do a useful job of work, "and nothing else can prevent the mental and physical deterioration that so often accompany enforced idleness"—or ensure a reasonable standard of living

This M R C memorandum sets out clearly the main facts together with their statistical background from the Social Survey and elsewhere, and a dozen case histories bring the problem very much to life The authors make two recommendations (1) that suitable work be offered, and (2) that a regular medical follow up of certified men be instituted It is depressing to read how so many of the brave hopes of the Disabled Persons Employment Act, Remploy, the Grenfell factories, the reablement centres, and the Board of Trade's development scheme remain unfulfilled South Wales has more men unemployed than the rest of the country and more who are disabled Special measures are therefore necessary, and though on suitable light work men with lesser degrees of pneumoconiosis have no higher sickness and absenteeism rates than average, local private employers cannot be expected to carry the whole responsibility The follow up of certified men would provide specialised medical advice otherwise not available, and the results of the examinations would be used in an attempt to grade the men according to the type of employment for which they are fit, in this way more could be learnt about prognosis In the memorandum Hugh Jones and Fletcher give their preliminary ideas on possible methods of such an "aftercare" scheme, but more would have been welcome Could the scheme be joined, for instance, to that for the periodic examination of all South Wales coalminers which the unit is advocating?[2] Opinion, it is true, is divided about both the practicability and the advisability of this scheme,[3] and there has been far too little discussion of it.

The pneumoconiosis research unit is clearly taking full advantage of its great opportunity The South Wales coalfield has many problems,[4] and we look forward to further such reasoned and helpful studies The unit only discusses remedies which are "properly the responsibility of medical men", but this need not be unduly restricting, since for more than a century everything that affects the health of the people has been regarded as such a responsibility Wider opportunities will no doubt be found in the reablement centre for miners with pneumoconiosis which, the Minister of Health announced in Cardiff last week, is to be set up near the unit's headquarters at Llandough Hospital

SECOND THOUGHTS ON THE COLOMBO PLAN

JUDGING by reports in the press, the American reaction to the Colombo plan is uncertain and wavering If what we believe[5] to be a great and imaginative conception has not been received with the full sympathy that it merits, we must remember the recent American agreement to ship one million tons of wheat to India. It is difficult to appreciate the significance of this huge figure, and to picture the bulk of food involved. It would suffice to supply each of the 347 million inhabitants of India with 12 oz of cereal (the daily cereal ration in some parts of India) for between seven and eight days. The value of this to a people accustomed to awaiting with trepidation an uncertain harvest cannot be exaggerated In economic terms the cost is $100 million At individual level, each citizen of the U S A has contributed about 70 cents, and to pay the debt each citizen of India must provide rupees 1 annas 6 The thoughtful American may well wonder how this account can be settled, and hesitate before rushing into new and uncertain investments in South-east Asia

We can only reiterate that on public health grounds alone it is imperative to develop the latent wealth of South east Asia by schemes along the broad lines of the Colombo plan The financial difficulties are immense it would be folly to minimise them World economists have before them the great task of finding means of developing the backward parts of the world without impoverishing more fortunate areas at the same time Essentially it is a problem of credit, which means faith

THE INDEX and title-page to Vol II, 1950, which was completed with THE LANCET of December 30, is published with our present issue A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W C 2 Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now

---

[1] Hugh Jones P Fletcher, C M Social Consequences of Pneumoconiosis Among Coalminers in South Wales Medical Research Council memorandum no 25 1951 H.M Stationery Office Pp 54 1s 9d

[2] Fletcher, C M Gough, J *Brit med Bull* 1950 7 42

[3] Meiklejohn A *Brit J industr Med* 1950 7, 105

[4] Morris J N *Lancet* 1947 ii, 341

[5] Leading article *Ibid* 1950 ii 808

Special Articles

W. R. HESS.

THE CONTROL OF THE AUTONOMIC NERVOUS SYSTEM BY THE HYPOTHALAMUS

D. A. McDONALD
M.A., B.M. Oxfd
SENIOR LECTURER IN PHYSIOLOGY, ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE, LONDON

Professor Hess in Zürich has been studying the autonomic and central nervous systems for the past quarter-century and more. His method of stimulating the hypothalamus in a fully conscious and freely moving animal is of particular interest, for it forms the closest parallel that experimental physiology has made to clinical observation.[1] Yet current teaching of the functions of the hypothalamus is based almost entirely on American and British work. Even research publications have few references to Hess's results.

The reasons for this neglect of his writings, here and in America, are difficult to determine. Though the papers are mainly published in German, they have all appeared in easily accessible journals, and two summaries have been published recently—namely *Die funktionelle Organisation des vegetativen Nervensystems* (1948) and *Das Zwischenhirn: Syndrome, Lokalisationen, Funktionen* (1949).[2] These books summarise work on the nervous system for which he was awarded a half-share of the Nobel prize in 1949. A review of his contributions to present knowledge is, therefore, appropriate now. It is based on the two monographs named, and on personal observations.[3]

METHODS

Das Zwischenhirn covers the results of experiments on the diencephalon, the thalamus, subthalamus, hypothalamus, and adjacent regions. The animals used throughout are cats. They are stimulated by steel needle electrodes (about 0·25 mm. thick and insulated to within 1·0 mm. of the tip), which are placed in the brain, under nitrous-oxide anæsthesia at the beginning of the experiment. They are fastened by means of a rectangular frame screwed to the skull. This fixes their direction and each experiment is based on the study of stimulation of these fixed electrode positions. The placing is afterwards checked by a complete histological investigation of the brain in each case. Symbols of the type of response seen are then mapped on to diagrams of the diencephalon at the site where they were obtained and they may be seen in these monographs. One is reproduced below.

Stimulation is by direct current pulses. Although this is the standard method of stimulation nowadays, using electronic apparatus, Hess designed his own machine over 20 years ago as a result of studies of the optimal conditions of stimulating autonomic nerves. Destructive lesions can be made by coagulation at the tip of a given electrode with diathermy current (see Hess 1932).

It is the study of the unnarcotised animal which is the unique feature of Hess's work on the central nervous system. The advantages of eliminating the unknown factors of anæsthesia, and operative trauma, need hardly be stressed. Correspondingly, experimental recording of an untrammelled animal is difficult and interpretation of its complex behaviour with its idiosyncrasies, and individual peculiarities of character, raises its own special problems. Records, therefore, consist of detailed observations dictated throughout the experiment; together with cinematic recording of all significant findings. It is a truly biological way of studying animal behaviour, an approach that is too easily lost in the increasing technicalities of physiology. Bird-watching has been raised to quite a respectable branch of biology, but cat-watching has relatively few supporters. Professor Hess is undoubtedly the world's greatest cat-watcher. That is not to decry his wide range as an experimental scientist, for he made early fundamental contributions to the study of blood viscosity (between 1907 and 1920), and to the investigation of squint (Hess screen) (Hess 1911), in addition to the work under review. Perhaps it is the slightly unorthodox attitude of wishing to study the intact animal, instead of a refined "preparation" such as the isolated brain, or a single segment of spinal cord, that has led to his neglect by Anglo-American physiologists. Also, without seeing his experiments, or the films of them, it is difficult to appreciate them.

AUTONOMIC ACTIVITIES

The technical details summarised here are to be found in the third section of *Das Zwischenhirn*. The first part deals with the autonomic nervous (vegetative) effects seen in over 400 animals. In the anæsthetised animal a large number of experiments have been performed recording blood-pressure changes. A rise in pressure is regularly obtained from a wide region of the posterior hypothalamus. A fall was obtained from zones including the anterolateral hypothalamus, and parts of the subthalamus and anterior thalamus. In addition to the marked effect on blood-pressure there is usually an increase in heart-rate observed at the same points, while a slowing of the pulse is seen, on occasion, with a fall in pressure.

Respiration is also greatly modified by stimulating the diencephalon, both its amplitude and its rate and character. Increased respiratory activity is seen with stimulation in the lateral part of the posterior hypothalamus. Decrease of rate and amplitude results from stimulation of the area supraoptica and also from widespread points in the septum pellucidum, and laterally in the subthalamus and inferior thalamus. An increase of rate alone (paroxysmal tachypnœa) is seen in the anæsthetised cat with stimulation of the anterior superior part of the hypothalamus and the neighbouring regions.

Comparison with the unanæsthetised animal suggests that the tachypnœa is not due to interference with normal respiratory regulation but is, in fact, the same as panting and so a response to stimulation of the temperature-regulating mechanism. Without anæsthesia, however, the response is obtained from a much wider field. The analysis of such comparable responses in anæsthetised and unanæsthetised animals are obviously of great importance in assessing the significance of experiments on the central nervous system of narcotised animals.

Another autonomic activity noted in the hypothalamus is that controlling pupil size. Dilatation, with widening of the palpebral fissure, is obtained from the same zone as that causing a rise in blood-pressure. Pupillary narrowing is the response from a small region lateral to the supraoptic nuclei and also in the mid thalamus.

All these observations are of interest in so far as they confirm, or contrast with, the results of other workers using different techniques. Many medical men, however, may be more interested in the coördinated activity reactions that Hess has recorded as a response to stimulation in the intact cats. Sneezing is often caused by stimulating the septum pellucidum. Other effects functionally related are sniffing, licking movements, salivation, and vomiting In order that the biological significance of these functions may be assessed they must be considered in relation to the other effects occurring at the same time Thus, salivation occurs at virtually all points that produce panting, and in this case presumably is activated by the heat regulating mechanism In other places salivation accompanies licking and sniffing, and so, reasonably, is regarded as digestive in function Licking movements are of divers forms, from isolated or rhythmic licks to fully organised licking and chewing Rhythmic licking results from thalamic stimulation, whereas more fully developed mastication is localised in the septum pellucidum

---

[1] G. W. Harris at Cambridge has subsequently developed another technique for stimulation of the conscious animal.

[2] Both published by Benno Schwabe, Basle. Although the text is in German, all the numerous illustrations and charts are subtitled in English.

[3] I am grateful to the Leverhulme Foundation for a research grant that made possible a period of research in Professor Hess's laboratory in 1949.

Vomiting, although not commonly elicited, is divided into two types One is apparently like normal vomiting, and is obtained from the level of the corpora mammillaria but more laterally A second type, which is got from the ventral nucleus of the thalamus, is associated with "gagging" and choking, as though the vomiting was initiated by sensations in the back of the throat Rubbing at the mouth with a paw, "as though trying to remove a foreign body," and twitching of the nose occur as well, which, with the licking movements noted above, support the opinion that the cat is responding to sensory stimuli referred to these areas This provides a good example of the lines along which Hess's analysis of an experiment proceeds

Micturition and defæcation are also considered under two headings The first type is complete, in a biological sense The cat prospects a site, assumes the appropriate posture and performs the act This response is usually a result of stimulation of the septum pellucidum, rarely in the hypothalamus The second type is that in which excreta are passed without the accompanying posture of the body This is probably because of suddenly increased peristalsis, or bladder contraction, and arises principally from supraoptic stimulation This is because the hypothalamic influence is almost solely on the viscera, whereas more anteriorly somatic movements are coördinated with visceral activity

A further group of responses merit psychophysiological analysis A complex reaction can be elicited which has been named the "attack reaction" which may turn into a "defence reaction," and later be associated with flight A complete picture of a cat preparing to rebuff a dog can be produced by stimulation of points in the periformical region of the hypothalamus This brings into prominence the relation between autonomic activity and the sensation of emotion Experimentally it must be compared to the "sham rage" of decorticate animals Hess regards the attack reaction as a genuine rage, being an instance of an emotion generated purely by subcortical structures

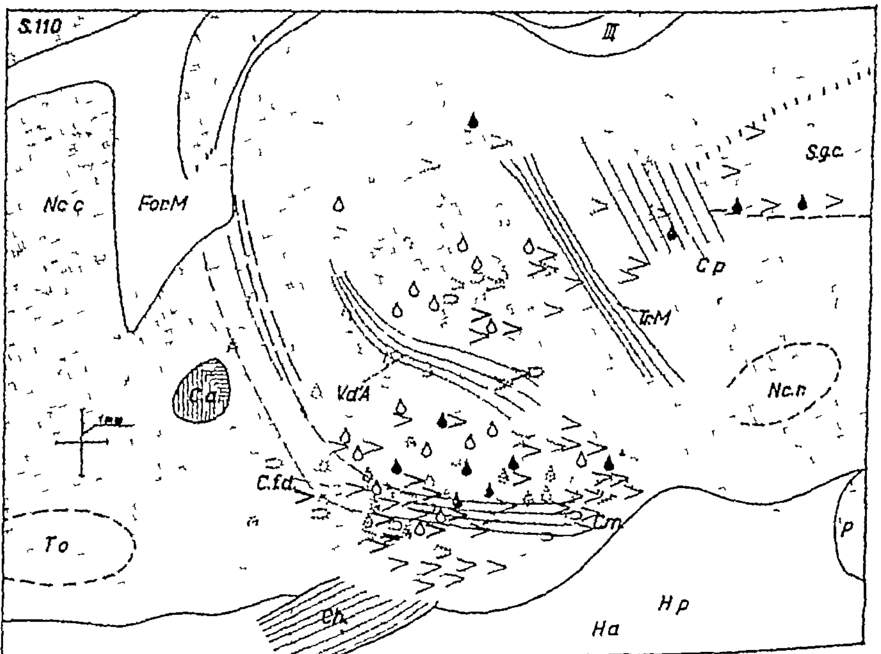
Related responses, caused by more lateral stimulation, are the appearance of abnormal appetites Bulimy, where the cat is apparently so hungry that it will chew any object given to it, or abnormal thirst, where even unpatatable fluids will be drunk, are seen

SLEEP

Finally, there is an all too short discussion of the production of sleep by diencephalic stimulation In Hess's interpretation sleep, as a restorative mechanism, is also a vegetative function, and in the sense of being an inhibition of motor activity it provides a link with the section on somatic functions of the 'tween brain

The production of sleep by electrical stimulation is the most widely known of Professor Hess's findings and has aroused much controversy Ranson and his colleagues, in particular, have asserted that sleep is only produced by destructive lesions and have failed to repeat Hess's results Here, more than anywhere in following the work on the freely moving animal, study of the film records is important

Hess distinguishes three syndromes—true sleep, adynamy, and atony Sleep is a reversible phenomenon, and involves a characteristic posture A cat is asleep (Hess says) when it has curled up in a corner but can be roused by noise, or particularly by putting food near it, afterwards it will return to sleep This only occurs with stimulating anywhere in a broad zone, the *hypnogenous zone*, in the lateral thalamus and subthalamus (at the level of the upper part of the massa intermedia) Atony can be produced by electrical stimulation and is an active inhibition, whereas adynamy, lack of initiative, is due to a locus of destruction in the hypothalamus Adynamic animals show no interest in their surroundings, will flop in any attitude when dropped on to a table, and are quite unrousable These lesions need to be in the *dynamogenous zone* in the hypothalamus, and apart from physical inactivity there is, apparently, a "running down" of the whole organism, with effects such as a fall in body temperature and a fall in the red cell count The difference between adynamy and sleep is as real as that between coma and normal sleep in human patients, and the failure to make the distinction has led to confusion in investigations of the physiology of sleep



A representative conventional diagram illustrating the collected results of stimulating discrete points in the diencephalon. The symbols represent :

> Panting Ↄ Vomiting → Sneezing O Salivation

Symbols heavily lined indicate points where the response was obtained with the lowest voltage.

Anatomical landmarks : C.a. anterior commissure ; C.f d descending column of the fornix ; Ch., optic chiasma ; C.m mammillary body ; C.p , posterior commissure ; For M foramen of Munro , Nc.c. caudate nucleus ; Nc.r , red nucleus ; P , pons ; S g.c. substantia grisea centralis T o., olfactory tubercle Tr M tract of Meynert ; Vd A., bundle of Vicq d Azyr ; III th

MOVEMENTS CAUSED BY DIENCEPHALIC STIMULATION

The second section of *Das Zwischenhirn* deals with the somatic motor effects produced by diencephalic stimulation This is of considerable importance because few other workers have paid attention to it, and none have used unanæsthetised animals Only the briefest outline of the findings will be given here, because they need to be analysed in detail to appreciate their full significance

The movements seen comprise a group involving movements of the head—raising, lowering, and rotating —a group in which turning the body to one side is seen, and a group consisting in isolated or combined movements of limbs, vibrissæ, pinna, or face Movements may be synchronous with the rhythm of the stimulus, characteristically seen in the first group mentioned, and presumably involving a simpler, more direct pathway than other effects in which smoothly executed responses showed no relation to the rhythm of stimulation None of the effects were obtained from regions in the hypothalamus proper, they were responses from the subthalamus and thalamus Rotation of the head resulted from stimulating the most anterior and superior field, slightly posterior to it, turning to the same side as the stimulus was seen, while rostro lateral to the rotation field there was turning to the opposite side The most posterior field caused lowering of the head, while raising of the head was obtained from a region somewhat anterior, but more medial and extending inferiorly into the subthalamus There is, however, considerable overlapping of the fields although their efferent tracts are distinct For details of the individual limb movements, &c, reference must be made to the published maps

ERGOTROPE AND TROPHOTROPE

Professor Hess's interest in the autonomic nervous system is not confined to the rôle of the hypothalamus, as is shown by the wide sweep of ideas in *Die funktionelle Organisation des vegetativen Nervensystems* His concept of the ever present activity of this system in maintaining the economy of the body is put forward in detail The interested reader should study the original work, although he must be prepared for hard toil with complex thought in German

The property of autonomous activity without nervous control, which is possessed by all organs in some degree, is discussed in an opening chapter Then follows a short account of the way in which this inherent autonomicity is coordinated, before considering the much more important integration by the peripheral autonomic system Hess considers the vegetative nervous system as composed of the *ergotrope,* and the *endophylactic* or *trophotrope* parts This terminology needs explanation

The concept of two opposing systems has pervaded all work on the subject, the original terms, sympathetic and parasympathetic, were never precise functionally, and became synonymous with the more purely anatomical categories thoracolumbar and craniosacral outflows. With the discovery of the chemical mediation of their effects, the pharmacological terms adrenergic and cholinergic have come into more general use Hess has coined his names to give them functional significance His views are somewhat similar to those of W B Cannon *Ergotrope* indicates organisation for work and external activity and is a function of the adrenergic part of the autonomic nervous system *Endophylactic* (*trophotrope*) signifies organisation for repair of wear and tear, for maintenance This is largely carried out by cholinergic nerves The concept is wider than those usually accepted Sleep, for instance, is a trophotropic function but would not fall within most classifications as a parasympathetic activity Control of respiration is also considered as a vegetative function, which logically it is, in spite of the fact that the respiratory muscles are striated

This part of the book reviews and recapitulates much earlier work on the control of the circulatory system (Hess 1930) and of respiration (Hess 1931, 1938) Hess's observations on the relation of diaphragm *tone* to the extent of inflation of the lungs, and the importance of this in relation to the Hering Breuer reflex mechanisms regulating the character of breathing, should be more widely known

The sensory visceral nerves are included in the discussion of the peripheral autonomic nervous system, this is of interest, because since Langley's original definition there has been a tendency to regard this as a purely efferent, effector system

INTEGRATION

The organisation of the central nervous control of vegetative functions is coordinated at spinal cord level to some extent, is more highly organised at the medullary level, but is supreme in the diencephalon The experimental findings have been detailed above The rôle of the hypothalamus can best be summarised, as Sherrington might have done it, by saying that the " hypothalamus is the head ganglion of the vegetative nervous system " All normal coordinations of autonomic activity is controlled and carried out at this level, in Professor Hess's view

The cerebral cortex can influence this coordination The emotional and visceral responses to external events perceived by the eyes or other senses show that this must be so (see Hess 1925) In the past decade much interest has been shown in the physiological mechanisms underlying this, and many cortical areas have been shown to mediate autonomic activity The fact that electrical stimulation can produce these effects, however, does not prove that it is a normal controlling mechanism Professor Hess is convinced that in fact the normal visceral control is quite unrelated to conscious activity (which is generally agreed) and that this control is exerted from the hypothalamus, or the diencephalon. The cortex can alter the hypothalamic control, but it plays only a small part, just as we know that conscious events, although they can influence visceral activity, play no part in regulating it

Thus an integrated concept of the organisation of the autonomic nervous system emerges For the younger generation of physiologists, impatient for precision but using increasingly artificial preparations, this work of an outstanding researcher of the older generation is exemplary For medical men working by the bedside the work should be an assurance that experimental physiology has not lost its power of integration It can still study the whole animal and, from the very complexity of this approach, derive results that are more directly applicable to understanding the whole patient than many other types of laboratory experiment

REFERENCES

Hess W R (1911) Graphische Darstellung von Bewegungsstörungen der Augen *Arch Augenheilk* 70 10
— (1925) Über die Wechselbeziehungen zwischen psychischen und vegetativen Funktionen *Schweiz Arch Neurol* 16 285
— (1930) Die Regulierung des Blutkreislaufes Leipzig
— (1931) Die Regulierung der Atmung Leipzig
— (1932) Beiträge zur Physiologie des Hirnstammes I Die Methodik der lokalisierten Reizung und Ausschaltung subkortikaler Hirnabschnitte Leipzig
— (1938) Beiträge zur Physiologie des Hirnstammes II Das Zwischenhirn und die Regulation von Kreislauf und Atmung Leipzig

---

We see that most people would rather be fooled than told truths which they do not feel that they can face Hence an economy that is always capsizing and the politics of international anarchy We prefer luxuries to necessities debt to solvency, nationalistic wars to peace Further we see that words have done all they can to caulk the gap in our gaping seams—far more than the last century thought possible With word fantasies ranging from psycho analysis to frank farce we have kept a film of pretence, a play of fun and fairy tale, over the widening fissure But now words are at the end of their tether Their elasticity is worn out, their credit exhausted We have to come back to Thought, to what we really think things to be and not what we say they are or should be '—GERALD HEARD *Morals Since 1900* London, 1950, p 144

Robinson (1943), and the 51% of Dummer (1949) The mother's employment was a factor in only 2 2%, this is very much lower than the figure given by Neale et al (1942) for Birmingham where in 1938 15% and in 1941 11% of mothers abandoned breast feeding because they went to work

THE ARTIFICIAL FOODS USED

The artificial feeds in use were

	No of cases	%
National Dried Milk	268	63
Cow's milk	82	19
Proprietary milk foods	74	18

(Sometimes several of these milk foods were given to the same child on different occasions)

It will be seen that the place of breast milk has usually been taken by National Dried Milk Indeed at 10½*d* for the equivalent of 7 pints of cow's milk it is difficult for mothers to resist its use, though of course it is the same price as the 7 pints per week priority milk for the under fives In Bristol, as elsewhere, it is distributed at infant welfare clinics and private shops, and is very easily obtainable by any mother

SUMMARY

The incidence of breast feeding in Bristol has fallen considerably in the past twenty years In 1949 36 2% of babies were breast fed at three months, compared with 77% in 1929–30

In 1947–48, fewer patients delivered in nursing homes had established lactation at fourteen days than patients delivered at home or in hospital at six months the incidence of breast feeding in these groups was the same

Mothers belonging to the Registrar General's classes I and II appear to breast feed their children longer than mothers belonging to classes IV and V

At six months, the weight of artificially fed babies is more variable than that of breast fed babies, this suggests that breast feeding is preferable for the majority of children

64 4% of mothers weaned their babies because their breast milk failed for no obvious reason only 2 2% because they went to work

National Dried Milk was the food most often used (63%) for artificial feeding Cow's milk was given to 19% of infants, and proprietary brands of milk to 18%

Our thanks are due to Prof A V Neale, department of child health, Bristol University, for his help in the preparation of the questionnaire of the 1947–48 survey, to Prof R H Parry, medical officer of health, City of Bristol, for his advice and permission to undertake the work, to Mr H S Twiggs, deputy city treasurer, and Miss M C M Hooper, of the city treasurer s department, for their help in recording the information on punched cards, to Mr H A Bywater for his help in preparing figures and graphs, to Mr A R Sherman, Miss K G Wright, and other members of the maternity and child welfare department, for their help in the analysis, and finally to the health visitors who made the work possible, and who went to great trouble to complete the special forms required

REFERENCES

Dummer F H M (1949) *Brit med. J* 2 14
Dykes, R.M. (1949) *Publ Hlth Lond* 62 118
Gordon, I (1942) *Arch Dis Childh* 17 139
Hughes, E L (1948) *Brit med J* 2 597–
Maternity in Great Britain (1948) Joint Committee of the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee London
Ministry of Health (1944) Reports on Public Health and Medical Subjects no 91 H M Stationery Office
Neale, A V Cassie E Braid F Pierce M (1942) *Arch Dis Childh* 18 59
Robinson, M (1943) *Lancet* 1 66
Spence J C (1938) *Brit med J* 2 729
Waller H (1947) *Month Bull Min Hlth P H.L.S* 6 73
Williams E J (1947) *Publ Hlth Lond* 60, 201

Measles

During the week ended March 3, 29,154 cases of measles were notified in England and Wales—an increase of 1378 over the previous week, when there was a record incidence The number of cases notified in this biennial epidemic surpasses that of 1943, previously the most severe, by a considerable margin The majority of cases continues to be in the southern part of the country London notified 3315 (3746), Essex 2403 (2094), Middlesex 2246 (2136), Surrey 1869 (1861), and Kent 1503 (1509), the previous week's cases are in parentheses High totals also occurred in the West Riding of York shire with 2540 (2073) and in Lancashire with 2496 (2422), while of the county boroughs Leeds with 498 and Southampton with 446 were most affected

Whooping-cough

Weekly notifications of whooping-cough continue to rise, and during the week ending March 3 the previous record was again exceeded, the 6096 cases in this week exceeded by 168 the number in the previous week During the corresponding week of 1950 notifications totalled 1614 Most cases again occurred in London and the home counties, although in this locality the position improved somewhat Totals were London 396, Essex 449, Kent 531, Surrey 293, and Middlesex 341 The first three showed reductions of 29, 49, and 61, but in the last two there were increases of 31 and 49 Notable increases were also experienced in Lancaster with 637 (588), the West Riding of Yorkshire with 390 (307), and Devon with 211 (129), the figures for the previous week are in parentheses In Stafford there was a drop of 97 cases, bringing the total to 208 Liverpool and Manchester, with 141 and 108 cases, had the highest incidence among county boroughs

Influenza

The latest figures show that throughout England and Wales the prevalence of influenza continues to decrease sharply In the week ended March 3, the incidence of influenza deaths per million population in the great towns was 8 58, deaths in these towns totalled 178, compared with 1099, 1239, 1269, 865, 492, and 317 in each of the six weeks from that ended Jan 20 to that ended Feb 24 New claims to sickness benefit under the National Insurance Act numbered 146,200 in the week ended Feb 27, compared with 267,400, 200,300, and 161,600 in the three earlier weeks of the month

Poliomyelitis

In the week ended March 3, notifications of poliomyelitis in England and Wales were as follows paralytic 19 (16), non-paralytic 9 (5), total 28 (21) Thus there was an increase of 7 compared with the previous week, for which the figures are in parentheses Total uncorrected notifications for the first nine weeks in each of the past five years have been as follows 1947, 99, 1948, 339, 1949, 178, 1950, 395, 1951, 270

Parliament

Clean Upholstery

In the House of Lords on March 6 Lord MACDONALD OF GWAENYSGOR moved the second reading of the Rag, Flock and Other Filling Materials Bill The original Rag Flock Act, he said, was before Parliament 40 years ago in 1911 A similar Bill was passed in 1928 Since then a helpful report had been received from the Merthyr Committee in 1946 But the passing of time had shown that the existing legal safeguards were inadequate The present Bill provided for registration and licensing of premises used for upholstery and kindred activities Registration would take place unconditionally on demand, but no licence would be issued for the making of rag flock for upholstery unless the premises contained adequate appliances for securing cleanliness

Lord AMULREE, who was among those who welcomed the Bill, said, however, that this must not necessarily be looked at purely as a health matter It was a strange and curious thing that, as far as he knew, there was no vidence that any sickness or disease had been caused by illing materials which were below the standards here aid down The Merthyr Committee's report said that rom an æsthetic point of view it was repugnant that pholstery should be filled with filthy material What his Bill was intended to do was to ensure that nothing f that sort should happen

Lord HADEN-GUEST said that in his work as a doctor he had seen something of the conditions under which the filling of upholstery and bedding was carried out, and it was alarming The percentage of traders who offended in this matter might not be large, but nevertheless control was necessary The Bill was read a second time

QUESTION TIME

Care of Children

In answer to a question Mr CHUTER EDE, Home Secretary, stated that on March 1 1951, 15 children committed to the care of local authorities were accommodated in remand homes with the Home Office authorisation given under Section 13 (6) of the Children Act, 1948 The normal length of stay of such children in remand homes was about six weeks While he deprecated using remand homes for this purpose, it was necessary to do so as an exceptional measure at present, but the need would disappear as more reception centres were provided under the Children Act

Mr K P THOMPSON asked if the Home Secretary was aware that this matter was a cause of great disquiet among those concerned with the welfare of this small number of children[1] They were liable to be overlooked because their numbers were small Six weeks in this sort of home could do these children more harm than they would have come to in the place from which they were removed for care and protection.—Mr EDE said he was concerned about this matter, and he was hoping that the new powers given to local authorities and to the Home Office under the Children Act 1948, would be used to reduce this number still further He was afraid, however that even then there might, in some exceptional cases be a necessity for one or two children to be detained temporarily in such places

G P Hospitals

Mr H A MARQUAND, in reply to Sir IAN FRASER, said that according to his present information 9 hospitals in which general practitioners formerly provided, for their own patients, treatment not of a specialist nature had been converted into specialist hospitals or for other uses Specialist staff had also been introduced into a number of small general hospitals where general practitioners formerly provided special forms of treatment, but in many of these, and also in some other hospitals, some beds had been reserved for patients under the care of general practitioners The following was the list of the 9 hospitals

Warde Adam Cottage Hospital South Elmsale Mirfield Memorial Hospital Alfred Bean Hospital Driffield Beverley Dispensary and Hospital Wirksworth Cottage Hospital Staines Hospital, Stanmore Cottage Hospital Epping Cottage Hospital Arundel Hospital

Hearing-aids

In answer to a question Mr MARQUAND stated that 118,699 patients in England and Wales had been supplied with Medresco hearing aids and evidence derived from a recent survey suggested that about 90% continued to use them regularly The services of research development and distribution were so widely spread over various Government agencies that he could not give any useful figure of total costs The manufacturing cost was remarkably low He expected that deliveries to distribution centres would continue at a rate of over 6000 a month during 1951 but some of these would be required for replacements

Checking the Doctor's List

Colonel O E CROSTHWAITE EYRE asked the Minister of Health what reasons prompted him to adopt the policy set out in circular E C L 6 51 dated January 11 1951, for the purpose of eliminating inflation in doctors records—Mr MARQUAND replied The present inflation makes it impossible accurately to assess the total amount of remuneration due to general practitioners or to distribute this remuneration equitably as between one doctor and another Colonel CROSTHWAITE EYRE Why has the Minister adopted this method? Does he realise that in Hampshire alone 26 lorry-loads of documents have to be moved from the food offices to the executive council offices and that neither has enough staff to deal with them? Why could he not have put a simple question in the forthcoming Census which would have given him all the information he needed?—Mr MARQUAND Possibly because the hon and gallant gentleman did not make that suggestion in time

Charge for Road Accident Treatment

Mr HUGH FRASER asked the Minister whether he was aware that anyone suffering a road accident in which a motor vehicle was involved could be charged 12s 6d by hospital management committees for emergency treatment, and what action he proposed to take—Mr MARQUAND replied The liability to meet the charge for emergency treatment under Section 16 of the Road Traffic Act, 1934, is upon the person using the vehicle at the time of the accident Mr FRASER As all people subscribe to the National Health Service today, and anticipate a free service, is it not time this section of the 1934 Act was repealed?—Mr MARQUAND The National Health Service Act expressly states that this section should continue in operation

Number of Medical Students

Mr SOMERVILLE HASTINGS asked the Minister what steps he was taking to augment the present facilities for training medical students and thus ensure a sufficient number of doctors, in view of the necessity for expansion of the National Health Service and of the estimated wastage of members of the medical profession.—Mr MARQUAND replied I am advised that the present output of the medical schools should be sufficient to provide for some expansion as well as to replace wastage, and I am not at present satisfied that any special steps to increase it are required

British Red Cross in Korea

Replying to a question Mr K G YOUNGER, Minister of State for Foreign Affairs, stated that the British Red Cross Society s welfare team was due to leave Japan on March 1 for Korea, where it would assist under the Unified Command in welfare and public health work among the local inhabitants In addition, British Red Cross and St John Naval V A.D.s were employed on a hospital ship in Korean waters, and the society had made grants to the International Red Cross Committee for relief work in Korea British Red Cross and St John personnel and stores were being used to help Service casualties in hospitals in Japan.

Exemption of Medical Students from Z Reserve Call-up

In answer to a question Mr JOHN STRACHEY, Secretary of State for War stated that no medical students whose studies were approaching completion should be called up under the Z Reserve call up scheme If they should receive a call up notice they might apply for exemption, submitting supporting evidence, and exemption would be allowed

Model By-laws on Hygiene

Mr MAURICE WEBB, Minister of Food replying to a question, stated that up to Feb 25 this year he had confirmed by laws on the handling wrapping delivery, and sale of food which had been made by 1062 local authorities, and he was expecting to take similar action shortly in a further 193 cases He had no information about the remaining 189 authorities

Infant Vaccination

In answer to a question Mr ARTHUR BLENKINSOP stated that the 1946 acceptance rate of infant vaccination was just over 41%, and for 1949 it has been roughly estimated as about 28%

Subnormal Children

In answer to a question Mr GEORGE TOMLINSON, Minister of Education, stated that at the beginning of last year there were approximately 28 000 children in England and Wales known to require education in special schools for educationally subnormal pupils, and there was provision for rather more than 15 000 He intended to do all he could within the limits of available building resources to increase this provision In this way he hoped that it would be possible for more of those educationally subnormal children, who drifted towards delinquency, to be dealt with preventively by special educational treatment

---

[1] See *Lancet* March 3 1951 p 519

In England Now

A Running Commentary by Peripatetic Correspondents

O what can ail thee, babe in arms,
  Perpetually bellowing?
Hideous is the noise you make
  And deafening.

O what can ail thee, babe in arms?
  Pipe down, you little so-and-so.
Mum says your guts are working fine
  —And Mum should know.

Your face is anything but pale,
  Your urine is a great success,
Throat, abdo, chest, and ears are clear
  And C.N.S.

Nurse diagnosed and cured the babe
  And silenced his unearthly din.
Piercing his buttock she espied
  A safety-pin.

* * *

The blossom is out once more—not in our rain-sodden gardens, but at the *Daily Mail* Ideal Home Exhibition, which remains open at Olympia until March 31. Here can be seen azaleas, camellias, clematis, magnolias, prunus, rhododendrons, and many other shrubs in full bloom, with bulbs and rock plants at their bases and beside them roses and carnations. The gardens as always wake us up from the dull, dreary months of winter, and our thoughts turn from the tiresome controversies of today to the colour, splendour, and peace of a cool summer evening. This year the houses in the Village of Ideal Homes have been set off by a central garden. Of special interest among the six houses is that of the Women's Institutes; this house embodies the ideas of 400,000 women who filled in questionaries. On an electricity stand a house-parlour-maid and cook are sitting in a kitchen; this tableau will certainly be of historic interest to the younger generation. The Fashion and Beauty section supplies sound factual evidence for the advocates of "make-up." There is an excellent demonstration of a new window cleaner, and a well-known product for killing indoor smells strives valiantly but unsuccessfully beside a demonstration of frying. There is a new section exhibiting books, where many hundreds can be examined. The Royal Air Force shows the improvements in the design and furnishing of their married quarters, while the Army's new barrack block must surely amaze many old and not so old soldiers, as also will the modern private's choice of bedside books. In another part of the exhibition the NAAFI show models of some of their clubs.

Interwoven into this exhibition are lessons for everyone. The police advise about protection against burglary, the Royal Society for Prevention of Accidents teach road sense and manners, and the W.V.S. look after a model of an accident-prone house. The Grand Hall is lit by ten chandeliers, and dominating it at one end is a replica of an arch of the Crystal Palace. Although there is one exhibit showing the South Bank, it is surprising how little the Festival is in evidence. It is still an exhibition of every aspect of home life.

* * *

"Darling, isn't 'Cortisone' a sort of linoleum?"

* * *

Broadcast health talks are all very well, but listeners will keep fitting the wrong caps on their heads or their family's. For instance, the best way to reduce one's weight no doubt is to eat less, but some qualifying words of warning are required. A little starvation will do no harm to the overweight man or woman of middle age whose fires are beginning to die down, but how about young people? One cold evening, soon after listening to the talks on fat-reduction, I was visited by the chairman of the parish council; he came ostensibly for a specimen of my signature, but actually to talk about his secretary, a girl of twenty. Apart from asthma since the age of two, she seemed healthy until this autumn, when she had pleurisy. After that she was repeatedly radiographed and was reported to have a "doubtful shadow." Finally she was pronounced non-tuberculous and fit to return to work shortly, though she must come again every month for examination.

Mr. Chairman wanted to unburden himself about two things. One was slimming. Like many girls of her age, his secretary was plump but not fat, and—like most of them—she wished she was slim and elegant. Having learnt from women's magazines and B.B.C. talks that the proper way to get thinner is to eat less, she reduced her intake so thoroughly that by the autumn her lunch was down to one rye biscuit and an orange. I agreed heartily with my visitor that this was wrong. Next he asked whether I thought the girl really had tuberculosis. This is one of the awkward and unanswerable questions that people ask when they get a doctor alone, and, as ever, there was more behind it. Mr. Chairman confessed that his mother died of tuberculous kidneys, and her long and painful illness gave him as a boy a horror of the disease. Obviously he does not want a T.B. secretary, and would be glad of a clearer diagnosis than "We think not, but ..."

He talked to me because no doctor in the Health Service ever seems to have time to listen. Laments of this kind reach me from all sides. "My doctor never explains anything. Can you tell me why ...?" or "The doctors are always run off their feet these days and I don't like to bother them." They catch me when I am out for a walk or posting letters at windy corners; they grab me as I pass their garden gate, confide in me over shop counters, or whisper in my ear at parish council meetings. The worst (except for the windy corners) is when they telephone. An unknown woman rang me up last week and talked about her distressing problem for about five minutes before she drew a breath and I could interrupt to ask, "Why are you telling me all this?" Her only reply was, "Mrs. X said you might be able to advise," and then she started off again. Mentally anathematising Mrs. X, a doctor's grass widow and a friend of mine, who should have known better, I listened for ten to fifteen minutes and spent another five persuading the voice that, willing as I was to help her, the right person to consult was her own doctor, whom I knew to be kind and sensible even if overworked.

Now that much of the old family doctor relationship has gone, many people are feeling the lack of someone they can talk to about the health problems which overflow into their daily lives. My G.P. colleagues give me the reverse side of the picture. When they are so rushed that there is no time for any but snap diagnoses, they clearly cannot listen to long tales of their patients' worries and give them the reassurance and common-sense advice which is all that most of them want.

It is easy to see why the radio talks and newspaper and magazine articles on health are increasingly popular. But though many of these are ably constructed, easy to understand, and correct in substance they cannot take the place of the spoken interview, with question and answer and mutual consideration of the individual situation. How would it be if those of us who are no longer physically fit to join actively in the fray were given an official niche—like a citizens' advice bureau, only more medical—where we could do some weeding out and lighten a little the burdens of both our overworked colleagues and our anxious fellow citizens?

* * *

The scene was the medical outpatients department of a children's hospital, where a mother had brought her small daughter because she had fits. After eliciting a long family history of fits the registrar asked whether there was any backwardness in the family. Like a flash came the reply: "Aye, Doctor, her sister comes down the stairs backwards."

* * *

"Who is arranging the funeral, Mrs. Jones?"

"The Co-op. They do it ever so nice, doctor, and you get your divi too."

* * *

Aphorism of the Week

Colostomies are easier opened than closed.

Letters to the Editor

THEORY OF CEREBRAL LOCALISATION

SIR,—The paper in your issue of March 3 by Dr Gooddy and Mr McKissock propounds, if I understand it aright, some strange beliefs Its authors seem to hold that neurological theory inclines to, or even insists on, an absolutist hypothesis of cerebral function, which they demand should be abandoned forthwith.

Those who have had the chance of reading Dr Gooddy's earlier paper[1] will know that the idea of an absolute functional topography, as though the living brain were engraved with the neat labels and figurines so familiar in textbooks, is a spectre which most perplexingly haunts him , and it now appears that he has persuaded Mr McKissock into joining him in his torment It must be emphasised, however, that such a doctrine is quite foreign to the thought of serious neurologists, whether they be physician or surgeon, physiologist or anatomist Indeed, it is doubtful whether it has ever been an acceptable tenet, though Ferrier probably came near to holding it The teachings of Hughlings Jackson contain nothing that could be so interpreted, for he argued that the clinical experiments of disease upon cerebral physiology indicate primarily not a functional, but a symptomatic, localisation Sherrington is equally blameless For example, in writing[2] of the excitable cortex, the "so called motor area," he specifically comments that "the student looking over the political map of a continent may little realise the complexity of the populations and states so simply represented We looking at the brain chart of the textbook may never forget the unspeakable complexity of the reactions thus rudely symbolized and spatially indicated " Latter day writers are also free from guilt Thus Denny Brown and Botterell[3] have lately recorded their conviction that "the phenomena of electrical excitation of the cortex demonstrate an important and localised motor effect, rather than a specialised motor act " In other words, this is the expression of a strictly empiricist attitude, applicable *mutatis mutandis* to all aspects of cerebral physiology

Having delivered their initial onslaught against what I submit to be a non existent doctrinal error, Dr Gooddy and Mr McKissock then apparently fall swiftly into the very heresy they have been attacking They write of the re allocation of functional sites and fancifully imagine the peregrinations of a centre concerned with reading, for all the world as though they themselves believed "centres" and "functional sites" to have a real and absolute existence, and not to be simply convenient abbreviatory terms, which in use briefly imply a host of more or less well known empirical facts Having next reminded us of the self evident proposition that the retention of a function necessarily indicates the preservation of the anatomical substrate requisite for its performance, they proclaim that any form of experimental approach to determine the situation of the structures involved must be forgone as "reactionary"

This egregious ukase evidently stems from over great timidity in face of the truism that the appearance of a certain disability after a particular anatomical lesion does not mean that the function of the locus injured is in health merely to prevent that defect They do not seem to realise the corollary—that the normal function of a part is always something positive, and never a mere negation, a device for warding off disorder To exemplify this if a wretch should lose both eyes he is blind, but only the very tortuous would choose to assert from this that the eyes are to prevent blindness, instead of accepting the everyday verdict that their use is to see Or again, the man in the street knows that his kidneys are to make water with , it takes the most vile addict of modern "scientific medicine" to protest the negative hypothesis—that they are only to prevent uræmia To give a final example nearer home, the use of the precentral gyrus is not to prevent paralysis, nor yet as some perhaps once thought to beget movement , rather it provides a facilitating mechanism by means of which we practise all those delicate motor skills, both major and minor, of which Dr Gooddy himself has written so lyrically elsewhere

Perhaps, after further reflection, Dr Gooddy and Mr McKissock will be more leniently inclined towards the exercise of experimental techniques However, that may be, they can at least console themselves with the thought that repetition of "methodological postulate" is a most excellent clinical test for dysarthria

Birmingham MICHAEL JEFFERSON

---

[1] Gooddy W G *Brain*, 1949 72 312

[2] Sherrington C S The Integrative Action of the Nervous System London 1906

[3] Denny Brown D Botterell E H The Frontal Lobes Baltimore 1918

ÆTIOLOGY OF CHRONIC GASTRIC ULCER

SIR,—I am interested to learn from Professor Bentley and Dr Barlow (Feb 24) that there is no difference in the vascular density of the lesser curve mucosa as compared with that lining the rest of the stomach in cases of gastric ulcer

As far as I am aware, a differential analysis of the number of vessels to the square inch of mucosal surface in normal and abnormal stomachs has not been published I assume, therefore, that Professor Bentley and Dr Barlow are speaking from personal experience I would like to ask two questions Is their opinion based mainly upon specimens removed at routine post mortem examinations and at operations for chronic duodenal ulcer, or exclusively upon those removed in the treatment of chronic gastric ulcer ? In a "normal" stomach, and in the stomach of a patient with a duodenal ulcer, there is little difference between the vascular density of the lesser and greater curvatures Secondly, if their material was solely from cases of gastric ulcer, was the mucous membrane dissected off the underlying structures before being micro radiographed ? In a recent paper from the department of surgery at Newcastle upon Tyne, by Mr Key,[1] no mention of this step is made, and the surface radiographs illustrated are of the full thickness of the stomach wall The vascular density of the mucosa can hardly be assessed in such a film Only surface films of the lesser curve are shown Moreover, his description of the comparison between the "vascular pattern" in the normal and the abnormal is drawn from transverse sections , in which plane the difference in the vascular density is not apparent

The risk of artefacts occurring with injection methods is well recognised, and I mentioned it in my article The lower density of the lesser curve in cases of gastric ulcer may prove ultimately to be an artefact , but the simple technique employed is unlikely to have been the main factor To draw conclusions from quantitative variations between different preparations is hazardous, as Professor Bentley and Dr Barlow correctly assert , but to draw conclusions from quantitative variations occurring in individual specimens is quite sound, because it is unlikely that the conditions of the injection would vary between different areas of the same stomach. Only the various regions of each organ were compared , in no instance was the mucosa of one specimen compared with that of another Moreover, as the observation consisted of a relative difference between the vascular density of the mucosa on the lesser and greater curvatures, the efficiency of the mucosal filling is of secondary importance The difference between two weights can be detected without knowing the absolute weight of either

---

[1] Key J A *Brit med J* 1950 ii 1464

To compare various areas of one preparation is always safer than comparing the same area in various preparations, because, as Professor Fisher [2] points out, "careful control" in experiments may be fallacious owing to the tacit assumption that the experimentor knows all the factors which might influence the result, which is seldom the case

Bromsgrove, Worcestershire F S A DORAN

FOOD WORKERS AND INFECTIOUS-DISEASES REGULATIONS

SIR,—The Catering Trade Working Party refers in its report [3] to the Public Health (Infectious Diseases) Regulations, 1927, and in paragraph 75 advocates their *modification to include within their scope excretors of food poisoning organisms*—a very desirable change Further it is suggested (paragraph 74) that advice can be given to those found in hospital to be carriers of enteric and dysentery and discharged as such, "*to avoid employment in the catering trade*" So far so good But then the report proceeds "if a Medical Officer of Health thinks it necessary in order to prevent the spread of infection he should take statutory action under the P H (I D) Regs—E & W 1927, Scotland 1932—if the worker is a carrier" It is my submission that unless the worker is *already* engaged in the food trade the M O H cannot take any statutory action

The relevant paragraphs are in part III of the first schedule to the regulations The first refers to a "case," which by the wording of paragraphs 1 (i) (*a*) and 1 (ii) must be in a person already engaged in the food trade since clearly the person *specified* in the notice referred to in section 1 (i) (*a*) cannot *discontinue* an occupation unless he has already *begun* it, and it would be idle to address the notice referred to in paragraph 1 (ii) to the patient or relatives, &c, unless the patient is the food worker The second *paragraph refers to a* suspected "carrier" already engaged in the food or drink trade In both cases the procedure is slow, involving a report to the local authority and action by that body (notice of restriction of employment) With regard to the case, the notice of restriction applies until revoked, with regard to the carrier, the notice is for a defined period

Now the regulations are presumably framed for the protection of the public, and also with a view to their usefulness in dealing with recalcitrant persons We know that in 99% or more of cases there is no need to invoke them formally But on the other hand they *may* be necessary, and the powers *may* be needed in a hurry Most of us would agree that typhoid or paratyphoid carriers, or suspected cases, should not work in food preparation, &c Yet we cannot under the present regulations exclude them (if they object) *at once* but only after the local authority has agreed Secondly we cannot require any carrier to abstain from *entering* such an occupation (but only require him to discontinue if he is already in it) We must wait till the risk has been run before we take the obvious precautionary steps It will be remembered that strict compliance by the medical officer of health and the local authority with the regulations is necessary in such an important matter affecting a person's livelihood

I maintain that

1 The medical officer of health should have immediate suspensory powers in respect of suspected cases and carriers of dysentery, typhoid, paratyphoid, and food poisoning occupied in a trade or business concerned with the preparation or handling of food

2 The authority should have powers to require, until revocation of the notice known carriers of these diseases to abstain from any occupation concerned with the preparation or handling of food or drink intended for sale for human consumption whether then engaged in such an occupation or not

These suggestions were made in 1949 in a note by Dr T G Galvin and myself on an outbreak of paratyphoid fever [4] It is simple enough to procure protection for the worker (*a*) by a compensation clause operative in the event of unreasonable action by the medical officer of health, and (*b*) by right of appeal to the courts

The consideration of compensation for workers for loss of earnings referred to in paragraph 68 of the *report* might also be extended to contacts *temporarily* excluded for examination, &c In my presidential address to the Yorkshire branch of the Society of Medical Officers of Health in 1946 I made reference to this [5] To some extent the point has been met by the Ministry of National Insurance (acting I believe on Dr J Grant's suggestion at the York meeting of the county borough group of the Society of Medical Officers of Health in 1947), which allows benefit equal to the ordinary sickness benefit *on certification* by the medical officer of health, but is this quite enough ?

There is a further point not referred to in the report. At present there is mounting public anxiety about open cases of tuberculosis being allowed to handle food for sale for human consumption

If the regulations are to be modified, as they should be, it is to be hoped that these considerations will be borne in mind

E D IRVINE
Exeter Medical Officer of Health.

LARYNGEAL VERTIGO

SIR,—Your leading article of July 15 prompts me to describe the following case

A plethoric, obese, European man, aged 49, with deeply nicotine stained fingers and cheery countenance, was warded with bronchitis and emphysema During a bout of coughing he fell off his bed and cut his nose He had been sitting on the edge of the bed and had reached the stage in the paroxysm of having "no breath left" in his chest when he lost consciousness He came round a second or two later on the floor, and was helped up by the dresser who witnessed the attack. He had soft arteries and a blood pressure of 135/90 mm Hg Skull, nervous system, blood sugar, and urine examinations were negative He admitted to a cigarette consumption of not less than forty a day and a beer intake of ten pints a week, but he did not consider he was a heavy eater

Questioning revealed two previous attacks, with an interval of three months, while working in the Middle East The first occurred, when he was sitting "having a beer with a friend," at the end of a paroxysm of coughing, he sustained a bruised neck from the table edge The second occurred when he was walking away from the lunch table His newly lit cigarette precipitated a bout of coughing ending in his pitching forward unconscious, sustaining lacerations on his face Extensive hospital investigations were then made, apparently with negative result

Is it not possible that such attacks in this well defined group of patients are due, not to any particular anatomical or pathological peculiarity, but rather to the fact that these people are, next to those with whooping cough, the most prone to the type of coughing bout which may end in syncope ? Might not the mechanism of these attacks be comparable to the sudden loss of consciousness that may take place during vomiting ? This is, I believe, a fairly common phenomenon In recent experience I recall a man, aged 28, who lost consciousness for a few seconds during a bout of vomiting from food poisoning, not associated with significant fluid loss Another example was a young woman, otherwise in robust health, who had three times fainted in the act of vomiting Diaphragm and glottis activities during vomiting must produce intrathoracic pressure changes and consequent events akin to those suggested in your leading article

---

[2] Fisher R A Statistical Methods for Research Workers Edinburgh 1946 Design of Experiments Edinburgh 1947

[3] Ministry of Food Hygiene in Catering Establishments H M Stationery Office, 1951 See *Lancet* Feb 10 1951 p 333

[4] *Lancet*, 1949, ii 904

[5] *Public Health*, 1947 60, 93

A preferable name for the syndrome might be "paroxysmal post tussive syncope" It might then be possible to rescue the condition from the limbo of the larger ear, nose, and throat textbooks, and to reduce the number of patients who are at present worried by their label of "epileptiform attacks" without the reassurance that is possible with accurate diagnosis

Kuala Belait Brunei
British Borneo　**MICHAEL FLINDT**

UNFAIR QUESTIONS

SIR,—Those of us whose duties involve teaching are sometimes astonished at questions set in examination papers or asked in viva voce examinations For instance, in a recent final examination in surgery one of the five questions required the candidate to discuss the surgical complications of typhoid fever In the last last ten years at Guy's Hospital only 4 cases of typhoid fever have been admitted and none of them had surgical complications A surgical colleague who is particularly interested in intestinal ailments tells me that he has never encountered any surgical complication of the disease It seems then that in a qualifying examination such a question is needlessly academic The surgical textbooks in common use among students contain only the briefest mention of the surgical complications of typhoid fever—certainly not enough to enable a student to write a reasonably good answer

The following question was set in a paper for a higher qualification in medicine "Discuss the diagnosis *in a young woman* presenting herself with the complaint of double vision" The italics are mine, but even without them the candidate is surely entitled to infer from the wording that the examiner had in mind certain conditions in which the patient's sex is important in diagnosis So far I have not found any physician who can give an adequate explanation

Again, is it reasonable to expect candidates to memorise the doses of large numbers of drugs, many of which are not commonly used? Surely to try to remember doses is not only unnecessary but dangerous In promotion examinations in the Services candidates are provided with the official books normally available to them, such as *King's Regulations* and the *Manual of Military Law* Why not allow candidates for examinations in the clinical subjects to consult the *British Pharmacopœia* or even the *National Formulary*? It is perhaps only fair to say that the examiners who most often ask doses are not clinicians

London, S E 1　**J J CONYBEARE**

A C T.H IN THE DIAGNOSIS OF GOUT

SIR,—The diagnosis of gout, up to the present, rests on clinical assessment, a history of intermittent attacks, a family history of the disease, a raised plasma uric acid and normal hæmoglobin levels, rapidity of change in the sedimentation rate X ray appearances, and the therapeutic test with full doses of colchicine Even consideration of all these factors will sometimes leave the diagnosis in doubt

In 1949 Hellman [1] and Wolfson [2] showed that, between the third and sixth day of administration of adrenocorticotropic hormone to gouty subjects, there was a "low corticoid" phase and this was often associated with an exacerbation of the disease By giving 150 mg A C T H daily for four days Hellman provoked an attack in 3 out of 5 trials in typical cases in the interval phase On the other hand, Gutman,[3] using 100 mg daily for four days in 5 interval gout cases on a low protein diet, only produced 1 attack in 8 trials

Early last year we observed in hospital 3 cases of typical gout Each patient was given a "shock" dose of 100 mg A C T H in an interval phase, to see whether an acute attack would occur during the low-corticoid phase regularly enough to make administration of A C T.H a useful test for gout Only 1 patient, however, had an acute attack within a week of the injection, and this was on the sixth day Four hours after the injections of A C T H there was a drop in the circulating eosinophils and lymphocytes, with an increase in the number of polymorphonuclear cells, together with a rise in plasma cholesterol level and a slight fall in plasma uric acid There was an increase in urinary uric acid and 17 ketosteroids, involving the crude, ketonic and β fractions, during the period of A C T H administration

In view of the failure of A C T H alone to cause regularly an exacerbation of gout, a further patient was first given 300 mg A C T H spread over twenty-four hours—with no effect except that she stated that she felt better in herself than she had for years After ten days she was put on a ketogenic high purine diet, containing 66 g carbohydrates and 263 g fat, and given 1 0 g purine (largely in fish roes) After three days she was given another 300 mg A C T.H and the diet was continued for four more days This combination of ketogenic high purine diet with shock dosage of A C T.H again failed to provoke an attack of gout

The failure of these attempts in 4 classical cases makes us think this method unlikely to be of value for excluding the presence of gout

G D KERSLEY
L MANDEL
M R JEFFREY

Royal National Hospital for
Rheumatic Diseases Bath

SUPPRESSION OF DIGITALIS-INDUCED VENTRICULAR PREMATURE BEATS BY A NEW PROCAINE DERIVATIVE

SIR,—Recently 'Pronestyl' (procaine amide hydrochloride) has been introduced for the treatment of ventricular arrhythmias, injected intravenously it has proved successful in cases of paroxysmal ventricular arrhythmia not yielding to other drugs, and also in cases of ventricular premature beats induced by cyclopropane anæsthesia

Pharmacologically the new compound has notable advantages over procaine Its central stimulating effect is less than 40% of that from procaine Whereas procaine is fully hydrolysed in blood plasma at 37°C within six minutes, hydrolysis of the amide amounts to $7^1/_2\%$ in nineteen hours under the same conditions, and in the body the plasma level of this substance falls only 10–15% per hour Thanks to its stability, oral administration is fully effective

In a case of coronary disease we applied the new drug with probably life saving effect, to control intolerance to digitalis glucosides due to numerous ventricular premature beats

The patient a man aged 50, had had manifestations of coronary disease for seven years The electrocardiogram showed the pattern of an old large anterior wall infarction, although there was no clinical history of this event The pulse rate was constantly 100 or more per min., with premature beats arising from two ventricular foci, their number varied at different times from a few up to 50 per min Radiologically the heart was notably enlarged to both sides. In the past six months the patient had also had recurrent phlebothrombosis of the left femoral vein, and during the second attack a severe pulmonary embolism occurred After a critical illness the patient recovered, but signs of increasing heart-failure appeared left hydrothorax, liver engorgement, pretibial œdema of both legs lumbar œdema, and dyspnœa on the slightest exertion Pulmonary embolism took place twice more, the emboli probably originating in the heart since no phlebothrombosis was discovered in a thorough search The second embolism gave rise only to slight and transient manifestations, but the third although far less severe than the first was serious

---

[1] Hellman L *Science*, 1949 109, 280
[2] Wolfson W Q *J lab clin Med* 1949 33 1473
[3] Gutman A B Yu T F *Amer J Med* 1950 9 211

Before the first pulmonary embolism the patient received 0 20 mg digitoxin daily with some benefit, although even with this minimal dosage the number of premature beats rose slightly, with 0 30 mg they became so frequent that the pulse rate actually increased With a change to other digitalis glucosides the result was the same, and thus digitalis administration in sufficient dosage was prevented After the first embolic episode, however, and simultaneously with the heart failure, complete intolerance to digitalis developed, so that even the small dosage previously tolerated gave rise to numerous ventricular beats with an increased pulse-rate With mercurial diuretics it was not possible to compensate for the lack of digitalis, and after the third pulmonary embolism the situation of the patient again became critical, owing to the steadily progressing heart failure

In an attempt to suppress the stimulating action of the digitalis on the ventricular foci from which the extrasystoles were originating, 2 5 g pronestyl was administered daily with 0 40 mg digitoxin This met with full success Within a fortnight, under this treatment combined with mercurial diuretics twice a week, complete compensation was achieved The side effect of the digitalis on the rhythm was almost entirely eliminated—only a very few premature beats were present from time to time—and the glucoside could now be given in a dosage never before tolerated which produced a sufficient inotropic action and slowed the pulse rate to 80 per min. The patient has now resumed his professional work on a reduced scale

It should, however, be borne in mind that pronestyl has not the same effect on auricular premature beats

Anglo-Swiss Hospital, Alexandria Egypt. FR MAINZER

CONGENITAL SYPHILIS IN A FIJIAN

SIR,—Stitt[1] states that amongst the Pacific Islanders a relative immunity to syphilis is found in spite of repeated exposure to infection from syphilitics of other races In Fiji syphilis is widespread amongst Indians and part Europeans, but it is doubtful if the disease has ever been recorded in a pure Fijian, though Lambert[2] quotes (without clinical details) one case described to him by Harper The following is a description of a case of congenital syphilis in a pure blooded Fijian

A Fijian girl, aged 23, of pure Fijian descent, born in the Tailevu district of Viti Levu, denied infection with yaws in childhood At the age of 13 she came to live in Suva, where she remained throughout the war In 1945 she was admitted to the Colonial War Memorial Hospital, Suva, where the Kahn reaction of her blood was found to be ++++ She received a total of 3 0 g neoarsphenamine and was then discharged Though unmarried she was living with a pure blooded Fijian when she became pregnant for the first time, and was admitted to the obstetrical annexe at the hospital on Aug 27, 1950, suffering from an antepartum hæmorrhage Shortly after her admission she was delivered of a macerated male fœtus, the placenta was removed manually as it was adherent The Kahn reaction of her blood was still ++++ After 4 injections of neoarsphenamine she absconded

Microscopically the placenta was fleshy Microscopical examination showed extensive fibrosis, endarteritis, and loss of blood vessels from the villi—all typically syphilitic changes The fœtus was almost full term and was well macerated Section of the liver stained by Levaditi s method showed numerous spirochætes indistinguishable from those of *Treponema pallidum*

It is generally admitted by authorities that no case of congenital yaws has ever been observed (Stitt[3]) yaws is said to be neither hereditary nor congenital[4] The present case therefore appears to be one of acquired syphilis in a Fijian girl with congenital syphilis in her offspring, and this indicates that there is no racial immunity to syphilis in Fijians

In the absence of racial immunity, the rarity of such a syphilitic infection must be ascribed to an acquired immunity It is thought that infection with yaws in childhood confers relative immunity to syphilis Should this immunity become less pronounced, then syphilis could be as readily acquired by Fijians as by other races

In the many Fijian women now attending the antenatal clinic at the Colonial War Memorial Hospital in Suva the Kahn reaction of the blood is often found to be negative It is therefore probable that, owing to the efficient control of yaws which has been established, many Fijian girls are never infected with it in childhood. The girl in question evidently escaped infection in early life, but was then exposed during the war years to syphilitic infection in Suva

In planning extensive anti yaws campaigns amongst primitive people, consideration should be given to the possibility that their immunity to syphilis might thereby be destroyed

I have to thank Dr J M Cruikshank, Inspector-General, South Pacific Health Service, for permission to publish this case

P E C MANSON BAHR
Physician-Specialist, Fiji

THE FALSE "ACUTE ABDOMEN"

SIR,—In his letter of Jan 13 Dr H M Royds Jones quotes a paper which Le Marquand and I wrote five years ago[1] We described a series of cases which clinically simulated perforated duodenal ulcer, instead of operating immediately we observed them for a few hours and we were rewarded by a complete change in the clinical picture with spontaneous recovery Dr Royds Jones describes a series which also recovered rapidly and spontaneously He then proceeds to discuss our paper he writes that we described an "epidemic of Bornholm disease" Reference to our article will show that we were not, at the time, convinced that we were dealing with an epidemic, we considered many possible explanations but Bornholm disease was not among them We suggested that the syndrome may have been due to a *forme fruste* of perinephric infection However in the course of time I have modified my own opinions perinephric infection does, in a transient phase, mimic the "acute abdomen," but this explanation cannot be stretched to cover all the cases we described I believe now that our series was a minor epidemic, but I cannot allow these cases to be labelled as Bornholm disease

The original epidemic of Bornholm disease occurred on the Danish island of Bornholm, and the main features observed were severe fleeting pain and rigidity of muscles innervated by the thoracic part of the cord Since the work of Lewis and Kellgren[2] we know that lesions of almost any deep structure will elicit the response of rigidity and pain in the muscles of its segment With the march of time Bornholm disease will prove to have been an all embracing title for many different lesions (their theoretical limit is equal to the total number of deep structures within the thoracic nerve territory multiplied by the total number of their pathogens!) Scientifically the diagnosis of Bornholm disease should command as little respect as, for example, the diagnoses of sciatica or rheumatism Certainly we must acknowledge that there are epidemics of severe transient pain and rigidity in the great trunk muscles, but these epidemics must be due to many different causes Dr Royds Jones's case histories are consistent with my speculations He is to be congratulated on a series of observations, under difficult conditions, extending over twenty three years

Suspected ulcer perforation was once an immediate signal for operation The possibility of a "false acute abdomen" as discussed in this correspondence, should give pause for thought There is now further additional argument against great haste to operate the work of

---

[1] Stitt s Tropical Diseases London 1942 vol i p 397

[2] Lambert S M *J trop Med Hyg* 1931 34 117

[3] *Op cit* (footnote 1) p 422

[4] Manson Bahr P H Manson s Tropical Diseases London, 1950, p 626

[1] Goldstone B W Le Marquand H S *Lancet* 1940 ii 207

[2] Lewis, T Kellgren J H *Clin Sci* 1939 4, 47

Hedley Visick,[3] later amplified by Hermon Taylor [4] and by Stead,[5] suggests that some cases of perforation are better treated conservatively It should also be realised that very early cases are in a state of acute shock , lately Selye [6] has defined this phase in more precise biochemical terms, calling it the "damage phase of the alarm reaction" It is, of course, the wrong time for operation Twenty-seven years ago Pannett [7] was teaching this, he instanced the case of a man who perforated on the steps of the Royal Free Hospital. At first it was a matter for congratulation that he was rushed to the theatre within an hour, but he died soon after a straightforward operation. There are many obstacles which delay the progress of the "acute abdomen" from his home to the operating-theatre. One may speculate that these irritating difficulties must have saved thousands of lives

East London,
South Africa

BERNARD GOLDSTONE

VACCINATION AGAINST SMALLPOX

SIR,—Commenting on my letter published in your issue of Feb 10, Dr Millard (Feb 24) writes 'I am also in favour of such people being inoculated against typhoid, but I do not think it necessary that everyone in this country should be similarly inoculated." I did not suggest that, because Dr Millard favours vaccination of all who visit the East, he should therefore advocate universal vaccination, but pointed out that, taking his argument to its logical conclusion, the vaccination of such travellers would increase the number of undetected cases of smallpox among them

Dr Millard's main argument against vaccination was that it is liable to render attacks so mild and atypical that they pass unnoticed and constitute a danger to others. He then recommended vaccinating the very people most likely to bring the disease into the country There is surely an inconsistency here. At the same time Dr Millard would leave unprotected those who remain at home and will be exposed to infection from the unrecognised case of smallpox in the vaccinated traveller It is difficult to imagine a policy more calculated to increase the number and severity of epidemics

Arlesheim
Switzerland.

A. M WOOLMAN

SIR,—Dr Millard's delightfully provocative article raises the question whether variola minor and variola major are the same disease and caused by the same virus

For the last six years in the Upper Nile province of the Sudan we have had a slowly developing epidemic of variola minor, with about 270 notified cases and 5 deaths The disease was at first regarded as chickenpox, but after a few reported deaths it was diagnosed as variola major Vaccination campaigns were organised, but because of the nature of the country they were largely ineffective and vaccination was abandoned as soon as the disease was recognised as variola minor The infection spread through the province slowly by traceable tribal contacts On two occasions laboratory tests proved it was variola and not chickenpox. The clinical aspect of the cases, and the slow spread, gave the epidemic a totally different picture from that of variola major

The epidemic occurred in a comparatively primitive community of 80,000 people in an area of 90,000 sq miles, and the number of cases notified was probably less than half the total. In one area where we instituted quarantine the people asked us not to do so because they knew that the disease was different from variola major and conferred immunity against variola major in fact they welcomed its appearance

Contrast this slow epidemic with one seen in 1947 in a similarly primitive population at Yirrol in the Bahr el Ghazal province, where there were 280 cases with 117 deaths It was a flare up, rapid in growth, killing in its severity, and again rapid in its decline—thanks mainly to an intensive vaccination campaign

In the Upper Nile outbreak we abandoned vaccination on advice from laboratory specialists, and because climatic conditions and communication difficulties made it impossible to guarantee the supply of lymph vaccine *regularly* and in an *active* state In some areas, owing to such difficulties, we had less than 15% "takes."

I think there can be little doubt that there are two different diseases, both clinically and epidemiologically, and that the viruses are different The distribution of the rash is the same, and the rash is in one stage , but in variola minor it is less profuse, and not so confluent in the axillæ and the groin, though confluent cases occur with facial distributions. The patient is not so seriously ill when the rash is in its pustular stage as in cases of variola major The differentiation between variola minor and chickenpox is often difficult unless care is taken to examine the extremities and the rash itself Generally mistakes are made most when the prodromal rash is not regarded as such, and the main disease is missed.

The immunological reactions between vaccinia virus and the various geographical strains of the variola minor virus also vary [1] There is yet no evidence to prove that variola virus strains change their virulence the major runs true to type, and so does the minor virus The differences are evident epidemiologically and clinically variola minor gives a negligible mortality, rarely reaching 3% compared with 20–30% for variola major. I suggest that the two diseases are entirely different entities, and that to confuse the two is to confuse the whole issue

Dr Millard's note that in the past inoculation used to be resorted to, and that inoculation was preferably from serious rather than mild cases is of historic interest In the Sudan in the 18th century inoculation was also practised. A piece of rag was tied round the arm of a serious case and its price was haggled over The person to be inoculated eventually bought it, having a guarantee not to get more than so many pocks If he had a severe attack he claimed his money back, if he survived Possible explanations are that the virus had "burnt itself out" in the serious case, or that the patient's reactions had reduced its virulence

Malakal.

J F E BLOSS
P.M.L (M O.H)
Upper Nile Province
Anglo Egyptian Sudan

MUNCHAUSEN'S SYNDROME

SIR,—A further example of the Munchausen syndrome was recalled to my notice today when a query arrived from the Royal Victoria Hospital, Folkestone, about a man treated here last April. A few days after his irregular discharge from the Western Infirmary, Glasgow, early in May, 1950, he was admitted as an emergency to the West London Hospital.

This man is 23 or 24, Irish, and of somewhat prognathous appearance He claims to be aspiring to the priesthood , and his complaints usually take the form of bleeding from nose, eyes, ears and urinary tract along with great pain of a renal-colic type He has a rooted objection to cystoscopy or catheterisation, the threat of which leads to a demand for discharge No cause can be found for his bleeding but sharp instruments may be found in his bed, and many of the blood-stained sites show no bleeding point. He tends to ascribe his symptoms to trauma before admission, and is admitted following collapse in the street

I should be most interested to know if he has been an inmate of other hospitals. I feel sure that he has been in many in the past nine months.

Western Infirmary
Glasgow

IAN A SHORT

---

[3] Visick, H S *Brit med. J* 1946 ii 941
[4] Taylor H *Lancet* Jan. 6 1951 p. 7
[5] Stead J R. *Ibid* p 12.
[6] Selye H Stress. Montreal 1951 p. 96
[7] Pannett, C A. Personal communication. 1924

[1] Horgan, E S., Haseeb M. A. Satti M. H *Brit. J exp Path* 1948 29 347

LYSIVANE AND ARTANE IN PARKINSONISM

SIR,—Dr Garai's conclusions (Feb 24) are most interesting My experience has been that 'Artane' is much more effective in postencephalitic parkinsonism than in the idiopathic and arteriosclerotic varieties, and Dr Garai's findings support this Of 31 postencephalitic patients 7 (23%) showed no improvement, whereas of 18 patients suffering from idiopathic and arteriosclerotic parkinsonism 6 (33%) were not improved

The large doses used by Dr Garai invite comment I find that where artane is effective, improvement is apparent on the second or third day [1] Where this does not occur, persistence with the drug is unlikely to result in success. Canelis et al [2] noted improvement within three days, continuing up to the end of the second week Dr Garai writes "it was found necessary in most cases to exceed 50 mg before full benefit was obtained" Was this the optimum dose, and was the benefit so obtained any the less when this was reduced to 20 mg or less daily ?

I agree that amphetamine has a potentiating effect on artane, especially in the control of oculogyric crises Where the number and severity of these is not satisfactorily reduced by artane alone, the addition of amphetamine may bring about the desired effect

Liverpool B K ELLENBOGEN

CAFESTOL IN RHEUMATOID ARTHRITIS

SIR,—In their letter of a year ago, Ferrari and Allegri [3] reported good results with 'Cafestol,' a new preparation obtained from the unsaponifiable fraction of the seed of *Coffea arabica* L, in 16 patients with polyarthritis due to rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, or degenerative arthritis of the spine The beneficial effects were more evident in the acute inflammatory disorders than in the degenerative Pain was rapidly diminished and there was progressive reduction in the articular swelling, temperature, and erythrocyte sedimentation rate (E S R) A steroid configuration has been ascribed to this vegetable substance, which Ferrari and Allegri claim to have the same clinical applications as the most potent steroids of animal origin, such as 'Cortisone' Their letter gave only a brief preliminary report without any clinical or experimental details

Cafestol is manufactured in Italy and marketed by Messrs Simes, of Milan So far we have not obtained any literature on the pharmacological or clinical aspects of this substance However, we received 3000 mg of the original substance, as marketed in Italy, for clinical trial, in addition to 3000 mg of a British substitute prepared especially for research investigations The Italian preparation was dissolved in olive oil, whereas the British substitute was dissolved in propylene glycol, and both were packed in ampoules containing 100 mg In view of these very limited supplies the investigation has been made on two patients only, each preparation being used entirely on one patient

Italian Cafestol

A married woman aged 45 had had rheumatoid arthritis for 22 years The onset was afebrile, insidious, and polyarticular There was no family history of rheumatism Five days before this trial began, the patient was admitted to hospital as an urgent case because of a sudden relapse, both hands, knees, and ankles being painful swollen and tender Radiography of her hands showed that she had stage 3 rheumatoid arthritis, according to the Steinbrocker classification [4] After clinical and laboratory investigations she was given 400 mg of cafestol intramuscularly daily for three days, and then 200 mg daily for nine days, making a total of 3000 mg After this her joint pains were slightly less, movements of the affected joints were a little easier, and the range of movements was slightly greater The pain in the knees, which was severe at the beginning of the course, became much less by the end of the course, and there were no new sites of pain. The laboratory findings (see table) show no significant changes in the E S R., packed-cell volume, plasma viscosity, or serum levels of sodium, potassium, or chlorides

LABORATORY FINDINGS

Date 1950	Blood				Serum levels (mg per 100 ml)			Urinary ketosteroids (mg per 24 hr)
	E S R *	P C V (%)	Plasma viscosity	Eosinophils per c mm	Sodium	Potassium	Chlorides	
				CASE 1				
Nov 30	41	46	23 0					4 5
Dec 4	41	46	23 0	145	326 1	18 4	358 7	(Menstruation)
„ 7	41	40	21 6	40	328 4	18 0	368 6	(Menstruation)
„ 11				145	327 1	18 5	360 2	7 7
„ 14	41	42	21 8	80	327 0	18 0	350 5	6 9
„ 18	41	43	21 8	55	324 7	18 4	351 8	5 5
				CASE 2				
Nov 6	39	37	20 3	35	317 0	16 7	334 0	6 2
„ 9	34	36	19 8	100	331 0	16 2	327 0	5 5
„ 22	23	35	19 5	120	333 0	15 9	343 0	5·6
30	20	37	19 0	110	328 0	17 4	353 0	5 0
Dec 4				50	327 9	19 4	360 0	5 1
„ 7	19	37	19 1	45	326 1	18 8	343 1	4·6
„ 11				35	325 8	19 1	349 0	(Menstruation)
„ 14	20	39	19 4	65	324 4	18 2	359 0	(Menstruation)
„ 18	25	38	19 2	100	324 0	18 7	340 5	5 3

In both cases daily intramuscular injections were begun on Dec. 6
* Spa hospitals method corrected rate

On the fifth day of the injections the patient complained of intermittent nausea which had begun soon after she started the injections and had got worse each day She did not vomit at any time She also complained of a "persistent taste of chlorodyne," which became less intense on the fifth day Visiting relations and fellow patients all said they could smell chlorodyne in her breath, but we could not detect the smell. So far as could be ascertained, she had not eaten or drunk anything containing chlorodyne or similar substances, and so far as we know, none is present in cafestol This symptom became less pronounced on the day after the daily dose of cafestol was reduced from 400 to 200 mg Nothing abnormal was detected in the urine, and no explanation can be offered for the curious statements

At the end of the course the patient appeared to be happy, full of optimism and generally improved, in spite of the negative laboratory findings

British Substitute

A young unmarried woman, aged 22, had had rheumatoid arthritis in the interphalangeal joints of both hands for 2 years The onset was afebrile, insidious, and polyarticular, the hips, ankles, elbows, and shoulders being affected in turn She had been in hospital for six weeks when the present trial was begun All her interphalangeal joints and both wrists were swollen and painful, with much restriction of movements Radiography showed a stage 2 rheumatoid arthritis. The left acromioclavicular joint was also involved She walked with pain and some difficulty There was no family history of rheumatism The eosinophil count (80 per c.mm) showed no response to adrenaline

She was given 400 mg of the British substitute for cafestol intramuscularly daily for three days, followed by 200 mg daily for nine days, making a total of 3000 mg During the course there was a gradual reduction in her joint-pains and she became much more cheerful

At the end of the course she had improved slightly, more particularly as regards pain, but it would be hard to say whether the improvement was greater than might have been expected from her condition before the course The laboratory findings (see table) showed no significant changes

Both these patients showed some clinical improvement, mainly in a diminution of their pain The improvement was slightly greater in the patient given the Italian cafestol, but the results were much less definite than one might have expected from the letter of Ferrari and Allegri [3]

---

[1] Ellenbogen B K *Lancet* 1950 i 1034

[2] Canelis M., Farnell F J McGavack T H *Amer J med Sci* 1949 **218** 655

[3] Ferrari G Allegri A *Lancet* 1950 i 687

[4] Steinbrocker O Traeger C H Batterman R C *J Amer med Ass* 1949 **140** 659

It was unfortunate that only such a small amount of cafestol was obtainable

We wish to thank Messrs British Schering Ltd , for supplying the cafestol and the British substitute

Regional Medical Research Centre
Royal Bath Hospital
Harrogate
G NORMAN MYERS
D N ROSS

SULPHONAMIDES AND PENICILLIN IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—Since publication of my article (Feb 3), my attention has been drawn to the earlier papers of Barber on the administration of sulphonamides for chronic lupus erythematosus He was treating patients as early as 1938 [1] and made a report in 1940 [2] summarising his experiences It is quite evident that he was well aware of the hazards of this form of treatment He stated

> Apart from the serious and sometimes fatal effects that may follow the administration of sulphonamides even in moderate dosage the severity of the reactions that often result from their use in lupus erythematosus makes it imperative that they should be given with the greatest discretion It cannot be too strongly emphasised that the indiscriminate use of the sulphonamides is fraught with danger

Further confirmation of the responsibility of the sulphonamides has come from the U S A Wile [3] has stated

> The incidence of this group has increased amazingly during the past fifteen or twenty years I believe this increase is real rather than apparent At the University Hospital (Ann Arbor Mich.) there has been an increase of 450% over this period Coincident in time with this increase there came in to the picture the more or less general use of the sulphonamide drugs, first used for serious infections such as pneumonia It soon became a general habit for many people to use sulphonamides for common colds and for all types of infections Many of these patients are photo sensitive and these drugs have shown themselves to be photo sensitizing agents

I have also had many letters from other observers supporting this thesis

London W 1 STEPHEN GOLD

INTRAVENOUS IRON

SIR,—Dr Klopper, commenting (March 3) on the recent work of Dr Scott and Dr Govan (Feb 17) shares with them a difficulty in interpreting the percentage utilisation of iron administered intravenously during pregnancy I would like to draw attention to a mathematical observation which occurred to me when I was engaged in similar work three years ago

In the absence of iron deficiency as pregnancy advances there is a slight increase in the total amount of circulating hæmoglobin but for the purpose of this note let it be assumed that it remains constant In a perfectly normal pregnancy, where no iron deficiency can be shown to exist at about the 30th week of gestation quite a usual finding would be a hæmoglobin level of 75% Now this fall in percentage is due to fluid retention and consequent hæmodilution and a finding of 75% Hb is produced by the same total circulating hæmoglobin that gave a reading of 100% before pregnancy began Treatment of such a case on the non pregnant basis that 100 mg elemental iron will result in a 4% increase in the hæmoglobin level, will obviously result in a finding that the utilisation of iron is nil.

Further, assume a similar case, but one with demonstrable iron deficiency anæmia and in which the hæmoglobin level is 70% If the hæmodilution is the same in this case, this hæmoglobin level represents a non-pregnant level of $\frac{100}{75} \times 70 = 93\%$ Such a case is therefore not 30% deficient in hæmoglobin, but 7% , and the anæmia should be corrected by the injection of 200 mg iron, and not 750 mg as would appear at first sight If 750 mg iron were injected, it is evident that some large quantity, in the region of 500 mg , would be diverted to storage depots and the calculated percentage utilisation would be very low

It will be seen therefore, that the treatment by present methods of iron deficiency anæmia in pregnancy results in gross overdosage In practice this is a good thing, for the reason that the very presence of an iron-deficiency anæmia in pregnancy is an indication that depot stores of iron are very low and that they would benefit from the excess dosage

The problem of iron deficiency anæmia in pregnancy is obscured by a lack of clear understanding of the total circulating blood-volume during pregnancy

Kidsgrove Staffs. D G FRENCH

PERSONAL HYGIENE

SIR,—Dr Bourne (Jan 27), stressing the importance of cleansing the hands from any fæcal contamination, suggests the fitting of foot controls for flushing the cistern, opening the door of the W C , and turning the tap over the basin A far more practicable suggestion is that all elementary school teachers should instruct their children that what might be called the toilet paper hand should never be used for these operations until cleaned It is extraordinary how quickly this habit can be learned so that it is repulsive to the child for that hand to be used for these purposes until it has gone under the tap

Petworth Sussex A H SPICER

CORTISONE AND FAT METABOLISM

SIR,—It is generally assumed that adrenocorticotropic hormone and other anterior pituitary hormones influence fat mobilisation and increase the fat content of the liver , but the influence of ' Cortisone ' on fat metabolism has not yet been ascertained In clinical research Sprague et al ,[1] Adlersberg et al.,[2] and Sala et al.[3] have found that cortisone increases plasma phospholipids and cholesterol. According to Winter et al ,[4] Kobernick and More,[5] and Rich et al.,[6] it produces hyperlipæmia in rats and rabbits Payne,[7] on the other hand, minimises the rôle of adrenal cortex in fat metabolism, and Levin and Farber [8] deny that cortisone may provoke fatty liver

We have determined the fat content of the liver in two groups of adult male rats, respectively treated daily with 1 and 5 mg of cortisone for 70 and 20 days.

The rats were fed a diet consisting of 56% carbohydrate 30% protein 10% fat with adequate supplement of salts vitamins and lipotropic factors The experimental groups consumed the same quantity of food daily Dried and powdered liver was extracted with ether by reflux distillation The fat content of the livers was significantly higher in cortisone treated animals than in controls (P values of 0·99 determined by the use of Student's *t*) Post-mortem examination showed varying degrees of hepatic perilobular steatosis without necrotic foci or fibrous proliferation body fat was

---

[1] Barber H W *Lancet* 1938 ii 668
[2] *Ibid* 1940 i 553
[3] Wile J U *Arch. Derm Syph Chicago* 1931 63 49

---

[1] Sprague R G Power M H P Mason H L Albert A Mathieson D R Hench P S Kendall E C Slocumb C H Polley H F *Arch intern Med* 1950 85 199
[2] Adlersberg D Schaefer L E Dritch R *Proc Soc exp Biol Med* 1950 74 877
[3] Sala G Fasoli A Bonelli M Bonomo E Ratti G Migliavacca A Ballabio C B *Reumatismo* 1950 suppl 3 p 33
[4] Winter C A Silber R H Stoerk, H C *Endocrinology* 1950 47 60
[5] Kobernick, S D More R H *Proc Soc exp Biol Med.* 1950 74 602
[6] Rich A. R. Cochran T H. McGoon D C *Bull Johns Hopk Hosp* 1951 88 101
[7] Payne R W *Endocrinology* 1949 45 305
[8] Levin L Farber R K. *Proc Soc exp Biol Med* 1950 74 758

LYSIVANE AND ARTANE IN PARKINSONISM

SIR,—Dr Garai's conclusions (Feb 24) are most interesting My experience has been that 'Artane' is much more effective in postencephalitic parkinsonism than in the idiopathic and arteriosclerotic varieties, and Dr Garai's findings support this Of 31 postencephalitic patients 7 (23%) showed no improvement, whereas of 18 patients suffering from idiopathic and arteriosclerotic parkinsonism 6 (33%) were not improved

The large doses used by Dr Garai invite comment I find that where artane is effective, improvement is apparent on the second or third day [1] Where this does not occur, persistence with the drug is unlikely to result in success Canelis et al [2] noted improvement within three days, continuing up to the end of the second week Dr Garai writes "it was found necessary in most cases to exceed 50 mg before full benefit was obtained" Was this the optimum dose, and was the benefit so obtained any the less when this was reduced to 20 mg or less daily ?

I agree that amphetamine has a potentiating effect on artane, especially in the control of oculogyric crises Where the number and severity of these is not satisfactorily reduced by artane alone, the addition of amphetamine may bring about the desired effect

Liverpool B K ELLENBOGEN

CAFESTOL IN RHEUMATOID ARTHRITIS

SIR,—In their letter of a year ago, Ferrari and Allegri [3] reported good results with 'Cafestol,' a new preparation obtained from the unsaponifiable fraction of the seed of *Coffea arabica* L, in 16 patients with polyarthritis due to rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, or degenerative arthritis of the spine The beneficial effects were more evident in the acute inflammatory disorders than in the degenerative Pain was rapidly diminished and there was progressive reduction in the articular swelling, temperature, and erythrocyte sedimentation rate (E S R) A steroid configuration has been ascribed to this vegetable substance, which Ferrari and Allegri claim to have the same clinical applications as the most potent steroids of animal origin, such as 'Cortisone' Their letter gave only a brief preliminary report without any clinical or experimental details

Cafestol is manufactured in Italy and marketed by Messrs Simes, of Milan So far we have not obtained any literature on the pharmacological or clinical aspects of this substance However, we received 3000 mg of the original substance, as marketed in Italy, for clinical trial, in addition to 3000 mg of a British substitute prepared especially for research investigations The Italian preparation was dissolved in olive oil, whereas the British substitute was dissolved in propylene glycol, and both were packed in ampoules containing 100 mg In view of these very limited supplies the investigation has been made on two patients only, each preparation being used entirely on one patient

Italian Cafestol

A married woman aged 45 had had rheumatoid arthritis for 22 years The onset was afebrile, insidious, and polyarticular There was no family history of rheumatism Five days before this trial began, the patient was admitted to hospital as an urgent case because of a sudden relapse, both hands, knees, and ankles being painful, swollen and tender Radiography of her hands showed that she had stage 3 rheumatoid arthritis, according to the Steinbrocker classification [4] After clinical and laboratory investigations she was given 400 mg of cafestol intramuscularly daily for three days and then 200 mg daily for nine days, making a total of 3000 mg After this her joint pains were slightly less, movements of the affected joints were a little easier, and the range of movements was slightly greater The pain in the knees, which was severe at the beginning of the course, became much less by the end of the course, and there were no new sites of pain The laboratory findings (see table) show no significant changes in the E S R , packed cell volume, plasma viscosity, or serum levels of sodium, potassium, or chlorides

LABORATORY FINDINGS

Date 1950	Blood: E S R *	Blood: P C V (%)	Blood: Plasma viscosity	Blood: Eosinophils per c mm	Serum levels (mg per 100 ml): Sodium	Serum levels (mg per 100 ml): Potassium	Serum levels (mg per 100 ml): Chlorides	Urinary ketosteroids (mg per 24 hr)
				CASE 1				
Nov 30	41	46	23 0					4 5
Dec 4	41	46	23 0	145	326 1	18 4	358 7	(Menstruation)
, 7	41	40	21 6	40	328 4	18 0	368 6	(Menstruation)
,, 11				145	327 1	18 5	360 2	7 7
,, 14	41	42	21 8	80	327 0	18 0	350 5	6 9
, 18	41	43	21 8	55	324 7	18 4	351 8	5 5
				CASE 2				
Nov 6	39	37	20 3	35	317 0	16 7	334 0	6 2
,, 9	34	36	19 8	100	331 0	16 2	327 0	5 5
,, 22	23	35	19 5	120	333 0	15 9	343 0	5 6
, 30	20	37	19 0	110	328 0	17 4	353 0	5 0
Dec 4				50	327 9	19 4	360 0	5 1
,, 7	19	37	19 1	45	326 1	18 8	343 1	4 6
, 11				35	325 8	19 1	349 0	(Menstruation)
, 14	26	39	19 4	65	324 4	18 2	359 0	(Menstruation)
,, 18	25	38	19 2	100	324 0	18 7	340 5	5 3

In both cases daily intramuscular injections were begun on Dec. 6
* Spa hospitals method corrected rate

On the fifth day of the injections the patient complained of intermittent nausea which had begun soon after she started the injections and had got worse each day She did not vomit at any time She also complained of a "persistent taste of chlorodyne," which became less intense on the fifth day Visiting relations and fellow patients all said they could smell chlorodyne in her breath, but we could not detect the smell So far as could be ascertained, she had not eaten or drunk anything containing chlorodyne or similar substances, and so far as we know, none is present in cafestol This symptom became less pronounced on the day after the daily dose of cafestol was reduced from 400 to 200 mg Nothing abnormal was detected in the urine, and no explanation can be offered for the curious statements

At the end of the course the patient appeared to be happy, full of optimism and generally improved, in spite of the negative laboratory findings

British Substitute

A young unmarried woman, aged 22, had had rheumatoid arthritis in the interphalangeal joints of both hands for 2 years The onset was afebrile, insidious, and polyarticular, the hips, ankles, elbows, and shoulders being affected in turn She had been in hospital for six weeks when the present trial was begun All her interphalangeal joints and both wrists were swollen and painful, with much restriction of movements Radiography showed a stage 2 rheumatoid arthritis. The left acromioclavicular joint was also involved She walked with pain and some difficulty There was no family history of rheumatism The eosinophil count (80 per c mm) showed no response to adrenaline

She was given 400 mg of the British substitute for cafestol intramuscularly daily for three days, followed by 200 mg daily for nine days, making a total of 3000 mg During the course there was a gradual reduction in her joint pains and she became much more cheerful

At the end of the course she had improved slightly, more particularly as regards pain, but it would be hard to say whether the improvement was greater than might have been expected from her condition before the course The laboratory findings (see table) showed no significant changes

Both these patients showed some clinical improvement, mainly in a diminution of their pain The improvement was slightly greater in the patient given the Italian cafestol, but the results were much less definite than one might have expected from the letter of Ferrari and Allegri [3]

---

1 Ellenbogen B K *Lancet* 1950 i 1034
2 Canelis M Farnell F J McGavack T H *Amer J med Sci* 1949 218 655
3 Ferrari G Allegri A *Lancet* 1950 i 687
4 Steinbrocker O Traeger C H Batterman, R C *J Amer med Ass* 1949 140 659

It was unfortunate that only such a small amount of cafestol was obtainable

We wish to thank Messrs British Schering Ltd, for supplying the cafestol and the British substitute

Regional Medical Research Centre,
Royal Bath Hospital,
Harrogate
G NORMAN MYERS
D N ROSS

SULPHONAMIDES AND PENICILLIN IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—Since publication of my article (Feb 3), my attention has been drawn to the earlier papers of Barber on the administration of sulphonamides for chronic lupus erythematosus He was treating patients as early as 1938[1] and made a report in 1940[2] summarising his experiences It is quite evident that he was well aware of the hazards of this form of treatment He stated

> “Apart from the serious and sometimes fatal effects that may follow the administration of sulphonamides even in moderate dosage, the severity of the reactions that often result from their use in lupus erythematosus makes it imperative that they should be given with the greatest discretion It cannot be too strongly emphasised that the indiscriminate use of the sulphonamides is fraught with danger ”

Further confirmation of the responsibility of the sulphonamides has come from the U S A Wile[3] has stated

> ‘The incidence of this group has increased amazingly during the past fifteen or twenty years I believe this increase is real rather than apparent At the University Hospital (Ann Arbor, Mich) there has been an increase of 450% over this period Coincident in time with this increase there came in to the picture the more or less general use of the sulphonamide drugs, first used for serious infections such as pneumonia It soon became a general habit for many people to use sulphonamides for common colds and for all types of infections Many of these patients are photo sensitive and these drugs have shown themselves to be photo sensitizing agents ’

I have also had many letters from other observers supporting this thesis

London W 1
STEPHEN GOLD

INTRAVENOUS IRON

SIR,—Dr Klopper, commenting (March 3) on the recent work of Dr Scott and Dr Govan (Feb 17), shares with them a difficulty in interpreting the percentage utilisation of iron administered intravenously during pregnancy I would like to draw attention to a mathematical observation which occurred to me when I was engaged in similar work three years ago

In the absence of iron deficiency, as pregnancy advances there is a slight increase in the total amount of circulating hæmoglobin but for the purpose of this note let it be assumed that it remains constant In a perfectly normal pregnancy, where no iron deficiency can be shown to exist, at about the 30th week of gestation quite a usual finding would be a hæmoglobin level of 75% Now this fall in percentage is due to fluid retention and consequent hæmodilution, and a finding of 75% Hb is produced by the same total circulating hæmoglobin that gave a reading of 100% before pregnancy began Treatment of such a case on the non pregnant basis that 100 mg elemental iron will result in a 4% increase in the hæmoglobin level, will obviously result in a finding that the utilisation of iron is nil

Further, assume a similar case, but one with demonstrable iron deficiency anæmia, and in which the hæmoglobin level is 70% If the hæmodilution is the same in this case, this hæmoglobin level represents a non pregnant level of $\frac{100}{75} \times 70 = 93\%$ Such a case is therefore not 30% deficient in hæmoglobin, but 7%, and the anæmia should be corrected by the injection of 200 mg iron, and not 750 mg as would appear at first sight If 750 mg iron were injected, it is evident that some large quantity, in the region of 500 mg, would be diverted to storage depots and the calculated percentage utilisation would be very low

It will be seen therefore, that the treatment by present methods of iron deficiency anæmia in pregnancy results in gross overdosage In practice this is a good thing, for the reason that the very presence of an iron deficiency anæmia in pregnancy is an indication that depot stores of iron are very low and that they would benefit from the excess dosage

The problem of iron deficiency anæmia in pregnancy is obscured by a lack of clear understanding of the total circulating blood volume during pregnancy

Kidsgrove Staffs
D G FRENCH

---

1 Barber H W *Lancet* 1938 ii 668
2 *Ibid* 1940 i 583
3 Wile J U *Arch Derm Syph Chicago* 1951 63 49

PERSONAL HYGIENE

SIR,—Dr Bourne (Jan 27), stressing the importance of cleansing the hands from any fæcal contamination, suggests the fitting of foot controls for flushing the cistern, opening the door of the w c, and turning the tap over the basin A far more practicable suggestion is that all elementary school teachers should instruct their children that what might be called the toilet paper hand should never be used for these operations until cleaned It is extraordinary how quickly this habit can be learned so that it is repulsive to the child for that hand to be used for these purposes until it has gone under the tap

Petworth Sussex
A H SPICER

CORTISONE AND FAT METABOLISM

SIR,—It is generally assumed that adrenocorticotropic hormone and other anterior pituitary hormones influence fat mobilisation and increase the fat content of the liver, but the influence of ‘Cortisone’ on fat metabolism has not yet been ascertained In clinical research Sprague et al,[1] Adlersberg et al,[2] and Sala et al[3] have found that cortisone increases plasma phospholipids and cholesterol According to Winter et al,[4] Kobernick and More,[5] and Rich et al,[6] it produces hyperlipæmia in rats and rabbits Payne,[7] on the other hand, minimises the rôle of adrenal cortex in fat metabolism, and Levin and Farber[8] deny that cortisone may provoke fatty liver

We have determined the fat content of the liver in two groups of adult male rats, respectively treated daily with 1 and 5 mg of cortisone for 70 and 20 days

The rats were fed a diet consisting of 56% carbohydrate, 30% protein, 10% fat, with adequate supplement of salts vitamins, and lipotropic factors The experimental groups consumed the same quantity of food daily Dried and powdered liver was extracted with ether by reflux distillation The fat content of the livers was significantly higher in cortisone treated animals than in controls (P values of 0 99 determined by the use of Student s *t*) Post-mortem examination showed varying degrees of hepatic perilobular steatosis, without necrotic foci or fibrous proliferation, body fat was

---

1 Sprague R G Power M H P Mason H L Albert, A Mathieson D R Hench P S Kendall E C Slocumb C H Polley H F *Arch intern Med* 1950 85 199
2 Adlersberg D Schaefer L E Dritch R *Proc Soc exp Biol Med* 1950 74 877
3 Sala G Fasoli A Bonelli M Bonomo E Ratti G Migliavacca A Ballabio C B *Reumatismo* 1950 suppl 3 p 33
4 Winter C A, Silber R H Stoerk H C *Endocrinology* 1950 47 60
5 Kobernick S D More R H *Proc Soc exp Biol Med* 1950 74 602
6 Rich A R Cochran T H, McGoon D C *Bull Johns Hopk Hosp* 1951 88 101
7 Payne R W *Endocrinology* 1949 45 305
8 Levin L Farber R K *Proc Soc exp Biol Med* 1950 74 758

LYSIVANE AND ARTANE IN PARKINSONISM

SIR,—Dr Garai's conclusions (Feb 24) are most interesting My experience has been that 'Artane' is much more effective in postencephalitic parkinsonism than in the idiopathic and arteriosclerotic varieties, and Dr Garai's findings support this Of 31 postencephalitic patients 7 (23%) showed no improvement, whereas of 18 patients suffering from idiopathic and arteriosclerotic parkinsonism 6 (33%) were not improved

The large doses used by Dr Garai invite comment I find that where artane is effective, improvement is apparent on the second or third day [1] Where this does not occur, persistence with the drug is unlikely to result in success Canelis et al [2] noted improvement within three days, continuing up to the end of the second week Dr Garai writes "it was found necessary in most cases to exceed 50 mg before full benefit was obtained" Was this the optimum dose, and was the benefit so obtained any the less when this was reduced to 20 mg or less daily ?

I agree that amphetamine has a potentiating effect on artane, especially in the control of oculogyric crises Where the number and severity of these is not satisfactorily reduced by artane alone, the addition of amphetamine may bring about the desired effect

Liverpool B K ELLENBOGEN

CAFESTOL IN RHEUMATOID ARTHRITIS

SIR,—In their letter of a year ago, Ferrari and Allegri [3] reported good results with 'Cafestol,' a new preparation obtained from the unsaponifiable fraction of the seed of *Coffea arabica* L , in 16 patients with polyarthritis due to rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, or degenerative arthritis of the spine The beneficial effects were more evident in the acute inflammatory disorders than in the degenerative Pain was rapidly diminished and there was progressive reduction in the articular swelling, temperature, and erythrocyte-sedimentation rate (E S R) A steroid configuration has been ascribed to this vegetable substance, which Ferrari and Allegri claim to have the same clinical applications as the most potent steroids of animal origin, such as 'Cortisone' Their letter gave only a brief preliminary report without any clinical or experimental details

Cafestol is manufactured in Italy and marketed by Messrs Simes, of Milan So far we have not obtained any literature on the pharmacological or clinical aspects of this substance However, we received 3000 mg of the original substance, as marketed in Italy, for clinical trial, in addition to 3000 mg of a British substitute prepared especially for research investigations The Italian preparation was dissolved in olive oil, whereas the British substitute was dissolved in propylene glycol, and both were packed in ampoules containing 100 mg In view of these very limited supplies the investigation has been made on two patients only, each preparation being used entirely on one patient

Italian Cafestol

A married woman, aged 45 had had rheumatoid arthritis for 22 years The onset was afebrile, insidious, and polyarticular There was no family history of rheumatism Five days before this trial began, the patient was admitted to hospital as an urgent case because of a sudden relapse, both hands, knees, and ankles being painful, swollen, and tender Radiography of her hands showed that she had stage 3 rheumatoid arthritis, according to the Steinbrocker classification [4] After clinical and laboratory investigations she was given 400 mg of cafestol intramuscularly daily for three days, and then 200 mg daily for nine days, making a total of 3000 mg After this her joint pains were slightly less, movements of the affected joints were a little easier, and the range of movements was slightly greater The pain in the knees, which was severe at the beginning of the course, became much less by the end of the course, and there were no new sites of pain. The laboratory findings (see table) show no significant changes in the E S R , packed cell volume, plasma viscosity, or serum levels of sodium, potassium, or chlorides

LABORATORY FINDINGS

Date 1950	Blood: E S R *	Blood: P C V (%)	Blood: Plasma viscosity	Blood: Eosinophils per c.mm	Serum levels (mg per 100 ml): Sodium	Serum levels (mg per 100 ml): Potassium	Serum levels (mg per 100 ml): Chlorides	Urinary ketosteroids (mg per 24 hr)
CASE 1								
Nov 30	41	46	23 0					4 5
Dec 4	41	46	23 0	145	326 1	18 4	358 7	(Menstruation)
„ 7	41	40	21 6	40	328 4	18 0	368 6	(Menstruation)
„ 11				145	327 1	18 5	360 2	7 7
„ 14	41	42	21 8	80	327 0	18 0	350 5	6 9
„ 18	41	43	21 8	55	324 7	18 4	351 8	5 5
CASE 2								
Nov 6	39	37	20 3	35	317 0	16 7	334 0	6 2
„ 9	34	36	19 8	100	331 0	16 2	327 0	5 5
„ 22	23	35	19 5	120	333 0	15 9	343 0	5 6
„ 30	20	37	19 0	110	328 0	17 4	353 0	5 0
Dec 4				50	327 9	19 4	360 0	5 1
„ 7	19	37	19 1	45	326 1	18 8	343 1	4 6
„ 11				35	325 8	19 1	349 0	(Menstruation)
„ 14	26	39	19 4	65	324 4	18 2	359 0	(Menstruation)
„ 18	25	38	19 2	100	324 0	18 7	340 5	5 3

In both cases daily intramuscular injections were begun on Dec. 6
* Spa hospitals method corrected rate

On the fifth day of the injections the patient complained of intermittent nausea which had begun soon after she started the injections and had got worse each day She did not vomit at any time She also complained of a "persistent taste of chlorodyne," which became less intense on the fifth day Visiting relations and fellow patients all said they could smell chlorodyne in her breath, but we could not detect the smell. So far as could be ascertained, she had not eaten or drunk anything containing chlorodyne or similar substances, and so far as we know, none is present in cafestol This symptom became less pronounced on the day after the daily dose of cafestol was reduced from 400 to 200 mg Nothing abnormal was detected in the urine, and no explanation can be offered for the curious statements

At the end of the course the patient appeared to be happy, full of optimism and generally improved, in spite of the negative laboratory findings

British Substitute

A young unmarried woman, aged 22, had had rheumatoid arthritis in the interphalangeal joints of both hands for 2 years The onset was afebrile, insidious, and polyarticular, the hips, ankles, elbows, and shoulders being affected in turn. She had been in hospital for six weeks when the present trial was begun All her interphalangeal joints and both wrists were swollen and painful, with much restriction of movements Radiography showed a stage 2 rheumatoid arthritis. The left acromioclavicular joint was also involved She walked with pain and some difficulty There was no family history of rheumatism The eosinophil count (80 per c.mm.) showed no response to adrenaline

She was given 400 mg of the British substitute for cafestol intramuscularly daily for three days, followed by 200 mg daily for nine days, making a total of 3000 mg During the course there was a gradual reduction in her joint-pains and she became much more cheerful

At the end of the course she had improved slightly, more particularly as regards pain, but it would be hard to say whether the improvement was greater than might have been expected from her condition before the course The laboratory findings (see table) showed no significant changes

Both these patients showed some clinical improvement, mainly in a diminution of their pain The improvement was slightly greater in the patient given the Italian cafestol, but the results were much less definite than one might have expected from the letter of Ferrari and Allegri [3]

---

[1] Ellenbogen B K *Lancet* 1950 i 1034
[2] Canelis M Farnell F J McGavack, T H *Amer J med Sci* 1949 218 655
[3] Ferrari G Allegri A *Lancet* 1950 i 687
[4] Steinbrocker, O Traeger C H Batterman, R C *J Amer med Ass* 1949 140 659

It was unfortunate that only such a small amount of cafestol was obtainable.

We wish to thank Messrs British Schering Ltd., for supplying the cafestol and the British substitute.

Regional Medical Research Centre
Royal Bath Hospital,
Harrogate

G. NORMAN MYERS
D. N. ROSS

SULPHONAMIDES AND PENICILLIN IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—Since publication of my article (Feb. 3), my attention has been drawn to the earlier papers of Barber on the administration of sulphonamides for chronic lupus erythematosus. He was treating patients as early as 1938[1] and made a report in 1940[2] summarising his experiences. It is quite evident that he was well aware of the hazards of this form of treatment. He stated:

> "Apart from the serious and sometimes fatal effects that may follow the administration of sulphonamides even in moderate dosage the severity of the reactions that often result from their use in lupus erythematosus makes it imperative that they should be given with the greatest discretion. . . . It cannot be too strongly emphasised that the indiscriminate use of the sulphonamides is fraught with danger."

Further confirmation of the responsibility of the sulphonamides has come from the U.S.A. Wile[3] has stated:

> "The incidence of this group has increased amazingly during the past fifteen or twenty years. I believe this increase is real rather than apparent. At the University Hospital (Ann Arbor, Mich.) there has been an increase of 450% over this period. . . . Coincident in time with this increase there came in to the picture the more or less general use of the sulphonamide drugs, first used for serious infections such as pneumonia. It soon became a general habit for many people to use sulphonamides for common colds and for all types of infections. Many of these patients are photosensitive . . . and these drugs have shown themselves to be photo-sensitizing agents."

I have also had many letters from other observers supporting this thesis.

London, W.1 STEPHEN GOLD

INTRAVENOUS IRON

SIR,—Dr. Klopper, commenting (March 3) on the recent work of Dr. Scott and Dr. Govan (Feb. 17), shares with them a difficulty in interpreting the percentage utilisation of iron administered intravenously during pregnancy. I would like to draw attention to a mathematical observation which occurred to me when I was engaged in similar work three years ago.

In the absence of iron deficiency, as pregnancy advances there is a slight increase in the total amount of circulating hæmoglobin, but for the purpose of this note let it be assumed that it remains constant. In a perfectly normal pregnancy, where no iron deficiency can be shown to exist, at about the 30th week of gestation quite a usual finding would be a hæmoglobin level of 75%. Now this fall in percentage is due to fluid retention and consequent hæmodilution, and a finding of 75% Hb is produced by the same total circulating hæmoglobin that gave a reading of 100% before pregnancy began. Treatment of such a case on the non-pregnant basis that 100 mg. elemental iron will result in a 4% increase in the hæmoglobin level, will obviously result in a finding that the utilisation of iron is nil.

Further, assume a similar case, but one with demonstrable iron-deficiency anæmia, and in which the hæmoglobin level is 70%. If the hæmodilution is the same in this case, this hæmoglobin level represents a non-pregnant level of $\frac{100}{75} \times 70 = 93\%$. Such a case is therefore not 30% deficient in hæmoglobin, but 7%, and the anæmia should be corrected by the injection of 200 mg. iron, and not 750 mg. as would appear at first sight. If 750 mg. iron were injected, it is evident that some large quantity, in the region of 500 mg., would be diverted to storage depots and the calculated percentage utilisation would be very low.

It will be seen, therefore, that the treatment by present methods of iron-deficiency anæmia in pregnancy results in gross overdosage. In practice this is a good thing, for the reason that the very presence of an iron-deficiency anæmia in pregnancy is an indication that depot stores of iron are very low and that they would benefit from the excess dosage.

The problem of iron-deficiency anæmia in pregnancy is obscured by a lack of clear understanding of the total circulating blood-volume during pregnancy.

Kidsgrove, Staffs D. G. FRENCH

PERSONAL HYGIENE

SIR,—Dr. Bourne (Jan. 27), stressing the importance of cleansing the hands from any fæcal contamination, suggests the fitting of foot controls for flushing the cistern, opening the door of the w.c., and turning the tap over the basin. A far more practicable suggestion is that all elementary school teachers should instruct their children that what might be called the toilet-paper hand should never be used for these operations until cleaned. It is extraordinary how quickly this habit can be learned so that it is repulsive to the child for that hand to be used for these purposes until it has gone under the tap.

Petworth, Sussex A. H. SPICER

CORTISONE AND FAT METABOLISM

SIR,—It is generally assumed that adrenocorticotropic hormone and other anterior pituitary hormones influence fat mobilisation and increase the fat content of the liver, but the influence of 'Cortisone' on fat metabolism has not yet been ascertained. In clinical research Sprague et al.,[1] Adlersberg et al.,[2] and Sala et al.[3] have found that cortisone increases plasma phospholipids and cholesterol. According to Winter et al.,[4] Kobernick and More,[5] and Rich et al.,[6] it produces hyperlipæmia in rats and rabbits. Payne,[7] on the other hand, minimises the rôle of adrenal cortex in fat metabolism, and Levin and Farber[8] deny that cortisone may provoke fatty liver.

We have determined the fat content of the liver in two groups of adult male rats, respectively treated daily with 1 and 5 mg. of cortisone for 70 and 20 days.

The rats were fed a diet consisting of 56% carbohydrate, 30% protein, 10% fat, with adequate supplement of salts, vitamins, and lipotropic factors. The experimental groups consumed the same quantity of food daily. Dried and powdered liver was extracted with ether by reflux distillation. The fat content of the livers was significantly higher in cortisone-treated animals than in controls (P values of 0·99 determined by the use of Student's *t*). Post-mortem examination showed varying degrees of hepatic perilobular steatosis without necrotic foci or fibrous proliferation; body fat was

---

[1] Barber, H. W. *Lancet*, 1938, ii, 668.
[2] *Ibid*, 1940, i, 583.
[3] Wile, J. U. *Arch. Derm. Syph., Chicago*, 1951, 63, 41.

---

[1] Sprague, R. G., Power, M. H., P. Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S., Kendall, E. C., Slocumb, C. H., Polley, H. F. *Arch. intern. Med.* 1950, 85, 199.
[2] Adlersberg, D., Schaefer, L. E., Dritch, R. *Proc. Soc. exp. Biol. Med.* 1950, 74, 877.
[3] Sala, G., Fasoli, A., Bonelli, M., Bonomo, E., Ratti, G., Migliavacca, A., Ballabio, C. B. *Reumatismo*, 1950, suppl. 3, p. 33.
[4] Winter, C. A., Silber, R. H., Stoerk, H. C. *Endocrinology*, 1950, 47, 60.
[5] Kobernick, S. D., More, R. H. *Proc. Soc. exp. Biol. Med.* 1950, 74, 602.
[6] Rich, A. R., Cochran, T. H., McGoon, D. C. *Bull. Johns Hopk. Hosp.* 1951, 88, 101.
[7] Payne, R. W. *Endocrinology*, 1949, 45, 305.
[8] Levin, L., Farber, R. K. *Proc. Soc. exp. Biol. Med.* 1950, 74, 758.

LYSIVANE AND ARTANE IN PARKINSONISM

SIR,—Dr Garai's conclusions (Feb. 24) are most interesting. My experience has been that 'Artane' is much more effective in postencephalitic parkinsonism than in the idiopathic and arteriosclerotic varieties, and Dr Garai's findings support this. Of 31 postencephalitic patients 7 (23%) showed no improvement, whereas of 18 patients suffering from idiopathic and arteriosclerotic parkinsonism 6 (33%) were not improved.

The large doses used by Dr Garai invite comment. I find that where artane is effective, improvement is apparent on the second or third day.[1] Where this does not occur, persistence with the drug is unlikely to result in success. Canelis et al.[2] noted improvement within three days, continuing up to the end of the second week. Dr Garai writes: "it was found necessary in most cases to exceed 50 mg. before full benefit was obtained." Was this the optimum dose, and was the benefit so obtained any the less when this was reduced to 20 mg. or less daily?

I agree that amphetamine has a potentiating effect on artane, especially in the control of oculogyric crises. Where the number and severity of these is not satisfactorily reduced by artane alone, the addition of amphetamine may bring about the desired effect.

Liverpool. B. K. ELLENBOGEN.

CAFESTOL IN RHEUMATOID ARTHRITIS

SIR,—In their letter of a year ago, Ferrari and Allegri[3] reported good results with 'Cafestol,' a new preparation obtained from the unsaponifiable fraction of the seed of *Coffea arabica* L., in 16 patients with polyarthritis due to rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, or degenerative arthritis of the spine. The beneficial effects were more evident in the acute inflammatory disorders than in the degenerative. Pain was rapidly diminished and there was progressive reduction in the articular swelling, temperature, and erythrocyte sedimentation rate (E.S.R.). A steroid configuration has been ascribed to this vegetable substance, which Ferrari and Allegri claim to have the same clinical applications as the most potent steroids of animal origin, such as 'Cortisone.' Their letter gave only a brief preliminary report without any clinical or experimental details.

Cafestol is manufactured in Italy and marketed by Messrs. Simes, of Milan. So far we have not obtained any literature on the pharmacological or clinical aspects of this substance. However, we received 3000 mg. of the original substance, as marketed in Italy, for clinical trial, in addition to 3000 mg. of a British substitute prepared especially for research investigations. The Italian preparation was dissolved in olive oil, whereas the British substitute was dissolved in propylene glycol, and both were packed in ampoules containing 100 mg. *In view of these very limited supplies the investigation has been made on two patients only, each preparation being used entirely on one patient.*

Italian Cafestol

A married woman aged 45 had had rheumatoid arthritis for 22 years. The onset was afebrile, insidious, and polyarticular. There was no family history of rheumatism. Five days before this trial began, the patient was admitted to hospital as an urgent case because of a sudden relapse, both hands, knees, and ankles being painful, swollen, and tender. Radiography of her hands showed that she had stage 3 rheumatoid arthritis, according to the Steinbrocker classification.[4] After clinical and laboratory investigations she was given 400 mg. of cafestol intramuscularly daily for three days, and then 200 mg. daily for nine days, making a total of 3000 mg. After this her joint pains were slightly less, movements of the affected joints were a little easier, and the range of movements was slightly greater. The pain in the knees, which was severe at the beginning of the course, became much less by the end of the course, and there were no new sites of pain. The laboratory findings (see table) show no significant changes in the E.S.R., packed cell volume, plasma viscosity, or serum levels of sodium, potassium, or chlorides.

LABORATORY FINDINGS

Date 1950	Blood				Serum levels (mg. per 100 ml.)			Urinary ketosteroids (mg. per 24 hr.)
	E.S.R.*	P.C.V. (%)	Plasma viscosity	Eosinophils per c.mm.	Sodium	Potassium	Chlorides	
				CASE 1				
Nov. 30	41	46	23.0					4.5
Dec. 4	41	46	23.0	145	326.1	18.4	358.7	(Menstruation)
,, 7	41	40	21.6	40	328.4	18.0	368.6	(Menstruation)
,, 11				145	327.1	18.5	360.2	7.7
,, 14	41	42	21.8	80	327.0	18.0	350.5	6.9
,, 18	41	43	21.8	55	324.7	18.4	351.8	5.5
				CASE 2				
Nov. 6	39	37	20.3	35	317.0	16.7	334.0	6.2
,, 9	34	36	19.8	100	331.0	16.2	327.0	5.5
,, 22	23	35	19.5	120	333.0	15.9	343.0	5.6
,, 30	20	37	19.0	110	328.0	17.4	353.0	5.0
Dec. 4				50	327.9	19.4	360.0	5.1
,, 7	19	37	19.1	45	326.1	18.8	343.1	4.6
,, 11				35	325.8	19.1	349.0	(Menstruation)
,, 14	26	39	19.4	65	324.4	18.2	359.0	(Menstruation)
,, 18	25	38	19.2	100	324.0	18.7	340.5	5.3

In both cases daily intramuscular injections were begun on Dec. 6.
* Spa hospitals method: corrected rate.

On the fifth day of the injections the patient complained of intermittent nausea which had begun soon after she started the injections and had got worse each day. She did not vomit at any time. She also complained of a "persistent taste of chlorodyne," which became less intense on the fifth day. Visiting relations and fellow patients all said they could smell chlorodyne in her breath, but we could not detect the smell. So far as could be ascertained, she had not eaten or drunk anything containing chlorodyne or similar substances, and so far as we know, none is present in cafestol. This symptom became less pronounced on the day after the daily dose of cafestol was reduced from 400 to 200 mg. Nothing abnormal was detected in the urine, and no explanation can be offered for the curious statements.

At the end of the course the patient appeared to be happy, full of optimism and generally improved, in spite of the negative laboratory findings.

British Substitute

A young unmarried woman, aged 22, had had rheumatoid arthritis in the interphalangeal joints of both hands for 2 years. The onset was afebrile, insidious, and polyarticular, the hips, ankles, elbows, and shoulders being affected in turn. She had been in hospital for six weeks when the present trial was begun. All her interphalangeal joints and both wrists were swollen and painful, with much restriction of movements. Radiography showed a stage 2 rheumatoid arthritis. The left acromioclavicular joint was also involved. She walked with pain and some difficulty. There was no family history of rheumatism. The eosinophil count (80 per c.mm.) showed no response to adrenaline.

She was given 400 mg. of the British substitute for cafestol intramuscularly daily for three days, followed by 200 mg. daily for nine days, making a total of 3000 mg. During the course there was a gradual reduction in her joint pains and she became much more cheerful.

At the end of the course she had improved slightly, more particularly as regards pain, but it would be hard to say whether the improvement was greater than might have been expected from her condition before the course. The laboratory findings (see table) showed no significant changes.

Both these patients showed some clinical improvement, mainly in a diminution of their pain. The improvement was slightly greater in the patient given the Italian cafestol, but the results were much less definite than one might have expected from the letter of Ferrari and Allegri.[3]

---

1 Ellenbogen B K *Lancet* 1950 i 1034
2 Canelis M Farnell, F J McGavack T H *Amer J med Sci* 1949 **218** 655
3 Ferrari G Allegri A *Lancet* 1950 i 687
4 Steinbrocker, O Traeger C H Batterman, R C *J Amer med Ass* 1949 **140** 659

will be far greater in number than ever before. In the outer zone of a bombed area there may be thousands of injured and the majority will have limb injuries. Admittedly radiation effects may complicate management, and at the moment this problem occupies much attention. At the same time it seems essential to plan for a more adequate instruction of surgeons who can handle these casualties. Just as with burns, some standard method of treatment is necessary, so some direction is urgently required for the care of large numbers of limb injuries.

There is a danger of complacency here with the suggestion that anyone can sew up a few flesh wounds or set fractures. This is the careless attitude which produced the disasters of primary suture, inadequate wound excision or decompression, and faulty splintage—disasters repeated so often in the last war. Such errors are avoidable and there should be no excuse for their repetition.

Department of Surgery,
University of Liverpool
JOHN A. SHEPHERD

Obituary

PERCY STANLEY TOMLINSON

K.B.E., C.B., D.S.O., F.R.C.P., F.R.C.P.E.

MANY who served in the Royal Army Medical Corps during the late war will have learnt with deep regret of the death on March 6 of Major-General Sir Percy Tomlinson.

Born in 1884, he was the son of Colonel W. W. Tomlinson, R.A.M.C., and was educated at Clifton College and Bristol University. He entered the Corps in 1909, and during the first world war served in France and Macedonia, gaining three mentions in despatches and the D.S.O. After service at home and in India, he found himself at the outbreak of the second world war D.D.M.S. to British troops in Egypt. In April, 1940, he was appointed D.M.S. to the Middle East Force, and he held that post during the critical years of the fighting in Africa. In 1943 he handed over this post to Major-General W. C. Hartgill, and in 1944 he was appointed D.M.S. in North-west Europe.

[Stoneman

He will be remembered above all for his magnificent work in Egypt, where he faced problems of the greatest difficulty, many of them new to military medicine. He was in charge of a large composite force, whose medical units came from every part of the British Empire and its Allies. He was dealing with a territory that stretched two thousand miles from north to south and two thousand miles from east to west, in which every terrain and every climate might be encountered, in which epidemic diseases were as much a danger to the armies as the warfare of the enemy, and in which hygiene and preventive medicine were of supreme importance. He directed the medical service of a force that till the last phases was outnumbered and under-equipped, that had to face misfortune and retreat as well as victory. He held office during the lightning changes of the early desert campaigns, and during the fighting in Greece and Crete, in Syria, Iraq, and Eritrea. He had to plan for possible disaster when Rommel stood within a day's march of the Cairo-Alexandria road, and had to improvise an emergency medical base on the Red Sea near the Abyssinian border in preparation for a possible loss of the Suez Canal; within a few months he was organising the medical preparations for the battle of Alamein, and coping with the difficulties of the chase of Rommel from Alexandria to Tunis—the longest and fastest advance in military history, with the sole exception of Cunningham's dash from Kenya to Addis Ababa.

In all this work he was not merely accessible to his subordinates; he sought out experts in every branch of medicine, posed his problems, and used their advice. He had a sound knowledge of clinical medicine, a fine administrative brain, and the power of leadership to an unusual degree. He could think clearly and decide quickly and impartially.

The changes that occurred under his leadership were fundamental. Forward surgery was reorganised to meet the needs of mechanised warfare. The field surgical units were planned and improved. The blood-transfusion service was organised and developed till blood became the chief factor in the remarkable rise in recovery from abdominal injuries and fall in the incidence of gas gangrene that marked the desert campaigns, and the field transfusion officer became the key man of the advanced operating centres. Advanced parties of the neurosurgical, faciomaxillary, and ophthalmic units were for the first time grouped at casualty-clearing stations within a few hours of the front line. At the same time our armies were kept almost free from the infective diseases, particularly the dysenteries, that seriously hampered our enemies.

In the second world war Tomlinson was mentioned four times in despatches. In 1941 he was made an honorary physician to the King and was appointed C.B.; in 1943 he received a knighthood in the Order of the British Empire, and he held the Croix de Guerre, the Legion of Honour, and the Legion of Merit of the U.S.A. He was elected a fellow of the Royal College of Physicians in 1943, and an honorary fellow of the Royal College of Physicians of Edinburgh in 1946.

General Tomlinson married Miss Gertrude Barr in 1920. He had one son, who was killed on active service, and one daughter.

GEORGE MILTON SMITH

M.D. Columbia, LL.D. Yale

As director of the Anna Fuller Fund Dr. G. M. Smith was able to foster Anglo-American coöperation in medical research, and many scientific workers will remember the warm kindliness which he added to official grants.

George Milton Smith graduated A.B. at Yale in 1901 and M.D. at Columbia University three years later. In 1910 he became associate professor of pathology in Washington University, St. Louis, where he worked till 1934. He then returned to Yale to take up his appointment with the Anna Fuller Fund, which he still held at the time of his death. While in Yale he also acted as research associate in anatomy. In later years his research interests lay mainly in the comparative pathology of tumours, on which he published papers in *Zoologica* and elsewhere, and in historical medicine. His greatest achievement, however, rests in the advancement of medical research, not only in the United States but in other countries, through his work for the Anna Fuller Fund and as adviser to the Jane Coffin Childs Memorial Fund for Medical Research. Much of his contribution lay in cancer research, and he also acted as a member of the National Advisory Cancer Council from 1939 to 1942. Yale conferred on him the honorary degree of LL.D. in 1947. A devoted supporter of the Allied cause in the late war, he served as chairman of the National Research Council committee on armoured vehicles.

A British colleague writes: "In George Smith we admired his intense loyalty to his country and to Yale, his complete unselfishness, and his lasting belief in international coöperation in science and medicine. He was also able, and wont, to accompany his practical benefactions with the warmth of encouragement to a rare degree. His loss will be mourned, and his memory honoured, by a host of colleagues and friends the world over."

decreased considerably, interscapular brown fat was reduced in amount and had taken the appearance of white adipose tissue

From our results it appears that cortisone increases the fat content of liver, probably through an increase of fat mobilisation Fatty liver produced by A C T H may be regarded as a consequence of adrenal stimulation

G SALA
A AMIRA
M BORASI
C CAVALLERO

Anatomo Pathological Institute
University of Milan and Farmitalia
Research Laboratories

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—In their letter last week, Dr Hirson and Dr Kelsall describe a fatality due to excessive low blood pressure after administration of hexamethonium An attempt was made to raise the blood-pressure by an intravenous drip containing adrenaline, and the report notes that the "pressure always dropped precipitately during the brief periods when the drip was discontinued"

It does not appear to be generally known that this result is to be expected, since it has been shown that *adrenaline itself has a blocking action on sympathetic ganglia* If an intravenous infusion of adrenaline is given, the adrenaline by direct action on the vessel walls causes vasoconstriction, but, by its action on sympathetic ganglia, it prevents the stream of impulses emitted by the vasomotor centres from reaching the vessels When the adrenaline infusion is stopped, the direct action on the vessels disappears, and, because tonic impulses from the centre cannot pass the ganglia, the blood-pressure falls precipitately In this respect noradrenaline has the same action as adrenaline

Fortunately, however, posterior lobe extract of the pituitary gland has no such effect, and, so far as animal experiments afford a guide, the right treatment of a patient in whom the blood pressure has fallen low because of the action of hexamethonium would seem to be to give an intravenous drip containing 10 units pituitary (posterior lobe) extract in each 50 ml. saline We have some evidence, which is too little to be conclusive, that posterior lobe extract may increase ganglionic transmission, and therefore it may prove to be a positive antidote to ganglionic block However this may be, the interruption of a drip containing posterior lobe extract would certainly not be followed by the precipitate fall of blood pressure which occurs at the end of an adrenaline drip

In using an intravenous drip containing posterior lobe extract, the effect on the coronary vessels will be constrictor, and therefore the drip should be given slowly

The evidence for the action of adrenaline on ganglionic transmission will be found in the *Journal of Physiology* (1942, **101**, 289)

Department of Pharmacology
Oxford University
J H BURN

ANTITOXINS AND ANTIBIOTICS

SIR,—Some of the most potent poisons known at the present time are bacterial toxins, so called "bacteriological warfare" is based on knowledge of these substances

Antibiotics deal faithfully with bacteria but offer no protection against their products Antitoxic treatment is a routine for cases of diphtheria, tetanus, and botulism, and with less effect for gas gangrene due to *Clostridium welchii* with its multiplicity of toxins, occupying half the letters of the Greek alphabet It is not generally realised that *Streptococcus pyogenes* can produce a powerful multi type toxin, and also the common *Staphylococcus pyogenes*, in certain instances, can produce an "enterotoxin" and, more often, cell destroying and blood clotting toxins Before antibiotics came into use, streptococcal antiserum and staphylococcal antitoxin were often used, with uneven results

The brilliant effects of treatment with antibiotics seem to have discouraged the serologists who formerly worked enthusiastically on the improvement of antisera. One or two recent tragedies have underlined our lack of effective sera, and also the fact that the present generation seems to have forgotten that such things exist or can be used with success

One such case was a young woman with a (staphylococcal) infected wisdom root This was operated on, and the woman died two days later of a pulmonary embolism despite active antibiotic therapy I think she might have been saved by simultaneous antibiotic and staphylococcal antitoxin treatment *Another young woman developed localised osteo*myelitis in a metatarsal bone, and died of general peripheral circulatory failure, despite the exhibition of astronomical doses of antibiotics

I think that a streptococcal toxin was to blame for the unfortunate outcome in the second case, but it never occurred to anybody to try antistreptococcal serum Nobody was really to blame for the fatal termination in either case, but I would like to suggest that the serologists be encouraged to get busy again, and develop their art to the utmost, and perhaps advertise their products

Epping, Essex FRANK MARSH

WILL WE NEVER LEARN ?

SIR,—After an interval of five weeks the first comment appears on a report by Surgeon Commander Latta (*Lancet*, Jan 27) on casualties in the Korean campaign He stressed two important points (1) that primary suture of war wounds is usually disastrous, (2) that rapid evacuation of casualties from a war zone can be a mixed blessing That he has to stress these points bears out Sir Heneage Ogilvie's text "Will we never learn ?" I think Commander Latta has done a considerable service in making his clear and unbiased report

As Sir Heneage indicates (March 3), there is something wrong with the training of the military surgeon As a reservist in one Service before the late war I used to do periods of training In my youthful enthusiasm I expected to be taught something about war surgery But no one seemed very interested, and the Service journals in periods of peace bear witness to this extraordinary lack of attention to a subject which should be very much in the minds of Service doctors—particularly surgical specialists The non-medical branches of the Services in peace time prepare for war, but for some reason the doctors do not There should be intensive training in the surgery of trauma for both regulars and reservists Suitable courses could easily be arranged and interested tutors would not be lacking The individual is not usually prepared to educate himself in these matters, and so he must be subjected to some discipline as Sir Heneage suggests *It would at least be possible* to drum into everyone concerned the principles of treatment of soft tissue wounds No one would expect to train abdominal surgeons, thoracic surgeons, or neurosurgeons in a night, but it ought to be feasible to teach most Service medical officers how to diminish mortality and morbidity in the major group of war wounds

I have long believed that the conscientious perusal of Professor Trueta's small monograph on war surgery published in 1939 would have saved a lot of needless suffering I still think that most of the answers are in this book (For one thing it scarcely mentions chemotherapy or antibiotic therapy—an unwarranted faith in these has often lead to the neglect of surgical principles) Jolly's *Field Surgery in Total War* was another book of great value in those early years The point is that remarkably few bothered to read these books in 1939 and 1940, and it does look as if appropriate study must be directed

If there is another war and if, as is *all too likely*, there is intensive bombing—atomic or otherwise—casualties

Congress at Evian

An international medical congress will be held at Evian from Sept 7 to 9 under the presidency of Prof. E Chabrol The topic chosen for discussion is L eau en biologie et en clinique Further particulars may be had from Prof Jean Hamburger 29, Boulevard de Courcelles, Paris

Gerontological Congress

The second International Gerontological Congress will be held at St Louis, Missouri, from Sept. 9 to 14 under the presidency of Dr E. V Cowdry Further information may be had from the secretary of the congress, Washington University Medical School, 660, South Kingshighway, St Louis 10 Mo

European Congress on Rheumatism

The Sociedad Española de Reumatismo is organising the second European Congress on Rheumatism, which is to take place at Barcelona from Sept 24 to 27 The English speakers will include Dr W S C Copeman, Dr R. M Mason, and Dr L G C Pugh. Further particulars may be had from the general secretary, Via Layetana, 31, Barcelona Spain.

Medical Research Council Publications

The list of Medical Research Council publications is brought up to date at March 31, 1950 by a new Stationery Office pamphlet (Government publications, sectional list no 12) This catalogue does not include publications in scientific journals, which are listed in the Council s annual reports Those wishing to be notified when new M.R C publications appear should notify the director of publications (P 2), H.M. Stationery Office, 429, Oxford Street, London W 1 Those ordering by post may if they wish, open deposit accounts with the Stationery Office deposits (minimum £1) should be sent to P O box 569 London, S.E 1

Institute of Biology

A symposium on Freeze-drying will be held in London on June 29 and 30 Provisional arrangements have been made to hold four sessions At the first there will be discussions on Physical Principles including freezing and drying of proteins and protein-containing materials such as plasma and foodstuffs, and Dr R L N Greaves will be in the chair At the second the Drying of Bacteria and Antibiotics will be discussed (chairman Sir Alexander Fleming, F.R.S), at the third the Drying of Viruses and Vaccines (chairman Dr C H. Andrewes, F.R.S.), at the fourth the Drying of Tissues and Tissue Sections (chairman Prof J F Danielli D.SC) Attendance will not be limited to members of the institute, and those who are interested are invited to apply to the general secretary of the institute Tavistock House South, Tavistock Square, W C 1

Medical Society of London

At this society's 171st anniversary dinner, on March 8, Lord Woolton spoke genially of medicine past and present. He recalled that just after the society was founded Guy's Hospital—the hospital of the society's president, Dr A. H. Douthwaite—was well known for the number of bugs and vermin that it harboured. There had been great changes. As to present-day medical practice ' You are such experts on such small parts of the anatomy that I wonder what chance the human being has of being understood as a whole' Speaking of his own experience as war time Minister of Food, he said that he had deliberately attempted to preserve the health of the country s children and the public having grasped this aim, coöperated whole-heartedly Lord Woolton was proposing The Society , and in reply the President paid tribute to his policy of fair shares for all. Some, he said had been confused by the expedients of war one nursing candidate had described rose hips as the first indication of a threatening bedsore Turning to the National Health Service, the President suggested that this could be a success if the cleavage between specialist and practitioner were ended, and if the practitioner received a just reward As to the society itself, its special features were friendliness and the habit it had of drawing together those working in different fields The President went on to speak gratefully of the gift from Colchester Medical Society of an antique wax medallion of John Coakley Lettsom, the Quaker physician and philanthropist who founded both societies. The Guests were toasted by Mr H R. Thompson, and Dr W Russell Brain, F.R.C.P , replied

Pneumoconiosis as a Prescribed Disease

The Industrial Injuries Advisory Council is considering further the method of prescribing pneumoconiosis as an industrial disease under the National Insurance (Industrial Injuries) Act 1946 Those interested are invited to submit, by May 1, written evidence to the council's secretary, Mr. S E Waldron, O.B.E., Ministry of National Insurance, 30, Euston Square, London, N W 1 An explanatory memorandum may be had on request

Association of Workers and Schools for Maladjusted Children

The inaugural meeting of this society was held earlier in the year A second meeting, to which all who are interested are invited, will be held on Monday, March 19, at the London School of Hygiene, Keppel Street, W C 1, at 5 15 P.M. The purpose of the meeting is to receive the report of the interim committee, draft rules, and appoint the officers of a permanent committee. The main objects of the association are to find means by which all maladjusted children may be treated, educated, and reabled, to provide a professional body whose opinion would have weight with other bodies, and to encourage research and experiment

Prescribing and Dispensing in Scotland

The Department of Health for Scotland has told executive councils that in future a selection of prescription forms dispensed each month will be scrutinised centrally to detect and deal with extravagant prescribing under the National Health Service in the light of the Cohen Committee s recommendations. Executive councils will be notified, for consideration in the first place by the local medical committee, of prescriptions which seem extravagant either (*a*) because they contain proprietary preparations for which less expensive standard equivalents may be had, which are not of recognised therapeutic value, or which are advertised direct to the public or (*b*) because they relate to unduly large quantities of drugs or other items such as lint and cotton wool The General Medical Services Subcommittee is urging local medical committees to consider very seriously apparent instances of extravagance These committees will communicate with practitioners concerned where necessary invite them to attend for discussion with the committee, and in the case of serious or repeated extravagance recommend to executive councils the recovery of appropriate sums Brief reports of action taken will be furnished by local medical committees to executive councils, which are asked to forward reports to the Department In appropriate instances the Department will publicise this action (omitting particulars identifying the doctor concerned) and executive councils are asked to supplement, as necessary such publicity

Scottish pharmacists have now completed their case for abolishing the 8% cut on earnings imposed last September

Doctors in the U S.A

In 1954 the U S.A. will have 22,000 fewer doctors than it needs This estimate was made by Dr Howard Rusk, chairman of the health resources advisory committee of the U.S National Security Resources Board, at a meeting in Chicago of the Federation of State Medical Boards According to B U.P Dr Rusk based his estimate on a military strength of 5 million , if the Forces were not increased beyond $3^{1}/_{2}$ million the deficit would be some 20 000 Dr Rusk was supported by Dr Joseph Hinsey, of Cornell University Medical College who declared The nation needs more physicians today Dr Stockton Kimball, dean of the University of Buffalo Medical College, told the meeting that during the past ten years medical schools had increased their intake to an extent equal to the opening of fifteen new medical schools. Today he said, there were 26 913 students in medical schools—1090 more than last year and almost 5000 more than ten years ago The need for more doctors was denied by Mr Frank Dickinson, PH.D , economist and statistician of the American Medical Association. Medical progress had, he claimed brought about an increase in ' output " of at least one third by each doctor No-one could foresee the duration of the present emergency and doctors ' cannot become war surplus after a war Dr Dickinson pointed out that during the late war about 40% of the active U.S doctors joined the Forces, but under the care of the remaining 60% the 90% of the total population that was still civilian continued to improve in health.

Notes and News

A SCHOOL FOR HANDICAPPED GIRLS

There were few residential schools for physically handicapped children before 1939, but during the war some 500 of them were evacuated to Peckforton Castle, near Cheshire, and this school remained in action for five years Thanks to the successful experience gained there, similar schools have been established since, and one of these, the London County Council's school at Stapleford Place, near Haywards Heath, in Sussex, was opened by the Minister of Education on Feb 24, The house, built as a private residence in 1911, has been converted according to plans prepared by the architect to the council By August, 1950, it was ready to receive 32 girls and members of the staff who until then had been housed in requisitioned quarters near Sherborne Now there are 49 girls in residence, between the ages of 5 and 16

Some of the children are without homes of their own, others come from homes which are not suitable for a disabled child to live in, and most of them need more medical and nursing care than they could reasonably get in their own homes Parents may visit every month, and the children can go home for holidays if they wish The house is on the village green, which places it well in the middle of the community life, and the neighbours are already taking a friendly interest in the children and in the life of the school Stapleford Place has spacious gardens, plenty of trees and lawns, and a lake of its own—always a gratifying piece of property to a child Its rooms are large and airy, and its windows overlook a lovely stretch of country The alterations have been considerable—a new water supply and sewage disposal system, the installation of modern heating, lighting and cooking equipment, proper fire precautions and a generous increase in bath and lavatory accommodation The panelling and the broad oak staircase have been carefully repaired, and all has been done skilfully, and with the comfort of the children well in mind The aim is to give these girls as nearly as possible a normal education and to fit them for as full an adult life as their disabilities will allow The new venture deserves every success

PORPHYRIN METABOLISM AND PORPHYRIA

With regard to Professor Watson's article last week (p 539), further information has been received about some of the references, as follows

Schmid R Schwartz S, Watson, C J (1950) *Proc Soc exp Biol N Y* 75 705

Schwartz S Zieve, L, Everts C, Watson, C J (1951) *J Lab clin Med* (in the press)

Sutherland D S Watson C J (1951) *Ibid* 37 29

Watson C J (1950) *Trans Ass Amer Phys* 63 219

— Hawkinson, V E, Sutherland, D S (1951) *J Lab clin Med* 37 8

A NEW NORWEGIAN JOURNAL

Norway has a new monthly in the *Journal of the Oslo City Hospitals* Printed in English, this somewhat resembles in form and intention the *Proceedings of the Staff Meetings of the Mayo Clinic* The journal, which will be sent without charge to hospitals in Norway and other countries, is published by Christian Plesner, Hospital and Medical Equipment, Oslo

LYMPHATIC PATHWAYS

A film on the *Lymphatic System* made by the medical film unit of Imperial Chemical Industries in conjunction with Dr J M Yoffey, professor of anatomy at Bristol University, has as its main purpose the instruction of medical students Animated diagrams and beautiful colour cinematography of animal injection experiments with indian ink and Evans blue show in striking terms many features of the mammalian lymphatic system of which students can usually only read Lymphatic trunks in the anæsthetised animals are well seen, and one particularly striking sequence illustrates the passage of substances instilled into the nose reaching the cervical lymphatic pathways The approach of the film is that of experimental physiology, and there is nothing therefore of immediate clinical bearing on lymphatic problems in the human body But as a demonstration of the way in which lymphatic systems work it is a vivid and useful presentation There are two small criticisms the first that some of the animated diagrams go on too long, and the second that the skin incision is shown in the making before each experiment—this might be taken as read after the first time or two

The film, which was briefly reviewed in these columns last year when it was shown at the annual meeting of the British Medical Association,[1] runs for 45 minutes and is 16 mm.

University of Cambridge

Dr F G J Hayhoe has been appointed lecturer in medicine for three years

On March 3 the following degrees were conferred

M A—G K Harrison

M D—P F Borrie, D B Cater, A E Flatt.

M B, B Chir—*Graham Harvey Evers, *Helen M Roseveare *I M Simmonds

*By proxy

University of London

At recent examinations for the academic postgraduate diploma in medical radiology (diagnosis) the following were successful

Raghubar Baidya, A T Broadbridge R J Callander, Phyllis A M. Crozier, David Datt Joseph Friedman J J Geere, J B Hearn, Maurice Hurwitz, Philip Jacobs Edward Mercieca, Victor Roseverne, Morris Simon, D G C Whyte Mary I Wray

Royal College of Surgeons of England

At a meeting of the council on March 8, with Sir Cecil Wakeley, the president, in the chair, a past president's badge was presented to Sir Holburt Waring

Mr A Wallis Kendall and Mr E L Farquharson were elected members of the court of examiners

Mr C D Read was elected to the fellowship ad eundem. The Hallett prize was presented to Mr M W Reece (St. Thomas's Hospital) The council decided that the first award of the James Berry prize would be made in 1952 The subject for essays will be the Treatment and Preservation of the Injured Hand

Prof H H Stones was appointed Charles Tomes lecturer for 1951 It was reported that Dr Loyal Davis (Chicago) will deliver a Moynihan lecture on Oct 9

Scottish Conjoint Board

The following candidates, having passed the final examination, were admitted on March 9 to the licentiateship of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow

Patricia F D Anderson John Boyd G McG Campbell, C MacP Christie Gordon Clarke, D M Cunningham, Anthony de Mello J Y N Devine J A Eykelenboom, Hannah Furman, James Goldie, A E D J Hellegers D W Kidd, Ruth Kope June M Litt, J T Lunn, Rankin Martin Joseph Minsky M H Pinsky Thomas Rice, June Rosin W S Thompson

Royal Society Lectures

Prof R A Peters, M.D, F R S, will deliver the Croonian lecture on June 7 on Lethal Synthesis Dr C H. Andrewes, F.R S, will deliver the Leeuwenhoek lecture on Dec 13 He is to speak on the Place of Viruses in Nature

Postgraduate Course at Hampstead

The Royal Free Hospital group is holding a postgraduate course at the Hampstead General and North West London Hospital, The Green, Haverstock Hill, N W 3, on Thursday of each week from April 5 to June 14 Lecture-demonstrations will begin at 3 P M and 4 15 P M Sir Dan Davies will give the inaugural lecture on April 5 Applications for enrolment should be sent to the secretary of the hospital

Encephalitis and Rabbit Myxomatosis in Australia

Last December the Australian Scientific and Industrial Research Organisation released in rural New South Wales a virus causing myxomatosis in rabbits, to test its effectiveness in controlling the rabbit pest B U.P reports that the disease spread rapidly among rabbits in New South Wales, Victoria, South Australia, and Queensland, but then several people in these areas contracted encephalitis More than 30 cases have been reported in Victoria, and 11 are believed to have died of the disease in Victoria and New South Wales. Government scientists, supported by medical advisers, deny any connection between the release of the virus and the cases of encephalitis, pointing out that exhaustive tests showed that only rabbits were susceptible to the virus and that the 1917 encephalitis outbreak in Queensland and New South Wales attacked people in rural areas but not in large cities. Newspapers have, however, expressed continuing uneasiness, and have cited reports that kangaroos and at least one dog have been found dead with a disorder resembling myxomatosis

---

[1] See *Lancet* 1950 ii 223

THE RISKS OF GASTROSCOPY

A SURVEY OF 49,000 EXAMINATIONS

F AVERY JONES *
M.D Lond , F.R C.P
PHYSICIAN IN CHARGE OF THE GASTRO ENTEROLOGICAL DEPARTMENT, CENTRAL MIDDLESEX HOSPITAL, LONDON

RICHARD DOLL
M.D Lond., M.R C.P
MEMBER OF STATISTICAL RESEARCH UNIT, MEDICAL RESEARCH COUNCIL, HONORARY ASSOCIATE PHYSICIAN, CENTRAL MIDDLESEX HOSPITAL

CHARLES FLETCHER
M.D Camb , F.R C.P
DIRECTOR OF PNEUMOCONIOSIS RESEARCH UNIT, MEDICAL RESEARCH COUNCIL

H. W RODGERS
F.R C S
PROFESSOR OF SURGERY IN THE QUEEN S UNIVERSITY, BELFAST

In the twenty years that have elapsed since Wolf and Schindler introduced their flexible gastroscope, gastroscopy has become established as a useful, if limited, method of investigation At the same time it has become clear that accidents occur and that flexibility alone is not enough to ensure complete safety

Perforation of the upper œsophagus has taken the place of perforation of the stomach and perforation of the lower œsophagus as the most common accident, and Golligher (1948), in reporting one case, was able to collect 17 others from the literature A bare figure, however, is of little value in assessing the risk of gastroscopy, without some indication of the corresponding number of examinations made Schindler (1940) surveyed 22,351 gastroscopies performed in America by gastroscopists of varying experience Among these there was 1 fatal case of hypopharyngeal perforation , also 8 cases of gastric perforation, and 1 of jejunal perforation, all of which recovered. Many English gastroscopists have the impression that accidents are commoner than this , so we have made a survey in this country to determine how often they happen and how they can be prevented.

METHOD OF INVESTIGATION

Forty gastroscopists were invited to coöperate by supplying the following information

(1) The approximate number of gastroscopies performed under their supervision (*a*) with the Wolf-Schindler gastroscope, and (*b*) with the Hermon Taylor gastroscope

(2) The number of mishaps, including cases in which the patients recovered, with brief clinical details and a note of the type of instrument and tip used and whether any accidents had been due to the local anæsthetic

(3) Whether accidents had happened when an assistant was passing the instrument

(4) Special precautions recommended to prevent accidents

All the gastroscopists supplied information, but it was not always complete The number of gastroscopies performed could often be only roughly estimated, particularly as regards the number performed with each instrument It must also be supposed that minor non-fatal accidents were less likely to have been recorded than fatal ones. The accident-rates death rates, and case fatality rates are therefore not exact The reported accident rate is probably too low, and the case fatality rate too high , but even if the errors are as great as 50% (which is unlikely), the general conclusions will not be invalidated

So far as is known, no bias was shown in the selection of gastroscopists written to because all who were known to one or other of us were included The large number involved makes it likely that their experience is reasonably representative

RESULTS

Altogether, 49,000 gastroscopies, with 75 accidents and 32 deaths, were reported In addition, information was provided about 5 other accidents (with 3 deaths), but the corresponding number of gastroscopies was not known These have been excluded from table I, in which the main complications with their corresponding incidence and death-rates are recorded, but they have been included in subsequent tables

Perforation of Œsophagus

Table I shows that the main danger has been perforation of the œsophagus In most cases the presence of a perforation was either proved at operation or necropsy or demonstrated radiologically In some the diagnosis of an upper œsophageal perforation was clinical—i.e , based on surgical emphysema of the neck, with or without a localised abscess—in others insufficient evidence was provided for the site to be determined, the report merely referring to " mediastinitis " In 7 cases coming to necropsy no tear could be found, though in 4 of them there was bruising or scratching of the œsophageal mucosa Since these patients had all died of mediastinal infection, they have been included under the heading of perforation, though they might more accurately be described as cases of perœsophageal infection.

TABLE I—INCIDENCE OF COMPLICATIONS ASSOCIATED WITH 49,000 GASTROSCOPIES

Complication	No of cases	No of deaths	Death rate per 10 000 gastroscopies
Perforation of œsophagus	50	21	4·3
Perforation of stomach	9	1	0·2
Hæmorrhage	7	2	0·4
Miscellaneous	4	4	0·8
Reaction to anæsthetic	5	4	0·8
Total	75	32	6·5

In 1 patient the perforation took place nineteen hours after the passage of the gastroscope and was immediately preceded by violent vomiting The perforation was in the lower œsophagus, and the case clinically resembled a spontaneous perforation , but it is reasonable to assume that the œsophagus had been damaged at the time of the gastroscopy

The numbers of cases of each type of perforation reported are shown in table II

Table II confirms that the preponderant site for perforation is in the upper œsophagus or hypopharynx.

In table III the cases of œsophageal perforation have been subdivided to show the incidence of various possible ætiological factors.

TABLE II—PERFORATION OF ŒSOPHAGUS AND SITE OF LESION*

Site	No of cases	No of deaths
Upper œsophagus proved	23	13
Upper œsophagus clinical	9	1
Lower œsophagus proved	4	2
Site indefinite	11	0
No recognisable perforation at necropsy		
Upper œsophageal lesion	4	4
Lower œsophageal lesion	1	1
Site indefinite	2	2
Total	54	23

* Including 4 cases with 2 deaths excluded from table I.

In receipt of an expenses grant from the Medical Research Council.

Merchant-shipping Medical Scales

From April 1, penicillin, chloramphenicol, anti venereal disease outfits, and other items will be added to merchant-shipping medical scales 1 and 2

Malayan Artificial Limbs for South-east Asia

Malaya now makes its own artificial limbs and orthopædic appliances, and also supplies other countries in South east Asia A grant of £7500 from the government of the Federation resulted in the building of a modern factory where 25 craftsmen are employed

How to Look After the Old

A 3–4 months' course, for men and women who wish to become wardens or matrons of homes for old people, will be held in London in October Where necessary some grants are available towards the cost of training Further particulars may be had from the secretary, National Old People's Welfare Committee, 26, Bedford Square, W C 1

Society for the Study of Fertility

The annual conference of this society is to be held at Cambridge on June 20 and 21 The hon. secretaries are Dr G I. M Swyer, University College Hospital, London, W C 1, and Mr A Walton, PH D, A.R C unit of animal reproduction, Animal Research Station, Cambridge The first issue of the society's *Proceedings*, dealing with the Edinburgh conference in 1949, has been published by Messrs W Heffer & Sons Ltd, Cambridge, at 10*s*

Belgian Society of Gastro-Enterology

This society are once more asking their colleagues from other countries to take part in their annual meeting, which they are holding this year at 9 A M on Sunday, June 3, at the Institute of Tropical Medicine, 155, rue Nationale, Antwerp The subject chosen for discussion is Diseases of the Blood and Affections of the Digestive Tract Further particulars may be had from the secretary general Dr G Brohée, 64, rue de la Concorde, Brussels

United Hospitals Festival Choir

More than fifty London hospitals are taking part in this choir which is to sing Mendelssohn's Elijah, accompanied by the London Symphony Orchestra and conducted by Mr Joseph Krips, in the Albert Hall, on Wednesday, May 30, at 7 30 P M The concert is in aid of the Royal College of Nursing Educational Fund. Tickets may be obtained from Mr Colin H Ratcliffe, the chorus master, 10, Waldegrove Park, Twickenham, Middlesex Some more male voices, particularly tenors, are still needed

The M O.H and Mental Health

This year the National Association for Mental Health is again arranging a course for medical officers of health or their deputies The course, which will be held at the London School of Hygiene, Keppel Street, W C 1, from June 4 to 9, will deal with preventive aspects of mental-health work and with provisions for the mentally handicapped, especially those living in the community who are the responsibility of the local authorities It is hoped to arrange some visits of observation in connection with the course Further particulars may be had from the education department of the association, 39, Queen Anne Street, W 1

Prof W Melville Arnott is visiting Cyprus from March 17 to April 7 on behalf of the British Council

---

CORRIGENDA *Standardisation of X ray Films*—Our annotation last week should have stated that the committee's recommendations appeared in the *British Journal of Radiology* (1950, 23, 272, 500)

Alkali dissolved Diphtheria Toxoid antitoxin Floccules—In this article by Mr J H Mason (March 3) the units of antitoxin per ml of serum before immunisation in each of the first three members of the institute staff who were immunised should have been given as <0 005

Treatment of Burns in Large Numbers—In our account of the discussion of this subject by the Royal Society of Medicine (*Lancet*, Feb 24, p 449) remarks were wrongly attributed to Surgeon Captain S G Rainsford In fact Captain Rainsford said that he thought that the present neglect of antisera was unwise

Diary of the Week

MARCH 18 TO 24

Monday, 19th

INSTITUTE OF OPHTHALMOLOGY Judd Street, W C 1
5 30 P M Mr F W Law Radiology of the Lacrimal Apparatus.

Tuesday, 20th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields, W C 2
5 P M Mr B N Brooke Surgery of Ulcerative Colitis (Hunterian lecture)

BRITISH POSTGRADUATE FEDERATION
5 30 P M (London School of Hygiene, Keppel Street, W C.1) Dr E E Pochin Application of Radioactive Isotopes to Medical Research Problems

INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle Street, W C 2
5 P M Dr W R Bett Medical Writing

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray s Inn Road W C 1
5 30 P.M Dr Hallowell Davis (St Louis) Effects of Noise upon the Ear

Wednesday, 21st

ROYAL COLLEGE OF SURGEONS
3 45 P M Dr L W Proger Recent Additions to the Museum (Erasmus Wilson demonstration)

INSTITUTE OF NEUROLOGY, National Hospital Queen Square W C.1
5 30 P M Dr Hallowell Davis Recent Work on the Neurophysiology of the Cochlear Mechanism and its Bearing upon Clinical Problems

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mr B W Rycroft Surgical Reconstruction of the Orbit.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION
8 30 P M (Royal Free Hospital School of Medicine, W C.1) Dr Keith Simpson Murder

MEDICO LEGAL SOCIETY
8 15 P M (26, Portland Place, W 1) Mr J A F Wilson, J.P Juvenile Delinquency

Appointments

COPE, EDWARD M D Leeds, M R.C.O G consultant obstetrician and gynæcologist, Birmingham group of hospitals

HENNEBRY, T M, M B, M CH N U I F R.C.S I D M R.E consultant orthopædic surgeon North Middlesex Hospital

HERD, J A, M.D Manc, D P M, D I.M consultant in mental health, public health department London County Council

HURFORD, F R., M.B Brist F R.C S consultant surgeon, Lichfield Sutton and Tamworth group of hospitals

MCSHANE, EILEEN M B Birm D A consultant anæsthetist, Dudley and Stourbridge group of hospitals

PARKINSON ROY, M B Lond, F R.C.S consultant general surgeon, Mildmay Mission Hospital, London

SCRASE, W H, M B Birm, M CH ORTH Lpool, F R.C.S.E. asst. orthopædic surgeon Birmingham group of hospitals

WILSON, W C M. M.D Belf, D P H consultant pathologist Coventry group of hospitals

WOOD, B S B, B M Oxfd M R C P D C H consultant pædiatrician, Birmingham group of hospitals

University College Hospital, London

COUCHMAN J M. D S O M A B M Oxfd senior hospital M.O venereal diseases department

GOODDY W W M D Lond M R C P consultant neurologist.

HARRIES B J M B Lond F R C.S consultant general surgeon

SWYER G I M M A, D M D PHIL Oxfd M.R.C P consultant endocrinologist to obstetric department

Births, Marriages, and Deaths

BIRTHS

BORRIE—On March 4 in Newcastle upon Tyne the wife of Mr John Borrie, M.B E, F R C.S—a son

FISK—On March 6 at Cambridge to Dr Susan Airey, wife of Mr Geoffrey Fisk F R C S—a son

HALLE—On Feb 20, in Sheffield the wife of Dr H M. Halle—a son

MCDONALD—On Feb 24 at Beckenham Kent, the wife of Dr Donald M McDonald—a son

MCGOWAN—On March 7 at Bristol, to Dr Rosalind McG (née Barclay), wife of Dr G K McGowan—a daughter

MANNING—On March 5, in London the wife of Dr Geoffrey C Manning—a son

PRATT—On March 3, at Cambridge the wife of Dr C L G a daughter

MARRIAGES

MCFADYEAN—CASS—On March 3 at South Ascot, Michael McFadyean, M R.C S, to Barbara Marjorie Joan

DEATHS

DAVIES—On March 5, in Manchester, Evan Sherrah Davi M R C S

DRAPER—On March 3, at Croydon, John Robert Draper, M.B. Camb aged 73

GILL—On Feb 28, at Oldham Lancs, Harry Gill M B R U.I

HAMER—On March 2, at Chorlton-cum Hardy, Lancs, W Myring Hamer L.M S S A

MONTGOMERY—On March 4, at Chichester Edwin Cecil Montgomery M R.C.S, aged 79

PENNELL—On March 7 at Findon Sussex Alice Maude O B E M B Lond

TOMLINSON—On March 6 at Hove Percy Stanley T K.B E C B, D S O F R C P aged 66 gastroscopy without any cause for death being discovered, 1 who died of rupture of what was presumed to be a chronic œsophageal abscess, and 1 case of phlegmonous gastritis.

The first 2 cases may not have had anything to do with the gastroscopy, but in the absence of any other recognised cause of death they have been included.

One was in a man, aged 30, who was inadvertently allowed to start his lunch immediately on returning to the ward and was found dead in bed half an hour after gastroscopy and forty minutes after the application of an amount of "percaine" which was "within the normal dosage range." At necropsy no abnormality was found, apart from hyperæmia of the duodenum; no foreign body was found in the bronchial tree.

The other patient, a man of 60, who ate lunch two hours after gastroscopy (somewhat sooner than usual) and then went to sleep. He was awakened by a severe pain in the right upper abdomen, became collapsed, and on examination showed epigastric rigidity. He recovered from the state of collapse, but ten hours after gastroscopy the rigidity was still present and the pulse rate had risen. The abdomen was opened, but no abnormality was found. He died twenty-two hours after gastroscopy. A necropsy was not done. The probability is that he had had a coronary thrombosis.

The third patient was a woman of 60 who was examined with a Wolf-Schindler gastroscope with a rubber finger tip. Instrumentation was straightforward, but she developed surgical emphysema of the neck and, despite sulphonamides, died three days later. Necropsy showed "an old chronic para-œsophageal abscess, extending one third the length of the œsophagus, with a perforation into the right pleura. No obvious damage was found in the œsophageal mucosa itself." A chronic abscess could hardly have developed within three days, and the case has therefore been classified as one of rupture of a previously existing abscess. Nevertheless the occurrence of surgical emphysema is in favour of there having been a small perforation, and if this were the primary lesion it would provide the second instance in this series of a fatal œsophageal perforation associated with the use of the Wolf-Schindler instrument.

The case of phlegmonous gastritis occurred in an elderly man with a pyloric carcinoma and complete achlorhydria. Twenty-four hours after gastroscopy he had severe epigastric pain and he died a few hours later. Necropsy showed an acute phlegmonous gastritis from a 5 mm. abrasion in the posterior wall which had become infected by a virulent streptococcus.

Reactions to Anæsthetic

In addition to the 5 cases shown in table I a 6th case was also reported, but the corresponding number of gastroscopies was not known. The doses given and the types of anæsthetic used are shown in table IV.

In all instances, toxic reactions developed within a few minutes. In 4 death was clearly due to overdosage; the 5th was not unreasonably attributed by the coroner to idiosyncrasy, and the dosage was similar to that often used without ill effect. In the sole case in which recovery took place the dose was not reported.

PREVENTION OF ACCIDENTS

In 1 case perforation followed instrumentation while a Ryle's tube was also down the œsophagus. It is not ordinarily necessary to pass the gastroscope in these circumstances, and any tube already in the œsophagus should clearly be withdrawn first.

Contra-indications which might have been recognised, accounted for 2 deaths. In one case the examiner did not recognise the extent of the patient's kyphosis, and difficulty at the cardia caused a tear at the lower end of the œsophagus; in the other, necropsy revealed a benign stricture of the upper œsophagus, which had been split. These experiences reinforce the need for a preliminary examination of the spine and for a barium swallow. In cases with a moderately severe degree of kyphosis the Wolf-Schindler gastroscope may be passed safely, but the Hermon Taylor instrument is probably much more hazardous. Those more familiar with the Wolf-Schindler must be specially careful in their selection of cases for the Hermon Taylor gastroscope.† A preliminary barium examination will usually demonstrate gross lesions of the œsophagus and cardia, but it will not always do so. It did not, in fact, demonstrate the œsophageal stricture which was split, or the carcinoma at the cardia in 1 of the 2 patients in whom a lower œsophageal tear was produced in association with a carcinoma.

TABLE IV—REACTIONS TO ANÆSTHETIC

Local anæsthetic	Dose	Result
Cocaine	Gross overdosage with 20% solution	Death
Amethocaine	3 ml. of 1% spray and 2 ml. of 2% solution	Death
	12 ml. of 2% solution*	Death
"	15 ml. of 2% solution	Death
"	12 ml. of 4% solution†	Death
	?	Recovery

* A smaller dose had been given at a previous examination without ill effect.

† Dispensed in error as 2% solution.

Goligher (1948) has suggested that accidents are most likely to happen in the presence of gross osteo-arthritis of the cervical spine, and has recommended routine radiography of the neck before endoscopy. We have knowledge of the state of the cervical vertebræ in only 4 cases: a fatal perforation of the hypopharynx, in which necropsy showed no arthritis, and perforation of the upper œsophagus in 3 patients who recovered. Radiography of the neck showed no abnormality in one case, "insignificant" osteo-arthritis of the cervical vertebræ in another, and moderate osteo-arthritis of the fifth cervical vertebra in the third. In the absence of stronger evidence we do not feel that routine radiography of the neck would be helpful. It is, however, a wise precaution to test the mobility of the neck when considering a gastroscopy.

Perforation of the œsophagus could be practically eliminated by giving up the use of the Hermon Taylor gastroscope. This instrument has, however, great practical advantages and provides a more certain view of the distal part of the antrum and of the posterior wall of the stomach. For this reason many gastroscopists (including ourselves) are unwilling to abandon its use completely. A very great reduction in the number of accidents could still be brought about by giving up the use of the Hermon Taylor gastroscope in women over 50, unless its use is specially indicated; for it is in this group that the great majority of accidents are found. It might also be wise to use the Hermon Taylor instrument only on inpatients, so that treatment can be instituted immediately in the event of perforation.

All gastroscopists agree that it is important to maintain flexion of the head and to use the fingers to keep the tip of the gastroscope from pressing against the posterior wall of the pharynx during its passage through the hypopharynx. With this technique, Hermon Taylor has personally made several thousand examinations without causing a fatal perforation of the œsophagus. On the other hand, several of the reported accidents occurred in the hands of the most experienced examiners, and only a few could be attributed to inexperience. In our opinion it is generally safer to reduce the use of the Hermon Taylor instrument in women over 50 to the minimum, rather than to rely on the examiner's skill. The possibility of pressure necrosis cannot in all cases be excluded

---

† Since this paper was written the G U Manufacturing Co. Ltd. have succeeded in greatly increasing the flexibility of the Hermon Taylor instrument. This modification should diminish the risk of instrumentation.—F. A. J.

The most striking finding is that nearly all the perforations occurred with the use of the Hermon Taylor instrument A death from perforation was reported with the Wolf Schindler gastroscope, and it is possible that a death in the miscellaneous group should have been properly classified as another (see below) To determine the relative risk of the two instruments, it is necessary to know the proportion of examinations made with each of them The estimates made cannot be claimed to be accurate, but neither can it reasonably be held that they are so far out as to account for the different accident-rates It cannot be argued that the lower rate with the Wolf Schindler instrument springs from its being used by more skilful examiners, for, if the comparison is confined to the results reported by the eight gastroscopists who had made more than 500 examinations with each instrument, the same sort of difference is obtained In 14,000 gastroscopies performed by them with the Hermon Taylor gastroscope there were 22 perforations, while in 9000 gastroscopies done with the Wolf Schindler gastroscope there was 1 It must therefore be concluded that the Hermon Taylor instrument is the more dangerous On the other hand, Schindler's claim that his instrument is "completely safe" is shown to be very close to the truth, though it is not entirely substantiated

The blunt metal and the rubber finger tips have been associated with about equal numbers of accidents Both types are in common use, hence there is probably no great difference in the accident rates The blunt rubber (or sponge) tip, which was associated with only 2 accidents, was probably used correspondingly rarely

An interesting observation is that there was no difficulty in instrumentation in 60% of the perforations in which evidence on this point was recorded In fact, the proportion in which there was no difficulty was probably even higher, since it may be presumed that when difficulty was encountered it was more likely to be reported, in view of the end result of the examination Evidently, even with the greatest caution, and if the examination had been abandoned at the slightest abnormal resistance, there would still have been an appreciable number of perforations Accidents were, however, relatively more frequent when there was difficulty, since difficulty is only ordinarily encountered in a small proportion of gastroscopies

Analysis by sex and age of the patient leads to an important finding It has been recognised for some time that the risk is greater in middle aged and elderly women, but the survey demonstrates the very great differences involved If the proportion of examinations made in each age and sex subgroup at one clinic are typical of the whole survey—and gastroscopists who have been asked agree that they are not far out—it can be concluded that the risk in women aged more than 50 is some nine or ten times that in men aged more than 50 and that in younger women, and thirty times that in younger men. The relative risks may be even greater, because many gastroscopists have been accustomed to using the Wolf Schindler instrument in old women, thereby decreasing the risk of perforation

TABLE III—PERFORATION OF ŒSOPHAGUS AND ASSOCIATED ÆTIOLOGICAL FACTORS *

Proportion of gastroscopies	Ætiological factor		No of cases	No of deaths
70 %	Type of instrument	Hermon Taylor	49	22
30 %		Wolf Schindler	4	1
—		Not known	1	0
?	Type of tip	Blunt metal	20	11
?		Rubber finger	25	8
?		Rubber sponge	2	1
?		Not known	7	3
?	Difficulty with instrumentation	Present	15	9
?		Absent	23	10
?		Not known	16	4
39 % †	Sex and age of patient	$M < 50$	3	1
37 %		$M > 50$	10	4
10 %		$F < 50$	3	1
14 %		$F > 50$	36	16
—		Not known	2	1
?	Gastric diagnosis	Gastric ulcer	15	8
?		Carcinoma	12	5
?		Atrophic gastritis	6	3
?		Other	9	6
?		Not known	12	1

* Including 4 cases with 2 deaths excluded from table I.

† Based on 898 gastroscopies done by one examiner

No figure has been obtained of the number of examinations made in different clinical conditions, hence it is not possible to compare with much confidence the accident rates in ulcer, carcinoma, and other conditions. Nevertheless it is unlikely that gastroscopy was performed in patients with carcinoma as often as in those with ulcer, and the number of perforations associated with carcinoma must be considered high The perforation was twice directly related to the growth, which had in these instances extended up into the œsophagus, in the remaining cases the lesions were independent. A possible explanation is the association of both carcinoma and perforation with an atrophic mucosa, and it is notable that the main pathological lesion in the stomach was described as "atrophic gastritis" in 6 other instances, and specially that 2 of these were cases of pernicious anæmia, a condition which can relatively seldom have been examined gastroscopically A higher proportion of the carcinoma patients than of the others examined would, admittedly, have been elderly women, and this alone may account for the findings On the other hand, it may well be that it is the frequent occurrence of an atrophic mucosa (in the œsophagus) which makes both elderly women and carcinoma patients specially vulnerable

Perforation of Stomach

After perforation of the œsophagus the next most common accident was perforation of the stomach, though it was responsible for only 1 death This accident used to be common when the rubber sponge tip was in general use (Schindler 1949), but it has become rare since The type of tip used is known in only 5 of the 9 cases in this series, the rubber sponge tip was used in 3 of these, and, in view of the rarity with which it is used, this is consistent with the belief that the rubber sponge tip predisposes to gastric perforation

Hæmorrhage

Little attention has been paid to the incidence of hæmorrhage following gastroscopy, doubtless because of the difficulty of distinguishing between hæmorrhage produced by the instrument and that occurring coincidentally In all, 7 cases were reported, including 2 in which 1 oz of blood was vomited shortly after the examination Slight hæmorrhage of this order may well have occurred on other occasions without being recorded in the series On the other hand, of the 2 deaths, 1 was due to a hæmorrhage which occurred the day after gastroscopy in a patient with hepatolienal fibrosis and may not have been due to instrumentation We have gastroscoped patients less than twenty four hours aft a profuse hæmorrhage and have often performed gastroscopies three or four days afterwards without producin any untoward result Though it would be natural t suppose that hæmorrhage was an appreciable risk of th examination, experience indicates that major hæmorrhag is remarkable for its rarity

Miscellaneous Complications

The 4 miscellaneous cases recorded in table I consiste of 2 patients who died within twenty four hours o jejunal ulcer not otherwise clearly demonstrated. In the small group of patients who bleed repeatedly and have not had a chronic ulcer demonstrated previously, gastroscopy may be of great value in defining the site of the bleeding and determining the need for surgery. In patients with unexplained hæmatemeses, gastroscopy within three to ten days of the hæmorrhage may demonstrate a rapidly healing acute ulcer. However, routine gastroscopy after hæmatemesis to demonstrate such ulcers is not justifiable; gastroscopy soon after hæmatemesis merely to save radiology should not be encouraged. Whether or not gastroscopy assists in the indication for operation in duodenal ulcer remains to be worked out; in such cases it is only justified as part of a planned research. Hermon Taylor (personal communication) has suggested that jejunal ulcers are particularly likely to develop after gastro-enterostomy in those cases in which a duodenal ulcer is associated with increased rugosity of the gastric mucosa. In our view generalised changes in the appearance of the gastric mucosa which have been supposed to indicate gastritis of various kinds are not consistently associated with symptoms. We do not regard the diagnosis of such cases of gastritis as a profitable use of gastroscopy—at least not until further evidence has been provided of their clinical significance.

When it is necessary to check the healing of gastric ulcers gastroscopically to relieve an overburdened X-ray department, it seems advisable to use the Wolf-Schindler gastroscope.

Gastroscopy has a limited but very useful sphere in the practical management of patients with gastric diseases, and the gastroscope still remains a valuable research instrument. Gastroscopy should not be regarded as a final diagnostic method, but the information it provides should be assessed with the clinical picture and other investigations.

SUMMARY AND CONCLUSIONS

The risks associated with gastroscopy have been assessed by means of a questionary sent to forty gastroscopists.

Altogether 75 accidents with 32 deaths were reported, following 49,000 gastroscopies; a further 5 accidents with 3 deaths were reported, but the corresponding number of gastroscopies was not known.

54—i.e., two thirds—of the accidents were perforations of the œsophagus, the great majority of which were in the upper part. Nearly all the perforations of the œsophagus followed the use of the Hermon Taylor gastroscope.‡ Most of them occurred in women over 50 and the risk in this age and sex group is estimated to be nine or ten times that in men aged more than 50 and in younger women, and thirty times that in younger men. It is recommended that the Wolf-Schindler gastroscope should be used routinely for gastroscopy in elderly women and in all outpatients.

An appreciable number of accidents have occurred with both the blunt metal and the rubber finger tips; insufficient evidence has been obtained to determine which is the safer.

Since the introduction of penicillin a considerable proportion of patients with œsophageal perforations have recovered on medical treatment. It is reasonable to treat mild cases conservatively in the first instance, but perforation of the lower œsophagus and cases in which a gross leak is apparent should be treated by immediate suture.

Perforation of the stomach has been rare following the abandonment of the rubber sponge tip; when it occurs it may be treated medically.

16 reactions to the anæsthetic were reported, 5 of which were fatal. Of the deaths 4 are attributable to overdosage; 4 ml. of 2% amethocaine should be the maximum used as a local surface anæsthetic.

The indications for gastroscopy are discussed.

We wish to record our thanks for the coöperation of all the gastroscopists who replied to our inquiries. We realise that it is easier to ask questions than to answer them, and we are therefore very grateful for the information and advice, which was often given in great detail, and for the expressions of opinion, which we found most helpful.

REFERENCES

Berk, J. E. (1946) *Gastroenterol.* 6, 218.
Chamberlin, D. T. (1947) *New Engl. J. Med.* 237, 843.
Goligher, J. C. (1948) *Lancet*, i, 355.
Jackson, C. A. (1949) *Brit. med. J.* i, 99.
Lichtstein, J., Wharton, G. K. (1948) *Gastroenterol.* 11, 127.
Schindler, R. (1940) *Amer. J. digest. Dis.* 7, 293.
— (1945) *Gastroenterol.* 5, 34.
— (1949) *Ibid.* 13, 473.

ACCIDENTAL PERFORATION DURING GASTROSCOPY

T. H. Boon
M.D. Durh., M.R.C.P.
PHYSICIAN, ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE

In carrying out nearly 4000 gastroscopies in the past thirteen years I have had 5 mishaps attributable to passing the instrument. Of these gastroscopies 3000 are included in a combined series published in the accompanying paper by Avery Jones and his associates. My mishaps include 4 of gastric perforation and 1 of damage to the posterior wall at the pharyngo-œsophageal junction. All the cases, particularly the gastric perforations, presented an undramatic picture so unlike what one would expect from a perforated viscus as to seem to justify a detailed description for the guidance of those who have not yet encountered such complications.

CASE-RECORDS

Case 1.—A woman, aged 47, was admitted to hospital with symptoms suggesting gastric carcinoma: for six months she had had weakness, loss of weight, anorexia, and vague upper abdominal discomfort. General examination and a barium meal revealed no abnormality. A gruel test-meal showed achlorhydria, and there was moderate hypochromic anæmia. Occult blood was absent from the stools. I was asked to perform a gastroscopy to exclude carcinoma.

Gastroscopy.—The gastroscope was passed easily and without any sensation of resistance at the cardia or elsewhere. I was at that time relatively inexperienced, and I tried repeatedly to inflate the stomach and make the mucosa visible, but I was unsuccessful and withdrew the gastroscope. The patient then complained of upper abdominal discomfort, and examination revealed abdominal distension and loss of hepatic dullness. Perforation of the stomach had evidently taken place, but the patient's general condition was not serious. There was little or no rigidity, and a house-surgeon with moderate experience of surgical emergencies doubted the diagnosis on general inspection of the patient.

Operation.—A perforation in the upper posterior part of the stomach near the greater curve was found and sutured. The gastric mucosa was seen to be atrophic. Recovery was uneventful.

Case 2.—A woman, aged 58, had six months' history of upper abdominal pain, relieved by "Maclean's powder," with poor appetite and loss of weight. A barium meal showed irregularity and probably thickening of the greater curvature of the stomach, and a gruel test-meal showed no free hydrochloric acid.

Gastroscopy.—I had no difficulty in passing the gastroscope, but after the insertion of a little air I saw omentum, which proved that perforation had occurred. Examination of the abdomen showed some general tenderness but far short of the usual board-like rigidity following perforation of a peptic ulcer. The patient was examined by a surgeon with considerable experience of surgical emergencies who was not entirely satisfied with the diagnosis until radiography demonstrated gas beneath both cupolæ of the diaphragm.

---

‡ See footnote p. 649.

as a cause of the perforation, and with tight instrumentation, particularly in short-necked patients, the examination should be concluded quickly

Accidents other than perforation of the œsophagus are very rare, but, nevertheless, some of them are readily preventable Abandonment of the rubber sponge tip practically eliminates perforation of the stomach Schindler (1949) maintains that the rubber finger tip is the only safe tip to use, but the experience of this survey provides no conclusive reason for preferring it to the blunt metal tip The rubber finger tip may act as a dilator and so make instrumentation easier when difficulty is encountered in passing the gastroscope through the pharyngo œsophageal sphincter, but many gastroscopists prefer the blunt metal tip in the straightforward case, and on the evidence available it is not necessary to discourage its use

Deaths under anæsthesia can be almost eliminated by strict limitation of the dose of local anæsthetic 4 ml. of 2% amethocaine hydrochloride should be regarded as the maximum to be administered Attention to this rule would have prevented 4 of 5 deaths under anæsthesia In our experience it is seldom necessary to use more than 2 ml., an additional 2 ml is required only when the first dose has been swallowed too rapidly

Sensitivity and toxic reactions to amethocaine hydrochloride have been studied by Jackson (1949), who makes the following recommendations about prophylactic measures

(1) A barbiturate should be given by mouth in preoperative preparation—e g , phenobarbitone gr 3 (0 2 g), or 'Sodium amytal' or nembutal gr 1½ (0 1 g) 40 minutes before gastroscopy

(2) An amethocaine pastille gr 1 (65 mg) should be given to the patient to suck 30 minutes before gastroscopy

(3) Amethocaine, when used for surface analgesia, should have adrenaline, 1 in 1000 solution, added in a proportion of 4 to 1 by volume, and the total dose of amethocaine should not exceed 4 ml of a 2% solution (80 mg) or the corresponding amount of a more dilute solution

(4) Application with a laryngeal spray should be avoided, since it can easily lead to overdosage

(5) Amethocaine should never be applied to an inflamed, traumatised, or highly vascular epithelial surface

(6) Amethocaine should be avoided in patients giving a history of allergy or in severely debilitated or cachectic persons

Though some gastroscopists find that an amethocaine pastille is adequate, our own experience leads us to prefer 2% solution of amethocaine hydrochloride We have no experience of adding adrenaline and have so far not found it necessary with the limited amount of amethocaine that has been used If a reaction develops, an unobstructed airway should be secured as quickly as possible with an endotracheal tube, and convulsions should be controlled by the intravenous administration of a rapidly acting barbiturate—e g , sodium thiopentone—an ampoule of which should be kept in the clinic According to Jackson (1949) 0 5 g is usually sufficient

TREATMENT

It is difficult to make accurate comparisons of the results of different treatments from the sort of material which has been collected in this survey, and the difficulty has been increased by the fact that part of the series occurred before the introduction of penicillin Since penicillin has been available we have records of 22 patients who were treated conservatively and 6 who were treated by immediate suture Of the former, 5 died, and of the latter, 2 These figures cannot be compared directly, for the types of case in the two groups are probably not comparable For example, there were 2 lower œsophageal perforations in the immediate suture group and none in the conservatively treated group Some of the fatal cases which were treated medically were so treated because the patient's condition did not permit surgical intervention, and others were so mild that surgery was never considered Again, as has been mentioned, mild cases which resolved are less likely to have been reported than fatal cases , hence the fatality rate is likely to be overestimated It is clear, however, that in a considerable proportion of cases the patients recovered on conservative treatment, including some in which the lesion resolved without drainage despite the initial presence of surgical emphysema All that can be concluded is that cases which have mild symptoms and are diagnosed early may reasonably be treated conservatively It is, on the other hand, the consensus of opinion that immediate suture should be undertaken for perforations in the lower œsophagus and when there is evidence of a gross leak The need for early treatment makes it desirable that all patients should be examined three or four hours after gastroscopy , outpatients should be detained for this period and then given instructions to report immediately if they develop a severe sore throat or difficulty in swallowing When there is doubt, radiography of the chest and neck will usually demonstrate the presence of air outside the œsophagus if a perforation is present

Perforation of the stomach during gastroscopy is quite a different condition from that occurring spontaneously, the essential difference being that the stomach is empty when the perforation is produced instrumentally These cases are eminently suitable for medical treatment, in fact, if laparotomy is carried out it will not infrequently be impossible to find the perforation The literature contains 4 such cases (Schindler 1945, Berk 1946, Chamberlin 1947, Lichstein and Wharton 1948) and a 5th, with recovery, occurred in this series Of the gastric perforations in the present series, 3 were treated medically and 5 had laparotomy , all recovered The method of treatment of the patient who died is not known

INDICATIONS FOR GASTROSCOPY

Owing to the definite risk attached to gastroscopy it is important that the indication for each examination should be clearly defined Gastroscopy is particularly useful when there is a disparity between the clinical history and the radiological findings. In patients in whom radiography reveals no abnormality of the stomach, but who nevertheless have symptoms suggesting peptic ulcer or neoplasm, gastroscopy may reveal an organic lesion It is not uncommon to find gastric ulcers which have escaped recognition previously, but the number of carcinomas so discovered is small , however, when a carcinoma is discovered, the case is usually early

Gastroscopy is also of value when an unusual gastric radiological appearance has been demonstrated which does not tally with the clinical picture The deformity may be found to have no intrinsic pathology , what is apparently a large symptomless ulcer high up on the lesser curve may turn out to be a diverticulum of the stomach , a suspected neoplasm may not be confirmed, and laparotomy may be saved Considerable caution must be exercised with distal pyloric defects and, even if the gastroscopy does not confirm the radiological findings, the patient must still be kept under observation and be re examined radiologically Caution must again be observed in assessing the malignancy or innocence of gastric ulcers Gastroscopy will demonstrate that certain ulcers are clearly malignant and others clearly simple, but there is an intermediate group in which it is very hard to be certain, and further observations are needed If the radiological appearance clearly suggests a simple ulcer, gastroscopy is not needed as a routine unless the ulcer fails to heal In patients with gross radiological appearance of neoplasm, little is gained by gastroscopy

In patients with dyspepsia following gastro enterostomy or partial gastrectomy, gastroscopy may define a junal ulcer not otherwise clearly demonstrated In the nall group of patients who bleed repeatedly and have ot had a chronic ulcer demonstrated previously, gastro copy may be of great value in defining the site of the leeding and determining the need for surgery In patients ith unexplained hæmatemeses, gastroscopy within hree to ten days of the hæmorrhage may demonstrate rapidly healing acute ulcer However, routine gastro copy after hæmatemesis to demonstrate such ulcers is ot justifiable, gastroscopy soon after hæmatemesis erely to save radiology should not be encouraged. Whether or not gastroscopy assists in the indication for peration in duodenal ulcer remains to be worked out, n such cases it is only justified as part of a planned esearch Hermon Taylor (personal communication) has uggested that jejunal ulcers are particularly likely to levelop after gastro enterostomy in those cases in which duodenal ulcer is associated with increased rugosity of the gastric mucosa In our view generalised changes n the appearance of the gastric mucosa which have been upposed to indicate gastritis of various kinds are not onsistently associated with symptoms We do not regard the diagnosis of such cases of gastritis as a profitable use of gastroscopy—at least not until further evidence has been provided of their clinical significance

When it is necessary to check the healing of gastric ulcers gastroscopically to relieve an overburdened X ray department, it seems advisable to use the Wolf Schindler gastroscope

Gastroscopy has a limited but very useful sphere in the practical management of patients with gastric diseases, and the gastroscope still remains a valuable research instrument Gastroscopy should not be regarded as a final diagnostic method, but the information it provides should be assessed with the clinical picture and other investigations

SUMMARY AND CONCLUSIONS

The risks associated with gastroscopy have been assessed by means of a questionary sent to forty gastroscopists

Altogether 75 accidents with 32 deaths were reported, following 49,000 gastroscopies, a further 5 accidents with 3 deaths were reported, but the corresponding number of gastroscopies was not known

54—i e, two thirds—of the accidents were perforations of the œsophagus, the great majority of which were in the upper part Nearly all the perforations of the œsophagus followed the use of the Hermon Taylor gastroscope ‡ Most of them occurred in women over 50 and the risk in this age and sex group is estimated to be nine or ten times that in men aged more than 50 and in younger women, and thirty times that in younger men It is recommended that the Wolf Schindler gastroscope should be used routinely for gastroscopy in elderly women and in all outpatients

An appreciable number of accidents have occurred with both the blunt metal and the rubber finger tips, insufficient evidence has been obtained to determine which is the safer

Since the introduction of penicillin a considerable proportion of patients with œsophageal perforations have recovered on medical treatment It is reasonable to treat mild cases conservatively in the first instance, but perforation of the lower œsophagus and cases in which a gross leak is apparent should be treated by immediate suture

Perforation of the stomach has been rare following the abandonment of the rubber sponge tip, when it occurs it may be treated medically

6 reactions to the anæsthetic were reported, 5 of which were fatal Of the deaths, 4 are attributable to over dosage 4 ml of 2% amethocaine should be the maximum used as a local surface anæsthetic

The indications for gastroscopy are discussed

We wish to record our thanks for the coöperation of all the gastroscopists who replied to our inquiries We realise that it is easier to ask questions than to answer them, and we are therefore very grateful for the information and advice, which was often given in great detail, and for the expressions of opinion, which we found most helpful

REFERENCES

Berk J E (1946) *Gastroenterol.* 6 218
Chamberlin D T (1947) *New Engl J Med* 237 843
Goligher J C (1948) *Lancet*, i 985
Jackson C A (1949) *Brit med J* i, 99
Lichstein J, Wharton G K (1948) *Gastroenterol* 11, 127
Schindler R (1940) *Amer J digest Dis* 7 293
— (1945) *Gastroenterol* 5, 34
— (1949) *Ibid* 13 473

ACCIDENTAL PERFORATION DURING GASTROSCOPY

T H Boon
M D Durh, M R C P
PHYSICIAN, ROYAL VICTORIA INFIRMARY NEWCASTLE UPON TYNE

In carrying out nearly 4000 gastroscopies in the past thirteen years I have had 5 mishaps attributable to passing the instrument Of these gastroscopies 3000 are included in a combined series published in the accompanying paper by Avery Jones and his associates My mishaps include 4 of gastric perforation and 1 of damage to the posterior wall at the pharyngo œsophageal junction All the cases, particularly the gastric perforations, presented an undramatic picture so unlike what one would expect from a perforated viscus as to seem to justify a detailed description for the guidance of those who have not yet encountered such complications

CASE RECORDS

Case 1 —A woman, aged 47, was admitted to hospital with symptoms suggesting gastric carcinoma for six months she had had weakness, loss of weight, anorexia and vague upper abdominal discomfort General examination and a barium meal revealed no abnormality A gruel test-meal showed achlorhydria, and there was moderate hypochromic anæmia. Occult blood was absent from the stools I was asked to perform a gastroscopy to exclude carcinoma

Gastroscopy —The gastroscope was passed easily and without any sensation of resistance at the cardia or elsewhere I was at that time relatively inexperienced, and I tried repeatedly to inflate the stomach and make the mucosa visible, but I was unsuccessful and withdrew the gastroscope The patient then complained of upper abdominal discomfort, and examination revealed abdominal distension and loss of hepatic dullness Perforation of the stomach had evidently taken place, but the patient's general condition was not serious There was little or no rigidity, and a house surgeon with moderate experience of surgical emergencies doubted the diagnosis on general inspection of the patient

Operation —A perforation in the upper posterior part of the stomach near the greater curve was found and sutured The gastric mucosa was seen to be atrophic Recovery was uneventful

Case 2 —A woman, aged 58, had six months' history of upper abdominal pain, relieved by Maclean's powder,' with poor appetite and loss of weight A barium meal showed irregularity and probably thickening of the greater curvature of the stomach, and a gruel test-meal showed no free hydrochloric acid

Gastroscopy —I had no difficulty in passing the gastroscope, but after the insertion of a little air I saw omentum, which proved that perforation had occurred Examination of the abdomen showed some general tenderness but far short of the usual board like rigidity following perforation of a peptic ulcer The patient was examined by a surgeon with considerable experience of surgical emergencies, who was not entirely satisfied with the diagnosis until radiography demonstrated gas beneath both cupolæ of the diaphragm

---

‡ See footnote p 649

Operation —A perforation was found high up on the posterior wall near the greater curvature The stomach wall was atrophic Gall stones were present Recovery was uneventful, apart from some postoperative pulmonary collapse, which ultimately cleared well

Case 3 —A man, aged 75, was extensively investigated for hypochromic anæmia without obvious nutritional cause All investigations having proved negative, I was asked to gastroscope him to exclude carcinoma or other intermittently bleeding gastric lesion

Gastroscopy —The patient was somewhat uncoöperative, but the gastroscope was passed without any feeling of obstruction or unusual difficulty The assistant was unskilled in dealing with a difficult patient at gastroscopy, and the patient soon got completely out of position At the initial view the gastric mucosa could not be seen, nor could an illuminated field be detected. It was presumed that this was due to the patient's change of posture, and after repeated unsuccessful efforts had been made to correct it in difficult circumstances the instrument was withdrawn The patient's condition at the end of the examination gave no cause for concern, and he did not complain of any pain Since the field had not been detected, it was considered remotely possible that injury might have occurred, and instructions were given for the patient to be closely watched

Operation —Ten hours after gastroscopy he began to complain of upper abdominal pain, and upper abdominal tenderness was detected The presence of gas beneath the diaphragm was established by radiography and laparotomy was performed The perforation was found high up on the posterior wall near the greater curve, and this was sutured Unfortunately this patient developed fibrillation after operation and died three days later of acute pulmonary congestion

Case 4 —A woman, aged 68, gave a long gastric history, and a barium meal showed possible prepyloric carcinoma

Gastroscopy —The patient was coöperative, and the gastroscope passed without difficulty The initial view showed that the instrument was in the stomach and that the optic was somewhat obscured by mucus The instrument was therefore partly withdrawn to wipe it on the posterior wall at the cardia It was then reinserted without any difficulty, but after the introduction of a little air omentum was seen, showing that perforation had taken place The patient complained of no abdominal pain whatever, and the general condition was entirely satisfactory A Ryle's tube was immediately introduced into the stomach and half hourly suction instituted She was seen an hour later by a senior surgeon of considerable experience, who saw her lying comfortably in bed with a pulse rate of 84 and a normal temperature, stating that she had no abdominal pain While awaiting my arrival he expressed doubt about my diagnosis but had no doubt whatever when complete loss of liver dullness was demonstrated

Treatment—The patient was kept in Fowler's position, and hourly aspiration of the stomach continued Fluids were administered intravenously Sulphathiazole was included in the intravenous drip, and penicillin administered intramuscularly The patient remained completely comfortable without any abdominal rigidity or tenderness The highest temperature reached in the next two days was 99°F, and the pulse rate never rose above 90 After forty eight hours the intravenous medication and aspiration were discontinued, and fluid was administered by mouth Recovery was uneventful

Case 5 —A woman, aged 58, had had gastric symptoms for several years A barium meal suggested an ulcer, which might be malignant, in the prepyloric area

Gastroscopy was done with a little preliminary difficulty in passing the pharyngo œsophageal junction. The patient returned to the ward without any suspicion of damage from the examination Next morning her pulse rate was 100, and temperature 102°F, and she complained of some stiffness and soreness of the neck Examination showed a little tenderness in the mid cervical region on both sides Damage to the pharynx was suspected and radiography of the neck showed a bubble of air behind the pharyngo œsophageal junction

Treatment —With sulphathiazole by mouth and penicillin injections, the patient made an uneventful recovery

COMMENTS

All the aforesaid complications took place after the gastroscope had been passed without unusual difficulty In 3 cases of gastric perforation subjected to operation it was noted that the mucosa was atrophic, which may have been a factor in the perforation The clinical picture in all the complications was undramatic and quite unlike what one would expect from a perforated viscus This is understandable since the patient was premedicated with atropine and morphine or with 'Opoidine' and scopolamine, and the stomach was emptied immediately before the instrument was passed, so that there was no food residue or gastric juice to soil and irritate the peritoneum

The perforation in the 3 cases subjected to operation was in a situation difficult of access to the surgeon Such cases seem to be ideal for medical treatment in that the diagnosis is certain, the stomach is empty at the time of perforation, and the peritoneum cannot be soiled by food. Leakage from a high perforation of the stomach is also unlikely to recur in a patient in Fowler's position

The cases reported here illustrate the ease with which a perforation may be caused at gastroscopy, the lack of serious symptoms immediately after the event, and the desirability of instituting medical treatment without delay when even a slight suspicion of perforation exists

GENERAL ANÆSTHESIA FOR GASTROSCOPY

J C GOLIGHER
Ch M Edin, F R C S
ASSISTANT SURGEON

H L THORNTON
M.R C S, D A
ANÆSTHETIST

ST MARY'S HOSPITAL, LONDON

UNTIL comparatively recently, like most other gastroscopists, we have performed almost all our gastroscopies under local analgesia with amethocaine ('Decicain') supplemented by heavy premedication with 'Omnopon' and scopolamine or barbiturates With some patients, particularly frail elderly subjects, this technique has yielded excellent results, the instrument being easily and painlessly passed, and well tolerated whilst in situ, a few of the patients have indeed fallen asleep during the examination! More often there has been a certain amount of discomfort, either during introduction or subsequently, due to pressure on the gum, to the extended position of the head, or to the inflation of the stomach, and in some cases this has made the gastroscopy a distinctly unpleasant experience It must also be recorded that in a small proportion of the cases referred for gastroscopy—about 1 in 30—nervousness and lack of cooperation on the part of the patient have prevented the passage of the instrument and the attempt at examination under local analgesia has had to be abandoned Altogether it can fairly be stated that gastroscopy under local analgesia is an investigation that few patients relish or are readily willing to have repeated on them

The only reason why local analgesia has been tolerated, despite its obvious imperfections, is that it has been held to be much safer than any form of general anæsthesia for this purpose, but with the recent advances in general anæsthetic technique we have felt that there are now good grounds for challenging this contention During the last eighteen months or so we have been experimenting with several methods of administering general anæsthesia for gastroscopy and œsophagoscopy and have eventually arrived at a technique which we are satisfied is thoroughly practicable and possesses significant advantages over purely local analgesia In this paper we shall describe our experiences with general anæsthesia for these forms of endoscopy, particularly gastroscopy

METHODS TRIED

General Anæsthesia Alone —We have had a very limited experience of thiopentone alone for gastroscopy and œsophagoscopy, but found it unsatisfactory because, in order to produce anæsthesia deep enough to abolish all sensation in the pharynx and give complete relaxation of the cricopharyngeal constrictor, it was necessary to push the dose to dangerous levels. We had also considered the use of 1% bromethol ('Avertin') intravenously, with which one of us had already had considerable experience for maxillofacial surgery, as described by Thornton and Rowbotham (1945), but, in view of the one unexplained fatality encountered in the series of cases which formed the basis of that communication, we decided to seek a safer alternative.

General Anæsthesia and Local Analgesia Combined.—We next tried a combined thiopentone and local analgesia technique, it being hoped that the reduction of sensation in the pharynx produced by the local application would lessen the amount of general anæsthetic required. The local analgesia was achieved by the patients' preliminary sucking of amethocaine tablets and by the application of amethocaine solution by syringe or applicator to the oral and laryngeal parts of the pharynx. This method was certainly more successful, the amount of thiopentone needed being somewhat less, but to secure sufficient muscular relaxation and quiescence for easy endoscopy still necessitated the administration of what we regarded as dangerously depressant doses of thiopentone.

General Anæsthesia and Local Analgesia Assisted by Relaxant Drugs.—It was not until we supplemented general anæsthesia and local analgesia with relaxant drugs, using a technique similar to that described by Scurr (1950) to provide reliable muscular and sphincteric relaxation that we felt we had a really practicable and efficient method. So successful indeed was the addition of the relaxant that we thought the local analgesic might without disadvantage be omitted, but we soon came to the conclusion that a full topical analgesia was always a valuable adjunct in that it helped to reduce the quantities of thiopentone and relaxing drug needed.

It is this threefold method of general anæsthesia and local analgesia supplemented by a relaxant drug that we chose to elaborate and will describe in detail. Before doing so, one other technical question might be discussed, and that is the advisability or otherwise of carrying out laryngotracheal intubation. The advantage of intubation is that it provides a free airway and allows of easy artificial respiration by rhythmic pressure on the anæsthetic bag, if such should become necessary. On the other hand, if a tube is to be tolerated by the larynx and trachea a somewhat deeper plane of anæsthesia must be obtained. The presence of the anæsthetic tube extending from the nasopharynx across the oropharynx to the larynx is also a slight impediment during the passage of the gastroscope or œsophagoscope, though less so than might be anticipated. Our main reason for not using a tube, however, was that we feared it might increase the risk of injury to the posterior wall of the pharynx by forcing the cricoid cartilage and the endoscope backwards against the cervical spine, and in actual practice we found intubation to be unnecessary.

TECHNIQUE OF COMBINED GENERAL ANÆSTHESIA AND LOCAL ANALGESIA SUPPLEMENTED BY RELAXANTS

Premedication.—Omnopon and scopolamine is administered hypodermically $1^1/_4$ hours before the endoscopy in an average dosage of omnopon gr. $^1/_3$, scopolamine gr. $^1/_{150}$ for a healthy adult. Appropriate adjustments are made for extremes of age and weight. Tab. decicain gr. 1 is given 1 hour preoperatively and 30 minutes preoperatively, the patient being instructed to let the tablets dissolve in the mouth as slowly as possible.

Topical analgesia is obtained 10 minutes before endoscopy, using 2% amethocaine. A total volume of 4 ml. of the solution is divided between a galleypot and a Macintosh's laryngeal spray. The patient is supported in a sitting position, the tongue, wrapped in a gauze swab, is gently and fully retracted with the operator's left hand. The fauces are lightly sprayed with amethocaine. After an interval of about a minute to allow this to take effect the analgesic solution is applied to each pyriform fossa in turn with dental cotton rolls held in curved laryngeal forceps. The process is repeated twice on each side, the analgesic solution on the dental roll being held steadily in contact with the base of the pyriform fossa for 30 seconds. The tongue traction is relaxed between each manœuvre or as often as the patient's comfort demands. The patient is now lowered into the recumbent position and the head positioned for laryngoscopy. The solution remaining in the spray is introduced between the vocal cords under direct vision with a Macintosh's curved laryngoscope.

The patient is now turned on his left side and supported in the position for gastroscopy with the left arm extended on a padded board.

General Anæsthesia Combined with Myoneural Block.—Thiopentone 5% is now injected into a convenient vein in the extended arm until the patient falls asleep. After allowing enough time for the thiopentone to take effect, and noting that respiration is adequate and unobstructed, the thiopentone syringe is detached from the needle and a second syringe charged with gallamine triethiodide ('Flaxedil') substituted. Flaxedil is injected in divided doses of 0·5 ml., with pauses to allow each dose to take full effect, until full relaxation is obtained, at which time respiration will have become predominantly diaphragmatic. No attempt is made to pass the gastroscope until this stage is reached, when a change back to thiopentone is made. Once the gastroscope is in place a Denis Browne hook conveying a stream of oxygen is hooked into the angle of the mouth on the right side, and further thiopentone is administered intermittently throughout the examination, as required.

We aim at maintaining an adequate and even respiratory exchange throughout the endoscopy, with complete absence of reflex response to the passage of the instrument. An average total dosage of each drug is flaxedil 60–80 mg., thiopentone 0·5–0·75 g. We seldom find it necessary to repeat the administration of flaxedil once the change to thiopentone has been made.

At the conclusion of the examination the patient is left lying on the left side, and an oral airway is inserted. He is not allowed to return to the ward until we are satisfied that the reflexes are returning, that the airway is free, and that the respiratory excursion is adequate to maintain a good colour when the patient is breathing atmospheric air. Only in a few cases has it been considered necessary to administer oxygen after the examination has been concluded, and then only for the space of 10–15 minutes. By the divided dose method of administering flaxedil we have avoided the accidental overdosage which would result in diaphragmatic paralysis and necessitate the use of neostigmine after the operation.

DISCUSSION OF RESULTS

At first the combined general anæsthetic and local analgesic technique with relaxants was reserved for the more apprehensive patients on whom œsophagoscopy or gastroscopy had already been unsuccessfully attempted under local analgesia alone or who were deemed unlikely to submit to examination with that technique, but, encouraged by the effectiveness and apparent safety of the threefold method, we were soon using it as a routine for these forms of endoscopy. We have now performed 42 œsophagoscopies and 112 gastroscopies in this way without fatality or serious accident. The method has had both advantages and disadvantages which we shall now briefly discuss.

Ease of Introduction and Comfort of Patient

Introduction of the gastroscope or œsophagoscope under the combined anæsthetic technique was always very much easier than under local analgesia alone, even in the most cooperative patients, because the neck muscles were always completely relaxed and spasm of the cricopharyngeal sphincter was eliminated. The usual precautions, however, were observed in passing the instrument, the utmost gentleness being exercised throughout. In the gastroscopies, special care was taken to maintain the point of the instrument in the midline and prevent it falling into either pyriform fossa, and also to press it forwards against the base of the tongue and avoid dangerous impingement on the pharyngeal wall; and this forward manipulation was much more easily carried out in an anæsthetised than in a conscious patient. In no case was it found impossible to introduce the instrument. We anticipated that the complete bodily relaxation produced by the general anæsthetic might make maintenance of the patient's lateral position for gastroscopy more difficult, but this actually proved no problem, and in fact no additional assistance was required over and above the two nurses or dressers normally employed by us during a gastroscopic examination. The patients, of course, have had no discomfort during the investigation and no recollection of the event afterwards, though they may have complained of slight soreness of the throat for a few hours or a day or so. So far as the patients' sensations were concerned, therefore, the method may be looked upon as having been 100% successful.

Respiratory Difficulties

It will be appreciated that the presence of the gastroscope or œsophagoscope in the pharynx pushing the tongue forward is helpful in maintaining an unobstructed airway, and we have had no troubles due to falling back of the tongue. Another possible cause of respiratory obstruction is laryngeal spasm, but thanks partly to the combined use of local analgesia diminishing the sensibility of the pharynx and the larynx, and partly to the relaxant drug employed, this seldom occurred. In the 3 cases so complicated, the spasm was easily overcome by increasing the dose of the flaxedil. A third source of respiratory trouble is temporary apnœa due to overdosage of thiopentone and the relaxant. One of the advantages of the threefold technique that we employ is that the dosage of the general anæsthetic and relaxant usually does not need to be pushed to the point of producing respiratory arrest in order to secure adequate anæsthesia for the endoscopy, but temporary apnœa has occurred in 8 of our patients. This has not caused alarm, for, owing to the relaxation of the laryngeal sphincter, it has been found possible to maintain an unimpeded respiratory excursion by rhythmic pressure on the lower thorax by the anæsthetist without interfering with the course of the gastroscopy or œsophagoscopy—and indeed without the knowledge of the endoscopist! But if this proved insufficient it would be an easy matter to withdraw the instrument and carry out laryngotracheal intubation. We have always arranged for the instruments necessary for this manœuvre to be at hand during gastroscopy or œsophagoscopy under general anæsthesia, though so far we have not had occasion to use them.

Risk of Injury Due to Completely Anæsthetic Condition of Pharynx and Œsophagus

The striking ease of introduction of the gastroscope under this combined general anæsthetic technique has already been mentioned, and any risk of injury to the pharynx or œsophagus due to difficulty in negotiating a spastic cricopharyngeus is certainly eliminated. However it is notorious that postcricoid perforation during gastroscopy or œsophagoscopy may occur in cases in which the passage of the instrument was attended by no difficulty whatsoever, and probably the main factor in its production is compression of the posterior pharyngeal or œsophageal wall between the shaft or point of the instrument and the prominent extended cervical spine. It might be argued that this would be more likely in a completely anæsthetic patient such as is provided by our technique than in one being examined under local analgesia alone, who by virtue of some remaining sensation might feel pain if unusual pressure were exerted and might thereby warn the endoscopist before injury were produced. We very much doubt the validity of this argument, because neither of our only two cases of postcricoid pharyngo-œsophageal perforation due to gastroscopy under local analgesia had any special pain during the examination to indicate that an injury had been produced. But, apart from its manifest unreliability as a safeguard against injury in the forms of endoscopy now being discussed we think that regulation of the gentleness of an endoscopist's manipulations by the amount of pain produced should be condemned in principle. In our view endoscopy should always be conducted in such a way that the patient cannot suffer any pain at all, and we see no reason why the endoscopist should be any less gentle when working with a general anæsthetic technique instead of local analgesia alone. Indeed, so far as gastroscopy and œsophagoscopy are concerned, general anæsthesia and relaxant drugs, by producing complete paralysis of the cricopharyngeal sphincter and neck and jaw muscles, enable the examiner to gauge more accurately the resistance which the point of the instrument is encountering on the posterior pharyngeal wall and thereby to avoid the application of undue force to this dangerous area. As for excessive pressure of the shaft of the instrument, when in position, on the cervical spine due to over extension of the head under general anæsthesia, this need not occur if an experienced assistant is controlling the movement of the head during the examination.

As the accompanying paper by Avery Jones et al. indicates, the risks of gastroscopy are slight and a very large series of cases is required to reveal them in their correct proportions. The number of gastroscopies and œsophagoscopies performed by us with the general anæsthetic technique just described is relatively small, and many more cases would need to be examined in this way to provide conclusive proof of the safety of the method. This additional experience we are in the process of acquiring. We see no reason, however, to suppose that the use of a general anæsthetic technique *per se* should add to the risks of endoscopy any more than suitable general anæsthesia adds to the hazards of the numerous operations in otorhinolaryngology and dental surgery for which it is regularly employed.

CONCLUSIONS

Our experience demonstrates that gastroscopy and œsophagoscopy can be very satisfactorily performed under combined local analgesia and general anæsthesia assisted by relaxant drugs, apparently without increased risk. This technique eliminates all discomfort for the patient; it also provides much easier working conditions for the endoscopist than does local analgesia alone, and it abolishes failure to introduce the instrument. On the other hand, vigilance is required to deal promptly with any respiratory difficulties and avoid danger from this source. Necessitating as it does the presence of an experienced anæsthetist, the method is undoubtedly more elaborate and slightly more time consuming than a purely local analgesic technique. For that reason it may not commend itself to those working in large gastroscopic clinics where many of the cases gastroscoped may be outpatients. Though such workers may think it inconvenient for routine use, we are confident that they will find it indispensable for their more nervous patients who might not otherwise be successfully gastroscoped at all. To explore fully the safety of the method we propose to continue to use it for all our gastroscopies and œsophagoscopies.

We wish to express our indebtedness to Dr R M. Mackenzie and Dr C M Parrott, anæsthetic registrars, for administering the anæsthetics to some of the cases which form the basis of this report

REFERENCES

Scurr C F (1950) *Brit med J* ii 1311
Thornton H L Rowbotham S (1945) *Anæsthesiology* 6 580

USE OF HIGH-FREQUENCY ULTRASONIC WAVES FOR DETECTING CHANGES OF TEXTURE IN LIVING TISSUES

J J Wild
M.A M.B Camb
AT DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA

Donald Neal
B Aero Engng
U S NAVAL RESERVE, AT WOLD CHAMBERLAIN NAVAL AIR STATION

MINNEAPOLIS, MINNESOTA

The development of high frequency ultrasonic apparatus by the U S Navy during the late war provided an opportunity to make some pilot experiments at 15 megacycles on biological tissues The experiments (Wild 1950) were directed towards the measurement and the detection of changes in the texture of biological tissues Further pilot experiments are described below

PRINCIPLE

Electrical energy can be converted into sound energy by means of crystals that show the piezo electric phenomenon Sound waves of very high frequency—far above the audible range—can be obtained in this way If this sound energy is generated in pulses, the pulses of sound waves travel out from the crystal in a manner analogous to that of sound propagated in the larynx. These pulses of sound energy are reflected as echoes from interfaces—i e, surfaces at which density changes—in a manner analogous to that of an echo returning from a mountain

The echoes of the pulses of sound from interfaces can be multiple if enough power is put into the pulses to drive them through multiple interfaces. Thus, if it were possible to penetrate a series of mountains lying one behind the other in the path of a shout, then echoes would be obtained from each successive mountain as the shout passed on through air to the next mountain, and so on

The echoes returning from a mountain at which a shout is directed are picked up by the human ear The piezo electric crystal, in addition to propagating sound-waves, can also ' hear " sound waves Thus one crystal could generate pulses of sound waves while another received the pulses, and the time could be measured for the passage of the sound waves through permeable media placed between the sender and the receiver Or the same crystal can both transmit and receive the echoes—the method used in the experiments described here

MEASUREMENT

Two measurements can be made (1) the time taken for a pulse to travel through a given permeable medium and to return to the source of propagation of the pulse, and (2) the " strength " of the echo or echoes returning from interfaces in the path of the propagated pulses

If we use the analogy of the shout at a mountain face, the time could be measured for the shout to leave the larynx, hit the mountain face, and return to the ear In addition, the ' strength " of the returning echo could be appreciated A loud shout would return a more powerful echo than a less loud shout Again, if it were possible to penetrate a series of mountains of equal thickness and density spaced equally apart, it would be possible to detect a series of successive echoes returned from each successive mountain as the shout passed through The energy of the shout would gradually be lost as it passed through each successive mountain, hence the power of the echoes would gradually fall off until no energy would be left to give an echo However, the *times* to pass through the various " layers " of air and mountain would be a fixed quantity, no matter what the strength of the returning echoes

The value of the two measurements can be summarised as follows if the shouter were blind he could detect both the presence of a mountain in front of him and the nearness of the mountain to him This echo-ranging is used by bats, and by blind people employing electronic apparatus Further, if the speed of sound were known in air and in the various mountain masses traversed by the shout, it would be possible to determine the thickness of the mountains and their distances apart

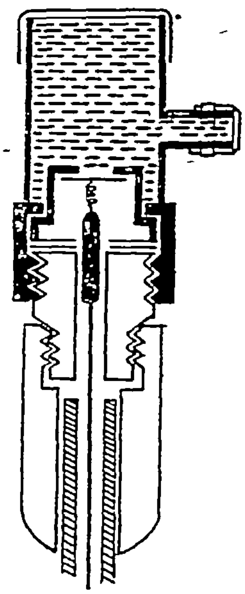


Fig 1—Ultrasonoscope consisting of a chamber filled with water so as to exclude air-bubbles Over one end is stretched a rubber membrane and at the opposite end a piezo-electric crystal is mounted in contact with the water The instrument can be held in the hand in any desired position and applied to the skin in the same manner as the end piece of a stethoscope.

FREQUENCY

The question of frequency of the ultrasonic energy is of vital importance theoretically, and is analogous to the resolution of an optical microscope The higher the frequency the better is the differentiation of texture changes Ludwig (1949) has recommended a frequency of 2 5 mega cycles for the detection of gall stones buried in the muscles of dogs Considerably higher frequencies were considered to be necessary for the differentiation of biological tissues. However, the higher the frequency for a given power output the less is the penetration of the pulses, so a compromise must be worked out for a given application

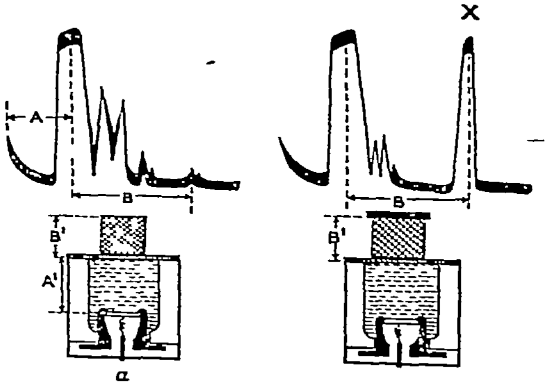


Fig 2—Ultrasonograms from normal brain tissue (*a*) without aluminium sheet interposed (*b*) with aluminium sheet interposed A time taken for ultrasonic wave to travel distance A (from crystal to rubber membrane and back), B time taken for ultrasonic wave to travel distance B (from rubber membrane to far side of brain tissue and back)

blastic The bone marrow, obtained by sternal puncture or at necropsy, appeared aplastic or hypoplastic in twenty six patients, marrow hyperplasia was observed in the remaining case, which followed exposure to radium

DIFFERENTIAL DIAGNOSIS FROM ALEUKÆMIC LEUKÆMIA

Cases of aleukæmic leukæmia may present as refractory anæmias of the macrocytic type, without enlargement of the liver, spleen, or lymph nodes (Scott 1939, Hynes 1940, Wintrobe and Mitchell 1940) Superficially these cases may closely simulate aplastic anæmia Usually in aleukæmic leukæmia the peripheral blood contains primitive cells, while the marrow is hypercellular and shows a hiatus leukæmicus This is not invariably so In aleukæmic leukæmia of the lymphatic type the marrow may be acellular Aplastic anæmia and leukæmia are disorders of the growth of blood cells, and possibly they may occur successively in one and the same patient as phases of one and the same illness

In three patients in the present series aplastic anæmia and aleukæmic leukæmia could not at first be clearly differentiated In one patient a few primitive cells were found in the peripheral blood, but the marrow was hypoplastic, although the primitive cells suggested aleukæmic leukæmia, necropsy a year later proved the case to be one of aplastic anæmia Another patient, who showed a similar combination of an acellular marrow, without preponderance of any one cell type, with the presence of scanty primitive cells in the peripheral blood, became frankly leukæmic shortly before death nine months later, and typical leukæmic infiltrations were seen at necropsy Repeated examinations of blood and marrow may therefore be necessary before a diagnosis between these two conditions can be made

ÆTIOLOGY

Wintrobe (1946) has collected the known causes of aplastic anæmia These are first the aromatic hydrocarbons, of which benzene is the most toxic, organic arsenicals, gold compounds, radioactive substances, and X rays Rare causes are mustard gas poisoning, bismuth, mercury, colloidal silver, dinitrophenol, trinitrotoluene, hair dyes, volatile insecticides, and various analgesics Recently tridione has been added to this list (Mackay and Gottstein 1946, Harrison et al 1946), as well as mepacrine (Custer 1946) Apart from these causes there is a large idiopathic group to which twenty four cases in the present series belong All our patients were closely questioned about possible bone marrow toxins, for removal from exposure may increase the slender chances of recovery Only three were exposed to potential marrow poisons—arsenic, lead, and radium This contrasts with the experience of Bomford and Rhoads (1941), who found a high incidence of toxic causes The discrepancy may be due to the fact that our patients were largely drawn from a rural population where industrial hazards are absent

CLINICAL FEATURES

There were fifteen male patients and twelve female The age of onset varied between 5 and 74 years, with an average of 43 years In most cases the disease presented as an insidious refractory anæmia, without other abnormal clinical features Eight patients first complained of purpuric symptoms such as bruising, bleeding from the gums, and menorrhagia In two the first symptoms were those of agranulocytosis The modes of onset in our cases were as follow

Mode of onset		*No of cases*
Insidious anæmia only		15
Anæmia and purpura	3	8
Purpura	5	
Anæmia and agranulocytosis	1	2
Chronic agranulocytosis	1	
Gross splenomegaly anæmia and agranulocytosis		1
Pyrexial illness with anæmia		1

The spleen was palpable in four cases, in one of them splenectomy was performed and a second came to autopsy

A familial incidence was found in only one patient, whose brother also died of aplastic anæmia Four patients gave family histories of other forms of anæmia, diagnosed as pernicious anæmia in two, leukæmia in one, and an unspecified anæmia in one Congenital defects were uncommon, an undescended testis, a second thumb, microcephaly, and a congenital cyst of the kidney The last occurred in the patient whose brother also had had aplastic anæmia, and this was thought to be an example of Fanconi's syndrome—the association of congenital defects and aplastic anæmia in several members of the same family (Fanconi 1927, Dacie and Gilpin 1944) Minor endocrine abnormalities were present in five patients

PROGNOSIS

Of the twenty seven patients seen during this period of 10 years, only two were alive 2 years after it ended A third patient recovered from the disease after it had run a course of 18 months, but died 6 years later from carcinoma of the colon All the rest have died from the disease, more than half within 2 years of the onset Clinically it seems that purpura and agranulocytosis both adversely affect the prognosis Occasionally it is possible to keep patients alive for long periods by blood transfusions In one patient with severe aplastic anæmia repeated transfusions maintained life for 9 years Nevertheless the results are disappointing, particularly in view of the fact that the patients were followed carefully and transfusions were given without stint

SIZE OF RED CELLS

Bomford and Rhoads (1941) stated that the mean corpuscular volume (M C V) in fifty three of their cases of refractory anæmia was 75–120 c µ, with a mean of 98 c µ Daland et al (1946) published data from seventeen cases of aplastic anæmia in a paper on the differentiation of macrocytic anæmias, but their cases were selected to include only those with a M C V greater than 100 c µ We have measurements of red cells in sixteen cases of aplastic anæmia, where the patient had not been transfused within the previous $3^1/_2$ months

Heparin was used as anticoagulant in determining red cell volumes Red cell diameters were measured by the Price Jones method, using a projection microscope with a high dry lens, as described by Biggs and Macmillan (1948) The dry lens gives diameters about 0 3 µ higher than does the oil immersion lens, owing to optical factors which have been discussed by Gunther (1928) and Mogensen (1938) Our normal values (table I), based on measurement of sixteen controls, are M C V 89 9 c µ ± 0 92, mean corpuscular diameter (M C D) 7 45 µ ± 0 074, and mean corpuscular thickness (M C T)

TABLE I—SIZES OF RED CELLS IN APLASTIC ANÆMIA

Case no	M C V (c µ)	M C D (µ)	S D (µ)	V (%)	Macro cytosis (%)	M C T (µ)
1	97 4	7 93	0 58	7 30	4 8	1 97
2	104 0	8 10	0 61	7 50	10 4	2 02
3	91 4	8 52	0 85	9 93	36 0	1 00
4	111 0	8 41	0 67	7 97	27 4	1 99
5	84 0	7 86	0 77	9 79	6 4	1 73
6	100 3	8 94	0 81	9 07	54 0	2 53
7	—	8 51	0 63	7 43	35 2	—
8	96 5	7 46	0 58	7 80	0	2 21
9	—	8 43	0 75	8 88	29 2	—
10	97 8	8 35	0 57	6 83	24 2	1 79
11	—	8 43	0 71	8 47	20 8	—
12	95 0	7 84	0 63	8 08	2 6	1 96
13	110 0	8 00	0 65	8 13	5 0	2 19
14	92 0	7 89	0 74	9 34	3 6	1 88
15	115 0	8 20	0 71	8 62	17 8	2 05
16	106 0	8 85	0 81	9 14	51 4	1 71

M C V mean 100 0 µ³ ± 2 30 M.C.D mean 8 23 µ ± 0 096, M C T mean 1 97 µ ± 0 066, V coefficient of variability

2 07 μ ± 0 034 The figure for macrocytosis indicates the percentage of red cells which are larger than any normally present in the blood. At least half of this unselected series of cases of aplastic anæmia show a considerable macrocytosis The M C V is abnormally high in twelve of the thirteen available figures, the M.C D is abnormally high in fifteen of the sixteen cases, and the means of both are significantly greater than our normal values The increments in M C V and M C D and the variability are smaller in aplastic anæmia than in pernicious anæmia, and, whereas asymmetry is observed in the Price Jones curves from pernicious anæmia, in aplastic anæmia all the curves tend to be symmetrical about the mean No relation was found between the size of the red cells and the severity of the disease, as measured by course and response to treatment, though probably the macrocytosis, like the anæmia, is due to reduction in the frequency of cell division

LIVER FUNCTION

Bomford and Rhoads (1941) reported decreased liver function in some of their cases They used only two tests of hepatic function—the bilirubin excretion test of Harrop and Barron (1930) and the sodium benzoate conversion test of Quick (1933) Higgins et al. (1944) showed that an estimation of the amount of bilirubin, alkaline phosphatase, albumin, and globulin in the plasma from a single sample of blood usually provides as much diagnostic and prognostic information as can be obtained from more elaborate tests of liver function. In table II the results of these biochemical estimations on our cases of aplastic anæmia are compared with the investigation made by Higgins et al (1944) of liver function in normal people and in proven liver disease On these criteria there is no evidence of impairment of liver function in our cases of aplastic anæmia, a fact which is verified by the absence of structural change in the livers at necropsy

TABLE II—LIVER FUNCTION IN APLASTIC ANÆMIA

Plasma constituents	Normal controls (100)	Liver diseases (71)	Aplastic anæmia
Serum bilirubin (mg per 100 ml)	0 5 ± 0 33	8 4 ± 3 46	0 38 ± 0 04 (27)
Alkaline phosphatase (units)	8 0 ± 2 0	33 0 ± 2 52	8 13 ± 0 64 (16)
Total protein (g per 100 ml)	7 1 ± 0 38	6 8 ± 0 12	6 58 ± 0 14 (18)
Albumin (g per 100 ml)	4 6 ± 0 29	3 2 ± 0 09	4 24 ± 0 2 (18)
Globulin (g per 100 ml)	2 2 ± 0 35	3 2 ± 0 13	2 13 ± 0 16 (13)

The figures in parentheses indicate the number of cases

TREATMENT

No treatment has been found to affect the anæmia, with the exception of blood transfusion. All the known hæmatinic drugs were tried without response Massive dosage of liver extract of known potency (intramuscular ‘Anahæmin’ 200 ml. over 10 days) proved ineffective, as did suprarenal cortical extract (intravenous ‘Eucortone’ 350 ml. in 6 days) Splenectomy, done in four cases, likewise failed to affect the course of the disease Although the anæmia can usually be controlled by transfusion, and the agranulocytic episodes by the antibiotics, we are usually powerless to alleviate the hæmorrhagic tendency

Where there is no loss of blood, as from purpuric lesions, transfusions of blood at regular intervals have maintained a few patients in fairly good health for long periods One patient received 217 pints of blood in 9 years, the transfusions being given at 3 month intervals Nowadays we prefer to transfuse smaller amounts of blood at shorter intervals—e g, one or two pints of blood a fortnight The patient can thus be treated as an outpatient without interruption of his activities In a few patients the transfused blood seemed to be destroyed faster than normal, although there was no rise in the serum bilirubin level One of these patients had his spleen removed, but this did not improve the state of affairs The skin may become pigmented after repeated transfusions of blood, but we have seen no evidence of visceral drainage, such as occurs in hæmochromatosis

DISCUSSION

The cases described here form one of the groups of anæmias which are refractory to all forms of treatment, and in which blood transfusion alone prolongs life For these cases Bomford and Rhoads (1941) have proposed the terms refractory anæmia, but there are other refractory anæmias, such as some of the acquired hæmolytic anæmias (Fisher 1947) To avoid confusion with these and with the refractory megaloblastic anæmias we prefer the older terms aplastic or aregenerative anæmia (Ehrlich 1888) It is true that in some cases of aregenerative anæmia the bone marrow is cellular, but a cellular marrow is infrequent in our experience Even when it is cellular, the marrow is presumably inactive as regards its function of delivering cells to the peripheral blood, and it is this functional aplasia in cases with histologically cellular marrows which justifies their inclusion in the aplastic anæmia group Chemical toxins, such as benzene, may lead to aplasia or to hyperplasia of the bone marrow (Mallory et al. 1939), and a wide variety of blood pictures has been recorded from such causes (Hunter 1939) In our series toxic causes were rare It is perhaps for this reason that so few hyperplastic marrow pictures were encountered, and that the cases were clinically more homogeneous than those described by Bomford and Rhoads (1941)

The pathological material—i e, that obtained at nine necropsies, the spleens from four patients submitted to splenectomy, and forty seven sternal-marrow smears—has not shown any unusual features apart from bone marrow hypoplasia and the excessive iron pigment deposits which usually follow transfusions of large amounts of blood. The underlying ætiology of aplastic anæmia remains unknown Although Bomford and Rhoads (1941) suggested that impaired liver function may be one of the causal factors, no evidence could be found in our cases that the liver is functionally or structurally affected The macrocytosis which has been shown to be a feature of aplastic anæmia can be simply explained by the retarded mitosis of the erythroblasts, as was demonstrated in pernicious anæmia by Japa (1945)

SUMMARY

The clinical features of twenty seven cases of aplastic anæmia are recorded, and the differential diagnosis from aleukæmic leukæmia is discussed The bone marrow was aplastic or hypoplastic in twenty six cases, hyperplasia was present in only one case Only three patients had been exposed to potential marrow poisons, the remainder falling into the idiopathic group

Macrocytosis is shown to be a feature of aplastic anæmia Liver function tests have revealed no impairment in hepatic function

Repeated blood transfusions have proved to be the only means of prolonging life in aplastic anæmia Nevertheless more than half of the patients died within 2 years

I should like to thank Prof L J Witts for his help in the preparation of this paper and his permission to present cases from his department, and also those members of the departments of medicine and biochemistry who made many of the routine investigations

References overleaf

EFFECT OF A C T H IN ACUTE DERMATOMYOSITIS

M M SUZMAN
M D Durh , M R C P
SENIOR PHYSICIAN
JOHANNESBURG HOSPITAL

J A RUDOLPH
M.B Witwatersrand

IN the United States 'Cortisone' and pituitary adrenocorticotropic hormone (A C T H) have been used with varying degrees of success in the treatment of diseases involving collagen tissue, such as rheumatic fever, acute disseminated lupus erythematosus, sclero derma, and dermatomyositis

DISCUSSION

A C T.H. has been used in seven cases of dermatomyositis

Elkinton et al (1949) report the case of a boy, aged 5 years, who had been critically ill for seven weeks with high fever, generalised cutaneous eruption, and œdema, and who was considered to be moribund with hepatomegaly, polyserositis, cardiac enlargement, and hypertension when A C T.H. therapy was begun. Two short courses of 40–80 mg daily were given, followed by a third course, of 80 mg daily, for four days and 10 mg daily for about twenty days After the first two courses relapses occurred, but after the third course a lasting remission was obtained Symptoms of potassium deficiency developed but were readily controlled by the administration of potassium salts

Two cases of dermatomyositis treated with A C T H are reported by Ragan (1950) In the first case, in which the disease had been present for three years, A C T H 100 mg daily was given for eighteen days, this was followed by improvement for twelve days, when a relapse occurred, In the second case, of two years' duration, A C T H 100 mg daily was given for nine days, and improvement was noted during the first five days of therapy, after which there was a great increase in muscular weakness not due to potassium deficiency, and A.C T.H. therapy had to be stopped In both of these patients the dermatomyositis was chronic, in which respect it differed from that of the present patient and of those of Elkinton et al (1949) and Oppel et al (1950)

Oppel et al (1950) report a case in a man, aged 30, who, in his second attack of acute dermatomyositis, made a prompt and dramatic recovery when treated with A.C T.H. 100 mg daily for two days On the seventh day of treatment, after the daily dosage had gradually been reduced to 25 mg , a relapse occurred, which was promptly controlled by increasing the daily dosage to 100 mg The patient remained free from symptoms for four months after having received almost 4 g of A C T H in fifty three days In the early improvement, the return of symptoms when the dosage of A.C T H was reduced, and the fall in the urinary output of creatine their case resembled the present one , but their daily and total dosages of A C T.H were considerably higher

Thorn et al (1950) report three cases A girl, aged 9 years, who had had dermatomyositis for two months, received A C T.H 740 mg in sixteen days in the dosage of 10–15 mg six hourly Her skin lesions improved, but remarkably her muscular strength did not increase appreciably until she had received additional therapy with testosterone In the second case a girl, aged 6 years, with joint symptoms for two months and severe progressive muscular weakness for one month, necessitating the use of a respirator, received A C T.H. 1560 mg in twenty-eight days in the dosage of 20 mg six hourly Gradual improvement took place, and after three weeks the respirator was dispensed with Supplementary therapy with testosterone was given, and after six months, although the girl had regained her strength, the disease was considered to be still active In the third case, in an adult female, after cortisone 100 mg daily for three weeks had brought about very little improvement in muscular strength, A C T H 25 mg six hourly was followed by slight but more definite improvement These workers express the opinion that A C T H can alter the acute inflammatory and destructive process within the affected muscles, but do not think that a lasting remission is likely to be obtained except with vigorous treatment in the very early cases They advocate the additional use of testosterone for its anabolic effect in restoring muscle function and in controlling the inflammation

We report here the effect of A C T H on a patient who was critically ill with acute dermatomyositis and improved dramatically within a few hours and finally recovered completely

CASE RECORD

A man, aged 38 and weighing 325 lb, who had had rheumatic fever at the age of 11 years, had remained well until Feb 15, 1950, when he developed sore throat, malaise, enlarged tender cervical lymph nodes, catarrhal otitis media, and mild pyrexia, for which intramuscular procaine penicillin 300,000 units daily was given for three days Two weeks later, after having shown slight temporary improvement, the patient complained of undue tiredness, profuse perspiration, and moderate pyrexia A preparation of sulphadiazine, sulphamerazine, and sulphathiazole 1 g four hourly given for three days produced only slight improvement

Six days later the symptoms returned with generalised aches and pains and a temperature of 101°F, no definite abnormal physical signs were detected, and "virus infection" was tentatively diagnosed, and the patient was given 'Aureomycin' 250 mg four hourly for two days, but without relief During the following week pyrexia (99–102°F), profuse sweats, and general aching of the body persisted, and the patient began to experience pain and tenderness of the right wrist and of the muscles of the shoulder girdle Acute rheumatic fever was diagnosed, and sodium salicylate gr 20 four hourly was given for four days, and later aspirin gr 20 two hourly was given for twelve days , but this medication, together with frequent 10 mg doses of 'Heptalgin' and 'Physeptone,' did not reduce the fever or relieve the pains

On March 13, the twenty eighth day from the onset of the illness, a blood count showed Hb 13 3 g per 100 ml , red cells 4,400,000 per c.mm , and leucocytes 8700 per c.mm. (neutrophils 68 5%, lymphocytes 20 5%, monocytes 9 5%, eosinophils 1 5%) The red cells showed diffuse polychromasia , the erythrocyte-sedimentation rate (E S R.) was 45 mm in an hour (Wintrobe) Agglutination tests were negative for *Salmonella typhi* O and H, *S paratyphi A*, *S paratyphi B*, and *S paratyphi C* in the dilution of 1/25, and for *Brucella abortus* and *Br melitensis*, and *Proteus O X 19*, *O X 2*, and *O X 4* in the dilution of 1/50 The streptococcal anti hæmolysin 0 titre was 300 units per ml of serum (normal 0–200) The urine contained no abnormal constituents

On the thirty first day of the illness the patient was given deoxycortone acetate 5 mg intramuscularly and ascorbic acid 1 g intravenously After two injections on consecutive days, this medication was discontinued because of a distinct exacerbation in symptoms The pains in the limbs were intensified, the patient could not move his right arm or hand, and, two days later, there developed swelling of the right wrist and pain and tenderness of the left knee The temperature ranged between 100° and 103°F, pulse rate

DR ADAMS REFERENCES

Adams, E B , Witts, L J (1949) *Quart J Med* 18, 173
Biggs, R , Macmillan, R L (1948) *J clin Path* 1, 269
Bomford, R R Rhoads C P (1941) *Quart J Med* 10, 175
Custer, R P (1946) *Amer J med Sci* 212, 211
Dacie J V Gilpin, A (1944) *Arch Dis Childh* 19, 155
Daland G A , Heath C W Minot G R (1946) *Blood*, 1 67
Ehrlich, P (1888) *Charité Ann* 13 300
Fanconi, G (1927) *Jb Kinderheilk* 117, 257
Fisher J A (1947) *Quart J Med* 16 245
Gunther H (1928) *Folia hæmat Lpz* 35 383
Harrison F F , Johnson, R D Ayer, D (1946) *J Amer med Ass* 132 11
Harrop G A jun Barron E S G (1930) *J clin Invest* 9, 577
Higgins G O Brien J R P Stewart A., Witts L J (1944) *Brit med J* i 211
Hunter F T (1939) *J industr Hyg* 21, 331
Hynes, M. (1940) *Quart J Med* 9 177
Japa J (1945) *Brit J exp Path* 26 111
Mackay, R P Gottstein W K (1946) *J Amer med Ass* 132 13
Mallory, T B , Gall, E A Brickley W J (1939) *J industr Hyg* 21 355
Mogensen E (1938) Studies on the Size of the Red Blood Cells Especially in Some Anæmias New York and London
Quick, A J (1933) *Amer J med Sci* 185, 630
Rhoads C P Miller D K (1938) *Arch Path* 26 648
Scott R B (1939) *Proc R Soc Med* 32 1429
Smith L W (1919) *Amer J Dis Child* 17, 174
Wintrobe, M. M. (1946) Clinical Hematology Philadelphia and London
— Mitchell D M (1940) *Quart J Med* 9 67

84–88, and blood pressure 156/84 mm. Hg. For the next few days the patient's condition continued to deteriorate and he began to have severe dyspnœa; his neck muscles became stiff and painful, causing difficulty in turning his head, and both ankles became painful and swollen.

On March 22, the thirty-seventh day of the illness, treatment with procaine penicillin 600,000 units twice daily was begun again, and a blood count showed Hb 14.0 g. per 100 ml., red cells 4,400,000 per c.mm., and leucocytes 16,000 per c.mm. (neutrophils 87.0%, lymphocytes 10.5%, monocytes 2.5%). The E.S.R. (Wintrobe) was 30 mm. in an hour, and the packed cell volume was 42.5%. Blood cultures in bile and broth showed no growth. Agglutination tests for the typhoid, brucella, and proteus groups of micro-organisms again proved negative. The urine contained a large amount of albumin and a large excess of urobilin, but no sugar, bile pigments, or acetone; the sediment contained scanty red cells and pus cells, but no casts.

Clinical examination at this stage showed a very ill man, extremely weak, unable to sit up unaided or to raise his arms from his sides, and hardly able to move his legs. He had severe pains in the muscles of his neck, shoulders, and limbs, was perspiring profusely, and had difficulty in breathing and talking. There was a complete lack of appetite, he was mentally depressed, and weeping spells were frequent. There was swelling of the ankles and wrists, œdema of subcutaneous tissues of the forearm and hands, and rapidly progressing wasting of the arms and legs, involving mostly the deltoid muscles, the outer muscles of the thighs, and the small muscles of the hands, with extreme weakness of the grip. The skin over the left ankle and right wrist was red, and a fine erythematous maculopapular rash had appeared on the skin of the back. The skin had become thickened and firm, offering a greater degree of resistance to the insertion of the hypodermic needles. On examination of the chest, extensive moist sounds were heard throughout both lungs posteriorly. The heart was enlarged to the left, no murmurs could be heard, and the second aortic sound was not heard. The pulse was collapsing in type and the sounds of the peripheral pulsations—so-called "pistol shots"—could be heard on auscultation of the extremities. The systolic blood-pressure was 120–180 mm. Hg, and the diastolic was constantly 0. The liver and spleen were impalpable. The deep reflexes were all present and normal.

Radiography of the chest revealed gross cardiac enlargement, widening of the superior mediastinum, and diminished transradiancy throughout both lung fields, interpreted as being due to congestive changes. Acute dermatomyositis was diagnosed.

On March 27, the forty-second day of the illness, a blood count showed Hb 11.7 g. per 100 ml., red cells 4,100,000 per c.mm., and leucocytes 13,800 per c.mm. (neutrophils 78%, lymphocytes 20%, monocytes 2%). The serum-protein level was 7 g. per 100 ml. (albumin 2.6 g. per 100 ml., globulin 4.4 g. per 100 ml., the A/G ratio being 1 : 1.7). The prothrombin index was 90%, the serum-bilirubin level 1.2 mg. per 100 ml., thymol turbidity 2 units, and thymol flocculation negative; and the cephalin-cholesterol flocculation test gave a one-plus positive reaction. The antistreptolysin 0 titre was 200 units (normal maximum 200 units). Cold agglutinins were not detected. The urine contained a moderate amount of albumin, no sugar, a trace of bile pigment, and a moderate excess of urobilin; the sediment contained no red cells, pus cells, or casts.

Biopsy of Skin and Muscle.—Dr. I. Webster, of the South African Institute for Medical Research, reported as follows:

Sections of this specimen of skin and muscle biopsy show the presence of a keratotic stratified squamous epithelium in which there is a reduction in the stratum granulosum. The rete pegs are irregular and in parts consist of a few layers of cells. There is well-marked increase in the collagen of the corium, and in parts the fibres are swollen and have a necrotic appearance. Adnexal structures are present but are widely separated by the connective tissue. The muscle fibres are swollen in parts, and in an occasional area the cells have a granular appearance. The cross-striations are still present, and no evidence of homogenisation, vacuolation, or necrosis has been found. Although there is no interstitial cellular infiltration, in parts there is a slight increase in interstitial connective tissue. The histological features suggest one of the collagen disease group, but no definite features of dermatomyositis have been detected.

Treatment.—Since neither cortisone nor a potent preparation of A.C.T.H. was available, it was thought that the combined administration of a steroid hormone, such as testosterone, with ascorbic acid, might prove effective. These two preparations were given once daily for seven days: intramuscular testosterone 25 mg. daily, followed immediately by intravenous ascorbic acid 1 g. Concurrently with this therapy, procaine penicillin 900,000 units was given once daily and intramuscular aneurine chloride 100 mg. daily, because of the resemblance of the cardiovascular features to those found in acute vitamin-B_1 deficiency.

After three days of this medication, there having been no improvement, a course of pregnenolone 100 mg. by mouth four-hourly was given for five days as additional therapy. During this treatment the patient's condition continued to deteriorate rapidly, his temperature remaining between 100° and 103°F, with increasing respiratory rate and pulse-rate, extension of the maculopapular eruption on the back, and progressive muscular paralysis and wasting, with severe pains and tenderness in the muscles and joints necessitating the frequent use of pethidine for its relief; swallowing had begun to become difficult, and the breathing more and more distressed.

At this stage, on April 4, when it was considered that the immediate outlook for survival was extremely grave, a substantial supply of A.C.T.H. ('Corticotrophin,' Organon) was obtained.* The 24-hour urinary excretion of 17-keto-steroids was 7 mg., uric acid 0.46 g., preformed creatinine 2.33 g., and creatine 0.56 g. The high figure for creatine was regarded as an important diagnostic feature of acute dermatomyositis. The blood-sodium level was 331 mg. per 100 ml., and blood-potassium level 20.5 mg. per 100 ml. A blood count showed Hb 12.1 g. per 100 ml., red cells 4,100,000 per c.mm., and leucocytes 17,500 per c.mm. (neutrophils 84%, lymphocytes 7.5%, monocytes 6%, eosinophils 0.5%, basophils 1%, myelocytes 1%). The red cells showed diffuse polychromasia. The administration of intramuscular A.C.T.H. 10 mg. six-hourly was begun at 6 P.M. on April 5, 1950, the fifty-first day of illness.

During that night the patient slept well, and next morning, after he had had three doses of 10 mg. each, his condition had improved dramatically. His temperature had fallen to 98.6°F, and his pulse-rate and respiratory rate were lower. He felt very much better, the pain and tenderness in the muscles and joints had diminished appreciably, and he could raise his arms above his head and sit up unaided. His breathing was less distressed, dysphagia had disappeared, and his appetite had improved to the extent that he enjoyed a hearty breakfast for the first time since the onset of his illness. During the first 24 hours of treatment the urinary excretion of preformed creatinine and of creatine showed a pronounced decrease to 1.17 g. and 0.14 g. respectively.

After 48 hours the temperature fell to subnormal levels, there was an appreciable further increase in muscular strength, the swelling of the wrists had disappeared, and all pain and tenderness in the muscles and joints had gone. The patient was now bright and cheerful, whereas previously he had been despondent, depressed, and highly emotional, with frequent weeping spells.

On the fourth day of treatment, his condition generally was found to have improved still further with the return of still greater muscular power. The blood-pressure was 150/0, with "pistol shots" still to be heard at the extremities.

On the seventh day of treatment a blood count showed Hb 12.8 g. per 100 ml., red cells 4,400,000 per c.mm., and leucocytes 31,000 per c.mm. (neutrophils 81%, lymphocytes 11%, monocytes 3%, neutrophil myelocytes 5%). The E.S.R. (Wintrobe) had diminished to 16 mm. in an hour, with a packed cell volume of 41%. The blood-sodium and blood-potassium levels were unchanged at 331 mg. and 20 mg. respectively per 100 ml.; the blood-protein level was 5.5 g. per 100 ml. (albumin 2.8 and globulin 2.7 g. per 100 ml., making the A/G ratio 1 : 1). The fasting blood-sugar level was 120 mg. per 100 ml. On examination of the lungs scanty basal râles were still heard, but the breathing had become normal. The skin rash on the back had faded appreciably, was less erythematous, and had begun to show a faint brownish pigmentation. Two days later the lungs were completely free from moist sounds, and the patient's strength had so improved that he felt he could get out of advantage in skin grafting and the transfer of skin flaps and pedicles

---

* The potency of this preparation, which was furnished through the courtesy of Dr. W. J. Tindall, of Organon Laboratories Ltd., London, was stated to be equivalent to that of 'Lala' (Armour).

(4) More extensive surgery is possible at one operation when bleeding is no longer a deciding factor—e g , extensive skin grafts to face and neck

(5) The postoperative recovery of many patients seems to be considerably improved (see below)

Operations on the head and neck and body wall, particularly when it is necessary to graft large raw areas or to raise extensive skin flaps, where considerable hæmorrhage is expected and the use of tourniquets impossible, are obvious fields in which the low pressure technique has its greatest application In these cases the dry bed and absence of bleeding and reactionary œdema are a great advantage Skin flaps do not seem to suffer from a deficient circulation when blood pressure is low and the field ischæmic Indeed they appear clinically to be much improved The congestive cyanosis produced by a high blood pressure with a relatively restricted venous return is absent, and the flap seems to benefit thereby

Where distortion of skin and subcutaneous tissues is of no significance to the surgeon, an extensive infiltration with adrenaline and saline solution often produces an almost complete absence of bleeding In many fields of surgery this technique is satisfactory, but in plastic surgery it is unsatisfactory Hæmostasis obtained with adrenaline and saline solution in muscle is poor, but with postural ischæmia it is good In bone, where there is no other method of controlling bleeding except by tourniquet, it is particularly successful

Subcutaneous injections of adrenaline cause an intense constriction and emptying of blood vessels which makes effective clotting more difficult, particularly since these vessels retract when cut When the vessels relax, there may be a postoperative reactionary hæmorrhage, particularly if at the same time the blood pressure is rising or raised After hexamethonium bromide the vessels are dilated, lie open on the cut surface, and become thrombosed during the operation They constrict on to the clot during recovery, and for these reasons postoperative reactionary hæmorrhage is considered to be less likely than when local vasoconstrictors are used

Emphasis must be placed again on the need for elevation of the site of operation to produce adequate ischæmia The area will become pallid as ischæmia develops, while the more dependent parts, such as the feet, become congested and their veins stand out prominently Less advantage is gained in perineal surgery with the legs elevated in the lithotomy position, for the blood drains into this area from the legs Although the blood pressure may be reasonably low, there is still some considerable ooze A Trendelenburg tilt can be used to elevate the perineum and so reduce the oozing, but it tends to raise the blood pressure

Similarly, in lower abdominal operations the Trendelenburg position, in the absence of vasomotor control, so assists the venous return to the heart that the blood pressure is maintained at a figure high enough to have a noticeable effect on the pelvic organs There is here a conflict of principle between the drainage of the part concerned and the effect on the blood pressure In such cases it has been found that the horizontal position is the most satisfactory , for, if an adequate drop of blood pressure can be obtained in this position, or by the help of lowered legs only, operations in and around the pelvis receive considerable assistance Where hypotension and postural ischæmia are only partially satisfactory it is observed that hæmostasis is nevertheless more quickly and satisfactorily obtained

TECHNIQUE AND MANAGEMENT

Little change has been made in the method and technique of anæsthesia reported previously (Enderby 1950) A muscle relaxant drug is now added to the thiopentone for induction to assist intubation when this is indicated, and such drugs do on occasion assist the autonomic ganglionic blocking of the methonium compounds We tend to use intratracheal anæsthesia more widely than before because of our anxiety to maintain a perfect airway under all conditions Maintenance of anæsthesia is by nitrous oxide and oxygen (2 1) in a semi closed circle absorber assisted occasionally by very small doses of ether, but intermittent thiopentone is the basal anæsthetic Cyclopropane is avoided Indeed there does not seem to be need for agents stronger than nitrous oxide in the usual conduct of these cases The Gordh needle, which is always used, is placed in the most convenient vein, usually on the dorsum of the foot for most operations on the head and neck Even with steep reverse Trendelenburg positions of 30–40° the circulation time, as judged by the injection of agents via this needle, is not prolonged

The initial dose of hexamethonium bromide varies with age and the preoperative blood pressure, the normal young adult receiving 50 mg , the effects of drug and posture are assessed in 3 minutes Patients over 40 years of age receive 30–40 mg , and hypertensives, arteriosclerotics, and those over 60 years of age begin with 20 mg It is becoming clear that the response to hexamethonium bromide falls roughly into two categories the young healthy patient shows an increase of pulse rate to 120–140 per min and the postural hypotension is not profound , and the older patient, particularly if hypertensive and arteriosclerotic, shows little rise of pulse rate, indeed occasionally a bradycardia, and the postural hypotension is profound The first group requires considerably more hexamethonium bromide and the maintenance of extreme posture (e g , up to 40° reverse Trendelenburg) to preserve surgically useful hypotension The second group may require an increase of an initially small dose of hexamethonium bromide but moderate posture (e.g., 5–10° reverse Trendelenburg) suffices to maintain an adequate hypotension, which when once stabilised at the optimum shows little tendency to alter for $^1/_2$–1 hour Naturally this latter group is much easier to manage when once stabilised, although initially the response to hexamethonium bromide is very dramatic, and needs most careful observation

All hypotensive patients must have the undivided attention of the anæsthetist Repeated blood pressure and pulse estimations are necessary, together with a careful observation of the site of operation Much valuable information is provided by this, and an estimate of blood pressure can be obtained from the degree and nature of the bleeding Only arterial bleeding is observed when there is an optimal hypotension and postural ischæmia When postural ischæmia is poor, venous bleeding is increased Colour changes and the state of the peripheral circulation must be carefully watched It is unpardonable to leave these patients unattended for even short periods If constant attention is impossible, this method should not be used

The measurement of blood pressure requires some practice and the adoption of a standard method for all cases There is wide variation between the figures obtained by auscultation, palpation, and oscillometry Palpation was used when auscultation failed, as it so often did when the pressure was low, and after practice it became possible to palpate to 40 mm Hg More recently oscillometry has been used in all cases it is the most convenient method under theatre conditions It should be borne in mind that this method gives readings 5–10 mm Hg higher than does any other

With the patient prone the legs can be dropped by a combination of the jack knife and reverse Trendelenburg positions This effectively reduces blood pressure, but unfortunately causes pressure on the abdominal veins As a result operations in the spinal canal are accompanied by troublesome bleeding from the dural veins, which are prominent When the patient is supine, elevating the gall bladder bridge causes considerable hypotension The fall is increased when the abdominal incision releases the negative pressure normally transmitted to the upper abdomen by the respiratory excursion All these factors influence the blood pressure by affecting the venous return to the heart

Positive pressure respiration, either assisted or controlled, is another powerful factor affecting blood pressure, the importance of which has been shown by Sarnoff et al (1950) in dogs under total spinal sympathetic block The absence of respiratory movements and a raised pulmonary pressure diminish the venous return to the heart, and they thus have the same effect as posture

Reversion from the inclined to a more horizontal position raises the blood pressure considerably, but it is our policy to prevent any sudden rise of more than 15–20 mm Hg This may be accomplished on return to the ward by elevating the head end of the bed and raising the patient on extra pillows Thus a slow return to normal blood pressure is ensured—an essential factor in promoting coagulation in tissue planes Blood pressure must be higher than 70 mm Hg and rising slowly before the patient leaves the theatre In the hypotensive state danger arising from respiratory obstruction is very much greater, hence the airway must be most carefully preserved until consciousness enables full control to be exercised by the patient

RESULTS

Hæmorrhage

With a hypotension of 55–65 mm Hg assisted by postural ischæmia bleeding is insignificant, and it should not be necessary to produce more profound falls Where posture cannot be used to full advantage, bleeding is noticeable even though the blood pressure is low, and in those positions which cause back pressure on the venous system bleeding may be troublesome Increasing experience enables us to maintain the optimal pressure in most patients, and to obtain the full benefits of postural ischæmia in a wider field of surgery

In this series 170 cases have been conducted at pressures of 55–80 mm Hg and have been entirely satisfactory except occasionally when it has been impossible to use postural ischæmia 55 of our patients have been maintained at 80–100 mm Hg These were not so good as in the previous group, but were nevertheless helpful. This latter figure includes many of the original cases in which pentamethonium iodide was used The remaining 25 are the earliest records when the action of pentamethonium iodide was under investigation and the effect on bleeding was often small or insignificant

The postoperative return of blood pressure is slow, and normal levels are not reached for several hours This is important in the prevention of reactionary hæmorrhage In this series one patient had a small reactionary hæmorrhage soon after return to bed, and it was believed that owing to inadequate posture the blood pressure rose too quickly In two other patients there has been postoperative bleeding, but there were also complicating factors One patient had a large abdominal flap attached to the arm, and on recovery she was restless, and disturbed both the attachment and the dressings In the other patient, who had undergone excision of the head and neck of a femur, an injection of adrenaline and saline solution had been given into the subcutaneous tissues Local vasoconstrictors often raise the blood pressure by a generalised action on the peripheral vessels, and their local action may make reactionary hæmorrhage likely, hence they should not be used

The sudden loss of even a small quantity of blood after vasomotor control has been removed leads to a considerable fall of blood pressure It is dramatic how the pressure can be restored immediately by intravenous replacement of an equivalent volume Where bleeding is anticipated because of the position of the patient or of other factors, it is important to have intravenous therapy to hand Saline solution or dextrose saline solution, &c, may be used as an immediate measure, but blood loss must be replaced eventually by blood

Vomiting

Careful records made by the recovery ward sister and nurses at Queen Victoria Hospital, East Grinstead, have shown the vomiting rate in the first 12–24 hours in an unselected series of 1000 normal anæsthetic cases to be 38% In 100 cases in which hexamethonium bromide or pentamethonium iodide had been given, vomiting occurred in 18% This number is too small to be statistically significant, but the figures are encouraging Further, it is observed clinically that the vomiting of many patients who have undergone a long series of operations can be greatly diminished, and sometimes entirely prevented, by the action of these drugs This effect is more definite during the first three hours after their administration, and few patients vomited during this time, and of those who did vomit many did so only after 'Omnopon' (It is impossible to analyse further the above figures of 1000 cases into pre omnopon and post omnopon vomiting) The action of these drugs on gastric secretion and mobility (Kay and Smith 1950) is probably responsible for the lower rate of vomiting, and perhaps also for the condition sometimes observed where for one or two days after operation patients show little desire for food, whereas normally they enjoy a good appetite

Duration of Operation

It has been possible to shorten many intranasal and antral operations to 5–15 minutes In other regions operations lasting up to 225 minutes have been successfully completed with no apparent ill effects from the low pressure It is not recommended that this technique be used for such lengthy periods Before this method is used, operating time should be reduced by more rapid surgery or by more assistance, for it has long been realised that postoperative morbidity depends directly on the time taken to operate In very lengthy operations it is unwise, in the present state of our knowledge, to add this largely unknown factor of hypotension A plea is thus made for rapid surgery under these better operating conditions in the knowledge that for short periods controlled hypotension is a safe possibility, of great material assistance to both patient and surgeon

Age

The limits have been from 11 to 78 years The best hypotension and ischæmia are more difficult to obtain in the young than in the aged patient Aged patients should be treated with the greatest caution, with the pressure not lower than 75 mm Hg, nor should the operation time be prolonged The coronary circulation in aged patients may be poor Dr D A Robertson has made electrocardiograms of a few of these patients when hypotensive, and he has not found any evidence of coronary ischæmia It is considered that this technique should not be used if signs of coronary arterial insufficiency are already present

Other Findings

A few patients have complained of sleepiness for 24–48 hours after operation This is apparently due to the drug and not to the low pressure It has been observed where the pressure was not lower than 90–100 mm Hg, and has been absent in those with considerably lower pressures Further, it has not been observed in hypotensive patients who have not had hexamethonium bromide

Headaches are rarely complained of

One patient complained of difficulty in reading for 24 hours after operation, an effect probably due to the action of hexamethonium bromide on the nervous control of the eye advantage in skin grafting and the transfer of skin flaps and pedicles

(4) More extensive surgery is possible at one operation when bleeding is no longer a deciding factor—e g , extensive skin grafts to face and neck

(5) The postoperative recovery of many patients seems to be considerably improved (see below)

Operations on the head and neck and body wall, particularly when it is necessary to graft large raw areas or to raise extensive skin flaps, where considerable hæmorrhage is expected and the use of tourniquets impossible, are obvious fields in which the low pressure technique has its greatest application In these cases the dry bed and absence of bleeding and reactionary œdema are a great advantage Skin flaps do not seem to suffer from a deficient circulation when blood pressure is low and the field ischæmic Indeed they appear clinically to be much improved The congestive cyanosis produced by a high blood pressure with a relatively restricted venous return is absent, and the flap seems to benefit thereby

Where distortion of skin and subcutaneous tissues is of no significance to the surgeon, an extensive infiltration with adrenaline and saline solution often produces an almost complete absence of bleeding In many fields of surgery this technique is satisfactory, but in plastic surgery it is unsatisfactory Hæmostasis obtained with adrenaline and saline solution in muscle is poor, but with postural ischæmia it is good In bone, where there is no other method of controlling bleeding except by tourniquet, it is particularly successful

Subcutaneous injections of adrenaline cause an intense constriction and emptying of blood vessels which makes effective clotting more difficult, particularly since these vessels retract when cut When the vessels relax, there may be a postoperative reactionary hæmorrhage, particularly if at the same time the blood pressure is rising or raised After hexamethonium bromide the vessels are dilated, lie open on the cut surface, and become thrombosed during the operation They constrict on to the clot during recovery, and for these reasons postoperative reactionary hæmorrhage is considered to be less likely than when local vasoconstrictors are used

Emphasis must be placed again on the need for elevation of the site of operation to produce adequate ischæmia The area will become pallid as ischæmia develops, while the more dependent parts, such as the feet, become congested and their veins stand out prominently Less advantage is gained in perineal surgery with the legs elevated in the lithotomy position, for the blood drains into this area from the legs Although the blood pressure may be reasonably low, there is still some considerable ooze A Trendelenburg tilt can be used to elevate the perineum and so reduce the oozing, but it tends to raise the blood pressure

Similarly, in lower abdominal operations the Trendelenburg position, in the absence of vasomotor control, so assists the venous return to the heart that the blood pressure is maintained at a figure high enough to have a noticeable effect on the pelvic organs There is here a conflict of principle between the drainage of the part concerned and the effect on the blood pressure In such cases it has been found that the horizontal position is the most satisfactory , for, if an adequate drop of blood pressure can be obtained in this position, or by the help of lowered legs only, operations in and around the pelvis receive considerable assistance Where hypotension and postural ischæmia are only partially satisfactory it is observed that hæmostasis is nevertheless more quickly and satisfactorily obtained

TECHNIQUE AND MANAGEMENT

Little change has been made in the method and technique of anæsthesia reported previously (Enderby 1950) A muscle relaxant drug is now added to the thiopentone for induction to assist intubation when this is indicated, and such drugs do on occasion assist the autonomic ganglionic blocking of the methonium compounds We tend to use intratracheal anæsthesia more widely than before because of our anxiety to maintain a perfect airway under all conditions Maintenance of anæsthesia is by nitrous oxide and oxygen (2 1) in a semi closed circle absorber assisted occasionally by very small doses of ether, but intermittent thiopentone is the basal anæsthetic Cyclopropane is avoided ! Indeed there does not seem to be need for agents stronger than nitrous oxide in the usual conduct of these cases The Gordh needle, which is always used, is placed in the most convenient vein, usually on the dorsum of the foot for most operations on the head and neck Even with steep reverse Trendelenburg positions of 30–40° the circulation time, as judged by the injection of agents via this needle, is not prolonged

The initial dose of hexamethonium bromide varies with age and the preoperative blood pressure, the normal young adult receiving 50 mg , the effects of drug and posture are assessed in 3 minutes Patients over 40 years of age receive 30–40 mg , and hypertensives, arteriosclerotics, and those over 60 years of age begin with 20 mg It is becoming clear that the response to hexamethonium bromide falls roughly into two categories the young healthy patient shows an increase of pulse rate to 120–140 per min and the postural hypotension is not profound , and the older patient, particularly if hypertensive and arteriosclerotic, shows little rise of pulse rate, indeed occasionally a bradycardia, and the postural hypotension is profound The first group requires considerably more hexamethonium bromide and the maintenance of extreme posture (e g , up to 40° reverse Trendelenburg) to preserve surgically useful hypotension The second group may require an increase of an initially small dose of hexamethonium bromide but moderate posture (e.g, 5-10° reverse Trendelenburg) suffices to maintain an adequate hypotension, which when once stabilised at the optimum shows little tendency to alter for ½-1 hour Naturally this latter group is much easier to manage when once stabilised, although initially the response to hexamethonium bromide is very dramatic, and needs most careful observation

All hypotensive patients must have the undivided attention of the anæsthetist Repeated blood pressure and pulse estimations are necessary, together with a careful observation of the site of operation Much valuable information is provided by this, and an estimate of blood pressure can be obtained from the degree and nature of the bleeding Only arterial bleeding is observed when there is an optimal hypotension and postural ischæmia When postural ischæmia is poor, venous bleeding is increased Colour changes and the state of the peripheral circulation must be carefully watched It is unpardonable to leave these patients unattended for even short periods If constant attention is impossible, this method should not be used

The measurement of blood pressure requires some practice and the adoption of a standard method for all cases There is wide variation between the figures obtained by auscultation, palpation, and oscillometry Palpation was used when auscultation failed, as it so often did when the pressure was low, and after practice it became possible to palpate to 40 mm Hg More recently oscillometry has been used in all cases , it is the most convenient method under theatre conditions It should be borne in mind that this method gives readings 5–10 mm Hg higher than does any other

With the patient prone the legs can be dropped by a combination of the jack knife and reverse Trendelenburg positions This effectively reduces blood pressure, but unfortunately causes pressure on the abdominal veins As a result operations in the spinal canal are accompanied

Case 6 —A married woman aged 44, with very advanced metastatic osseous deposits, began treatment with testosterone propionate 300 mg daily on Dec 1, 1949, and this was reduced to 300 mg on alternate days on Feb 28, 1950 While she was having the daily injections her libido was increased very much

Case 7 —A widow, aged 62, with carcinoma of the breast She had a Horner's syndrome and an effusion in the left chest

Treatment with 200 mg of testosterone propionate daily was started on Feb 14, 1950 There was general improvement, with a gain in weight of 14 lb , hirsuties, and a husky voice Libido increased after 14 days, and while the patient was having this massive dosage she was bothered by a constant warm irritation of her clitoris She also complained of an increased sensitivity of her right breast The clitoris measured 0·8 cm wide and was bright red By this time she had received 14 2 g in 71 days

Case 8 —A widow, aged 63, had cancer-en cuirasse involving the whole of the left breast and *osteolytic metastases* Therapy with testosterone propionate 200 mg daily was started in May, 1949, and 39 2 g was given in 196 days About a month after the injections began, the patient had sexual cravings She had a slight growth of beard, a low pitched voice, and an enlarged clitoris

Case 9 —A married woman aged 44, was treated for $9^1/_2$ months periodically with a total dose of 26 1 g of testosterone propionate She had very widespread metastases from breast carcinoma and later developed a pleural effusion.

At one period after doses of 300 mg and later 100 mg daily of testosterone propionate, totalling 11 5 g in 96 days, her libido was much increased, and intercourse was frequent, but her clitoris was not enlarged

Case 10 —A married woman who had the same dosage for about 2 months denied any sexual stimulation, but her reaction to treatment had not been so favourable as in some of the other cases and she still had symptoms of her disease

DISCUSSION

The action of these large doses of testosterone propionate in this small series confirms the earlier findings of numerous workers cited above The inhibitory action claimed by Rubinstein et al. (1940) and Greenblatt (1940) can probably be explained by their use of a small dose Before testosterone was used for metastatic breast carcinoma, large doses were rarely given to women

Perloff (1949) maintains that a genetic factor sets the sexual pattern, and that a hormone develops the organs needed for the sex act and increases their sensitivity to stimulation He states that the increased effect on libido observed in women treated with large amounts of testosterone for breast cancer occurs coincidently with hypertrophy of the clitoris the psychological sexual urge is not primarily increased, but rather the sensitivity of the organ

Any direct psychological effect of the injections received by these patients can be dismissed, because they were all in a poor state of health and some were ignorant of any possible sexual effect of this treatment for cancer Those who knew that they were being given male hormone with probable virilising effects, would not expect an increased stimulation of feminine desire.

In view of the fact that, in the married women, coital frequency was low or normal in their previous state of good health, it is remarkable that, coincident with partial physical improvement with androgen therapy, their sexual appetite should not merely return to its previous level but greatly exceed it

If this increased sexuality is merely due to clitoridal development, it does not explain why in Klein's (1950) rabbits the frequent acceptance of the male only lasted as long as the androgen effect, depending on the method of application, or why it was observed so soon after injection or why it occurred after administration of other steroids—e g , progesterone If the effect is due to clitoridal stimulation and development, one would expect the altered sexual behaviour to last longer It is not unreasonable in view of Klein's observations, to postulate that this effect of testosterone may be m general

In women with Simmonds's disease or Addis disease libido is absent but returns with testoster therapy Possibly androgens may be the normal fa influencing sexual behaviour in both male and fem the added gonadal androgen being responsible for aggressive male sexual behaviour In the female state of receptivity to the male may normally be trolled by adrenal cortical androgens and consider augmented by exogenous androgens In female an cortical adrenal androgens may fluctuate rhythmic as do œstrogens, and act synergically with their œstrus

So far as I know, there is no definite evidence that does occur, but Lobban (1949) has shown that in the ratio between the width of the zona fasciculata the width of zona reticularis, expressed as percen of the cortex width, excluding the glomerulosa, is able , and, when the cats were divided into groups according to the state of activity of their gonads, there was a characteristic ratio for each group, It was chiefly the variations in width of the reticularis which was responsible for the difference in F/R ratio If such variation in measurable histological ratios can be confirmed, it may well coincide with cyclical variations in output of cortical androgen

SUMMARY

During the treatment of advanced cases of mammary carcinomatosis with large amounts of testosterone propionate a considerable and abnormal increase in sexual desire was recorded in those patients who had shown temporary clinical improvement

These observations confirm those of some other workers on the effect of androgens on sexual behaviour in females and are in accord with the experiments of Klein on animals

It is suggested that sexual behaviour in the female may normally depend more on suprarenal androgens than on œstrogens

I am indebted to the late Dr J P Raban and to Drs S Curwen and R C Tudway for referring cases for treatment, and to the faculty of the Bristol Royal Hospital for their permission to do this work which would not have been possible at least in the early stages, without the very liberal supplies of testosterone propionate kindly provided by Ciba Laboratories Organon Laboratories and British Drug Houses

REFERENCES

Abarbanel A R (1940) *Amer J Obstet Gynec* 39 243
Abel S (1945) *Ibid* 49 327
Adair F E Herrmann J B (1946) *Ann Surg* 123 1023
Bender, M X (1937) *C.R Soc franç Gynec* 7 222
Cotte G Martin J F Mankiewicz E (1937) *Gynécologie* 36 581
Desmarest E Capitain Mme (1937) *Pr Méd* 45 777 1109
— — (1938) *Ibid* 46 185
Farrow J H (1944) *Surgery* 16 141
— Woodard H Q (1942) *J Amer med Ass* 118 339
Fels E (1944) *J clin Endocrinol* 4 121
Foss G L (1938) *Lancet*, i 992
Goormaghtigh N (1938) Communication at congress of the Société Royale Médicale Ghent Jan 25
Greenblatt R B (1940) *J Amer med Ass* 115 120
— Mortara F Torpin R (1942) *Amer J Obstet Gynec* 44 658
— Wilcox E A (1941) *Sth Surgeon* 10 339
Groome J R (1939) *Lancet* ii 722
Herrmann J B Adair F E (1946) *J clin Endocrinol* 6 769
— — Woodard H Q (1947) *Surgery* 22 101
Klein, M. (1950) Symposium on steroid hormones Ciba Research Foundation London
Lobban M C (1949) *J Physiol* 109 P 25
Loeser A A (1938) *Lancet* i 373
— (1940) *Brit med J* i 479
— (1941) *Lancet* ii 698
Nathanson I T (1944) *Surgery* 16 108
Perloff W H (1949) *Psychosom Med* 11 133
Prudente A (1945) *Surg Gynec Obstet* 80 575
Rubinstein H S Shapiro H D Freeman W (1940) *Amer J Psychiat* 97 703.
Salmon U J (1937) *Proc Soc exp Biol N Y* 37 488
— (1941) *J clin Endocrinol* 1 162
Silberman D Radman H M Abarbanel A R (1940) *Amer J Obstet Gynec* 39 332
Turpault M (1937) *C R Soc franç Gynec* 7 181
Wilson L (1940) *Endocrinology* 27 29
Wyatt J (1948) *J Obstet Gynæc* 55 53
Zuckerman S (1937) *Lancet* ii 676

Greenblatt and Wilcox (1941), using 25–145 mg. by implantation in ten women, found a definite increase in sexual libido in every patient.

As the dosage used in women increased and workers were conscious of the possible effect on libido, more comments on the stimulation of the sexual urge were made.

Salmon (1941), who gave 500 mg. of testosterone monthly to his patients, reported increased libido during the course of injections and for several weeks after; in many the clitoris was very red and sensitive to touch.

Later Greenblatt et al. (1942) reported on the effect of testosterone on libido in the female, and deliberately treated fifty five patients, aged 22–53, by implantation of pellets to increase it; 100 mg. was the best dose by this method. There was a resurgence of libido in nearly all the patients who had previously had sexual desire.

After Loeser (1941) had reported a beneficial effect of implants of male hormone in cases of mammary carcinoma, several papers were published, mostly in America, on the effect of androgens on cancer of the breast.

Farrow and Woodard (1942), Nathanson (1944), Farrow (1944), Fels (1944), Prudente (1945), and Adair and Herrmann (1946) used gradually increasing doses, but none commented on the effect on libido in a fairly large number of women.

Herrmann and Adair (1946), discussing the effect of testosterone on soft-tissue metastases from carcinoma of the breast in six cases, stated that "facial hirsutism, deepening of voice, and acne, and an increase in libido were encountered to a greater or less degree in all the patients." Herrmann et al. (1947) said that an increase in libido was noted in some of his patients treated for breast cancer with 100–200 mg. of testosterone propionate twice a week or 100 mg. three times a week.

Abel (1945) reported on *androgenic therapy in malignant* disease of the genitalia in five patients who received 150 mg. weekly. One of these women, aged 60, who for two years had not had intercourse, was so stimulated that coitus took place twice weekly. Similar effects were reported in the other patients.

Wyatt (1948), who gave 150 mg. twice a week in one case to a total dose of 35 g., made no comment on a sexual effect.

Following these rather conflicting reports, Klein (1950) reported some remarkable results after administration of steroid hormones to rabbit does.

The spayed doe will not receive the buck unless she has been treated with œstrogens or with other hormones. With testosterone, however, a much more dramatic effect was observed than with œstrogens or with progesterone: the doe received the buck as many times as possible while the androgen effect lasted. When Klein implanted a pellet of testosterone subcutaneously, the doe accepted the male for full coitus six times daily for forty seven days until the implant was absorbed.

PRESENT INVESTIGATION

During a study* of the treatment of cases of very advanced metastases from breast cancer with massive doses of testosterone propionate in oil, a similar effect on sexual behaviour has been found.

The doses of testosterone propionate varied between 200 and 300 mg. daily for several weeks until improvement occurred or the patient was obviously not benefited and was deteriorating rapidly. In those in whom clinical improvement was found the doses were gradually reduced in amount and frequency. The highest total dose is 60 g. and several still under treatment have received over 40 g.

CASE RECORDS

Case 1.—A married woman, aged 42, had had a radical mastectomy in September, 1946, for carcinoma, followed a month later by deep X-ray therapy. In May, 1949, she had developed multiple and widespread osseous metastases involving all the vertebræ of the lower dorsal and lumbar spine, and also the sacrum, both pubic bones, and both ischii. The menses remained regular.

Treatment was started on Jan. 7, 1950, 300 mg. daily of testosterone propionate being given in oil by intramuscular injection. After 52 days her husband reported that *for some while she had lost all her pain and felt* much better, but during the last 14 days she had developed an almost insatiable desire for intercourse. Previously she had never been much interested in sex, and on an average intercourse had taken place about once a month; but she now sought sexual gratification at every opportunity. For the first time in her life she experienced orgasm.

When examined on March 3 she had increased in weight and had a high facial colour and plethora, though there was only a little fine down on her face and chin, and her voice was not much altered. Her clitoris was larger than normal, and she had a slight yellowish vaginal discharge. There had been no menstrual bleeding since Jan. 4. She had received 16 g. of testosterone propionate in 52 days. Radiography later showed that the bones had healed considerably, with union of the fractures.

Case 2.—A married woman, aged 51, had had a radical mastectomy in December, 1948, for scirrhous carcinoma, followed by deep X-ray therapy. Osseous metastases had, however, developed in ribs and vertebræ.

Therapy was started on Jan. 17, 1950, with 200 mg. of testosterone propionate daily while in hospital. She was discharged from hospital on Feb. 25, and when seen a month later she could walk with reasonable comfort. When questioned about any alteration in libido, she said that before her operation, when normally fit, she had usually had intercourse about twice weekly, but during her illness it became infrequent. On her return from hospital her desire had so increased that she sought intercourse four or five times a week. She had had a hysterectomy sixteen years before, and orgasm had been rare; but now she obtained full sexual satisfaction. There was also a slight vaginal discharge, and vulval secretions were increased.

On examination the clitoris protruded from its prepuce and measured 1.5 cm. long and 1 cm. wide. The total dose received by this time was 14 g. of testosterone propionate.

Case 3.—An unmarried woman, aged 42, had had a radical mastectomy for carcinoma in April, 1940. She later developed sciatica, and radiography showed destructive lesions in both ilia and in some vertebræ.

Treatment with testosterone propionate 300 mg. daily was started in November, 1948. The pain disappeared and the patient returned to work. She remained fit and free from any recurrence, and by April, 1950, she had received 38.7 g. of testosterone propionate.

When asked, she said that, since her general health had improved, she had noticed very definite sexual cravings, which she had rigidly to control. She had a sensation of fullness in both groins and was conscious of a continuous warm feeling in the clitoris. The glans clitoris was 1 cm. wide and protruded when the labia were parted. Other signs of virilism were considerable, with a growth of beard, acne, and a deep low pitched voice.

Case 4.—An unmarried woman, aged 53, had had a left radical mastectomy for carcinoma of the breast in November, 1946, followed by deep X-ray therapy. In September, 1948, she developed a pleural effusion and metastases in the right lung.

Injections of 300 mg. of testosterone propionate daily were started in November, 1948. By December, 1949, the pleural effusion had completely cleared and her general condition was excellent. By the end of March, 1950, she had received 52.6 g. of testosterone propionate. She said that while having the daily doses of 300 mg. she had noticed a sexual craving which she found difficult to understand and which was unusual for her. She denied any sensation in her clitoris, but this was 0.9 cm. wide.

Case 5.—A married woman, aged 37, had had a left radical mastectomy in 1942. In October, 1948, two large metastases in the lungs were found.

A bilateral oöphorectomy was done on Nov. 8, 1949, and injections of testosterone propionate 300 mg. daily were started on Nov. 21, 1949, this dose being later reduced to 200 mg. on alternate days. The patient's general health improved, with a gain in weight of 10 lb., but there was little change in the X-ray appearances in the chest. With increased libido, intercourse increased in frequency from once to twice a week. Her clitoris was enlarged; the glans was 0.9 cm. wide and bright red. Her voice was very husky, but there was only a little hair on her upper lip. She had then received 15.7 g. of testosterone propionate.

---

* This study was conducted during the tenure of a grant for a laboratory technician from the British Empire Cancer Campaign.

THE LANCET

LONDON SATURDAY, MARCH 24, 1951

On April 8

THE Census of 1951 is everybody's story, and nobody's. It belongs to everyone, because each of us contributes a brick to its immense structure; and to nobody, because not one of those bricks carries a name and address. The Census is one of the few human institutions that bring benefit to every citizen and harm to none. In its modern shape the information that it reveals tells us not only where we stand, in number and proportion, but also in what direction we are moving. At the present time our nation urgently needs this information, for the last numbering of the people took place as long ago as 1931. The intervention of the blitz ten years ago tore a great hole in our knowledge about population, life, and death, and the gap could only be loosely plugged by more or less inspired guesswork.

The broad general uses of a census are obvious enough, but it is just as well that we should count the blessings we derive from it. The national population returns, and their breakdown into the smallest units of local government, form the only accurate basis for the daily business of living. Some of the figures could be obtained by other means, but the Census is the most economical way of doing the job. Its records are props to trade at every level, and they are indispensable for the administrative activities of local authorities. The shifting pattern of modern industry and the disrupting forces of war have brought important regional changes in the distribution of our population; how great the changes are we can only estimate today, and we need the Census to give exact information to help in the convenient siting of industry and in town and country planning. Again, the vital statistics which are compiled from the Census returns—the tale of birth, death, marriage, and fertility rates—are the stuff out of which national calculations for insurance and retirement schemes are woven; and in the busy world the life assurance companies depend on them for their own livelihood. With an ageing population, and birth rates which—apart from a recent post war increase—have declined steadily over the last seventy years, it becomes of vital importance to know to what extent we are replacing ourselves as a people; it is for this reason that questions are included to discover women's age at marriage, and the number of children that each married woman has had during her lifetime.

In the sphere of medicine almost all the information derived from the Census is valuable: the returns form a well stocked laboratory of social medicine and public health. The rates that are handled in everyday estimates of health and social welfare, such as the birth and death rates, and many of the sensitive indices of social progress or failure, are referred back ultimately to the number of the people. The prevalence of certain diseases owes its discovery to an accurate knowledge of age and sex distribution, and epidemiology in all its length and breadth has the Census as its point of departure. Our knowledge of the principal hazards of industry is intimately related to the information that the Census provides about the number of persons in each occupation, and their age and sex distribution. The registration of deaths and the increasing quantity of facts we receive about injury and sickness join with the Census returns in giving us a clear picture of industrial health and sickness.

The information given for each citizen about his occupation is also used by the Registrars General to break down the population and its mortality experience into social classes, the contrasted experience of which has been helpful in suggesting different types of health hazard associated with varying social environments, and also as a challenge to complacency, holding before us the need to attain for the nation as a whole the standards of experience of the most fortunate. The particulars about occupation and social class depend for their usefulness on a sufficiently detailed description being given of the occupation of each employed person; to get this necessary detail not only must the occupation be described as fully as possible but also the trade in which the work is done, and the name and address of the employer have to be supplied. The Census will likewise give us much new knowledge of housing conditions. The return for Great Britain not only includes the more formal question about the number of living rooms per person; we are also to learn whether the householder has exclusive use of, or has to share, piped water supply, cooking stove, kitchen sink, water-closet, and bath. In the processing of previous censuses a disadvantage has been the long period that had to elapse before the full details could be published for general interest and trade and scientific research. A welcome innovation on this occasion will be the early publication of as much information as possible based on facts derived from a 1% sample of the whole Census population.

The householder scratching his head as he fills in his Census form on Sunday, April 8, may find the task less congenial than his normal sabbath routine; but he may comfort himself with the reflection that our Registrars-General are much more forbearing in their demands than their opposite numbers in most other countries. Relative to the mighty task it must perform, the schedule of questions is a masterpiece of brevity and simplicity, and to a generation trained on football pools the completing of this form should surely be child's play. Past generations have feared to learn unpleasant truths about themselves revealed by census: in a parliamentary debate in 1753 one legislator suggested that a census “may act as the most effective instrument of rapacity ever used against an injured people.” With a century and a half behind us of decennial census taking we now know that the dangers are imaginary and the benefits immense. Nevertheless the Registrars General go out of their way to give reassurance against abuse of privilege and to emphasise that the Census “has no connection whatever with assessing individuals for taxation, with pursuing them for insurance contributions, or with compelling them to perform any other social or national obligation. The personal details derived

It is richly illustrated with line drawings (there are almost five hundred) and it has been attractively printed Some sections will probably need rather regular revision, but this is one of the penalties of writing a book which is thoroughly up to date

Handbook of Child Health

Austin Furniss, L R C P E, L D S, D P H, chief assistant school medical officer, West Ham London Sylvirо Publications 1950 Pp 280 25s

This small but solid book is intended in the first place for the student taking a diploma in child health it will certainly be of more use to the examinee than to the pædiatrician or hygienist A wide field is covered, including the physiology of diet and nutrition, the administrative and other aspects of special schools, and the clinical features and treatment of some of the commoner and some of the rarer diseases of childhood Inevitably much of this is handled in only a superficial way, and the book is not a work of reference At its best this is a general survey of the work done in the school health service it is packed full of facts but is heavy reading

Problems in Cerebellar Physiology

G Moruzzi, M D, professor of physiology, University of Pisa, Italy Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 124 23s 6d

This monograph, based on four lectures given in the Northwestern University three years ago, discusses what is known of the functions of the anterior lobe of the cerebellum, also called the palæocerebellum, which includes the vermis Stimulating this part of the cerebellar mechanisms has important effects on muscle tone, and these are described Professor Moruzzi thus considers the manner in which the cerebellum affects the motor results of activity in the cerebral cortex and spinal cord and examines the intervening structures which might be involved The part played by the "old cerebellum" in modifying tone and movement is related to the activity of the brain stem reticular substance with which it is intimately connected Study of these integrating mechanisms in the central nervous system is now revolutionising our conception of the basis of purposive behaviour within the cerebrum This clear little monograph offers easy access to an aspect of this subject which might well escape the notice of those interested in behaviour in a more general way

Cytologic Diagnosis of Lung Cancer

Seymour M Farber, M D, Milton Rosenthal, M D, Edwin F Alston, M D, Mortimer A Benioff, M D Allen K McGrath, Jr, M D, University of California Medical Service and Department of Pathology, San Francisco Hospital, and the San Francisco Department of Public Health Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 79 45s

The growing importance of early diagnosis of carcinoma of the bronchus, now that thoracic surgery has made such strides in the operative treatment of this condition, has stimulated interest in the laboratory diagnosis, by means of the Papanicolaou technique, of malignant cells in the sputum In this country Dudgeon and his colleagues devised a wet-film technique for this purpose which has since been superseded by various modifications The volume from San Francisco is based upon the study of 1526 cases of non-neoplastic as well as neoplastic diseases of the respiratory tract A full account is given of the different types of normal and abnormal cell that may be encountered in films from sputum and bronchial washings These are illustrated by 60 excellent colour photomicrographs An impressive percentage of positive diagnoses, later confirmed either by biopsy or necropsy, was obtained by these workers, who made their examinations without clinical information to bias their judgment But they properly emphasise the caution required in using this type of diagnostic aid, in particular the novice needs long training to recognise the bizarre forms of non-malignant cells that may appear in films

The Anatomy of Man and Other Animals, or Brothers Under the Skin (London Watts 1951 Pp 158 18s) — This work by Dr D Stark Murray and Miss Grace M Jeffree is a clear elementary description of the probable course of evolution of the animal world, laying special emphasis on "the great variety of uses and of external form with which nature has endowed a fundamental structure which comes clearly from one source," and "the many ways in which nature has sought to do the same job with different types of organ." Within this limited field the authors have successfully performed what they set out to do The book would have been excellent for senior school children if it had been couched in simpler language It is worthy of a better index

Clinical Orthoptic Procedure (London Henry Kimpton 1950 Pp 393 56s) —Mr William Smith is an orthoptist in the Massachusetts School of Optometry, and his book illustrates, in our opinion, the harm that is done when practitioners without a medical training are allowed to treat the general public for such conditions as squint He refracts children of 16 months without a cycloplegic and prescribes glasses for them on this refraction he gives case histories without any follow up to show what happened to the patient, and nowhere does he clearly enunciate the axiom that orthoptic treatment for heterophoria is indicated only where there are symptoms due to the imbalance

Medical Dictionary (Berne Huber 1951 Sw fr [illegible]) —This enterprising new work, edited by Dr E Veillon with the help of a number of colleagues, is really three dictionaries in one cover, for German English French, French German English, and English French German translations are set out synoptically in separate sections, each of close on 500 pages Dr Veillon does not pretend that the dictionary is complete, but it is reasonably full and special heed is given to anatomical terms British readers may be a little daunted to find the Old World following the New in the spelling of such words as "anemia," "color," and "edema"

An Introduction to the Theory of Statistics (14th ed London Charles Griffin 1950 Pp 701 34s) —The title of this classical text by G Udny Yule, F.R.S., and M G Kendall D SC, does less than justice to its most recent revision and expansion, for Professor Kendall has imparted a fresh vitality to the work Of particular importance in medical work is the expansion of the treatment of small samples and the emphasis on both the theory and the practice of sampling inquiries Although primarily intended for use in the study of economics, the new chapters on index numbers and the elementary theory of time series have their potential value to research workers in social medicine and epidemiology

No profound mathematical knowledge is needed to assimilate the contents of this book, it is enough to have a nodding acquaintance with algebra up to the binomial theorem, and a little analytical geometry No serious student of the quantitative aspects of any branch of medical research should be dissuaded by the occasional burst of symbolism from reading it

Microanalysis in Medical Biochemistry (2nd ed London J & A Churchill 1951 Pp 222 14s) —In this new edition of Prof E J King's book, the first chapter, on normal values has been considerably altered A new table of levels of the major constituents of blood, based on a statistical survey of some 80 normal subjects, replaces the former table which quoted generally accepted values Some of the figures listed are so controversial that readers will want to know whether an adequate foundation has been provided for such drastic revision of limits, and though Professor King indicates that the table is intended only for use with the methods described in the text, its publication can only be justified if it stimulates more widespread investigations on similar lines The general plan of the book remains very much the same, but some methods have been revised, and the inclusion of a further selection of biochemical procedures has increased the size Most workers in medical biochemistry have their own tried and trusted methods which they are loth to desert, and for this reason any criticism of the methods selected here would be out of place Professor King is always ready to adopt or adapt the latest refinements in technique as they are published and this quality of progress is one of the most attractive features of a book which has become essential to the laboratory bookshelf

THE LANCET

LONDON SATURDAY, MARCH 24, 1951

On April 8

THE Census of 1951 is everybody's story, and nobody's. It belongs to everyone, because each of us contributes a brick to its immense structure, and to nobody, because not one of those bricks carries a name and address. The Census is one of the few human institutions that bring benefit to every citizen and harm to none. In its modern shape the information that it reveals tells us not only where we stand, in number and proportion, but also in what direction we are moving. At the present time our nation urgently needs this information, for the last numbering of the people took place as long ago as 1931. The intervention of the blitz ten years ago tore a great hole in our knowledge about population, life, and death, and the gap could only be loosely plugged by more or less inspired guesswork.

The broad general uses of a census are obvious enough, but it is just as well that we should count the blessings we derive from it. The national population returns, and their breakdown into the smallest units of local government, form the only accurate basis for the daily business of living. Some of the figures could be obtained by other means, but the Census is the most economical way of doing the job. Its records are props to trade at every level, and they are indispensable for the administrative activities of local authorities. The shifting pattern of modern industry and the disrupting forces of war have brought important regional changes in the distribution of our population; how great the changes are we can only estimate today, and we need the Census to give exact information to help in the convenient siting of industry and in town and country planning. Again, the vital statistics which are compiled from the Census returns—the tale of birth, death, marriage, and fertility rates—are the stuff out of which national calculations for insurance and retirement schemes are woven; and in the busy world the life assurance companies depend on them for their own livelihood. With an ageing population, and birth-rates which—apart from a recent post-war increase—have declined steadily over the last seventy years, it becomes of vital importance to know to what extent we are replacing ourselves as a people; it is for this reason that questions are included to discover women's age at marriage, and the number of children that each married woman has had during her lifetime.

In the sphere of medicine almost all the information derived from the Census is valuable: the returns form a well stocked laboratory of social medicine and public health. The rates that are handled in everyday estimates of health and social welfare, such as the birth and death rates, and many of the sensitive indices of social progress or failure, are referred back ultimately to the number of the people. The prevalence of certain diseases owes its discovery to an accurate knowledge of age and sex distribution, and epidemiology in all its length and breadth has the Census as its point of departure. Our knowledge of the principal hazards of industry is intimately related to the information that the Census provides about the number of persons in each occupation, and their age and sex distribution. The registration of deaths and the increasing quantity of facts we receive about injury and sickness join with the Census returns in giving us a clear picture of industrial health and sickness.

The information given for each citizen about his occupation is also used by the Registrars General to break down the population and its mortality experience into social classes, the contrasted experience of which has been helpful in suggesting different types of health hazard associated with varying social environments, and also as a challenge to complacency, holding before us the need to attain for the nation as a whole the standards of experience of the most fortunate. The particulars about occupation and social class depend for their usefulness on a sufficiently detailed description being given of the occupation of each employed person; to get this necessary detail not only must the occupation be described as fully as possible but also the trade in which the work is done, and the name and address of the employer have to be supplied. The Census will likewise give us much new knowledge of housing conditions. The return for Great Britain not only includes the more formal question about the number of living rooms per person; we are also to learn whether the householder has exclusive use of, or has to share, piped water-supply, cooking stove, kitchen sink, water closet, and bath. In the processing of previous censuses a disadvantage has been the long period that had to elapse before the full details could be published for general interest and trade and scientific research. A welcome innovation on this occasion will be the early publication of as much information as possible based on facts derived from a 1% sample of the whole Census population.

The householder scratching his head as he fills in his Census form on Sunday, April 8, may find the task less congenial than his normal sabbath routine; but he may comfort himself with the reflection that our Registrars General are much more forbearing in their demands than their opposite numbers in most other countries. Relative to the mighty task it must perform, the schedule of questions is a masterpiece of brevity and simplicity, and to a generation trained on football pools the completing of this form should surely be child's play. Past generations have feared to learn unpleasant truths about themselves revealed by census: in a parliamentary debate in 1753 one legislator suggested that a census "may act as the most effective instrument of rapacity ever used against an injured people." With a century and a half behind us of decennial census-taking we now know that the dangers are imaginary and the benefits immense. Nevertheless the Registrars General go out of their way to give reassurance against abuse of privilege and to emphasise that the Census "has no connection whatever with assessing individuals for taxation, with pursuing them for insurance contributions, or with compelling them to perform any other social or national obligation. The personal details derived

It is richly illustrated with line drawings (there are almost five hundred) and it has been attractively printed Some sections will probably need rather regular revision, but this is one of the penalties of writing a book which is thoroughly up to date

Handbook of Child Health

AUSTIN FURNISS, L R C P E , L D S , D P H , chief assistant school medical officer, West Ham London Sylviro Publications 1950 Pp 280 25*s*

THIS small but solid book is intended in the first place for the student taking a diploma in child health it will certainly be of more use to the examinee than to the pædiatrician or hygienist A wide field is covered, including the physiology of diet and nutrition, the administrative and other aspects of special schools, and the clinical features and treatment of some of the commoner and some of the rarer diseases of childhood Inevitably much of this is handled in only a superficial way, and the book is not a work of reference At its best this is a general survey of the work done in the school health service it is packed full of facts but is heavy reading

Problems in Cerebellar Physiology

G MORUZZI, M D , professor of physiology, University of Pisa, Italy Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 124 23*s* 6*d*

THIS monograph, based on four lectures given in the Northwestern University three years ago, discusses what is known of the functions of the anterior lobe of the cerebellum, also called the palæocerebellum, which includes the vermis Stimulating this part of the cerebellar mechanisms has important effects on muscle tone, and these are described Professor Moruzzi thus considers the manner in which the cerebellum affects the motor results of activity in the cerebral cortex and spinal cord and examines the intervening structures which might be involved The part played by the " old cerebellum " in modifying tone and movement is related to the activity of the brain-stem reticular substance with which it is intimately connected Study of these integrating mechanisms in the central nervous system is now revolutionising our conception of the basis of purposive behaviour within the cerebrum This clear little monograph offers easy access to an aspect of this subject which might well escape the notice of those interested in behaviour in a more general way

Cytologic Diagnosis of Lung Cancer

SEYMOUR M FARBER, M D , MILTON ROSENTHAL, M D , EDWIN F ALSTON M D , MORTIMER A BENIOFF, M D , ALLEN K MCGRATH, Jr , M D , University of California Medical Service and Department of Pathology San Francisco Hospital, and the San Francisco Department of Public Health Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 70 45*s*

THE growing importance of early diagnosis of carcinoma of the bronchus, now that thoracic surgery has made such strides in the operative treatment of this condition, has stimulated interest in the laboratory diagnosis, by means of the Papanicolaou technique, of malignant cells in the sputum In this country Dudgeon and his colleagues devised a wet film technique for this purpose which has since been superseded by various modifications The volume from San Francisco is based upon the study of 1526 cases of non-neoplastic as well as neoplastic diseases of the respiratory tract A full account is given of the different types of normal and abnormal cell that may be encountered in films from sputum and bronchial washings These are illustrated by 60 excellent colour photomicrographs An impressive percentage of positive diagnoses, later confirmed either by biopsy or necropsy, was obtained by these workers, who made their examinations without clinical information to bias their judgment But they properly emphasise the caution required in using this type of diagnostic aid , in particular the novice needs long training to recognise the bizarre forms of non-malignant cells that may appear in films

The Anatomy of Man and Other Animals, or Brothers Under the Skin (London Watts 1951 Pp 158 18*s*)—This work by Dr D Stark Murray and Miss Grace M Jeffree is a clear elementary description of the probable course of evolution of the animal world, laying special emphasis on " the great variety of uses and of external form with which nature has endowed a fundamental structure which comes clearly from one source," and " the many ways in which nature has sought to do the same job with different types of organ." Within this limited field the authors have successfully performed what they set out to do The book would have been excellent for senior school children if it had been couched in simpler language It is worthy of a better index

Clinical Orthoptic Procedure (London Henry Kimpton 1950 Pp 393 56*s*)—Mr William Smith is an orthoptist in the Massachusetts School of Optometry, and his book illustrates, in our opinion, the harm that is done when practitioners without a medical training are allowed to treat the general public for such conditions as squint He refracts children of 16 months without a cycloplegic and prescribes glasses for them on this refraction , he gives case histories without any follow up to show what happened to the patient and nowhere does he clearly enunciate the axiom that orthoptic treatment for heterophoria is indicated only where there are symptoms due to the imbalance

Medical Dictionary (Berne Huber 1951 Sw fr 75) —This enterprising new work, edited by Dr E Veillon with the help of a number of colleagues, is really three dictionaries in one cover , for German English French, French German English, and English French German translations are set out synoptically in separate sections, each of close on 500 pages Dr Veillon does not pretend that the dictionary is complete, but it is reasonably full and special heed is given to anatomical terms British readers may be a little daunted to find the Old World following the New in the spelling of such words as " anemia," color," and "edema "

An Introduction to the Theory of Statistics (14th ed London Charles Griffin 1950 Pp 701 34*s*)—The title of this classical text by G Udny Yule, F.R.S , and M G Kendall, D SC , does less than justice to its most recent revision and expansion , for Professor Kendall has imparted a fresh vitality to the work Of particular importance in medical work is the expansion of the treatment of small samples and the emphasis on both the theory and the practice of sampling inquiries Although primarily intended for use in the study of economics, the new chapters on index numbers and the elementary theory of time series have their potential value to research workers in social medicine and epidemiology

No profound mathematical knowledge is needed to assimilate the contents of this book it is enough to have a nodding acquaintance with algebra up to the binomial theorem, and a little analytical geometry No serious student of the quantitative aspects of any branch of medical research should be dissuaded by the occasional burst of symbolism from reading it

Microanalysis in Medical Biochemistry (2nd ed London J & A Churchill 1951 Pp 222 14*s*)—In this new edition of Prof E J King's book, the first chapter, on normal values has been considerably altered A new table of levels of the major constituents of blood, based on a statistical survey of some 80 normal subjects, replaces the former table which quoted generally accepted values Some of the figures listed are so controversial that readers will want to know whether an adequate foundation has been provided for such drastic revision of limits , and though Professor King indicates that the table is intended only for use with the methods described in the text, its publication can only be justified if it stimulates more widespread investigations on similar lines The general plan of the book remains very much the same, but some methods have been revised, and the inclusion of a further selection of biochemical procedures has increased the size Most workers in medical biochemistry have their own tried and trusted methods which they are loth to desert, and for this reason any criticism of the methods selected here would be out of place Professor King is always ready to adopt or adapt the latest refinements in technique as they are published and this quality of progress is one of the most attractive features of a book which has become essential to the laboratory bookshelf

Anticoagulants in Cardiac Infarction

OUR cardiologists have been slow to accept the claims made for the anticoagulants in cardiac infarction, and even today, though some are enthusiastic believers, others remain unconvinced It is only reasonable to demand strong evidence, for anticoagulant therapy involves a considerable expenditure of time, trouble, and money, the technique must be scrupulous, and the coagulability of the blood must be maintained at exactly the right level for several weeks Then there are the hazards inherent in any interference with blood clotting—bleeding into the tissues generally, into the wall of the atheromatous coronary artery, and into the cardiac infarct itself with perhaps an increased risk of ventricular rupture However, aggravation of the cardiac lesion has not been observed in animal experiments, and, judging by the clinical reports, rupture of the ventricle has not become any more common in patients treated with anticoagulants The proportion of cases in which a hæmorrhage into the coronary wall leads directly or indirectly to obstruction of the lumen has been variously assessed at 5–65%, and there can be no doubt that cardiac infarction very often occurs without any recent thrombosis Thus among the 114 cases of gross infarction analysed by **YATER** and his colleagues [1] there were 35 without coronary thrombosis, and less than half of the 336 other fatal cases of coronary disease showed coronary thrombosis These considerations, however, are of no practical importance if it can be shown clinically, in a large series of properly controlled cases, that anticoagulants have a beneficial effect in major attacks of cardiac ischæmia—that is, in the cases clinically termed coronary thrombosis

In Denmark, **HOLTEN** [2] has collected the results of a two-year trial at 21 clinics in which 174 patients were treated with anticoagulants and 256 without It was intended to allot patients to the treated and control groups on alternate days, and, though this rule was not strictly adhered to, the variations have been shown not to affect the results There was a substantial difference in the mortality of the two groups (presumably over a period of a few weeks) After excluding 52 patients who died within 24 hours of admission, the mortality of the treated patients was 22 5% and of the untreated 36% When the patients are divided into age groups the only groups with enough cases to be significant are 50–59, 60–69, and 70–79 in which there were 149 treated cases with mortality 23%, and 229 controls with mortality 37% But at ages 50–59 and 70–79 the mortality is only 4–5% lower in the anticoagulant-treated cases than in the controls Thus in the treated group as a whole the evidence in favour of anticoagulant therapy largely depends on the experience at age 60–69 (mortality of treated cases 17% and of controls 43%)—a peculiar result which requires explanation In the large American series reported by **WRIGHT** and colleagues [3] the benefit of anticoagulants appeared to be greatest in patients aged 70 and over, and the figures given by **TULLOCH** and **GILCHRIST** [4] in England are similar

When we turn to the causes of death, thrombo-embolism was $3^1/_2$ times as frequent in **HOLTEN**'s controls (14%) as in his treated patients, though it is impossible to assess the significance of this complication in the fatal outcome Apart from shock in the earliest stages, the deaths presumably were either due to congestive failure or occurred suddenly from ventricular fibrillation or asystole, which is the general experience If anticoagulants are to prevent these disasters they must do so largely by preventing clotting in the coronary lumen, though embolism, particularly in the lung, may sometimes be a contributory cause of death **HOLTEN** and **TULLOCH** and **GILCHRIST** seem to agree with this view of their action, but **WRIGHT** et al regard the main rôle of anticoagulants as the prevention of thrombo embolism. Such theoretical considerations cannot affect the statistics, which, if they cannot be taken at their face value, certainly cannot be disregarded The time will soon come, it is to be hoped, when we shall know whether the routine use of anticoagulants in coronary thrombosis is worth while or not

Annotations

IMMERSION IN COLD WATER

Two world wars have taught us something of the chances for seafarers and others who are immersed in northern waters Critchley, in his Bradshaw lecture,[5] remarked that of 10 men from a torpedoed vessel who were immersed in water at −1 7°C, only 1 survived half an hour, but a corpulent man of 29, clad in indoor clothes and duffel coat, remained swimming in the Barents Sea in July at a temperature of −1 5°C for nine to fourteen hours Molnar [6] describes a group of 23 people who all survived four hours in a sea at 8°C, even though experiments in baths suggested that this should have lowered the rectal temperature to 24°C, and that few would survive in water near freezing point for more than half an hour and none for more than an hour and a half

This seeming anomaly is explained by Glaser [7] from observations on a man swimming in water at 20°C with a Douglas bag on his back. Glaser remarks that if this subject had been swimming in colder water his heat production would have been similar, for Spealman [8] has made it clear that, in the absence of shivering, heat production during immersion does not depend on water temperature, and, says Glaser

> ' a man who is swimming hard should produce about as much heat as he loses in water near freezing point and he should not die of cold as long as he is able to swim Stiffness of the muscles may eventually interfere with efficient swimming, but muscles which are being exercised hard may remain warm enough to prevent them from becoming stiff Men in baths may shiver but only after they have lost much heat, and they cannot produce enough heat by this means alone to balance their losses in very cold water

Glaser concludes "Fit men therefore, who are in danger of immersion in cold water, might be advised to swim or struggle as hard as they can for as long as they can If they try to preserve their strength by clinging to wreckage or floating on their lifebelts, they will die from cold Perhaps more lives would have been saved in the past if this had been understood " from the returns are treated by the Registrars General and their staffs and by all engaged in taking the Census in complete and absolute confidence and used for statistical purposes only—never in any circumstances to the detriment of the individual concerned "[1] The integrity of the Census administration can be taken for granted It is now up to all citizens to do their duty, for self knowledge is one of the badges of a free people

---

[1] Yater, W M et al *Amer Heart J* 1948 36 683

[2] Holten C *Ugeskr Læg* 1950 112 1205

[3] Wright I S Marple C D Beck D *Amer Heart J* 1948 36 801

[4] Tulloch J A Gilchrist A R *Brit med J* 1950 ii 965

[5] Critchley M Shipwreck Survivors London 1943

[6] Molnar G W *J Amer med Ass* 1946 131 1046

[7] Glaser E M *Nature Lond* 1950 166 1068

[8] Spealman C R *Proc Soc exp Biol N Y* 1945 60 11

The Pituitary and the Blood

IN man, the injection of a small dose of pituitary adrenocorticotropic hormone (A C T H) produces a fall in the eosinophil granulocytes of the peripheral blood which is maximal after about 4 hours In mice and rats, however, the most characteristic effect of A C T H is a reduction in the circulating lymphocytes, and it occurred to G W HARRIS and his physiologist colleagues at Cambridge[2] that this temporary lymphopenia could be used as an indicator of adrenocorticotropic hormone activity and as a means of studying the pathways in the central nervous system through which pituitary stimulation occurs They worked with rabbits, so they had first to confirm that A C T H does cause lymphopenia in these animals, and then to find out whether emotional stress in the rabbit has a similar effect on the lymphocytes, as it has in mice and rats It was soon established that immobilisation of a rabbit in clamps for 3 hours reduced its circulating lymphocytes by about 30%, whereas its granulocytes increased They were able to show that rabbits which have had their hypophysis removed no longer develop lymphopenia after stress, but if the animal is injected intravenously with crude anterior pituitary extract beforehand emotional stress will again produce lymphopenia The conclusions drawn from these findings are that emotional lymphopenia is mediated by stimulation of the pituitary, and that the adrenocorticotropic hormone secreted is the actual lymphopenic agent The possibility of direct nervous stimulation of the adrenal was excluded by denervating the adrenal glands and showing that the reaction was unaffected, the adrenal medulla was unlikely to be involved because injections of adrenaline normally have no effect on the blood lymphocytes

Next, DE GROOT and HARRIS[3] tackled the nerve pathways It seemed that the lymphopenic reaction could again be used, for MIKKELSEN and HUTCHENS[4] had found in man that electric shock therapy is followed by a lymphopenia 3 hours later The Cambridge workers adopted an ingenious indirect electrical method of stimulating the relevant parts of the central nervous system in unanæsthetised but quiescent rabbits Local stimulation of the posterior part of the tuber cinereum or of the mamillary bodies, in the floor of the third ventricle produced a typical lymphopenic response, which could be abolished by cutting transversely through these areas or the zona tuberalis of the pituitary body itself Thus there is good reason for believing that the secretion of the anterior pituitary which causes lymphopenia presumably A C T H, is controlled by the hypothalamus Stimuli from the hypothalamus do not reach the pituitary via the cervical sympathetic nerves, since cutting them does not affect the lymphopenic response GREEN and HARRIS[5] had previously suggested that the hypothalamus influences pituitary secretion by two steps nerve fibres pass from the hypothalamus to the median eminence, where a humoral transmitter is liberated into the portal vessels of the pituitary gland and so carried to the anterior lobe cells The experimental findings are said to support this view

Lymphopenia is uncommon in man It occurs after over exposure to radium, and the textbooks vaguely associate it with severe illnesses and bad prognoses SHILLITOE[6] has analysed the 647 routine differential white cell counts done in his laboratory during a year, and has found 87 lymphocyte counts of 1000 per c mm or less, but these counts were not constantly associated with any particular clinical state HEINLE and colleagues[7] have been trying to find out where the lymphocytes go when they disappear from the peripheral blood The original hypothesis of DOUCHERTY and WHITE was that they lost their cytoplasm and were then picked up by the lymphoid tissues, where they regenerated When HEINLE et al transfused rats with lymphocytes labelled with radioactive phosphorus (P^{32}), after a quarter of an hour most of the labelled lymphocytes had left the circulation and accumulated in the lungs and to less extent in the spleen They repeated the experiment with rats which had been injected with A C T H or 'Cortisone' 4 hours previously and obtained the same results It does not necessarily follow that when patients develop a lymphopenia their lymphocytes congregate in the lungs or spleen It is unfortunate for the hæmatologist that rodents are the easiest laboratory animals to maintain, because the reactions of their blood and blood forming tissues to various drugs and other stimuli are sometimes strikingly different from those in man The most notable difference of this kind has been in the effects of folic acid deficiency In the rat the predominant change is a diminution in the granulocyte producing tissues, erythropoiesis being little affected, in man, on the other hand, lack of folic acid seems to be accompanied by megaloblastic erythropoiesis, of which no hint could be gleaned from the rat experiments Such differences have also made it difficult to interpret the experimental work on the relation between the pituitary gland and blood cells For instance, PILIERO et al[8] have shown in rats that adrenalectomy *increases granulopoiesis and decreases* erythropoiesis in the bone marrow, besides causing abnormalities of maturation, and that cortisone restores the picture to normal But such changes have not been observed in, for example, patients with Addison s disease For the present it seems wise not to draw clinical conclusions about the influence of the pituitary gland on blood cells from the theories based on observations in rodents

---

[1] April 8 1951 The Census Explained H M Stationery Office, London 1951 Pp 20 6*d*

[2] Colfer H F De Groot J Harris G W *J Physiol* 1950 **111** 328

[3] De Groot J Harris G W *Ibid* p 335

[4] Mikkelsen W P Hutchens T T *Endocrinology* 1948 **42** 391

[5] Green J D Harris G W *J Endocrinol* 1947 **5** 136

[6] Shillitoe A J *J clin Path* 1950 **3** 321

[7] Heinle R W Weisberger A S Guyton R A *J Lab clin Med* 1950 **36** 832

[8] Piliero S J Landau D Gordon A S *Science* 1950 **112** 559

Anticoagulants in Cardiac Infarction

OUR cardiologists have been slow to accept the claims made for the anticoagulants in cardiac infarction, and even today, though some are enthusiastic believers, others remain unconvinced It is only reasonable to demand strong evidence, for anticoagulant therapy involves a considerable expenditure of time, trouble, and money, the technique must be scrupulous, and the coagulability of the blood must be maintained at exactly the right level for several weeks Then there are the hazards inherent in any interference with blood clotting—bleeding into the tissues generally, into the wall of the atheromatous coronary artery, and into the cardiac infarct itself with perhaps an increased risk of ventricular rupture However, aggravation of the cardiac lesion has not been observed in animal experiments, and, judging by the clinical reports, rupture of the ventricle has not become any more common in patients treated with anticoagulants The proportion of cases in which a hæmorrhage into the coronary wall leads directly or indirectly to obstruction of the lumen has been variously assessed at 5–65%, and there can be no doubt that cardiac infarction very often occurs without any recent thrombosis Thus among the 114 cases of gross infarction analysed by YATER and his colleagues[1] there were 35 without coronary thrombosis, and less than half of the 336 other fatal cases of coronary disease showed coronary thrombosis These considerations, however, are of no practical importance if it can be shown clinically, in a large series of properly controlled cases, that anticoagulants have a beneficial effect in major attacks of cardiac ischæmia—that is, in the cases clinically termed coronary thrombosis

In Denmark, HOLTEN[2] has collected the results of a two year trial at 21 clinics in which 174 patients were treated with anticoagulants and 256 without It was intended to allot patients to the treated and control groups on alternate days, and, though this rule was not strictly adhered to, the variations have been shown not to affect the results There was a substantial difference in the mortality of the two groups (presumably over a period of a few weeks) After excluding 52 patients who died within 24 hours of admission, the mortality of the treated patients was 22 5% and of the untreated 36% When the patients are divided into age groups the only groups with enough cases to be significant are 50–59, 60–69, and 70–79 in which there were 149 treated cases with mortality 23%, and 229 controls with mortality 37% But at ages 50–59 and 70–79 the mortality is only 4–5% lower in the anticoagulant-treated cases than in the controls Thus in the treated group as a whole the evidence in favour of anticoagulant therapy largely depends on the experience at age 60–69 (mortality of treated cases 17% and of controls 43%)—a peculiar result which requires explanation In the large American series reported by WRIGHT and colleagues[3] the benefit of anticoagulants appeared to be greatest in patients aged 70 and over, and the figures given by TULLOCH and GILCHRIST[4] in England are similar

When we turn to the causes of death, thrombo-embolism was 3½ times as frequent in HOLTEN's controls (14%) as in his treated patients, though it is impossible to assess the significance of this complication in the fatal outcome Apart from shock in the earliest stages, the deaths presumably were either due to congestive failure or occurred suddenly from ventricular fibrillation or asystole, which is the general experience If anticoagulants are to prevent these disasters they must do so largely by preventing clotting in the coronary lumen, though embolism, particularly in the lung, may sometimes be a contributory cause of death HOLTEN and TULLOCH and GILCHRIST seem to agree with this view of their action, but WRIGHT et al regard the main rôle of anticoagulants as the prevention of thrombo embolism. Such theoretical considerations cannot affect the statistics, which, if they cannot be taken at their face value, certainly cannot be disregarded. The time will soon come, it is to be hoped, when we shall know whether the routine use of anticoagulants in coronary thrombosis is worth while or not

---

[1] Yater W M et al *Amer Heart J* 1948 36 683
[2] Holten C *Ugeskr Læg* 1950 112 1205
[3] Wright I S Marple C D Beck D *Amer Heart J* 1948 36 801

Annotations

IMMERSION IN COLD WATER

Two world wars have taught us something of the chances for seafarers and others who are immersed in northern waters Critchley, in his Bradshaw lecture,[5] remarked that of 10 men from a torpedoed vessel who were immersed in water at −1 7°C, only 1 survived half an hour, but a corpulent man of 29, clad in indoor clothes and duffel coat, remained swimming in the Barents Sea in July at a temperature of −1 5°C for nine to fourteen hours Molnar[6] describes a group of 2 people who all survived four hours in a sea at 8°C even though experiments in baths suggested that this should have lowered the rectal temperature to 24°C and that few would survive in water near freezing point for more than half an hour and none for more than an hour and a half

This seeming anomaly is explained by Glaser[7] from observations on a man swimming in water at 20°C with a Douglas bag on his back. Glaser remarks that if this subject had been swimming in colder water his hea production would have been similar, for Spealman has made it clear that, in the absence of shivering heat production during immersion does not depend on water temperature, and, says Glaser

> " a man who is swimming hard should produc about as much heat as he loses in water near freezing point and he should not die of cold as long as he is able to swim Stiffness of the muscles may eventually interfere wit efficient swimming but muscles which are being exercis hard may remain warm enough to prevent them from becoming stiff Men in baths may shiver, but only after the have lost much heat, and they cannot produce enoug heat by this means alone to balance their losses in ver cold water '

Glaser concludes "Fit men therefore, who are i danger of immersion in cold water might be advised t swim or struggle as hard as they can for as long as the can If they try to preserve their strength by clingin to wreckage or floating on their lifebelts, they will di from cold Perhaps more lives would have been save in the past if this had been understood "

---

[4] Tulloch J A Gilchrist A R *Brit med J* 1950 ii 965
[5] Critchley M Shipwreck Survivors London 1943
[6] Molnar G W *J Amer med Ass* 1946 131 1046
[7] Glaser E M *Nature Lond* 1950 166 1068
[8] Spealman C R *Proc Soc exp Biol N Y* 1945 60 11

What of resuscitation ? Light cradles, heated sleeping bags, and friction are less effective than rapid rewarming by direct immersion in water at temperatures of up to 50°C, maintained until peripheral vascular spasm is dispelled Characteristically, the subject gives a sharp outcry, and then the laboured respiration and muscular rigidity disappear With brisk rubbing and wrapping in warm blankets the temperature is restored to normal in about three hours

MEDICAL SECRECY AND ABORTION

IN our leading article of Feb 24 we drew attention to the legal safeguards which foreign systems, in contrast to the common law, have established to protect confidential communications between doctors and their patients Happenings in two towns of Western Germany at the end of February show that even these measures to prevent breaches of medical secrecy may not go far enough They also illustrate how jealously the public on the Continent resist any attempt to whittle down, by official action, what they have come to regard as a fundamental right of the individual

Under a statute of 1935, re enacted in 1946–47, practitioners in Western Germany have to notify to the public health authorities, *for the purpose of registration and* statistics, any abortions among patients under their care There seemed to be no danger in such action until it occurred to the public prosecutor of the town of Weinheim (Baden) that the information thus assembled might be useful for tracking down professional abortionists, whose activities have lately increased The prosecutor asked the local health authority to give him a copy of the relevant list of women treated for hæmorrhages, &c , during the past six months, and in due course the police were told to summon and interrogate the women named in the list Perhaps in an excess of zeal, the local chief of police ordered a raid during which some 200 women and girls from the town and neighbourhood were taken in vans to the police station and kept there several hours for questioning and further investigation, on no other ground than that they had been treated within the last six months for miscarriage

How far this measure succeeded in its purpose is not yet known , for this aspect of the affair has been submerged by a wave of protests from the doctors of the district and from the public Concern has been aroused all over Germany, particularly since it became known that a similar attempt to get evidence of criminal abortions from official returns of miscarriages had been made by the police at Garmisch (Bavaria) In its indignation over the high handed action of the police, the German press has not lost sight of the wider principles involved, and much of the outcry has been directed against the public health officials for their " gross breach of medical secrecy " in passing the list of names to the public prosecutor The local medical organisation has advised its members to suspend all notifications of abortion until the legality of the recent police action has been investigated, and an information has been laid against the health officials concerned for breach of medical and official secrecy This step has been endorsed by the medical chamber of the Land, which demands new legislation to provide legal safeguards against such breaches of medical secrecy, if the present rules should be found insufficient After this sharp reaction of public and medical opinion in Western Germany such attempts to circumvent medical secrecy are not likely to be repeated, the more so since German law clearly says that in no circumstances can such a breach be ordered even for the purpose of pursuing punishable conduct

In this country the duties of medical practitioners in relation to cases of criminal abortion which have come to their knowledge in the course of treatment were the subject of a resolution passed by the Royal College of Physicians in 1916 After emphasising " the moral obligation to respect the confidence of the patient," this advised the practitioner to urge his patient to make a statement to the police , but if such a statement is refused, he is under no legal obligation to take further action and should continue to treat the patient It is less easy to give any definite answer to the further question which the incidents in Germany may raise here—namely, whether the records of patients and treatment which have to be forwarded to the local executive council under the National Health Service regulations, and the written clinical information which may be requested by the medical officer of health, are, in theory or even in practice, open to similar misuse There is, however, some authority for suggesting that, if the Government department concerned were to object to the revelation of such documents to the police, the courts would uphold the objection on the ground that the papers are protected as State documents

CARE OF THE TEETH

THOUGH its causes lie chiefly in diet, much dental caries could be prevented or checked if people could be induced to keep their mouths clean and see a dentist regularly Recognising that, for many years at least, *most dental surgeons will be occupied mainly in dental* repairs, Mr G H Leatherman[1] bases his scheme of preventive care on the employment of women dental ancillaries, or " hygienists," who would undertake scaling and polishing, and would help to instruct patients or parents in the elements of oral hygiene and home treatment Whereas adults, and possibly adolescents, should be seen first by the dental surgeon, who would refer the patient to the hygienist for any minor treatment required, Mr Leatherman thinks that for the very young the sequence should be reversed, because it is psychologically better for the child to be introduced to dental care by a woman He recommends that polishing of the teeth, mouth charting, and the taking of " wing bite " radiographs should be done by the hygienist before the child goes to the dental surgeon for detailed examination and treatment This proposal, however, when he made it before the British Dental Association at Birmingham was strongly criticised,[2] mainly on the ground that diagnosis should precede treatment and that scaling alters the diagnostic picture Mr A F Stammers did not regard scaling as by any means minor dental work it was, he said, the most important thing a dental surgeon could do for his patient Mr E Davies-Thomas, at the Children's Hospital, Birmingham, had made a rule that nobody should talk to the child except himself, and in this way he established a personal understanding

In the care of the teeth at home, Mr Leatherman believes that the basic need from childhood is to prevent gingivitis, and, where gingivitis and its sequelæ have developed, to see that the causes are removed and the supporting structures rendered healthy The patient should be made to understand that the supporting structures of the teeth require as much attention as the surfaces of the teeth themselves, and to this end the term toothbrush should be changed to mouthbrush He favours the use of a mouthwash of full strength hydrogen peroxide (10 volumes), or 'Milton' (1 part to 4 parts water), or sodium chloride and sodium bicarbonate (1/2 teaspoonful of each in half a glass of warm water) The teeth and mouth are brushed first thing in the morning and last thing at night with salt powder, or a powder of urea and ammonium , though what really matters is not what is on the brush but how and when the brush is used The brush of choice, according to Mr Leatherman, is one of natural bristle, of medium consistence, 6–8 rows long, the bristles being all of the same length , and more than one brush is necessary, for

each should be allowed to dry for at least 24 hours after use. He would have us all clean our dental spaces with wooden sticks or dental floss, and some people should massage the interdental epithelium with a wooden stick. At each mouth cleaning the gums are massaged with the fingers, and the session ends with a mouthwash.

---

[1] *Brit dent J* 1950 89, 119
[2] *Ibid* p 125

BLEEDING AT OPERATIONS

PERSISTENT oozing of blood during an operation may cause nothing worse than irritation and delay—in itself the loss of blood is not often serious nowadays, when it can easily be made up by transfusion—but it may obscure the surgeon's view and lead to damage of important structures, or by forming a hæmatoma it may delay healing and encourage infection. Surgeons and anæsthetists are inclined to blame each other for such oozing, and almost every anæsthetic agent has at some stage of its career been accused of increasing the bleeding tendency; so the subject has been keenly studied. It seems to be generally agreed that cyclopropane encourages bleeding, though whether this is a direct effect of the gas or a result of the absorption method of administration or of the presence of excess of oxygen is uncertain. Ether is also suspect, because, except in very deep anæsthesia, it stimulates cardiac and respiratory activity and dilates the peripheral vessels. Apart from drug action, bleeding can be aggravated by respiratory obstruction sufficient to raise the venous pressure, and also by breathing excessive amounts of carbon dioxide, whether this comes direct from the cylinder or from a faulty absorber or mismanaged anæsthetic apparatus. Then the surgeon himself may be responsible—for example, he can obstruct the venous return by leaning on the patient, or with his bandages, or, in tonsillectomy, with the tourniquet like straps of his gag jack.

Two methods of anæsthesia have long been noted for a striking absence of bleeding—chloroform and spinal anæsthesia. Their common feature is that they usually cause a considerable fall in blood-pressure. This effect has lately been developed in several directions to reduce bleeding, the two main techniques being (1) high spinal anæsthesia[1] extensive enough to cut off all the sympathetic outflow, and (2) the injection of drugs of the methonium group which act selectively on the sympathetic ganglia.[2] Both of these will produce a profound fall in blood pressure and ensure a bloodless field for the surgeon. In brain surgery, where bleeding is particularly apt to be troublesome, there is an additional factor—intracranial tension, on which ease of access and the avoidance of surgical trauma largely depend. Intracranial tension is in turn dependent on arterial blood pressure; so by reducing the B.P. it is possible both to control bleeding and keep the intracranial tension low. At Edinburgh Royal Infirmary Bilsland[3] has attained this end with the technique introduced by Gardner[4] in the U.S.A. as "controlled induced hypotension by arteriotomy," an adaptation of the method used experimentally for inducing shock in animals. In this blood is rapidly withdrawn through a cannula in the radial artery until the desired reduction of B.P. is attained. The blood is run into a reservoir, from which, usually towards the end of the operation, it is returned to the patient by the same route, simply by raising the pressure in the reservoir to above the patient's systolic B.P. In 63 craniotomy cases a B.P. of under 100 mm. Hg has been maintained for up to 6 hours by withdrawing 300–2600 ml. of blood, and only one death could be put down to the hypotension.

Last year Dr. Enderby[2] published in these columns his preliminary results with "controlled hypotension," attained with penta- or hexa-methonium iodide or tetraethylammonium chloride, supplemented by a careful use of posture. The technique, though based on that described by Griffiths and Gillies[5] was exploratory; nevertheless, Enderby obtained a satisfactory reduction of bleeding in about half of his 85 cases, and the ill-effects were nil. In this issue (p. 663) he and Dr. Pelmore report subsequent experience. Using hexamethonium only, with posture when possible, the proportion of successes has risen to 85% in 250 cases. In fenestration, where the slightest bleeding at the wrong place reduces the chances of success, Dr. Hughes (p. 666) has lowered the systolic B.P. to 75–80 mm. Hg with pentamethonium and posture (plus pentothal and pethidine, "the four P's") and produced a completely bloodless field with no ill effects in 10 cases. But, as several speakers emphasised at the Royal Society of Medicine discussion on March 2, this is not a technique for the inexperienced or inattentive: unless the anæsthetist can keep a constant eye on B.P. and pulse, the behaviour of vessels at the operation site, colour changes, and the state of the peripheral circulation, he had better be content with preventing venous congestion, ensuring a free airway, and the other classical methods of minimising bleeding.

"FAMILY DOCTOR"

THE public appetite for information about medicine is so insatiable as to seem a little morbid; and in fact it is evidence of a deficiency disease. People ingest masses of information, supplied from various sources, in the hope of getting the small amounts of knowledge they need for bodily and mental efficiency. Often this knowledge is of a kind they could get in a few minutes' leisurely conversation with a trusted general practitioner; but for one reason or another they have not got it. In producing a journal that will supplement the efforts of clinicians, educationists, and publicists to meet the large and legitimate demand for sound instruction, the British Medical Association has chosen the title *Family Doctor*, and the editor, Dr. Harvey Flack, aims at making it friendly and dependable, like the good G.P. In a letter introducing the first issue, Dr. Hugh Clegg, editor of the *British Medical Journal*, says that the title "may remind you that the doctor's main concern is to make and keep people well," and he hopes that the new magazine will help everyone to lead a healthy and happy life—"by telling the reader all the medical profession knows about the rules of health for men and women, boys and girls, and for babies." Lord Horder, in a message of encouragement entitled Health is Your Right, speaks of the difficulty caused in this country by medical writers wanting to preserve their anonymity, whereas the newspapers have wanted "not only the 'story' but the signature and, for preference, the photograph also, of the writer." In this demand the newspapers have reflected the opinion of the public, who like to know that the person addressing them is an authority; but the difficulty will be largely overcome if readers can feel that, though an article bears no signature, it comes to them with the imprimatur of over 60,000 members of the B.M.A.[6] The success of the American Medical Association's popular magazine *Hygeia* (now called *Today's Health*) is an encouraging precedent, and we congratulate the *B.M.J.* on the birth of this seventeenth child, which will be the public relations officer for its more academic brothers and sisters.

LORD ADDISON

IN his new office as Lord President of the Council, Lord Addison will find himself on largely familiar ground; for the Privy Council is responsible for the General Medical Council, with which his name is registered, and the Privy Council also has under its ægis the Medical Research Council, of which he has been chairman since 1948. Lord Addison remains leader of the House of Lords.

---

[1] Gillies, J. *Ann. R. Coll. Surg. Engl.* 1950, 7, 204.

[2] Enderby, G. E. H. *Lancet*, 1950, i, 1145.

[3] Bilsland, W. L. *Anæsthesia*, 1951, 6, 20.

[4] Gardner, W. J. *J. Amer. med. Ass.* 1946, 132, 572.

[5] Griffiths, H. W. C., Gillies, J. *Anæsthesia*, 1948, 3, 134.

[6] The new magazine is published from B.M.A. House, Tavistock Square, London, W.C.1, monthly at 1s.

What of resuscitation? Light cradles, heated sleeping bags, and friction are less effective than rapid rewarming by direct immersion in water at temperatures of up to 50°C, maintained until peripheral vascular spasm is dispelled Characteristically, the subject gives a sharp outcry, and then the laboured respiration and muscular rigidity disappear With brisk rubbing and wrapping in warm blankets the temperature is restored to normal in about three hours

MEDICAL SECRECY AND ABORTION

IN our leading article of Feb 24 we drew attention to the legal safeguards which foreign systems, in contrast to the common law, have established to protect confidential communications between doctors and their patients Happenings in two towns of Western Germany at the end of February show that even these measures to prevent breaches of medical secrecy may not go far enough They also illustrate how jealously the public on the Continent resist any attempt to whittle down, by official action, what they have come to regard as a fundamental right of the individual

Under a statute of 1935, re enacted in 1946–47, practitioners in Western Germany have to notify to the public health authorities, for the purpose of registration and statistics, any abortions among patients under their care There seemed to be no danger in such action until it occurred to the public prosecutor of the town of Weinheim (Baden) that the information thus assembled might be useful for tracking down professional abortionists, whose activities have lately increased The prosecutor asked the local health authority to give him a copy of the relevant list of women treated for hæmorrhages, &c, during the past six months, and in due course the police were told to summon and interrogate the women named in the list Perhaps in an excess of zeal, the local chief of police ordered a raid during which some 200 women and girls from the town and neighbourhood were taken in vans to the police station and kept there several hours for questioning and further investigation, on no other ground than that they had been treated within the last six months for miscarriage

How far this measure succeeded in its purpose is not yet known, for this aspect of the affair has been submerged by a wave of protests from the doctors of the district and from the public Concern has been aroused all over Germany, particularly since it became known that a similar attempt to get evidence of criminal abortions from official returns of miscarriages had been made by the police at Garmisch (Bavaria) In its indignation over the high handed action of the police, the German press has not lost sight of the wider principles involved, and much of the outcry has been directed against the public health officials for their "gross breach of medical secrecy" in passing the list of names to the public prosecutor The local medical organisation has advised its members to suspend all notifications of abortion until the legality of the recent police action has been investigated, and an information has been laid against the health officials concerned for breach of medical and official secrecy This step has been endorsed by the medical chamber of the Land, which demands new legislation to provide legal safeguards against such breaches of medical secrecy, if the present rules should be found insufficient After this sharp reaction of public and medical opinion in Western Germany such attempts to circumvent medical secrecy are not likely to be repeated, the more so since German law clearly says that in no circumstances can such a breach be ordered even for the purpose of pursuing punishable conduct

In this country the duties of medical practitioners in relation to cases of criminal abortion which have come to their knowledge in the course of treatment were the subject of a resolution passed by the Royal College of Physicians in 1916 After emphasising "the moral obligation to respect the confidence of the patient," this advised the practitioner to urge his patient to make a statement to the police, but if such a statement is refused, he is under no legal obligation to take further action and should continue to treat the patient It is less easy to give any definite answer to the further question which the incidents in Germany may raise here—namely, whether the records of patients and treatment which have to be forwarded to the local executive council under the National Health Service regulations, and the written clinical information which may be requested by the medical officer of health, are, in theory or even in practice, open to similar misuse There is, however, some authority for suggesting that, if the Government department concerned were to object to the revelation of such documents to the police, the courts would uphold the objection on the ground that the papers are protected as State documents

CARE OF THE TEETH

THOUGH its causes lie chiefly in diet, much dental caries could be prevented or checked if people could be induced to keep their mouths clean and see a dentist regularly Recognising that, for many years at least, most dental surgeons will be occupied mainly in dental repairs, Mr G H Leatherman[1] bases his scheme of preventive care on the employment of women dental ancillaries, or "hygienists," who would undertake scaling and polishing, and would help to instruct patients or parents in the elements of oral hygiene and home treatment Whereas adults, and possibly adolescents, should be seen first by the dental surgeon, who would refer the patient to the hygienist for any minor treatment required, Mr Leatherman thinks that for the very young the sequence should be reversed, because it is psychologically better for the child to be introduced to dental care by a woman He recommends that polishing of the teeth, mouth charting, and the taking of "wing bite" radiographs should be done by the hygienist before the child goes to the dental surgeon for detailed examination and treatment This proposal, however, when he made it before the British Dental Association at Birmingham was strongly criticised,[2] mainly on the ground that diagnosis should precede treatment and that scaling alters the diagnostic picture Mr A F Stammers did not regard scaling as by any means minor dental work it was, he said, the most important thing a dental surgeon could do for his patient Mr E Davies-Thomas, at the Children's Hospital, Birmingham, had made a rule that nobody should talk to the child except himself, and in this way he established a personal understanding

In the care of the teeth at home, Mr Leatherman believes that the basic need from childhood is to prevent gingivitis, and, where gingivitis and its sequelæ have developed, to see that the causes are removed and the supporting structures rendered healthy The patient should be made to understand that the supporting structures of the teeth require as much attention as the surfaces of the teeth themselves, and to this end the term toothbrush should be changed to mouthbrush He favours the use of a mouthwash of full strength hydrogen peroxide (10 volumes), or 'Milton' (1 part to 4 parts water), or sodium chloride and sodium bicarbonate ($^1/_2$ teaspoonful of each in half a glass of warm water) The teeth and mouth are brushed first thing in the morning and last thing at night with salt powder, or a powder of urea and ammonium, though what really matters is not what is on the brush but how and when the brush is used The brush of choice, according to Mr Leatherman, is one of natural bristle, of medium consistence, 6–8 rows long, the bristles being all of the same length, and more than one brush is necessary, for each should be allowed to dry for at least 24 hours after use He would have us all clean our dental spaces with wooden sticks or dental floss, and some people should massage the interdental epithelium with a wooden stick At each mouth cleaning the gums are massaged with the fingers, and the session ends with a mouthwash

---

[1] *Brit dent J* 1950 89, 119
[2] *Ibid* p 125

BLEEDING AT OPERATIONS

PERSISTENT oozing of blood during an operation may cause nothing worse than irritation and delay—in itself the loss of blood is not often serious nowadays, when it can easily be made up by transfusion—but it may obscure the surgeon's view and lead to damage of important structures, or by forming a hæmatoma it may delay healing and encourage infection Surgeons and anæsthetists are inclined to blame each other for such oozing, and almost every anæsthetic agent has at some stage of its career been accused of increasing the bleeding tendency, so the subject has been keenly studied It seems to be generally agreed that cyclopropane encourages bleeding, though whether this is a direct effect of the gas or a result of the absorption method of administration or of the presence of excess of oxygen is uncertain Ether is also suspect, because, except in very deep anæsthesia, it stimulates cardiac and respiratory activity and dilates the peripheral vessels Apart from drug action, bleeding can be aggravated by respiratory obstruction sufficient to raise the venous pressure, and also by breathing excessive amounts of carbon dioxide, whether this comes direct from the cylinder or from a faulty absorber or mismanaged anæsthetic apparatus Then the surgeon himself may be responsible—for example, he can obstruct the venous return by leaning on the patient, or with his bandages, or, in tonsillectomy, with the tourniquet like straps of his gag jack

Two methods of anæsthesia have long been noted for a striking absence of bleeding—chloroform and spinal anæsthesia Their common feature is that they usually cause a considerable fall in blood pressure This effect has lately been developed in several directions to reduce bleeding, the two main techniques being (1) high spinal anæsthesia[1] extensive enough to cut off all the sympathetic outflow, and (2) the injection of drugs of the methonium group which act selectively on the sympathetic ganglia[2] Both of these will produce a profound fall in blood pressure and ensure a bloodless field for the surgeon In brain surgery, where bleeding is particularly apt to be troublesome, there is an additional factor—intracranial tension, on which ease of access and the avoidance of surgical trauma largely depend Intracranial tension is in turn dependent on arterial blood pressure, so by reducing the B P it is possible both to control bleeding and keep the intracranial tension low At Edinburgh Royal Infirmary Bilsland[3] has attained this end with the technique introduced by Gardner[4] in the U S A as "controlled induced hypotension by arteriotomy," an adaptation of the method used experimentally for inducing shock in animals In this, blood is rapidly withdrawn through a cannula in the radial artery until the desired reduction of B P is attained The blood is run into a reservoir, from which, usually towards the end of the operation, it is returned to the patient by the same route, simply by raising the pressure in the reservoir to above the patient's systolic B P In 63 craniotomy cases a B P of under 100 mm Hg has been maintained for up to 6 hours by withdrawing 300–2600 ml. of blood, and only one death could be put down to the hypotension

Last year Dr Enderby[2] published in these columns his preliminary results with "controlled hypotension," attained with penta or hexa methonium iodide or tetraethylammonium chloride, supplemented by a careful use of posture The technique, though based on that described by Griffiths and Gillies[5] was exploratory, nevertheless, Enderby obtained a satisfactory reduction of bleeding in about half of his 85 cases, and the ill-effects were nil In this issue (p 663) he and Dr Pelmore report subsequent experience Using hexamethonium only, with posture when possible, the proportion of successes has risen to 85% in 250 cases In fenestration, where the slightest bleeding at the wrong place reduces the chances of success, Dr Hughes (p 666) has lowered the systolic B P to 75–80 mm Hg with pentamethonium and osture (plus pentothal and pethidine, "the four P's") and produced a completely bloodless field with no ill effects in 10 cases But, as several speakers emphasised at the Royal Society of Medicine discussion on March 2, this is not a technique for the inexperienced or inattentive unless the anæsthetist can keep a constant eye on B P and pulse, the behaviour of vessels at the operation site, colour changes, and the state of the peripheral circulation, he had better be content with preventing venous congestion, ensuring a free airway, and the other classical methods of minimising bleeding

"FAMILY DOCTOR"

THE public appetite for information about medicine is so insatiable as to seem a little morbid, and in fact it is evidence of a deficiency disease People ingest masses of information, supplied from various sources, in the hope of getting the small amounts of knowledge they need for bodily and mental efficiency. Often this knowledge is of a kind they could get in a few minutes' leisurely conversation with a trusted general practitioner, but for one reason or another they have not got it In producing a journal that will supplement the efforts of clinicians, educationists, and publicists to meet the large and legitimate demand for sound instruction, the British Medical Association has chosen the title *Family Doctor*, and the editor, Dr Harvey Flack, aims at making it friendly and dependable, like the good G P In a letter introducing the first issue, Dr Hugh Clegg, editor of the *British Medical Journal*, says that the title "may remind you that the doctor's main concern is to make and keep people well," and he hopes that the new magazine will help everyone to lead a healthy and happy life—"by telling the reader all the medical profession knows about the rules of health for men and women, boys and girls, and for babies" Lord Horder, in a message of encouragement entitled Health is Your Right, speaks of the difficulty caused in this country by medical writers wanting to preserve their anonymity, whereas the newspapers have wanted "not only the 'story' but the signature and, for preference, the photograph also, of the writer" In this demand the newspapers have reflected the opinion of the public, who like to know that the person addressing them is an authority, but the difficulty will be largely overcome if readers can feel that, though an article bears no signature, it comes to them with the imprimatur of over 60,000 members of the B M A[6] The success of the American Medical Association's popular magazine *Hygeia* (now called *Today's Health*) is an encouraging precedent, and we congratulate the *B M J* on the birth of this seventeenth child, which will be the public relations officer for its more academic brothers and sisters

LORD ADDISON

IN his new office as Lord President of the Council, Lord Addison will find himself on largely familiar ground, for the Privy Council is responsible for the General Medical Council, with which his name is registered, and the Privy Council also has under its ægis the Medical Research Council, of which he has been chairman since 1948 Lord Addison remains leader of the House of Lords.

---

[1] Gillies J *Ann R Coll Surg Eng* 1950 7 204

[2] Enderby G E H *Lancet*, 1950 1 1145

[3] Bilsland W L *Anæsthesia*, 1951 6 20

[4] Gardner W J *J Amer med Ass* 1946 132 572

[5] Griffiths H W C Gillies, J *Anæsthesia* 1948 3 134

[6] The new magazine is published from B M A House Tavistock Square London, W C 1 monthly at 1s

What of resuscitation ? Light cradles, heated sleeping bags, and friction are less effective than rapid rewarming by direct immersion in water at temperatures of up to 50°C, maintained until peripheral vascular spasm is dispelled Characteristically, the subject gives a sharp outcry, and then the laboured respiration and muscular rigidity disappear With brisk rubbing and wrapping in warm blankets the temperature is restored to normal in about three hours

MEDICAL SECRECY AND ABORTION

In our leading article of Feb 24 we drew attention to the legal safeguards which foreign systems, in contrast to the common law, have established to protect confidential communications between doctors and their patients Happenings in two towns of Western Germany at the end of February show that even these measures to prevent breaches of medical secrecy may not go far enough They also illustrate how jealously the public on the Continent resist any attempt to whittle down, by official action, what they have come to regard as a fundamental right of the individual

Under a statute of 1935, re enacted in 1946–47, practitioners in Western Germany have to notify to the public health authorities, for the purpose of registration and statistics, any abortions among patients under their care There seemed to be no danger in such action until it occurred to the public prosecutor of the town of Weinheim (Baden) that the information thus assembled might be useful for tracking down professional abortionists, whose activities have lately increased The prosecutor asked the local health authority to give him a copy of the relevant list of women treated for hæmorrhages, &c , during the past six months, and in due course the police were told to summon and interrogate the women named in the list Perhaps in an excess of zeal, the local chief of police ordered a raid during which some 200 women and girls from the town and neighbourhood were taken in vans to the police station and kept there several hours for questioning and further investigation, on no other ground than that they had been treated within the last six months for miscarriage

How far this measure succeeded in its purpose is not yet known , for this aspect of the affair has been submerged by a wave of protests from the doctors of the district and from the public Concern has been aroused all over Germany, particularly since it became known that a similar attempt to get evidence of criminal abortions from official returns of miscarriages had been made by the police at Garmisch (Bavaria) In its indignation over the high handed action of the police, the German press has not lost sight of the wider principles involved, and much of the outcry has been directed against the public health officials for their " gross breach of medical secrecy " in passing the list of names to the public prosecutor The local medical organisation has advised its members to suspend all notifications of abortion until the legality of the recent police action has been investigated, and an information has been laid against the health officials concerned for breach of medical and official secrecy This step has been endorsed by the medical chamber of the Land, which demands new legislation to provide legal safeguards against such breaches of medical secrecy, if the present rules should be found insufficient After this sharp reaction of public and medical opinion in Western Germany such attempts to circumvent medical secrecy are not likely to be repeated, the more so since German law clearly says that in no circumstances can such a breach be ordered even for the purpose of pursuing punishable conduct

In this country the duties of medical practitioners in relation to cases of criminal abortion which have come to their knowledge in the course of treatment were the subject of a resolution passed by the Royal College of Physicians in 1916 After emphasising " the moral obligation to respect the confidence of the patient," this advised the practitioner to urge his patient to make a statement to the police , but if such a statement is refused, he is under no legal obligation to take further action and should continue to treat the patient It is less easy to give any definite answer to the further question which the incidents in Germany may raise here—namely, whether the records of patients and treatment which have to be forwarded to the local executive council under the National Health Service regulations, and the written clinical information which may be requested by the medical officer of health, are, in theory or even in practice, open to similar misuse There is, however, some authority for suggesting that, if the Government department concerned were to object to the revelation of such documents to the police, the courts would uphold the objection on the ground that the papers are protected as State documents

CARE OF THE TEETH

Though its causes lie chiefly in diet, much dental caries could be prevented or checked if people could be induced to keep their mouths clean and see a dentist regularly Recognising that, for many years at least, most dental surgeons will be occupied mainly in dental repairs, Mr G H Leatherman[1] bases his scheme of preventive care on the employment of women dental ancillaries, or " hygienists," who would undertake scaling and polishing, and would help to instruct patients or parents in the elements of oral hygiene and home treatment Whereas adults, and possibly adolescents, should be seen first by the dental surgeon, who would refer the patient to the hygienist for any minor treatment required, Mr Leatherman thinks that for the very young the sequence should be reversed, because it is psychologically better for the child to be introduced to dental care by a woman He recommends that polishing of the teeth, mouth charting, and the taking of " wing bite " radiographs should be done by the hygienist before the child goes to the dental surgeon for detailed examination and treatment This proposal, however, when he made it before the British Dental Association at Birmingham was strongly criticised,[2] mainly on the ground that diagnosis should precede treatment and that scaling alters the diagnostic picture Mr A F Stammers did not regard scaling as by any means minor dental work it was, he said, the most important thing a dental surgeon could do for his patient Mr E Davies-Thomas, at the Children's Hospital, Birmingham, had made a rule that nobody should talk to the child except himself, and in this way he established a personal understanding

In the care of the teeth at home, Mr Leatherman believes that the basic need from childhood is to prevent gingivitis, and, where gingivitis and its sequelæ have developed, to see that the causes are removed and the supporting structures rendered healthy The patient should be made to understand that the supporting structures of the teeth require as much attention as the surfaces of the teeth themselves, and to this end the term toothbrush should be changed to mouthbrush He favours the use of a mouthwash of full strength hydrogen peroxide (10 volumes), or 'Milton' (1 part to 4 parts water), or sodium chloride and sodium bicarbonate ($^1/_2$ teaspoonful of each in half a glass of warm water) The teeth and mouth are brushed first thing in the morning and last thing at night with salt powder, or a powder of urea and ammonium , though what really matters is not what is on the brush but how and when the brush is used The brush of choice, according to Mr Leatherman, is one of natural bristle, of medium consistence, 6–8 rows long, the bristles being all of the same length , and more than one brush is necessary, for

each should be allowed to dry for at least 24 hours after use. He would have us all clean our dental spaces with wooden sticks or dental floss, and some people should massage the interdental epithelium with a wooden stick. At each mouth cleaning the gums are massaged with the fingers, and the session ends with a mouthwash.

---

[1] *Brit dent J* 1950 89 119

[2] *Ibid* p 125

BLEEDING AT OPERATIONS

PERSISTENT oozing of blood during an operation may cause nothing worse than irritation and delay—in itself the loss of blood is not often serious nowadays, when it can easily be made up by transfusion—but it may obscure the surgeon's view and lead to damage of important structures, or by forming a hæmatoma it may delay healing and encourage infection. Surgeons and anæsthetists are inclined to blame each other for such oozing, and almost every anæsthetic agent has at some stage of its career been accused of increasing the bleeding tendency; so the subject has been keenly studied. It seems to be generally agreed that cyclopropane encourages bleeding, though whether this is a direct effect of the gas or a result of the absorption method of administration or of the presence of excess of oxygen is uncertain. Ether is also suspect, because, except in very deep anæsthesia, it stimulates cardiac and respiratory activity and dilates the peripheral vessels. Apart from drug action, bleeding can be aggravated by respiratory obstruction sufficient to raise the venous pressure, and also by breathing excessive amounts of carbon dioxide, whether this comes direct from the cylinder or from a faulty absorber or mismanaged anæsthetic apparatus. Then the surgeon himself may be responsible—for example, he can obstruct the venous return by leaning on the patient, or with his bandages, or, in tonsillectomy, with the tourniquet like straps of his gag jack.

Two methods of anæsthesia have long been noted for a striking absence of bleeding—chloroform and spinal anæsthesia. Their common feature is that they usually cause a considerable fall in blood pressure. This effect has lately been developed in several directions to reduce bleeding, the two main techniques being (1) high spinal anæsthesia[1] extensive enough to cut off all the sympathetic outflow, and (2) the injection of drugs of the methonium group which act selectively on the sympathetic ganglia.[2] Both of these will produce a profound fall in blood-pressure and ensure a bloodless field for the surgeon. In brain surgery, where bleeding is particularly apt to be troublesome, there is an additional factor—intracranial tension, on which ease of access and the avoidance of surgical trauma largely depend. Intracranial tension is in turn dependent on arterial blood pressure; so by reducing the B.P. it is possible both to control bleeding and keep the intracranial tension low. At Edinburgh Royal Infirmary Bilsland[3] has attained this end with the technique introduced by Gardner[4] in the U.S.A. as "controlled induced hypotension by arteriotomy," an adaptation of the method used experimentally for inducing shock in animals. In this, blood is rapidly withdrawn through a cannula in the radial artery until the desired reduction of B.P. is attained. The blood is run into a reservoir, from which, usually towards the end of the operation, it is returned to the patient by the same route, simply by raising the pressure in the reservoir to above the patient's systolic B.P. In 63 craniotomy cases a B.P. of under 100 mm. Hg has been maintained for up to 6 hours by withdrawing 300–2600 ml. of blood, and only one death could be put down to the hypotension.

Last year Dr. Enderby[2] published in these columns his preliminary results with "controlled hypotension," attained with penta- or hexa-methonium iodide or tetraethylammonium chloride, supplemented by a careful use of posture. The technique, though based on that described by Griffiths and Gillies,[5] was exploratory; nevertheless, Enderby obtained a satisfactory reduction of bleeding in about half of his 85 cases, and the ill-effects were nil. In this issue (p. 663) he and Dr. Pelmore report subsequent experience. Using hexamethonium only, with posture when possible, the proportion of successes has risen to 85% in 250 cases. In fenestration, where the slightest bleeding at the wrong place reduces the chances of success, Dr. Hughes (p. 666) has lowered the systolic B.P. to 75–80 mm. Hg with pentamethonium and posture (plus pentothal and pethidine, "the four P's") and produced a completely bloodless field with no ill effects in 10 cases. But, as several speakers emphasised at the Royal Society of Medicine discussion on March 2, this is not a technique for the inexperienced or inattentive: unless the anæsthetist can keep a constant eye on B.P. and pulse, the behaviour of vessels at the operation site, colour changes, and the state of the peripheral circulation, he had better be content with preventing venous congestion, ensuring a free airway, and the other classical methods of minimising bleeding.

"FAMILY DOCTOR"

THE public appetite for information about medicine is so insatiable as to seem a little morbid, and in fact it is evidence of a deficiency disease. People ingest masses of information, supplied from various sources, in the hope of getting the small amounts of knowledge they need for bodily and mental efficiency. Often this knowledge is of a kind they could get in a few minutes' leisurely conversation with a trusted general practitioner; but for one reason or another they have not got it. In producing a journal that will supplement the efforts of clinicians, educationists, and publicists to meet the large and legitimate demand for sound instruction, the British Medical Association has chosen the title *Family Doctor*, and the editor, Dr. Harvey Flack, aims at making it friendly and dependable, like the good G.P. In a letter introducing the first issue, Dr. Hugh Clegg, editor of the *British Medical Journal*, says that the title "may remind you that the doctor's main concern is to make and keep people well," and he hopes that the new magazine will help everyone to lead a healthy and happy life—"by telling the reader all the medical profession knows about the rules of health for men and women, boys and girls, and for babies." Lord Horder, in a message of encouragement entitled Health is Your Right, speaks of the difficulty caused in this country by medical writers wanting to preserve their anonymity, whereas the newspapers have wanted "not only the 'story' but the signature and, for preference, the photograph also, of the writer." In this demand the newspapers have reflected the opinion of the public who like to know that the person addressing them is an authority; but the difficulty will be largely overcome if readers can feel that, though an article bears no signature, it comes to them with the imprimatur of over 60,000 members of the B.M.A.[6] The success of the American Medical Association's popular magazine *Hygeia* (now called *Today's Health*) is an encouraging precedent, and we congratulate the *B.M.J.* on the birth of this seventeenth child, which will be the public relations officer for its more academic brothers and sisters.

LORD ADDISON

IN his new office as Lord President of the Council, Lord Addison will find himself on largely familiar ground; for the Privy Council is responsible for the General Medical Council, with which his name is registered, and the Privy Council also has under its ægis the Medical Research Council, of which he has been chairman since 1948. Lord Addison remains leader of the House of Lords.

---

[1] Gillies, J. *Ann. R. Coll. Surg. Eng.* 1950, 7, 204.
[2] Enderby, G. E. H. *Lancet*, 1950, i, 1145.
[3] Bilsland, W. L. *Anæsthesia*, 1951, 6, 20.
[4] Gardner, W. J. *J. Amer. med. Ass.* 1946, 132, 572.
[5] Griffiths, H. W. C., Gillies, J. *Anæsthesia*, 1948, 3, 134.
[6] The new magazine is published from B.M.A. House, Tavistock Square, London, W.C.1, monthly at 1s.

What of resuscitation? Light cradles, heated sleeping-bags, and friction are less effective than rapid rewarming by direct immersion in water at temperatures of up to 50°C, maintained until peripheral vascular spasm is dispelled. Characteristically, the subject gives a sharp outcry, and then the laboured respiration and muscular rigidity disappear. With brisk rubbing and wrapping in warm blankets the temperature is restored to normal in about three hours.

MEDICAL SECRECY AND ABORTION

In our leading article of Feb. 24 we drew attention to the legal safeguards which foreign systems, in contrast to the common law, have established to protect confidential communications between doctors and their patients. Happenings in two towns of Western Germany at the end of February show that even these measures to prevent breaches of medical secrecy may not go far enough. They also illustrate how jealously the public on the Continent resist any attempt to whittle down, by official action, what they have come to regard as a fundamental right of the individual.

Under a statute of 1935, re-enacted in 1946–47, practitioners in Western Germany have to notify to the public health authorities, for the purpose of registration and statistics, any abortions among patients under their care. There seemed to be no danger in such action until it occurred to the public prosecutor of the town of Weinheim (Baden) that the information thus assembled might be useful for tracking down professional abortionists, whose activities have lately increased. The prosecutor asked the local health authority to give him a copy of the relevant list of women treated for hæmorrhages, &c., during the past six months, and in due course the police were told to summon and interrogate the women named in the list. Perhaps in an excess of zeal, the local chief of police ordered a raid during which some 200 women and girls from the town and neighbourhood were taken in vans to the police station and kept there several hours for questioning and further investigation, on no other ground than that they had been treated within the last six months for miscarriage.

How far this measure succeeded in its purpose is not yet known, for this aspect of the affair has been submerged by a wave of protests from the doctors of the district and from the public. Concern has been aroused all over Germany, particularly since it became known that a similar attempt to get evidence of criminal abortions from official returns of miscarriages had been made by the police at Garmisch (Bavaria). In its indignation over the high-handed action of the police, the German press has not lost sight of the wider principles involved, and much of the outcry has been directed against the public health officials for their "gross breach of medical secrecy" in passing the list of names to the public prosecutor. The local medical organisation has advised its members to suspend all notifications of abortion until the legality of the recent police action has been investigated, and an information has been laid against the health officials concerned for breach of medical and official secrecy. This step has been endorsed by the medical chamber of the Land, which demands new legislation to provide legal safeguards against such breaches of medical secrecy, if the present rules should be found insufficient. After this sharp reaction of public and medical opinion in Western Germany such attempts to circumvent medical secrecy are not likely to be repeated, the more so since German law clearly says that in no circumstances can such a breach be ordered even for the purpose of pursuing punishable conduct.

In this country the duties of medical practitioners in relation to cases of criminal abortion which have come to their knowledge in the course of treatment were the subject of a resolution passed by the Royal College of Physicians in 1916. After emphasising "the moral obligation to respect the confidence of the patient," this advised the practitioner to urge his patient to make a statement to the police; but if such a statement is refused, he is under no legal obligation to take further action and should continue to treat the patient. It is less easy to give any definite answer to the further question which the incidents in Germany may raise here—namely, whether the records of patients and treatment which have to be forwarded to the local executive council under the National Health Service regulations, and the written clinical information which may be requested by the medical officer of health, are, in theory or even in practice, open to similar misuse. There is, however, some authority for suggesting that, if the Government department concerned were to object to the revelation of such documents to the police, the courts would uphold the objection on the ground that the papers are protected as State documents.

CARE OF THE TEETH

Though its causes lie chiefly in diet, much dental caries could be prevented or checked if people could be induced to keep their mouths clean and see a dentist regularly. Recognising that, for many years at least, most dental surgeons will be occupied mainly in dental repairs, Mr G. H. Leatherman[1] bases his scheme of preventive care on the employment of women dental ancillaries, or "hygienists," who would undertake scaling and polishing, and would help to instruct patients or parents in the elements of oral hygiene and home treatment. Whereas adults, and possibly adolescents, should be seen first by the dental surgeon, who would refer the patient to the hygienist for any minor treatment required, Mr Leatherman thinks that for the very young the sequence should be reversed, because it is psychologically better for the child to be introduced to dental care by a woman. He recommends that polishing of the teeth, mouth charting, and the taking of "wing bite" radiographs should be done by the hygienist before the child goes to the dental surgeon for detailed examination and treatment. This proposal, however, when he made it before the British Dental Association at Birmingham was strongly criticised,[2] mainly on the ground that diagnosis should precede treatment and that scaling alters the diagnostic picture. Mr A. F. Stammers did not regard scaling as by any means minor dental work: it was, he said, the most important thing a dental surgeon could do for his patient. Mr E. Davies Thomas, at the Children's Hospital, Birmingham, had made a rule that nobody should talk to the child except himself, and in this way he established a personal understanding.

In the care of the teeth at home, Mr Leatherman believes that the basic need from childhood is to prevent gingivitis, and, where gingivitis and its sequelæ have developed, to see that the causes are removed and the supporting structures rendered healthy. The patient should be made to understand that the supporting structures of the teeth require as much attention as the surfaces of the teeth themselves, and to this end the term toothbrush should be changed to mouthbrush. He favours the use of a mouthwash of full strength hydrogen peroxide (10 volumes), or 'Milton' (1 part to 4 parts water), or sodium chloride and sodium bicarbonate (½ teaspoonful of each in half a glass of warm water). The teeth and mouth are brushed first thing in the morning and last thing at night with salt powder, or a powder of urea and ammonium; though what really matters is not what is on the brush but how and when the brush is used. The brush of choice, according to Mr Leatherman, is one of natural bristle, of medium consistence, 6–8 rows long, the bristles being all of the same length; and more than one brush is necessary, for

each should be allowed to dry for at least 24 hours after use. He would have us all clean our dental spaces with wooden sticks or dental floss, and some people should massage the interdental epithelium with a wooden stick. At each mouth cleaning the gums are massaged with the fingers, and the session ends with a mouthwash.

---

[1] Brit. dent. J. 1950, 89, 119.
[2] Ibid, p. 125.

BLEEDING AT OPERATIONS

PERSISTENT oozing of blood during an operation may cause nothing worse than irritation and delay—in itself the loss of blood is not often serious nowadays, when it can easily be made up by transfusion—but it may obscure the surgeon's view and lead to damage of important structures, or by forming a hæmatoma it may delay healing and encourage infection. Surgeons and anæsthetists are inclined to blame each other for such oozing, and almost every anæsthetic agent has at some stage of its career been accused of increasing the bleeding tendency, so the subject has been keenly studied. It seems to be generally agreed that cyclopropane encourages bleeding, though whether this is a direct effect of the gas or a result of the absorption method of administration or of the presence of excess of oxygen is uncertain. Ether is also suspect, because, except in very deep anæsthesia, it stimulates cardiac and respiratory activity and dilates the peripheral vessels. Apart from drug action, bleeding can be aggravated by respiratory obstruction sufficient to raise the venous pressure, and also by breathing excessive amounts of carbon dioxide, whether this comes direct from the cylinder or from a faulty absorber or mismanaged anæsthetic apparatus. Then the surgeon himself may be responsible—for example, he can obstruct the venous return by leaning on the patient, or with his bandages, or, in tonsillectomy, with the tourniquet-like straps of his gag jack.

Two methods of anæsthesia have long been noted for a striking absence of bleeding—chloroform and spinal anæsthesia. Their common feature is that they usually cause a considerable fall in blood pressure. This effect has lately been developed in several directions to reduce bleeding, the two main techniques being (1) high spinal anæsthesia[1] extensive enough to cut off all the sympathetic outflow, and (2) the injection of drugs of the methonium group which act selectively on the sympathetic ganglia.[2] Both of these will produce a profound fall in blood pressure and ensure a bloodless field for the surgeon. In brain surgery, where bleeding is particularly apt to be troublesome, there is an additional factor—intracranial tension, on which ease of access and the avoidance of surgical trauma largely depend. Intracranial tension is in turn dependent on arterial blood pressure, so by reducing the B.P. it is possible both to control bleeding and keep the intracranial tension low. At Edinburgh Royal Infirmary Bilsland[3] has attained this end with the technique introduced by Gardner[4] in the U.S.A. as ‘controlled induced hypotension by arteriotomy,” an adaptation of the method used experimentally for inducing shock in animals. In this, blood is rapidly withdrawn through a cannula in the radial artery until the desired reduction of B.P. is attained. The blood is run into a reservoir, from which, usually towards the end of the operation, it is returned to the patient by the same route, simply by raising the pressure in the reservoir to above the patient's systolic B.P. In 63 craniotomy cases a B.P. of under 100 mm. Hg has been maintained for up to 6 hours by withdrawing 300–2600 ml. of blood, and only one death could be put down to the hypotension.

Last year Dr. Enderby[2] published in these columns his preliminary results with “controlled hypotension,” attained with penta- or hexa-methonium iodide or tetraethylammonium chloride, supplemented by a careful use of posture. The technique, though based on that described by Griffiths and Gillies[5] was exploratory; nevertheless, Enderby obtained a satisfactory reduction of bleeding in about half of his 85 cases, and the ill-effects were nil. In this issue (p. 663) he and Dr. Pelmore report subsequent experience. Using hexamethonium only, with posture when possible, the proportion of successes has risen to 85% in 250 cases. In fenestration, where the slightest bleeding at the wrong place reduces the chances of success, Dr. Hughes (p. 666) has lowered the systolic B.P. to 75–80 mm. Hg with pentamethonium and posture (plus pentothal and pethidine, “the four P's”) and produced a completely bloodless field with no ill effects in 10 cases. But, as several speakers emphasised at the Royal Society of Medicine discussion on March 2, this is not a technique for the inexperienced or inattentive: unless the anæsthetist can keep a constant eye on B.P. and pulse, the behaviour of vessels at the operation site, colour changes, and the state of the peripheral circulation, he had better be content with preventing venous congestion, ensuring a free airway, and the other classical methods of minimising bleeding.

“FAMILY DOCTOR”

THE public appetite for information about medicine is so insatiable as to seem a little morbid, and in fact it is evidence of a deficiency disease. People ingest masses of information, supplied from various sources, in the hope of getting the small amounts of knowledge they need for bodily and mental efficiency. Often this knowledge is of a kind they could get in a few minutes' leisurely conversation with a trusted general practitioner, but for one reason or another they have not got it. In producing a journal that will supplement the efforts of clinicians, educationists, and publicists to meet the large and legitimate demand for sound instruction, the British Medical Association has chosen the title *Family Doctor*, and the editor, Dr. Harvey Flack, aims at making it friendly and dependable, like the good G.P. In a letter introducing the first issue, Dr. Hugh Clegg, editor of the *British Medical Journal*, says that the title “may remind you that the doctor's main concern is to make and keep people well,” and he hopes that the new magazine will help everyone to lead a healthy and happy life—“by telling the reader all the medical profession knows about the rules of health for men and women, boys and girls, and for babies.” Lord Horder, in a message of encouragement entitled Health is Your Right, speaks of the difficulty caused in this country by medical writers wanting to preserve their anonymity, whereas the newspapers have wanted “not only the ‘story’ but the signature and, for preference, the photograph also, of the writer.” In this demand the newspapers have reflected the opinion of the public, who like to know that the person addressing them is an authority, but the difficulty will be largely overcome if readers can feel that, though an article bears no signature, it comes to them with the imprimatur of over 60,000 members of the B.M.A.[6] The success of the American Medical Association's popular magazine *Hygeia* (now called *Today's Health*) is an encouraging precedent, and we congratulate the *B.M.J.* on the birth of this seventeenth child, which will be the public relations officer for its more academic brothers and sisters.

LORD ADDISON

IN his new office as Lord President of the Council, Lord Addison will find himself on largely familiar ground, for the Privy Council is responsible for the General Medical Council, with which his name is registered, and the Privy Council also has under its ægis the Medical Research Council, of which he has been chairman since 1948. Lord Addison remains leader of the House of Lords.

---

1. Gillies, J. *Ann. R. Coll. Surg. Eng.* 1950, 7, 204.
2. Enderby, G. E. H. *Lancet*, 1950, i, 1145.
3. Bilsland, W. L. *Anæsthesia*, 1951, 6, 20.
4. Gardner, W. J. *J. Amer. med. Ass.* 1946, 132, 572.
5. Griffiths, H. W. C., Gillies, J. *Anæsthesia*, 1948, 3, 134.
6. The new magazine is published from B.M.A. House, Tavistock Square, London, W.C.1, monthly at 1s.

What of resuscitation? Light cradles, heated sleeping-bags, and friction are less effective than rapid rewarming by direct immersion in water at temperatures of up to 50°C, maintained until peripheral vascular spasm is dispelled. Characteristically, the subject gives a sharp outcry, and then the laboured respiration and muscular rigidity disappear. With brisk rubbing and wrapping in warm blankets the temperature is restored to normal in about three hours.

MEDICAL SECRECY AND ABORTION

IN our leading article of Feb. 24 we drew attention to the legal safeguards which foreign systems, in contrast to the common law, have established to protect confidential communications between doctors and their patients. Happenings in two towns of Western Germany at the end of February show that even these measures to prevent breaches of medical secrecy may not go far enough. They also illustrate how jealously the public on the Continent resist any attempt to whittle down, by official action, what they have come to regard as a fundamental right of the individual.

Under a statute of 1935, re-enacted in 1946–47, practitioners in Western Germany have to notify to the public health authorities, for the purpose of registration and statistics, any abortions among patients under their care. There seemed to be no danger in such action until it occurred to the public prosecutor of the town of Weinheim (Baden) that the information thus assembled might be useful for tracking down professional abortionists, whose activities have lately increased. The prosecutor asked the local health authority to give him a copy of the relevant list of women treated for hæmorrhages, &c., during the past six months, and in due course the police were told to summon and interrogate the women named in the list. Perhaps in an excess of zeal, the local chief of police ordered a raid during which some 200 women and girls from the town and neighbourhood were taken in vans to the police station and kept there several hours for questioning and further investigation, on no other ground than that they had been treated within the last six months for miscarriage.

How far this measure succeeded in its purpose is not yet known; for this aspect of the affair has been submerged by a wave of protests from the doctors of the district and from the public. Concern has been aroused all over Germany, particularly since it became known that a similar attempt to get evidence of criminal abortions from official returns of miscarriages had been made by the police at Garmisch (Bavaria). In its indignation over the high-handed action of the police, the German press has not lost sight of the wider principles involved, and much of the outcry has been directed against the public health officials for their "gross breach of medical secrecy" in passing the list of names to the public prosecutor. The local medical organisation has advised its members to suspend all notifications of abortion until the legality of the recent police action has been investigated, and an information has been laid against the health officials concerned for breach of medical and official secrecy. This step has been endorsed by the medical chamber of the Land, which demands new legislation to provide legal safeguards against such breaches of medical secrecy, if the present rules should be found insufficient. After this sharp reaction of public and medical opinion in Western Germany such attempts to circumvent medical secrecy are not likely to be repeated, the more so since German law clearly says that in no circumstances can such a breach be ordered even for the purpose of pursuing punishable conduct.

In this country the duties of medical practitioners in relation to cases of criminal abortion which have come to their knowledge in the course of treatment were the subject of a resolution passed by the Royal College of Physicians in 1916. After emphasising "the moral obligation to respect the confidence of the patient," this advised the practitioner to urge his patient to make a statement to the police; but if such a statement is refused, he is under no legal obligation to take further action and should continue to treat the patient. It is less easy to give any definite answer to the further question which the incidents in Germany may raise here—namely, whether the records of patients and treatment which have to be forwarded to the local executive council under the National Health Service regulations, and the written clinical information which may be requested by the medical officer of health, are, in theory or even in practice, open to similar misuse. There is, however, some authority for suggesting that, if the Government department concerned were to object to the revelation of such documents to the police, the courts would uphold the objection on the ground that the papers are protected as State documents.

CARE OF THE TEETH

THOUGH its causes lie chiefly in diet, much dental caries could be prevented or checked if people could be induced to keep their mouths clean and see a dentist regularly. Recognising that, for many years at least, most dental surgeons will be occupied mainly in dental repairs, Mr. G. H. Leatherman[1] bases his scheme of preventive care on the employment of women dental ancillaries, or "hygienists," who would undertake scaling and polishing, and would help to instruct patients or parents in the elements of oral hygiene and home treatment. Whereas adults, and possibly adolescents, should be seen first by the dental surgeon, who would refer the patient to the hygienist for any minor treatment required, Mr. Leatherman thinks that for the very young the sequence should be reversed, because it is psychologically better for the child to be introduced to dental care by a woman. He recommends that polishing of the teeth, mouth charting, and the taking of "wing bite" radiographs should be done by the hygienist before the child goes to the dental surgeon for detailed examination and treatment. This proposal, however, when he made it before the British Dental Association at Birmingham was strongly criticised,[2] mainly on the ground that diagnosis should precede treatment and that scaling alters the diagnostic picture. Mr. A. F. Stammers did not regard scaling as by any means minor dental work: it was, he said, the most important thing a dental surgeon could do for his patient. Mr. E. Davies Thomas, at the Children's Hospital, Birmingham, had made a rule that nobody should talk to the child except himself, and in this way he established a personal understanding.

In the care of the teeth at home, Mr. Leatherman believes that the basic need from childhood is to prevent gingivitis, and, where gingivitis and its sequelæ have developed, to see that the causes are removed and the supporting structures rendered healthy. The patient should be made to understand that the supporting structures of the teeth require as much attention as the surfaces of the teeth themselves, and to this end the term toothbrush should be changed to mouthbrush. He favours the use of a mouthwash of full strength hydrogen peroxide (10 volumes), or 'Milton' (1 part to 4 parts water), or sodium chloride and sodium bicarbonate ($^1/_2$ teaspoonful of each in half a glass of warm water). The teeth and mouth are brushed first thing in the morning and last thing at night with salt powder, or a powder of urea and ammonium; though what really matters is not what is on the brush but how and when the brush is used. The brush of choice, according to Mr. Leatherman, is one of natural bristle, of medium consistence, 6–8 rows long, the bristles being all of the same length; and more than one brush is necessary, for

---

[1] *Brit. dent. J.* 1950, 89, 119.

[2] *Ibid*, p. 125.

The magnitude of this change is best appreciated in its reflection in the medical press Table I shows the number of articles in THE LANCET classified according to the number of contributors under the title of each, that is to say whether they were written by one, two, three, &c, contributors I have excluded articles which are essentially monographic, such as memorial lectures and presidential addresses, and also short clinical notes

These figures show that multiple authorship, uncommon fifty years ago, now exceeds single authorship

Table II shows the relative numbers of medical and lay contributors

TABLE II—MEDICAL AND LAY CONTRIBUTORS

Contributors	Year		
	1899	1924	1949
Medical	291	273	499
Lay	2	16	85
Ratio of lay to medical		1 17	1 6

Lay authorship, once a rarity, has increased at an accelerating rate and now forms a substantial part of the total If I had included the large number of postscript acknowledgments the figures would have been even more striking

Of the two lay contributors in 1899 one was a physiologist, the other a bacteriologist The occupations of those in the other years were

1924	
Chemists and biochemists	5
Physiologists	5
Botanist	1
Physicist	1
Protozoologist	1
Not stated	3
Total	16

949	
Chemists biochemists pathological and bacteriological chemists	39
Bacteriologists	8
Statisticians	4
Physicists	3
Pharmacologists	3
Physiologists	2
Biologists	2
Accountants	2
Laboratory technicians	2
Nurses	2
Pathologist	1
Medical artist	1
Engineer	1
Lecturer in experimental method	1
Cerebral palsy therapist	1
Holders of science degrees subjects not stated	13
Total	85

The 1949 list shows the wide range of occupations involved, the predominance of chemists, and the admission of technicians to partnership in publication

LAY PARTICIPATION AT ACADEMIC LEVEL

The extent of lay participation in research and teaching needs no emphasis It is, however, worth pointing out that a medical qualification is no longer essential for the directorship of the National Institute for Medical Research or for professorships of physiology, biochemistry, or even anatomy Of the 35 research units of the Medical Research Council no less than 9 are under lay directors Lay participation has become essential to almost every research team It sometimes provides the inspiration and it always exerts a disciplinary influence on a subject peculiarly prone to intellectual delinquency To change the metaphor, the concrete of clinical experience, formerly sufficient for the structure of medical progress, must now be poured round the iron skeleton of science

As the influence of the laboratory increases, individualism declines The discovery of the plantar reflex was complete and perfect in itself and required only one person, the discovery of a new drug is only the beginning of a process with endless ramifications involving a countless number of persons Sir Alexander Fleming, who in the medical field has made the greatest individualistic discovery of our day, has pointed out that the production of a new antibiotic involves in turn the biologist who discovers it, the chemist who purifies and if possible synthesises it, the pharmacologist who investigates its properties, the physician who assesses its therapeutic effects, and the pharmaceutical manufacturer who makes it in quantity Note that the physician takes fourth place The unlimited fecundity of science and the relative sterility of clinical observation make it certain that in the higher branches of medicine the worth of a medical qualification will undergo a further decline

HOSPITAL PERSONNEL

The value of a medical qualification is, however, more seriously affected by the growth of the auxiliary, administrative, and clerical staffs To illustrate this growth I give in table III the figures for Addenbrooke's Hospital, Cambridge

From the figures for 1950 a small deduction should be made for work in connection with satellite hospitals Neglecting this we see that in fifty years, though beds have only doubled, the labour involved has increased 7 times, the medical staff 12 times, and the nursing staff 5 times, while the auxiliary and administrative staffs have grown from almost nothing It may appear surprising that in 1900 one person should have sufficed for administration, but Dr G S Haynes, who was then house physician and who happily is still with us, tells me that the secretary, a solicitor practising in the town, was paraplegic and was wheeled into the hospital for board meetings All the administration, such as it

TABLE III—STAFF OF ADDENBROOKE S HOSPITAL

	1900 (170 beds)				1925 (190 beds)				1950 (360 beds)			
	Number				Number				Number			
—	Part time and full time		Estimated as full time labour		Part time and full time		Estimated as full time labour		Part time and full time		Estimated as full time labour	
Medical and dental staff												
Consultants and clinical assistants	10		4		25		10		50		30	
Registrars and house officers	3		3		4		4		55		55	
Total		13		7		29		14		105		85
Nursing staff												
Nurses	59		59		73		73		278		268	
Orderlies	0		0		0		0		22		18	
Total		59		59		73		73		300		286
Auxiliaries												
Pharmacists and dispensers	2		2		5		5		7		7	
Almoners	0		0		0		0		3		3	
Occupational therapists	0		0		0		0		3		3	
Physiotherapists	0		0		3		3		16		16	
Radiographers	0		0		1		1		12		12	
Dietitians	0		0		0		0		2		2	
Laboratory technicians	0		0		1		1		28		28*	
Others	0		0		0		0		6		6	
Total		2		2		10		10		77		77
Administrative and clerical staff		1		1		7		7		62		62
Grand total		75		69		119		104		544		510

* Including 20 in training

Points of View

THE ECONOMIC VALUE OF THE DOCTOR

FFRANGCON ROBERTS
M A, M D Camb, F F R

THE most significant feature of the threatened dismissal of the registrars is that under a Government committed to full employment the first departure from this principle should affect one of the higher-wage groups While hoping for a satisfactory solution of the problem we may profitably inquire whether it is an isolated malaise (teething trouble, to use the current jargon) due to special circumstances unlikely to recur, or whether it is the first symptom of a condition likely to become recurrent or chronic To find the answer we must examine the effects of medical and social evolution upon the economic value of the doctor to the community

The counsel given by the writer of *Ecclesiasticus* and the designation of medicine as a noble and learned profession may persuade us that the doctor has always been held in high honour, a state which the march of medical science cannot fail to enhance I propose to show that this view is mistaken, that in the doctor's prestige three periods can be discerned a long period when it was low, a short period when it rose very rapidly, and a third, the present, period when it is undergoing a *relative* decline

The attitude of the public on this point is mercurial and unreliable It fluctuates, according to circumstances, between extremes of emotional gratitude and hostile criticism The threat to the registrars was bewailed by one of our popular newspapers as the destruction of the hopes of "the brilliant young men and women," destined for Harley Street Such sentimental adulation, however, is one of those psychological devices invented by society to create a feeling of security When someone is going to remove your stomach you feel safer if you can deify him The opposite to this idolatry was evident in the unsympathetic attitude taken during the passing of the National Health Service Bill by a section of the press from which many had expected unflinching support

THE PERIOD OF LOW PRESTIGE

The history of medicine, as usually recounted, is misleading in that it concentrates on the high lights—on those who made notable advances in medical science, on those who gave valued personal service to their sovereigns, and on those who aped the flamboyant manners of high society These, however, were very few and were not typical of their profession The gold headed cane was conspicuous enough in Pall Mall to inspire the satirical brush of Hogarth, but that it was the customary adornment of doctors in general is hardly credible The surgeon was someone to be "fetched" when occasion arose Unlike the Church, the Services, and the Bar, medicine was always completely devoid of privilege, patronage, and sinecures, and was therefore never considered a suitable outlet for the energies or lucrative indolence of the cadets of the aristocratic families

To the wits of all times, from Aristophanes to G B Shaw, the doctor has been a favourite butt In Victorian fiction he cuts a sorry figure Mr Bob Sawyer and Mr Benjamin Allen of *Pickwick Papers* are obviously caricatures, as are Surtees's Dr Roger Swizzle and Dr Sebastian Mello, and Trollope's Sir Omicron Pie and Dr Fillgrave But even in his more serious mood Dickens depicts the doctor as kind hearted but fussy and incompetent George Eliot, who acquired a knowledge of medicine unequalled by any other novelist save possibly Flaubert, presents the provincial doctor in a more dignified light Nevertheless one of the characters in *Middlemarch* says

> 'Mr Brooke says he is one of the Lydgates of Northumberland, really well connected One does not expect it in a practitioner of that kind For my part, I like a medical man more on a footing with the servants they are all the cleverer I assure you I found poor Hicks' judgment unfailing, I never knew him wrong He was coarse and butcher like but he knew my constitution"

No, doctors were quite humble members of society, and their neglect of sanitation, which, though well within their competence, they left to a layman to reform, is alone sufficient to show that they deserved no better consideration

THE PERIOD OF RISING PRESTIGE

This situation was radically transformed by the discovery of the microbial origin of infection, with its corollary, antiseptic surgery, reinforced by the earlier discovery of anæsthesia For the first time in its history the medical profession became a power in the land The doctor who in Fildes's famous picture could only sit in helpless contemplation of his patient gave place to one who could save life dramatically by operation or quietly but no less surely by prophylaxis At the same time he acquired great civil powers He could influence legislators, condemn houses, close schools, and deprive citizens of their liberty by putting them in quarantine The new knowledge, combined with the high standard of refinement and cleanliness required in its practice, gave to the sons, and later the daughters, of the rising middle class an opening with unlimited possibilities which the more static professions lacked New medical schools were opened, the curriculum became more exacting and higher qualifications were instituted This period can be defined as the period during which the new gifts of science could be exploited by the doctors individually, with little help from their colleagues and none from lay sources apart from nurses and pharmacists Doctors stood alone in their glory, perched high above the city like muezzins on their minarets

THE PERIOD OF RELATIVE DECLINE IN PRESTIGE

Since the early 1920s, however, there has come over the scene another change the importance of which has been overlooked The progress in the knowledge of disease and in the complexity of technique has enforced an increasing degree of collaboration Individualism is giving place to team work This in itself would be of no great moment were it not for the fact that such collaboration is becoming progressively lay in character (I use the word lay as meaning the absence of a medical qualification) The contributions of science have now passed beyond the stage when they can be handed over to the doctor On the higher plane their complexity has enforced their retention in the hands of the lay scientists and on the lower plane their widespread application has enforced their delegation to technicians By the limitations of his training in the one case and by the exigencies of practice in the other the doctor has become incapable of applying them himself

TABLE I—AUTHORSHIP

Contributors under the title of each article	Year		
	1899	1924	1949
One	231	158	165
Two	28	55	125
Three	2	7	34
Four	0	0	11
Five	0	0	2
Six	0	0	1
Seven	0	0	1
Total articles	261	220	339
Total contributors	293	289	584

With regard to advertised vacancies, over 95% of the recommendations by executive councils were accepted.

Dr D. F. HUTCHINSON said that general practitioners were not happy about the service. They were making a just demand for improved remuneration, but the greatest source of discontent was the administration, which did not enable them to give the best possible service; they felt that they were tied with red tape and that the administration should be simplified. In England and Wales the delay in filling practice vacancies was now shorter, but still greater speed might be achieved by following the example of Scotland, where appeals against decisions in filling vacancies were heard by the Medical Practices Committee. As to the classification of areas, practitioners thought this was too rigid, and that the Medical Practices Committee gave insufficient weight to local opinion. Dr Hutchinson agreed about the need for cooperation between the three main divisions of the service; and from his experience as a member of both the Central Consultants and Specialists Committee of the B.M.A. and the General Medical Services Committee, he denied the existence of antagonism between practitioner and specialist. Nevertheless in some areas the practitioner was not given a proper opportunity to place his views before hospital bodies.

SIR WILLIAM MARSHALL was impressed by the difficulty of young doctors in establishing themselves in practice. The second world war, with the associated rise in income tax had made it almost impossible for the young graduate to purchase a practice unless he had substantial financial backing; even now, with sale and purchase of practices abolished, he might still have difficulty in buying a house, car and so on. Sir William was impressed, too, by the number of men, aged 30–40 and perhaps married, who applied for a place in one practice after another. Unless he gained an assistantship with a view to partnership, the outlook for him was almost hopeless. Related to this problem was the size of lists. He himself was convinced that a doctor with the maximum of 4000 patients could not give reasonable service and have leisure and a chance to keep himself up to date. Even with a list of 3000, on a basis of 5 items of service per patient per year the doctor would be giving 30–40 items per day and up to 70 in the winter. He hoped that any additional money would be used to aid the practitioner with small lists.

Dr H. S. HOWIE WOOD suggested that the two main causes of discontent among practitioners were (1) the Minister's failure to fulfil his promise to fix remuneration, and (2) the practitioner's reduced status. Young men seeking to enter practice should make full use of the trainee assistant scheme.

Mr A. N. WRIGHT, president of the Executive Councils Association (England), challenged Dr Rogers's assessment of the executive-council machinery; and he agreed that the method of filling practice vacancies should be revised, with appeal only to the Medical Practices Committee.

Dr J. L. MCCALLUM said that patients realised they were getting good service from practitioners, but they noticed that the doctor was hurried. This haste could not go on for ever: the patient would not put up with it and the doctor's health could not stand it; the wastage rate among practitioners was rising. The doctor should be given more time by providing him with ancillary help and suitable premises. "The doctor's best equipment is his time."

Mr A. J. FIELDER held that the average person, seeing his doctor with one new car after another, was not convinced that he was not faring well. The doctor, it perhaps seemed, was just in doubt whether he wanted to be a Civil Servant. If doctors wanted better conditions they must persuade the public that there was more to it than this.

More than one medical speaker referred to the difficulty created by thoughtless patients who applied needlessly late in the day for a visit; this meant that the doctor had to cover the same ground a second time, and he had no way of countering such heedlessness.

Answering questions, Dr ROGERS observed that the number of young men seeking to enter practice had fallen off a little, but the number would soon be swollen by ex-registrars. To place them suitably, executive councils and regional boards should possibly work together. The immediate need was for increase in the capitation fee for the first 1000 patients; this increase should apply only to principals, for otherwise there was little incentive to take on a partner rather than an assistant.

The Hospital Administrator

Mr J. CRAWFORD FIELD suggested that every job can be divided into policy (what shall be done) and execution (actually carrying out the work). With simple tasks both these functions could be exercised by the same person; but in a more complicated procedure, where several people took part, a third function, administration, was needed to coordinate their efforts. In a hospital, policy was settled by the chairman and the committee, and execution was carried out by the different departments. But who was to be administrator? In a multicraft organisation like a hospital, if the executive parts were to work together happily, it must be clear that administration was not the prerogative of one of the sections. This ruled out, in his view, the medical administrator with clinical duties. Similarly the administrator should stand apart from staff specialising in finance, supply, and maintenance. At present many hospitals and groups of hospitals had no true administrator, but the struggle for power between the different departments would make the appointment of a coördinating officer inevitable. Mr Field believed the position of the administrator was stronger if he had no part in policy making, and the staffs of the different services did not regard him as responsible for the decisions taken by the chairman and committee.

Dr T. ROWLAND HILL affirmed that the administrative problems of the doctor had been enormously increased by the suddenness with which the National Health Service was introduced. Medical organisation and practice, especially in large hospitals, were so intricate and delicately balanced that efficiency was easily impaired. To get the best doctor, he must in his work be both free and trusted. Save us, Dr Hill cried, from the purely technical doctor who becomes a subordinate officer in an administrative machine with no sense of independent professional and ethical authority. We would not achieve a contented service by creating a highly disciplined authoritarian organisation in which most of the staff felt they had merely to obey instructions. For this reason Dr Hill warmly advocated joint consultation with all grades of responsible staff, which he believed had been so far insufficiently developed in the National Health Service. He deprecated the present practice of obtaining advice not from the chosen representatives of the profession but from panels of experts chosen by the administrative department concerned.

Dr E. B. BROOKE agreed with Florence Nightingale that administration is the enlightened pursuit of economy; and true economy, he pointed out, was getting value for your money. The hospital administrator, he suggested, should be a good housekeeper. But a good housekeeper should have control of the housekeeping money, and he thought it would be better if the savings of hospital management committees could be reflected in local benefits. Another problem of hospital administration

4 Is the medical curriculum designed to provide a philosophic ascendancy sufficiently powerful to maintain control over events and sufficiently stable to withstand the changes which time brings?

It will no doubt be objected that to ask these questions strikes at the roots of medical freedom But economically medicine never has been and never will be free Those who imagine that the nationalisation of medicine gives them licence to do and have what they like will soon realise their error Medicine, having acquired the capacity for unlimited procreation, becomes subject to the Malthusian law the pressure which it exerts against its means of subsistence will, if we are not careful, inevitably lower its standard We make a great mistake if we imagine that its tension against the inexorable resistance of economics will be unaccompanied by internal disturbances It will develop the fretfulness of frustration

For what is to count in the medicine of the future? The qualities and experience which should result from a medical training, or the test tube and the machine? Is medicine to degenerate into mass production in which technicians multiply and leadership lies in the hands of those members of the profession with a flair for organisation and committee-work? If so, it is obvious that the State cannot at the same time continue to pay a number of four figure salaries which would drive a commercial concern to bankruptcy

We are concerned not with what is best for ourselves but with what is best for medicine At the same time we must remember that it takes at least six years to train a doctor and about fifteen to train a specialist We cannot foretell what medicine will be like in 1966, but we can confidently predict that at the present acceleration of progress it will differ from the medicine of 1951 far more than the medicine of 1951 differs from the medicine of 1936 We therefore owe it to those who come after us at least to make some attempt to read the signs of the times and to ask ourselves what we are doing and why we are doing it Unless man's capacity to induce changes in his environment is accompanied by an equal capacity to adapt himself to those changes he will not be master of his destiny

Special Articles

PROBLEMS OF THE HEALTH SERVICE

LONDON CONFERENCE

REPRESENTATIVES from the various branches of the National Health Service were brought together—for the first time in England—at a conference held in London last week by the Institute of Public Administration The chairman was Mr HENRY LESSER

General Practice

Dr A TALBOT ROGERS said that the executive councils had taken over the offices, staffs, methods, and outlook of the old insurance committees Initially this was an advantage, but this borrowed administration was "not so well suited to resolving in any radical manner the newer problems peculiar to the changed conditions of a service now available to all, and provided by doctors whose traditional methods of entering and leaving practice had been abruptly abolished" Many had hoped that the executive council might have become a forum for exchanging lay and professional views on policy and planning but the mass of detailed day to day work in which the councils and their officers were immersed had almost everywhere confined them to a managerial rôle Consequently, on the medical side, local medical committees had had to work out for themselves the solutions to new problems, and when in difficulty to apply for guidance to their own central committee—the General Medical Services Committee

As to entry into practice, the Medical Practices Committee had hesitated to close areas to new entrants unless these were most manifestly over doctored

> It has often had to resist local arguments in favour of closure of areas, and not infrequently has had to upset on appeal the choice of a successor for a practice, or the decision that no successor was needed In many of the cases where it has done this it has had to act, not from exact local knowledge but rather from rule of thumb methods based upon calculations of the numbers of doctors and the numbers of the population Some of the committee's decisions have undoubtedly given rise to heart burnings among the local medical committee members who feel that if they, with full local knowledge and acting as carefully, impartially and disinterestedly as they can have come to a decision this decision should not lightly be upset by a remote central committee

As to the tribunal which dealt with serious disciplinary offences, the main reasons for dissatisfaction were (1) the very long delays in some cases between commission of the offence and the tribunal's decision, and (2) the revelation in certain cases of the defendant's name and place of practice, even though the case against him had not been established Many doctors remained dissatisfied, too, that no provision was made for an appeal to a court of law

One weakness of the Act was that it sectionalised the administration of the service, and provided little, if any, local means of liaison between the administration of the hospitals, the local authority health services, and the general medical services Commonly local medical committees had gone some way towards overcoming this weakness by coopting the local medical officer of health Similarly, a place had been found for a general practitioner on the health committee of some local health authorities One example of the value of such cooption was in the provision of medical care on new housing estates All too often a new estate was developed "with no agreed conception of how and where medical care should be provided being reached by the health authority, the executive council, and the local medical committee, all of whom are concerned"

Professional members of the boards and committees administering hospitals were almost all consultants, and this, practitioners felt, often resulted in a failure by these boards and committees to understand the practitioner's point of view and how much sound advice he could give on what would best satisfy his patients' needs The problem of the over provision of registrars could not, it seemed, be solved satisfactorily without full and continuing consultation between bodies administering the hospitals and those administering general practice

Dr W E DORNAN, chairman of the Medical Practices Committee, insisted on the need for the stabilising influence of this central body, which was able to get a comprehensive picture denied to local committees The committee had never refused admission to local lists against the advice of executive councils, but in the fringe areas it had often admitted doctors against the advice of councils The committee was concerned, not to protect doctors in established practice, but to preserve the greatest freedom for any doctor to practise where he would, subject only to the interest of the public being served Though the right to sell goodwill had been lost, many of the best features of ownership had been retained, and the committee had jealously preserved the right of principals to nominate partners and assistants Over half the appointments to vacancies in established practices were now made in complete agreement with executive councils, local medical committees, and local doctors.

either a separate block or appropriate separate ward units in which patients are looked after by their own general practitioners. I am also in favour of selected general practitioners acting as part time assistants to consultants."

As to lay and medical hospital administration, either system "can work admirably if the officer is a man of high ability and suitable personality." But "*I doubt* whether hospital administrators of the necessary quality are likely to be recruited and retained under present conditions."

> "In these days of huge hospital regions and large hospital management groups there is not sufficient recognition of the fact that the local administration of one hospital of 200–800 *beds requires a man of very high ability and suitable* personality, and that this is more important than the question whether he should be medical or non medical — the more I have seen of organisation of hospital and other health services, the more I am convinced that in the end the quality of service depends on the quality of the individual in local charge of its various subsections—for example, the administrator of the individual hospital."

Finally, with regard to maternity beds, for the individual family institutional care was much cheaper than domiciliary care, and this anomaly should be corrected because it increased the demand for institutional care. The hospital service, having to refrain from unnecessary expansion, might wish to abandon schemes for extending institutional midwifery to deal with 75% or more of all births and be content with a target of 40% or so, according to local conditions.

Public Health

World Typhoid Survey

ONE of the legacies of the late war was a recrudescence of enteric fever throughout Europe. A survey published by the World Health Organisation in 1948 noted that the "safe areas" had been reduced to the United Kingdom, Switzerland, and the Scandinavian countries, and that in other areas the position was wholly unsatisfactory and showed no signs of improvement. The latest survey published by W.H.O. shows that since 1947 there has been an unexpected reduction in the number of cases in Europe, but not in Africa, America, Asia, and Oceania.

In Europe the number of cases fell from 162,000 in 1947 to 118,000 and 124,000 in the two following years, and an estimated 105 000 in 1950. In 1948 the greatest improvement was in Austria, Germany, Finland, Italy, and Poland, while in Belgium, Greece, Luxembourg, and the United Kingdom the incidence remained the same. In 1949 the downward trend continued except in France and Spain where there were severe outbreaks; and in 1950 the position was still improving despite moderately severe epidemics in Turkey and Yugoslavia and minor ones in Sweden and Switzerland.

In the other continents the total incidence has remained the same. In Africa the decline in the number of cases in Algeria, Madagascar, Mauritius, Morocco, and Tunisia was balanced by a steady rise during the three years, in Northern and Southern Rhodesia, and a considerable increase in the number of notifications in Egypt and Kenya during 1948 and 1949, and in the Union of South Africa in 1949.

For the whole of the American continent the total number of cases remained the same. There was an increase of incidence in Colombia in 1948 and 1949, and a decrease in Costa Rica, Cuba, Haiti, Jamaica, Peru, and St. Vincent. The United States had by far the fewest cases in proportion to the size of its population.

Of those countries in Asia for which figures are available the majority showed an increased incidence of enteric fever; they include Afghanistan, Ceylon, Cyprus, Iraq, Iran, Israel, Malaya, and Syria. Japan was an exception, for there was a spectacular drop in the number of cases from 1947 to 1950. In the Fiji Islands the incidence rose in 1947 and 1948 and fell again in 1950.

In England Now

A Running Commentary by Peripatetic Correspondents

OUR province extends from the incisor teeth to the anal sphincter, and strange things come our way. Last week we had our bezoar. It came to us in a quiet unassuming housewife, and our physician first spied it through his gastroscope, so we all queued up to cast an eye. Our radiologist was delighted; he showed it in his films, and even pushed it up into the pouch of the woman's diaphragmatic hernia. We showed her to the clinic and one student responded with the diagnosis of "a hairy ball in the stomach."

Such was the splash it made in our hospital; the ripples reaching the outside world were far more decorative. In the patient's home village the thing was a tropical beast (derivation: foreign body—foreign beast—tropical beast). The houseman in a neighbouring unit heard their lady-help telling his mother that it was four inches long, with a pointed beak, a furry coat, and short legs. The village postman knew it had a long neck, for surely it reached up for food when hungry. The patient's own doctor told us that everyone in the village knew how we had fed it for days on little crusts of bread dangled on a string down a tube and then one day had poisoned the bait and that was its end.

With his more direct approach our chief opened her stomach, and there are some who say that it took wings and flew round the theatre, chased by the anæsthetist with an ethyl chloride spray. At last we had it out and sent it to the Professor of Botany, who laid the ghost: the undigested skin of a citrous fruit—not a trichobezoar but a citrobezoar. The answer was in fact a lemon.

* * *

I am a confirmed air-traveller, and I travel B.O.A.C. whenever possible, but I wish the corporation would apply a little spit and polish to their service. I have just returned from a flight to the Far East, mainly by B.O.A.C. but using other lines now and then, which gave me an opportunity for comparisons.

The B.O.A.C. catering is reasonable by our present English austerity standards but inferior to that of K.L.M. or Quantas. There is some excuse for this but none for providing different qualities of sherry according to whether you pay for it separately or have it as a "complimentary" drink before dinner, when it is included in the price of the meal.

This happened on my flight back from Nairobi by the new and much-vaunted *Hermes* service. The sherry I paid for was drinkable; the complimentary sherry was not. Incidentally the prices of drinks are extortionate compared with those charged on ships, being the standard English hotel prices. Considering that the flights often include night flying, that there may be 40 passengers on board, and that the washing arrangements at most airports are poor, hot water can hardly be called a luxury, and the supply should not be as temperamental as it is; nor should one be expected to make do with paper towels, which are all that some B.O.A.C. lines provide. Sir Miles Thomas's attempts to make the corporation pay are no doubt laudable, but stinginess in the toilet department is not a worth-while economy.

Some of the airports are still pretty grim. Aden was the worst I sampled. We touched down there on the flight from Karachi to Nairobi by Air India International and were given a miserable breakfast with execrable tea (no coffee). Malta gave us a reasonable breakfast, but I have yet to meet a bleaker and draughtier spot on a blustery wet December morning than the Malta airport. Imagine a derelict railway waiting-room in some isolated corner of this country, with canine excreta on the floor, and you will be somewhere near it.

Finally—and this applies to several of the airlines I have sampled—when the departure of a plane is delayed, why are the passengers not told the reason? Any passenger who tries to obtain such information from the ground staff can be sure of a rebuff, and this is all the more irritating because the full details are always forthcoming from the crew once the plane is in flight. Two years ago we were delayed for hours at Gander on our return absurdity of having to increase administrative costs in order to bring down total outlay could be avoided if doctors, dentists, and opticians worked in publicly provided health centres or clinics ”

More fundamental was the basic dilemma of the N H S how with limited resources to meet a potentially unlimited demand for medical care—how to impose a ceiling on “ production ” when the lid was taken off “ consumption ” The service was based on the naïve idea that it was simple to decide what was medically necessary, and that all such needs must be met

> “ There are two objections to this view First, there is a large subjective element even in the professional view of what is ‘ medically necessary,’ especially in such matters as buildings, equipment, and ambulance rides If the head of every department of every hospital were to write down his ideal requirements for good work, and all the bills were added up, the present outlay on hospitals might have to be raised three or four times to meet the total Secondly, the subjective element is even stronger in the patient’s mind Medical care tends to reverse normal economic laws the supply tends to create the demand, rather than vice versa The priestly function of the doctor, for instance, is capable of indefinite expansion , so possibly is the cosmetic use of spectacles and dentures, and the use of hospitals as hostels for elderly relatives unwanted at home ”

For checks that were not merely arbitrary two sets of criteria were required (1) standards of quality of professional work, staffing, accommodation, and other aspects of care , and (2) standards of cost of necessary work efficiently performed

The problem of rational financing was made harder by the fatal division between responsibility for the use of resources and responsibility for providing them , this ran right through the N H S but was most marked in the hospitals The Ministry, lacking any sure means of judging how far their requests were reasonable, had yielded to the fatal temptation to control the affairs of the hospitals in detail The bureaucratic control predicted by the opponents of the N H S had in fact been imposed on the hospitals Economy was possible without this , and it even fostered waste

> “ I fail to see how the need for economy justifies these controls By fixing an annual sum not to be exceeded by the hospitals as a whole, the Government has already taken the first step towards making them unnecessary The second step would be to treat this as a pool to be shared among the regions for the time being according to some rough criterion of relative needs of a necessarily empirical kind The third step would be to leave each regional board free within broad limits to share its funds between its management committees as it chooses , the fourth to give the committees a reasonable freedom to manage their own ‘ block budgets, including a right to save money without forfeiting it Until the development of hospital costing yields reliable means of measuring efficiency and needs, such a system would of course be arbitrary But the present system is not only just as arbitrary it is also bureaucratic and damaging to the whole spirit of the hospital service ’

As to checking the public appetite for health service care, the first need was to examine the professional man’s position and to remove from his working environment any features tending to deprive him of incentives to economy, or giving him an incentive to be over lenient with his less sensible patients There was too, a certain scope for more direct measures, including charges to patients

> Generally I think there is a case now for introducing charges in the N H S for ‘ articles rather than for services but only in cases where without creating a new financial barrier to necessary care charges would result in a real overall economy There is little point in using charges to reduce the public cost of a service if this merely sends up private spending by an equivalent amount That is, I suspect, precisely what would happen if a charge were introduced for board and lodging in hospital ’

Ideally, said Mr Lafitte, the whole N H S budget should be directed to securing the rational deployment of all available medical resources It was arguable, too, that one aim should be to build up the “ front line ” services, so as to screen away from the hospitals and other services at the “ rear ” the greatest possible amount of work

> “ My impression is that such wider issues of strategy are not being sufficiently considered, although the long term fate of medicine in part depends on them, because it is no-one s job outside Whitehall to look at the pattern of needs and resources in medical care as a whole In most places I suspect that they [the hospital authorities] have the most influence in determining the whole pattern and trends of development of the medical care and services The shape they are imposing is, I suspect, derived from their own particular attitude to medical care, which is largely that of the specialist clinicians, and the general trend seems to be for them to claim all the work which interests them and to leave the rest to other agencies If I am right, the budgetary implications may be very great in the long run, since the hospital is the most expensive means of supplying medical care If specialists, general practitioners, and midwives—or ‘ general ’ and priority dentists—were all on the same payroll, is it not likely that developments in many places would be going along different lines ? It may well be that we shall have neither ‘ rational planning ’ nor economical budgeting until the power to allocate funds between the different branches of the N H S is vested in some authority, below the level of central government, which is competent to look at every aspect of the position in a particular place, and is responsible for finding part of the necessary funds from local, not central, sources ”

Planning and Coördination

Dr W G PATTERSON declared that major hospital planning should be considered by the appropriate local health authority, whose observations might be of great value At present there might be no consultation, not because the board was opposed to it, but because the board and its officers were so overworked that they did not go out of their way to initiate time consuming discussions Formal consultation should be obligatory, but, failing this, a suitable liaison committee should be set up As regards cooperation between board and management committee, Dr Patterson had seen great benefit result where the chairman of the management committee was a member of the board At regional board level administrative officers were at present overtaxed , and he believed that the gravest immediate impediment to an efficient service lay in the risk of a breakdown in the administrative medical and architect organisation of regional boards

Another difficulty was the poor general practitioner representation on regional boards , and Dr Patterson was convinced that this accounted in part for some failure in cooperation between boards and practitioners To secure committee member cooperation, on local matters, between the three branches of the service, each hospital region should have several liaison committees including members of local health authorities, local sanitary authorities executive councils, and hospital management committees , and each liaison committee should preferably cover a population of about 300,000 Officers should also have a local officer liaison committee At regional level there was need for a regional health services liaison committee, including members of the regional board, the board of governors, local health authorities, and executive councils To avoid unwieldy size, local health authorities and executive councils might have to agree to token membership

Observation had convinced Dr Patterson that the best domiciliary general practice was found where practitioners attended patients in a good cottage hospital ‘ Indeed, I hold that where there is no cottage hospital available the large general hospital should include either a separate block or appropriate separate ward units in which patients are looked after by their own general practitioners. I am also in favour of selected general practitioners *acting as part time assistants to* consultants."

As to lay and medical hospital administration, either system "can work admirably *if the officer is a man of* high ability and suitable personality." But "I doubt whether hospital administrators of the necessary quality . . . are likely to be recruited and retained under present conditions."

> 'In these days of huge hospital regions and large hospital management groups there is not sufficient recognition of the fact that the local administration of one hospital of 200–800 beds requires a man of very high ability and suitable personality, and that this is more important than the question whether he should be medical or non medical . . . the more I have seen of organisation of hospital and other health services the more I am convinced that in the end the quality of service depends on the quality of the individual in local charge of its various subsections—for example the administrator of the individual hospital.'

Finally, with regard to maternity beds, for the individual family institutional care was much cheaper than domiciliary care, and this anomaly should be corrected because it increased the demand for institutional care. The hospital service, having to refrain from unnecessary expansion, might wish to abandon schemes for extending institutional midwifery to deal with 75% or more of all births and be content with a target of 40% or so, according to local conditions.

Public Health

World Typhoid Survey

ONE of the legacies of the late war was a recrudescence of enteric fever throughout Europe. A survey published by the World Health Organisation in 1948 noted that the "safe areas" had been reduced to the United Kingdom, Switzerland, and the Scandinavian countries, and that in other areas the position was wholly unsatisfactory and showed no signs of improvement. The latest survey published by W.H.O. shows that since 1947 there has been an unexpected reduction in the number of cases in Europe, but not in Africa, America, Asia, and Oceania.

In Europe the number of cases fell from 162,000 in 1947 to 118 000 and 124 000 in the two following years, and an estimated 105 000 in 1950. In 1948 the greatest improvement was in Austria, Germany, Finland, Italy and Poland, while in Belgium, Greece, Luxembourg and the United Kingdom the incidence remained the same. In 1949 the downward trend continued except in France and Spain where there were severe outbreaks; and in 1950 the position was still improving despite moderately severe epidemics in Turkey and Yugoslavia, and minor ones in Sweden and Switzerland.

In the other continents the total incidence has remained the same. In Africa the decline in the number of cases in Algeria, Madagascar, Mauritius, Morocco, and Tunisia was balanced by a steady rise, during the three years in Northern and Southern Rhodesia, and a considerable increase in the number of notifications in Egypt and Kenya during 1948 and 1949, and in the Union of South Africa in 1949.

For the whole of the American continent the total number of cases remained the same. There was an increase of incidence in Colombia in 1948 and 1949, and a decrease in Costa Rica, Cuba, Haiti, Jamaica, Peru and St. Vincent. The United States had by far the fewest cases in proportion to the size of its population.

Of those countries in Asia for which figures are available the majority showed an increased incidence of enteric fever; they include Afghanistan, Ceylon, Cyprus, Iraq, Iran, Israel, Malaya, and Syria. Japan was an exception for there was a spectacular drop in the number of cases from 1947 to 1950. In the Fiji Islands the incidence rose in 1947 and 1948 and fell again in 1950.

In England Now

A Running Commentary by Peripatetic Correspondents

OUR province extends from the incisor teeth to the anal sphincter, and strange things come our way. Last week we had our bezoar. It came to us in a quiet unassuming housewife, and our physician first spied it through his gastroscope, so we all queued up to cast an eye. Our radiologist was delighted; he showed it in his films, and even pushed it up into the pouch of the woman's diaphragmatic hernia. We showed her to the clinic and one student responded with the diagnosis of "a hairy ball in the stomach."

Such was the splash it made in our hospital; the ripples reaching the outside world were far more decorative. In the patient's home village the thing was a tropical beast (derivation: foreign body—foreign beast—tropical beast). The houseman in a neighbouring unit heard their lady-help telling his mother that it was four inches long, with a pointed beak, a furry coat, and short legs. The village postman knew it had a long neck, for surely it reached up for food when hungry. The patient's own doctor told us that everyone in the village knew how we had fed it for days on little crusts of bread dangled on a string down a tube and then one day had poisoned the bait and that was its end.

With his more direct approach our chief opened her stomach, and there are some who say that it took wings and flew round the theatre, chased by the anæsthetist with an ethyl chloride spray. At last we had it out and sent it to the Professor of Botany, who laid the ghost: the undigested skin of a citrous fruit—not a trichobezoar but a citrobezoar. The answer was in fact a lemon.

* * *

I am a confirmed air-traveller, and I travel B.O.A.C. whenever possible, but I wish the corporation would apply a little spit and polish to their service. I have just returned from a flight to the Far East, mainly by B.O.A.C. but using other lines now and then, which gave me an opportunity for comparisons.

The B.O.A.C. catering is reasonable by our present English austerity standards but inferior to that of K.L.M. or Quantas. There is some excuse for this but none for providing different qualities of sherry according to whether you pay for it separately or have it as a "complimentary" drink before dinner, when it is included in the price of the meal.

This happened on my flight back from Nairobi by the new and much-vaunted *Hermes* service. The sherry I paid for was drinkable; the complimentary sherry was not. Incidentally the prices of drinks are extortionate compared with those charged on ships, being the standard English hotel prices. Considering that the flights often include night flying, that there may be 40 passengers on board, and that the washing arrangements at most airports are poor, hot water can hardly be called a luxury, and the supply should not be as temperamental as it is; nor should one be expected to make do with paper towels, which are all that some B.O.A.C. lines provide. Sir Miles Thomas's attempts to make the corporation pay are no doubt laudable, but *stinginess in the toilet department* is not a worth-while economy.

Some of the airports are still pretty grim. Aden was the worst I sampled. We touched down there on the flight from Karachi to Nairobi by Air India International and were given a miserable breakfast with execrable tea (no coffee). Malta gave us a reasonable breakfast, but I have yet to meet a bleaker and draughtier spot on a blustery wet December morning than the Malta airport. Imagine a derelict railway waiting-room in some isolated corner of this country, with canine excreta on the floor, and you will be somewhere near it.

Finally—and this applies to several of the airlines I have sampled—when the departure of a plane is delayed, why are the passengers not told the reason? Any passenger who tries to obtain such information from the ground staff can be sure of a rebuff, and this is all the more irritating because the full details are always forthcoming from the crew once the plane is in flight. Two years ago we were delayed for hours at Gander on our return absurdity of having to increase administrative costs in order to bring down total outlay could be avoided if doctors, dentists, and opticians worked in publicly provided health centres or clinics "

More fundamental was the basic dilemma of the N H S how with limited resources to meet a potentially unlimited demand for medical care—how to impose a ceiling on "production" when the lid was taken off "consumption" The service was based on the naïve idea that it was simple to decide what was medically necessary, and that all such needs must be met

> ' There are two objections to this view First, there is a large subjective element even in the professional view of what is ' medically necessary,' especially in such matters as buildings, equipment, and ambulance rides If the head of every department of every hospital were to write down his ideal requirements for good work, and all the bills were added up, the present outlay on hospitals might have to be raised three or four times to meet the total Secondly, the subjective element is even stronger in the patient's mind Medical care tends to reverse normal economic laws the supply tends to create the demand, rather than vice versa The priestly function of the doctor, for instance, is capable of indefinite expansion, so possibly is the cosmetic use of spectacles and dentures, and the use of hospitals as hostels for elderly relatives unwanted at home "

For checks that were not merely arbitrary two sets of criteria were required (1) standards of quality of professional work, staffing, accommodation, and other aspects of care, and (2) standards of cost of necessary work efficiently performed

The problem of rational financing was made harder by the fatal division between responsibility for the use of resources and responsibility for providing them, this ran right through the N H S but was most marked in the hospitals The Ministry, lacking any sure means of judging how far their requests were reasonable, had yielded to the fatal temptation to control the affairs of the hospitals in detail The bureaucratic control predicted by the opponents of the N H S had in fact been imposed on the hospitals Economy was possible without this, and it even fostered waste

> " I fail to see how the need for economy justifies these controls By fixing an annual sum not to be exceeded by the hospitals as a whole, the Government has already taken the first step towards making them unnecessary The second step would be to treat this as a pool to be shared among the regions for the time being according to some rough criterion of relative needs, of a necessarily empirical kind The third step would be to leave each regional board free within broad limits to share its funds between its management committees as it chooses the fourth to give the committees a reasonable freedom to manage their own ' block budgets including a right to save money without forfeiting it Until the development of hospital costing yields reliable means of measuring efficiency and needs such a system would of course be arbitrary But the present system is not only just as arbitrary it is also bureaucratic and damaging to the whole spirit of the hospital service '

As to checking the public appetite for health service care, the first need was to examine the professional man's position, and to remove from his working environment any features tending to deprive him of incentives to economy, or giving him an incentive to be over lenient with his less sensible patients There was too a certain scope for more direct measures, including charges to patients

> Generally, I think there is a case now for introducing charges in the N H S for articles rather than for services, but only in cases where without creating a new financial barrier to necessary care charges would result in a real overall economy There is little point in using charges to reduce the public cost of a service if this merely sends up private spending by an equivalent amount That is I suspect, precisely what would happen if a charge were introduced for board and lodging in hospital '

Ideally, said Mr Lafitte, the whole N H S budget should be directed to securing the rational deployment of all available medical resources It was arguable, too, that one aim should be to build up the "front line" services, so as to screen away from the hospitals and other services at the "rear" the greatest possible amount of work

> " My impression is that such wider issues of strategy are not being sufficiently considered, although the long term fate of medicine in part depends on them, because it is no-one's job outside Whitehall to look at the pattern of needs and resources in medical care as a whole In most places I suspect that they [the hospital authorities] have the most influence in determining the whole pattern and trends of development of the medical care and services The shape they are imposing is, I suspect, derived from their own particular attitude to medical care, which is largely that of the specialist clinicians, and the general trend seems to be for them to claim all the work which interests them and to leave the rest to other agencies If I am right, the budgetary implications may be very great in the long run, since the hospital is the most expensive means of supplying medical care If specialists, general practitioners, and midwives—or ' general' and priority dentists—were all on the same payroll, is it not likely that developments in many places would be going along different lines? It may well be that we shall have neither ' rational planning' nor economical budgeting until the power to allocate funds between the different branches of the N H S is vested in some authority, below the level of central government, which is competent to look at every aspect of the position in a particular place, and is responsible for finding part of the necessary funds from local, not central, sources "

Planning and Coördination

Dr W G PATTERSON declared that major hospital planning should be considered by the appropriate local health authority, whose observations might be of great value At present there might be no consultation, not because the board was opposed to it, but because the board and its officers were so overworked that they did not go out of their way to initiate time consuming discussions Formal consultation should be obligatory, but, failing this, a suitable liaison committee should be set up As regards cooperation between board and management committee, Dr Patterson had seen great benefit result where the chairman of the management committee was a member of the board At regional board level administrative officers were at present overtaxed, and he believed that the gravest immediate impediment to an efficient service lay in the risk of a breakdown in the administrative medical and architect organisation of regional boards

Another difficulty was the poor general practitioner representation on regional boards, and Dr Patterson was convinced that this accounted in part for some failure in cooperation between boards and practitioners To secure committee member cooperation, on local matters, between the three branches of the service, each hospital region should have several liaison committee including members of local health authorities, local sanitary authorities, executive councils, and hospital management committees, and each liaison committee should preferably cover a population of about 300,000 Officers should also have a local officer liaison committee At regional level there was need for a regional health services liaison committee, including members of the regional board, the board of governors, local health authorities, and executive councils To avoid unwieldy size, local health authorities and executive councils might have to agree to token membership

Observation had convinced Dr Patterson that the best domiciliary general practice was found where practitioners attended patients in a good cottage hospital ' Indeed, I hold that where there is no cottage hospital available the large general hospital should include demand for treatment that should follow a nationwide attempt at breaking down the fear of cancer

London, W C 1 SIDNEY RUSS

TUBERCULOSIS AND OVERCROWDING

SIR,—When our efforts against tuberculosis fall short of what we hope for, we are apt to give a disclamatory shrug of the shoulders and say "Well, after all, it's a social problem, for example, overcrowding is a major factor which we cannot influence" Time invalidates many generalisations and they become clichés obstructing thought and action

Do we really have to wait until the nation is properly housed before overcrowding ceases to be an important factor? Overcrowding in the absence of a case of tuberculosis is not a cause of tuberculosis—it merely facilitates gross infection in the presence of an open case If many cases of tuberculosis are unknown, this effect of overcrowding can only be abolished by the gigantic long term process of rehousing everyone who is living in overcrowded conditions If diagnosis was very efficient and most cases were known, it would only be necessary for tuberculosis control to rehouse the families of the tuberculous cases The overcrowding problem in relation to its effect on tuberculosis would then be almost abolished But a large proportion of cases are *unknown* and so cannot be rehoused

The problem of overcrowding (in relation to tuberculosis) therefore turns out to be a diagnostic one We do not know who should be rehoused because we do not know who has tuberculosis The problem of overcrowding can be overcome by better case finding Of course, it is generally accepted that known tuberculous cases shall be rehoused with priority (which is too low) What is not recognised is that, given rehousing, overcrowding is only a factor in the tuberculosis problem because the *unknown* cases (infection spreaders) cannot be rehoused The need for nation wide serial radiography of those living in overcrowded conditions follows as a corollary to this argument

F A NASH

Medical Director Mass X ray Service
South west Metropolitan London Area

COMPLICATIONS OF SPINAL ANÆSTHESIA

SIR,—May I be permitted to draw attention to an important omission from your annotation of March 3? Most of the serious sequelæ you listed—such as cauda equina syndrome and impotence—were probably due to the custom of keeping ampoules of local anæsthetics (used for spinal anæsthesia), in spirit or formaldehyde, or mixtures of these two Ampoules kept for long periods in this way may develop minute cracks due to movement of the containers and collisions between ampoules and the container-walls In this event the spirit or formaldehyde, having a low molecular weight, will readily diffuse into the ampoules, and the cases you mentioned were probably caused by the injection of these mixtures into the subarachnoid space

Nicholson and Eversole[1] first drew attention to this complication—mentioning that the cracks were invisible to the naked eye—and suggested the use of 'non irritating, *coloured* sterilizing solutions of high molecular weight such as benzalkonium chloride (Zephiran)" The addition of a dye (e g, methylene blue) to the solution in which ampoules are immersed ' is of value in detecting the occasional defective ampoule into which the sterilizing solution has leaked Although Kennedy et al.,[2] whose paper prompted your annotation, refer to Nicholson and Eversole they appear to have overlooked the portion of the paper I quote

Stenberg[3] later reaffirmed the usefulness of coloured sterilising solutions, mentioning that he had detected four defective ampoules by this method in a matter of months He also quoted two occasions when local-anæsthetic solutions kept in uncoloured spirit produced small sloughs when used to raise a skin weal prior to lumbar puncture

When using ampoules of dry procaine crystals (which are dissolved in cerebrospinal fluid immediately before injection) we are on safer ground for, should minute cracks allow spirit or formaldehyde to enter the ampoule, the contents would liquefy Macintosh[4] states that he has repeatedly proved such contents to be inflammable

Nowadays most hospitals autoclave the ampoules in the "spinal drum," which also contains rubber gloves, towels, syringes, needles, &c, which are necessary for an aseptic lumbar puncture From conversations with other anæsthetists it is my impression that where these precautions are taken the serious sequelæ of spinal anæsthesia have ceased to occur, I would be interested to know whether this opinion is shared by colleagues elsewhere

King's College Hospital
London S E 5

A H GALLEY
Anæsthetist.

VACCINATION AGAINST SMALLPOX

SIR,—For many years Dr Killick Millard has emphasised the difficulty of diagnosing variola major which is modified as a result of vaccination, and this difficulty has been demonstrated again and again at the start of outbreaks in the United Kingdom Dr Millard recommends that, by discouraging vaccination of the general population, as opposed to individuals who are particularly at risk, we should ensure that as many cases as possible of variola major are unmodified and therefore the more easily recognised He replies effectively to one objection of the orthodox vaccinists such as Dr Gemmill (Feb 10) by pointing out that herd immunity in this country has for many years been too low to play much part in preventing the spread of smallpox If this solution fails to take account of mild cases in the unvaccinated, and is regarded as otherwise incorrect and unpalatable, how should the problem be tackled?

To require all persons entering the country to produce evidence of recent vaccination, as advocated by Professor Taylor (March 10), would lessen, but would not end, the risk of variola major being introduced

Whatever else is done the standard of smallpox diagnosis must be improved Dr Rao (March 10) mentions laboratory methods of identifying the virus, but, efficient though these are in a high proportion of cases, neither they nor the help of medical officers of health and smallpox consultants can be used until the disease is suspected clinically Two things are therefore necessary (1) the patient should seek medical advice promptly, and (2) the doctor should include smallpox among the diagnostic pitfalls which he keeps constantly in mind The exacting responsibility which the doctor may have to bear is clear to all readers of THE LANCET, and the rule of regarding all doubtful cases as smallpox until the opposite is proved is indispensable Nor is it possible to be certain that the patient will come under observation before many others have suffered risk, but the standard of public information on this matter could be much improved Some still believe that vaccination prevents smallpox absolutely for at least seven years, few understand how greatly it may modify the attack without stopping the patient from infecting others journey in an American air liner, and the ground staff were so mysterious about it that the more nervous passengers began to wonder whether it would be safer to abandon the flight, and even we phlegmatic ones were reconciling ourselves to an uncomfortable night at the airport Yet directly we took off the crew told us all about it—there had been some trouble with the undercarriage which the captain had insisted on having repaired before we took off on the long hop to Heath Row Delays and hold-ups must occur occasionally, but these stony silences do not make them more bearable

---

[1] Nicholson M. J Eversole U H *J Amer med Ass* 1946 132 679

[2] Kennedy F Effron S A Perry G *Surg Gynec Obstet* 1950 91 385

[3] Stenberg B L *Anesthesiology* 1950 11 257

[4] Macintosh R R Lumbar Puncture and Spinal Anæsthesia. Edinburgh 1951 p 143

* * *

Through the vestibule of a ward dingy in everything except its eponym I reached the bedside of one of its more decrepit temporary inhabitants My breezy overtures produced a tale of suffering inconsequent as it was incoherent Not that my victim was uncoöperative —she was out to help all she could—but match a straight question with a straight answer she could not, though she reiterated the source of her afflictions, consumption contracted in 1917 taking her to and from hospital ever since, with a coronary thrombosis at Christmas, 1950 She was vague about her symptoms, but quite definite about the times when her sputum was positive When I came to examining her she could not lie straight or draw a decent breath, and she objected vehemently to the clamminess of my nervous hands, but she told me accurately the direction of her tracheal displacement, the site of her apex-beat, and the size of her cavity She would not tolerate my thumping her knees, but she assured me that no amount of reinforcement would restore her lost reflexes And her information was offered as amicably as one could wish So I prepared to meet the examiner with a respectable array of facts and a clear conscience I had even made an exhaustive though negative urine analysis when a sympathetic registrar led me to the place of execution Here the softening-up process was taken over by a caricature of a noteworthy examiner whose gimlet eyes and hectoring voice quelled his milder colleagues "Nought marks, nought marks! Write it down Nought marks! And I'll add a note to the censors that he must never again take the examination The fellow got the patient to tell him the diagnosis! I'll not be treated in this way " I did not wait for his peroration With terror in my heart I dashed for the door It was barred by white coated registrars I turned towards a window, burst it open, and jumped, to fall down and down, into pitch darkness

I did not know where I had landed, but I was shaken, literally physically shaken And then pinched "Wake up darling and say nice things to me"—it was my wife's voice—"I've just had a horrid dream that you failed your Membership again "

* * *

Stimulated by the good example of St Francis I take a bit of trouble about the birds in my garden I have rigged up a sort of platform on a stake driven into the ground, and each morning I spread upon it the remnants of the dog's dinner The local robin always gets there first and behaves in a dog-in-the-*salle-à-manger* manner, driving off not only the tits, chaffinches, and sparrows but also the thrushes, blackbirds, and starlings for a long time after he has eaten his fill. By lunch-time all is eaten and the birds are hanging around waiting for their next meal Now I do not object to feeding the birds during frosty or snowy weather, but when the ground is soft and wet I see no reason why the brutes shouldn't pick up their own living They, it seems, think otherwise and leave the job entirely to me—just one more example, I suppose, of the enervation of character produced by the Welfare State

* * *

Believe it or not, but the following is a verbatim extract from a patient's reply to a follow-up letter

"I have filled the form up best to my advantage But since my Home Help as had to exspire on account of me having to pay "

* * *

Aphorism of the Week

An observant parent's evidence may be disproved but should never be ignored

Letters to the Editor

PUBLICITY IN CANCER

SIR,—It is timely perhaps to inquire whether a policy of publicity in relation to cancer would serve a useful purpose If it can be shown that some lives can be saved by this means, then it should be asked of those who oppose the policy, in what ways would harm be done if it were put into practice?

I venture to draw attention to one feature of treatment and suggest that publicity should begin by attempting to drive it home One of the greatest handicaps to treatment at the present time is the late stage of the disease when cancer patients come to the clinics It is agreed that the chances of successful treatment diminish gravely as the later stages of the disease appear, if patients could be induced to pay more regard to the early signs of something being wrong, to overcome their scruples about worrying the doctor, and to banish from their minds the idea that the trouble will cure itself, then treatment would carry a greater hope and the mortality figures begin to decline

Relevant data have, through the courtesy of Dr Ralston Paterson, been supplied to me by the medical statistics department of the Christie Hospital and Holt Radium Institute, Manchester, which allow one to see the present position in a big clinic Restricting ourselves at the moment to cancer of the breast and of the cervix uteri we have the following

		Cases examined	
Site	*Clinical stage*	*1932–33*	*1948*
Breast	I	36	22
	II + III + IV	200	293
Cervix uteri	I	17	17
	II + III + IV	219	390

The data repay study, in some respects they tell a very grim story. Patients suffering from cancer of the breast who came to this clinic in 1932–33 numbered 236, and only 15% of them were in stage I of the disease. Any hope that the year 1948 would show an improvement in this deplorably low percentage has not been realised, in fact, the figure is 7 5% For the cervix uteri the percentages are even worse—7 8% in 1932–33 and 4 4% in 1948

These are appalling facts, surely the sign to a woman of a small lump in the breast or an unusual uterine happening is easily recognisable, yet they refuse to give word about it We may well ask is this false modesty or is it fear? In either case the attitude should be combated, thus helping to bring down the cancer death rate

One is tempted to essay an evaluation of what would accrue from a successful effort in publicity relating to early signs of the disease Let us suppose that as a result of enlightened publicity the proportion of patients at this clinic in the two categories of (*a*) stage I and (*b*) other stages, was reversed, a simple calculation shows that if 1000 patients suffering from cancer of the breast were treated by the same methods (surgical and radiological) as now, there would be 454 alive after five years instead of 213—a saving of 241 *extra* lives out of a total of 1000 Turning to uterine cancer, and assuming that the treatment is radiological, we find that the corresponding numbers would be 630 alive after five years instead of 275—a saving of 355 *extra* lives out of a total of 1000

In 1948 there were approximately 8000 deaths from cancer of the breast and about 3000 from cancer of the cervix uteri The *extra* lives that would be saved through early recognition of the disease by the patients themselves is so obviously considerable that one is convinced that it is a duty to take the public into official confidence, to lay the significant facts before them, and to make arrangements now for the increasing

When I wrote that immunisation should be considered here for the whole population in the event of war (rather than reserved for the 10% or so in the Armed Forces) it seemed to me that I was stating an obvious case—and one, furthermore, which committees responsible for advising the Government would have already very fully considered.

London W 1   PATRICK CLARKSON

INTRAVENOUS IRON

SIR,—We would like to thank Dr Klopper for his letter published in your issue of March 3. We would point out, however, that we make no claim regarding the existence of a renal threshold of iron, nor do we stress the significance of the iron lost in the urine. We merely report our findings and suggest that such hypotheses are worth considering in future investigations.

As regards the delayed cases, Dr Klopper appears to have misunderstood us. It is perhaps unfortunate that the two paragraphs relating to delayed cases and hæmodilution were in juxtaposition. The finding of hæmodilution was common to all cases whether the improvement was immediate or delayed, and was not specially related to the delay in response to treatment. The delay appeared to be related more to a protein deficiency than any change in blood-volume. Dr Klopper's hypothesis of the displacement of copper from the protein molecule by iron is also attractive and ingenious, but as yet he has supplied no proof of its occurrence.

We agree with Dr Fench (March 17) that hæmodilution is responsible for many of the mathematical aberrations noted in anæmia of pregnancy, but we are not convinced that it is the only factor of importance. Even allowing for hæmodilution, we find in our cases that the utilisation of iron does not reach the theoretical level. We are of the opinion that more important factors are the storage of iron in early pregnancy and fœtal demands in the last trimester. It is also relevant to point out that the hæmoglobin mass increases considerably in normal pregnancy (by as much as 20% of the total according to Smallwood[1] and 12% per sq. m. according to Roscoe and Donaldson[2]). Much of his argument is therefore negatived.

Glasgow Royal Maternity
and Women's Hospital

JEAN M SCOTT
A. D T GOVAN

EL TOR VIBRIO IN CHLORAMPHENICOL ESTIMATION

SIR,—The principle of our method for the quantitative estimation of antibiotics is to bring together different dilutions of blood serum or other substances with a micro organism sensitive to the antibiotic, and to note the dilutions in which growth of the organism is inhibited, using the micro method of Goslings.[3]

A strain of El Tor vibrio proved very sensitive to chloramphenicol, its growth being completely inhibited in the presence of 0·5 γ per ml. In tests on fifty sera, we found that inactivating them at 56°C for 30 minutes abolished their natural bactericidal effect, which may otherwise cause a false or "pseudo" titre.

The El Tor vibrio used was isolated twenty years ago from pilgrims in El Tor quarantine camp (Doorenbos) and has kept its capacity to produce active exohæmolysins in liquid media. It grows well in peptone water of pH 7·2 to which 5% defibrinated sheep's blood has been added; after incubation at 37°C for 18 hours the pH of the medium increases to 7·4. The optimum pH for the activity of chloramphenicol being 7·2, the conditions are satisfactory for its quantitative estimation, using hæmolysis as an indicator.

The inhibitory effect of urine on the vibrio can be abolished by keeping it for 15 minutes at 100°C. After adding a known quantity of chloramphenicol—e.g., 5 γ per ml.—to sixty different urines and to seven sputa, we found that heating at 100°C did not affect the quantity of the antibiotic. By rendering the vibrio resistant to penicillin (100 units per ml.) and to streptomycin (100 γ per ml.), it could be used to test the sera of patients undergoing simultaneous treatment with these antibiotics, especially for the presence of chloramphenicol.

Our conclusion is that quantitative estimation of chloramphenicol by the use of El Tor vibrio (Doorenbos) is of practical importance. The strain of El Tor vibrio can be obtained from the laboratory of the Academisch Ziekenhuis, Leiden, or from the National Collection of Type Cultures, Colindale Avenue, London, N W 9.

Laboratory University Hospital Leiden
and Antibiotics Research Laboratory
Gistfabriek, Delft Holland

W DOORENBOS
J KOP

---

[1] Smallwood W C *Brit med J* 1938 ii 573

[2] Roscoe M H Donaldson, G M M *J Obstet Gynaec* 1946 53 527

[3] Goslings W R O *Ned Tijdschr Geneesk* 1947 91 1542

VERATRUM IN HYPERTENSION

SIR,—Your leading article of March 10 gives an altogether misleading account of what is known of the mode of action of the veratrum alkaloids. The essential difference between these and, for instance, the methonium compounds is that whereas the latter cause a fall of blood-pressure by interfering with the transmission of impulses on the *efferent* side of the cardiovascular reflex systems, the veratrum alkaloids have their principal effect on the circulation by exciting receptors on the *afferent* side of the reflex arc.

As long ago as 1868 von Bezold and Hirt[1] described the fall of blood pressure and heart rate which follows the intravenous injection of crude veratrum preparations and came to the conclusion that this must be due to a reflex action initiated by the stimulation of receptors, probably in the heart itself. Interest in the subject was revived by Jarisch and his colleagues,[2] who confirmed Bezold's original observation that the circulatory response to the intravenous injection of veratrine was abolished by cutting both vagi, and came to similar conclusions as to the location of the receptors. By this time much more was known about the reflex control of the circulation, and Jarisch pointed out that the anatomical and physiological basis for the Bezold reflex had still to be discovered. A few years later Krayer and his colleagues[3] took up the story. They showed that if large doses of the pure alkaloids were used these had a direct action on the central nervous system, but that in considerably smaller doses—and this is most probably the case in man—the whole fall of blood pressure and heart-rate could be explained by the Bezold reflex. The receptors for the reflex are located in the area of distribution of the coronary arteries, probably in the left ventricle.[4] They have not yet been positively identified with any physiological mechanism, though the suggestion has been made[2,5] that they serve the purpose of limiting the pressure rise in the left ventricle. The further elucidation of the Bezold reflex mechanism has therefore considerable physiological interest.

Another feature of the actions of these alkaloids which interested physiologists for many years was the veratrine "contracture," which was eventually traced to excitation of repetitive discharges in muscle and in nerve.[6] The ability of veratrine and of the pure alkaloids to cause repetitive discharges in nerves and stretch receptors[5,7]

---

[1] von Bezold A Hirt L *Unters physiol Lab Würzburg* 1867 1 73.

[2] Jarisch A., Richter H *Klin Wschr* 1939 18 185 Jarisch A Richter H. *Arch exp Path Pharmak* 1939 193 347 355 Jarisch A *Arch Kreislaufforsch* 1940 7 260 *Ibid* 1941 9 1. Amann A Jarisch A *Arch exp Path Pharmak* 1943 201 46

[3] Krayer O Wood E H Montes G, *J Pharmacol* 1943 79 215 Krayer O Moe, G K Mendez R *Ibid* 1944 82 167

[4] Dawes G S. *Ibid* 1947 89 325 Aviado D M Pontius, R G., Schmidt C F *Ibid* 1949 97 420

[5] Jarisch, A. Zotterman, Y *Acta physiol scand* 1948 16 31 Schaefer H *Ergebn. Physiol* 1950 46 71

[6] Krayer O., Acheson, G H. *Physiol. Rev* 1946 26 383

[7] Amann A., Schaefer, H. *Pflüg Arch. ges. Physiol* 1943 246 757 Acheson G H Rosenblueth A *Amer J Physiol* 1941 133 736 Meier R Bein H J Helmich H. *Experientia* 1949 5 484 Dawes G S *Acta physiol scand* 1951 22 73

Each time vaccination is performed, could not a few minutes be spent in explaining what may, and what may not, be expected from it ? How often is this now done ?

Weston upon Trent
Stafford

C D L LYCETT

TREATMENT OF SMALLPOX A SUGGESTION

SIR,—Dr Alexander L Hoyne[1] says of confluent smallpox that " with an extensive destruction of the skin the situation is little different with that of a patient who has a burn involving a large area of the skin "

Dr M James Whitelaw[2] has successfully used adrenocorticotropic hormone (A C T H) for burns of the skin, notably in one case where 70% of the skin was destroyed Dr A Benson Cannon et al ,[3] using A C T H and ' Cortisone,' have had good results in severe cases of pemphigus vulgaris, one case of pemphigus vegetans, two cases of erythema multiforme pemphigoides, and two cases of epidermolysis bullosa

Is there not a possibility that cases of smallpox might be treated successfully with A C T H in early stages of the disease or even in severe cases after skin destruction ? It is impossible to make the experiment in the United States at present, since fortunately we have not enough cases, and those few we have are widely scattered

Smallpox is epidemic in India and China, where your journal goes If the experiment has been made, it has not come to my attention

Bristol Connecticut
U S A

ARTHUR S BRACKETT

PENICILLIN IN WEIL'S DISEASE

SIR,—Since the publication of my paper in your issue of Jan 13, my attention has been drawn to an article written in 1949 by Lurie,[4] describing the use of ' Aureomycin ' in a case of leptospirosis icterohæmorrhagica

An agricultural worker, aged 32, was admitted to hospital with all the classical signs of Weil's disease, confirmed on the fourth day after admission by a strongly positive agglutination test From the degree of hepatic and renal involvement it appears that this was a rather severe case of leptospirosis The patient was treated with aureomycin 2 g daily for the first three days, and thereafter 1 g daily for eleven days The response to aureomycin treatment was immediate and the patient recovered completely He was in hospital for twenty three days and on discharge blood urea, serum bilirubin, and urine were normal

In 1949 Brainerd et al[5] reported the use of aureomycin in one case of Weil's disease

A sewer worker was admitted to hospital unconscious and jaundiced, with nephritis and evidence of subarachnoid bleeding Leptospira were demonstrated on two consecutive days by dark field examination of blood Aureomycin was given in 1 g doses orally every six hours for twelve days, in addition, 100 mg of the drug was injected intravenously three times a day during the first five days Improvement was rapid The icteric index, originally 125, fell to 17 in about a week, and the blood urea from 120 mg per 100 ml to 21 mg per 100 ml in five days The patient made a full recovery, and the authors have this to say " Although the rapid improvement could not certainly be attributed to aureomycin, it was felt that specific anti spirochætal effect was most likely "

Another interesting case was reported by Batchelor and Todd[6] in 1950 They used aureomycin after penicillin had failed to halt the progression of toxæmia

The patient was a negro admitted to hospital with high fever hepatorenal syndrome, and subarachnoid bleeding When the diagnosis of Weil s disease was ascertained, treatment was started with 600,000 units of procaine penicillin in oil four times daily and 200,000 units of sodium penicillin intramuscularly every two hours After thirty six hours the patient became moribund Aureomycin was then started, an initial dose of 2 g was given, followed by 250 mg every three hours Twelve hours after starting aureomycin the patient improved sufficiently to take sips of water The dosage was then increased to 500 mg three hourly and was continued until 17 25 g had been given Convalescence started on the fifth day after admission It is to be noted, however, that penicillin was continued throughout the aureomycin therapy This makes it difficult to say which of the two antibiotics was the life saving drug

Lurie's and Brainerd's cases of Weil's disease were probably the first two on record to have been treated with aureomycin, and no doubt since 1949 many more patients with leptospirosis have been treated successfully with this antibiotic, thus confirming clinically the therapeutic results obtained by Heilman[7] in experimental leptospiral infection

St Charles Hospital
London W 10

A I SUCHETT KAYE

PROPHYLAXIS AGAINST TETANUS IN BURNS

SIR,—Dr Colebrook (March 10) raises an important question about which opinion is divided Some believe that the risk of tetanus in burns is negligible, others consider it sufficient to warrant routine prophylaxis for all burned patients

May I first answer Dr Colebrook's questions ? My own experience in burn patients is less than his (it comprises two thousand cases treated during the last ten years in Africa, Italy, Europe, and England) , but I have seen tetanus in three patients, one of them with a trivial burn, and know of its occurrence in four other burned patients during this period All seven of these patients were burned in the south west of England or in East Anglia (This is not surprising in the light of Conybeare and Logan's paper,[8] which draws attention to the fact that tetanus from all causes in civil life in England is most common in the South west and East) These were no cases in the burns seen outside England There were soldiers who had had both toxoid and anti tetanus serum injections

None of these seven cases has been published But as Dr Colebrook will of course be aware, tetanus as a complication in burns is reviewed in Harkins's textbook *Treatment of Burns* , references to over a hundred cases of tetanus following burns are given, including the one to Dupuytren which I mentioned in my review (Feb 24) on account of its historical interest

Although the complication is undoubtedly rare, I agree with those who believe that it is not so rare in civil life that it can be ignored The chance of tetanus is unpredictable , the nature of the disease and its still high mortality outweigh, in my view, the cost of prophylaxis and the undoubted disadvantages of serum sickness

In my general account of the management of burns, to which Dr Colebrook refers, I made it clear that my remarks were directed towards burns in any future war, with special reference to the effects of atomic explosions, in which lacerating injuries may be expected to be as common as burns Conybeare and Logan consider the risk of tetanus sufficiently high in peace time injuries to warrant consideration of active immunisation of the population in certain regions of England Truman Blocker at the Washington symposium on burns[9] expressed the opinion " that it is imperative that mass immunisation of our whole population be carried out "

---

1 Brennemann s Practice of Pædiatrics vol ii chap 25 p 10
2 *J Amer med Ass* Jan 13 1951 p 85
3 *Ibid* Jan 27 1951 p 201
4 Lurie, I *Acta med orient* 1949 10 188
5 Brainerd H Lennette E H Meiklejohn G Bruyn H B Clark W H *J clin Invest* 1949 28 992
6 Batchelor T M Todd C M *J Amer med Ass* 1950 143 21
7 Heilman F R *Proc Mayo Clin* 1948 23 569
8 Conybeare F T Logan W P D *Brit med J* March 10, 1951 p 504
9 See *Lancet* 1950 ii 635

When I wrote that immunisation should be considered here for the whole population in the event of war (rather than reserved for the 10% or so in the Armed Forces), it seemed to me that I was stating an obvious case—and one, furthermore, which committees responsible for advising the Government would have already very fully considered

London, W 1 **Patrick Clarkson**

INTRAVENOUS IRON

Sir,—We would like to thank Dr Klopper for his letter published in your issue of March 3 We would point out, however, that we make no claim regarding the existence of a renal threshold of iron, nor do we stress the significance of the iron lost in the urine We merely report our findings and suggest that such hypotheses are worth considering in future investigations

As regards the delayed cases, Dr Klopper appears to have misunderstood us It is perhaps unfortunate that the two paragraphs relating to delayed cases and hæmodilution were in juxtaposition The finding of hæmodilution was common to all cases whether the improvement was immediate or delayed, and was not specially related to the delay in response to treatment The delay appeared to be related more to a protein deficiency than any change in blood-volume Dr Klopper's hypothesis of the displacement of copper from the protein molecule by iron is also attractive and ingenious, but as yet he has supplied no proof of its occurrence

We agree with Dr Fench (March 17) that hæmodilution is responsible for many of the mathematical aberrations noted in anæmia of pregnancy, but we are not convinced that it is the only factor of importance. Even allowing for hæmodilution, we find in our cases that the utilisation of iron does not reach the theoretical level We are of the opinion that more important factors are the storage of iron in early pregnancy and fœtal demands in the last trimester It is also relevant to point out that the hæmoglobin mass increases considerably in normal pregnancy (by as much as 20% of the total according to Smallwood,[1] and 12% per sq in according to Roscoe and Donaldson [2]) Much of his argument is therefore negatived

Glasgow Royal Maternity and Women's Hospital **Jean M Scott**
A D T Govan

EL TOR VIBRIO IN CHLORAMPHENICOL ESTIMATION

Sir,—The principle of our method for the quantitative estimation of antibiotics is to bring together different dilutions of blood serum or other substances with a micro organism sensitive to the antibiotic, and to note the dilutions in which growth of the organism is inhibited, using the micro method of Goslings [3]

A strain of El Tor vibrio proved very sensitive to chloramphenicol, its growth being completely inhibited in the presence of 0 5 γ per ml. In tests on fifty sera, we found that inactivating them at 56°C for 30 minutes abolished their natural bactericidal effect which may otherwise cause a false or "pseudo" titre

The El Tor vibrio used was isolated twenty years ago from pilgrims in El Tor quarantine camp (Doorenbos) and has kept its capacity to produce active exohæmolysins in liquid media It grows well in peptone water of pH 7 2 to which 5% defibrinated sheep's blood has been added, after incubation at 37°C for 18 hours the pH of the medium increases to 7 4 The optimum pH for the activity of chloramphenicol being 7 2, the conditions are satisfactory for its quantitative estimation, using hæmolysis as an indicator

The inhibitory effect of urine on the vibrio can be abolished by keeping it for 15 minutes at 100°C After adding a known quantity of chloramphenicol—e g, 5 γ per ml—to sixty different urines and to seven sputa, we found that heating at 100°C did not affect the quantity of the antibiotic By rendering the vibrio resistant to penicillin (100 units per ml) and to streptomycin (100 γ per ml), it could be used to test the sera of patients undergoing simultaneous treatment with these antibiotics, especially for the presence of chloramphenicol

Our conclusion is that quantitative estimation of chloramphenicol by the use of El Tor vibrio (Doorenbos) is of practical importance. The strain of El Tor vibrio can be obtained from the laboratory of the Academisch Ziekenhuis, Leiden, or from the National Collection of Type Cultures, Colindale Avenue, London, N W 9

Laboratory, University Hospital Leiden
and Antibiotics Research Laboratory
Gistfabriek Delft, Holland

W Doorenbos
J Kop.

VERATRUM IN HYPERTENSION

Sir,—Your leading article of March 10 gives an altogether misleading account of what is known of the mode of action of the veratrum alkaloids The essential difference between these and, for instance, the methonium compounds is that whereas the latter cause a fall of blood-pressure by interfering with the transmission of impulses on the *efferent* side of the cardiovascular reflex systems, the veratrum alkaloids have their principal effect on the circulation by exciting receptors on the *afferent* side of the reflex arc

As long ago as 1868 von Bezold and Hirt [1] described the fall of blood pressure and heart rate which follows the intravenous injection of crude veratrum preparations and came to the conclusion that this must be due to a reflex action initiated by the stimulation of receptors, probably in the heart itself Interest in the subject was revived by Jarisch and his colleagues,[2] who confirmed Bezold's original observation that the circulatory response to the intravenous injection of veratrine was abolished by cutting both vagi, and came to similar conclusions as to the location of the receptors By this time much more was known about the reflex control of the circulation, and Jarisch pointed out that the anatomical and physiological basis for the Bezold reflex had still to be discovered A few years later Krayer and his colleagues [3] took up the story They showed that if large doses of the pure alkaloids were used these had a direct action on the central nervous system, but that in considerably smaller doses—and this is most probably the case in man—the whole fall of blood pressure and heart rate could be explained by the Bezold reflex The receptors for the reflex are located in the area of distribution of the coronary arteries, probably in the left ventricle [4] They have not yet been positively identified with any physiological mechanism, though the suggestion has been made [2,5] that they serve the purpose of limiting the pressure rise in the left ventricle The further elucidation of the Bezold reflex mechanism has therefore considerable physiological interest

Another feature of the actions of these alkaloids which interested physiologists for many years was the veratrine "contracture," which was eventually traced to excitation of repetitive discharges in muscle and in nerve [6] The ability of veratrine and of the pure alkaloids to cause repetitive discharges in nerves and stretch receptors [5,7]

---

[1] Smallwood W C *Brit med J* 1936 ii 573
[2] Roscoe M H Donaldson G M M *J Obstet Gynæc* 1946 53 527
[3] Goslings W R O *Ned Tijdschr Geneesk* 1947 91 1542

---

[1] von Bezold A Hirt, L *Unters physiol Lab Würzburg* 1867 1 73
[2] Jarisch A, Richter H *Klin Wschr* 1939 18, 185 Jarisch A Richter H *Arch exp Path Pharmak* 1939 193 347 355 Jarisch A *Arch Kreislaufforsch* 1940 7 260 *Ibid* 1941 9 1 Amann A Jarisch A *Arch exp Path Pharmak* 1943 201 46
[3] Krayer O Wood E H Montes G, *J Pharmacol* 1943 79 215 Krayer O Moe, G K Mendez R *Ibid* 1944 82 167
[4] Dawes, G S *Ibid* 1947 89 325 Aviado D M Pontius R G Schmidt C F *Ibid* 1949 97 420
[5] Jarisch A Zotterman, Y *Acta physiol scand* 1948 16, 31 Schaefer H *Ergebn Physiol* 1950 46 71
[6] Krayer O Acheson G H *Physiol Rev* 1946 26 383
[7] Amann A. Schaefer, H *Pflüg Arch ges Physiol* 1943 246 757 Acheson G H Rosenblueth A *Amer J Physiol* 1941 133 736 Meier R Bein H J Helmich H *Experientia* 1949 5 484 Dawes G S *Acta physiol scand* 1951 22 73

is almost certainly the explanation of their manifold actions upon the circulation. In smaller or larger doses they excite a number of different types of cardiovascular and respiratory receptors[4,5,7,8] and have an action upon the central nervous system too. But of all these receptor mechanisms the Bezold reflex appears to be the most sensitive. In addition, relatively very large concentrations may have a direct action on the heart somewhat resembling that of digitalis,[9] or, as Krayer has recently shown, antagonising the accelerator action of adrenaline.

The various pure alkaloids differ considerably in their activity and duration of action in causing a fall of blood pressure, which all authors are agreed is due to peripheral vasodilatation. It is difficult to see why the immediate mechanism of this vasodilatation should cause such controversy. Like other reflex depressor responses it is almost certainly due to a coordinated change in both sympathetic and parasympathetic systems. Thus the administration of atropine abolishes the bradycardia but not the decrease in peripheral vascular sympathetic tone, and hence not the fall in blood-pressure. These features of the action of the veratrum alkaloids should be of great interest to the clinician, since the fall of blood pressure and heart rate is produced reflexly one would not expect the general circulatory adaptations—the "cold pressor" rise for instance—to be interfered with, and that indeed has been the experience in man.[10] For this reason it has always been expected that these alkaloids would have certain advantages over other methods of reducing the blood pressure in hypertensive patients. On the other hand, toxic symptoms would also be anticipated from the ubiquity of their actions on muscle and nerve.

This ubiquity and the difficulties of tachyphylaxis have hindered progress in unravelling the complicated actions of the veratrum alkaloids in the whole animal. How much more difficult is this process in man? There does indeed seem very little hope of obtaining *direct* evidence for the reflex actions of these substances in man, unless it becomes practicable to block the afferent path of the reflex—the cervical vagus nerves—for a short while. As an experimental procedure this is hardly justifiable. On the other hand, the overwhelming weight of the experimental evidence in animals is in favour of the reflex mode of action with those alkaloids which do cause a profound fall of blood pressure. The one exception is the claim by Stutzman and Kusserow,[11] working with a new impure extract of veratrum viride named 'Veriloid' (which Kauntze and Trounce used for their investigations described on March 10), that veriloid causes a fall in blood pressure despite vagotomy. It will be interesting to see if these extracts contain alkaloids of such strikingly different properties from the pure substances already investigated. It is true that not all veratrum alkaloids, but only some of the ester alkaloids, are capable of producing the reflex fall in blood pressure and heart rate. But the inactive alkamines are also virtually inactive upon the circulation. Cevine, for instance, lacks the characteristic depressor property in a dose 2000 times the minimal effective dose of its ester alkaloid veratridine. And in any case, for the reasons given above, the use of substances which produce a fall of blood pressure by a reflex mechanism would seem to be preferable for clinical purposes.

Nuffield Institute for Medical Research
University of Oxford
G S DAWES

---

8 Heymans C de Vleeschhouwer G *Arch int Pharmacodyn* 1950 84 409

9 Krayer O Mendez R *J Pharmacol* 1942 74, 350 Moe G K Krayer O *Ibid*, 1943 77 220

10 Freis E D Stanton J R Culbertson J W Litter J Halperin M H Burnett C H Wilkins R W *J clin Invest* 1949 28 353 Meilman E Krayer, O *Circulation*, 1950 1 187

11 Stutzman J W Kusserow C W *Proc Soc exp Biol N Y* 1949 71 725

SLIMMING BY TELEVISION

SIR,—We have for some time been concerned by the publication of dietary advice in the daily press. Recently, however, this dissemination of gratuitous information has taken the form of a series of television programmes culminating in the free distribution of obesity diet sheets to any members of the public who cared to apply to the B B C for them.

This reducing diet, which is fairly strict, provides 1000 calories a day. It has been carefully constructed, and applicants are told to follow it under the guidance of their medical advisers. We feel, however, that this injunction will often be disregarded and that many of the 35,000 people already clamouring for diet sheets will endeavour to follow the instructions without recourse to their doctors.

It has always been a principle of our profession that no dietary advice should be given without specific instructions from the patient's doctor. No printed diet sheet should ever be handed out, moreover, without an interview during which the dietitian satisfies herself that the patient has understood the principles of the régime, that it is within his means, and that it is suited to the social conditions under which he lives. She will also arrange for the patient to be kept under supervision so that she can assure herself that the diet is proving suitable, that it has been understood, and that it is being applied.

None of these conditions is entirely fulfilled by the present large scale distribution of diet sheets. We feel that this situation is undesirable and even potentially dangerous.

K FITZPATRICK
Secretary British Dietetic Association

251 Brompton Road
London S W 3

CHRONIC NON-TUBERCULOUS ABSCESS AT SITE OF INJECTIONS

SIR,—I was interested in the paper of March 10 by Dr Fielding and Dr Norris, describing the unusually large number of abscesses seen by them in patients who had received penicillin injections. They report that most of these were sterile on culture, and the clinical and pathological features, which they carefully studied, suggested the presence of a common irritant.

Amongst the first 17 cases seen by me and treated with 'Cortisone' from different batches, no less than *5 large* abscesses developed. Of these 2 were opened by surgeons of repute, but seemed to heal unusually slowly; indeed one of these is still discharging slightly more than six months after operation. The other 3 ultimately subsided completely as the result of repeated aspirations. Cultures from 2 of these abscesses were reported to contain *Staphylococcus aureus*, but the other 3 were reported as sterile.

These abscesses developed very slowly but gave rise to considerable pain and disability. They appeared to be situated in the deep subcutaneous fatty tissue, and not intramuscularly. I find from conversation with both British and French colleagues that my experience is not unusual, so it seems strange that we seem to have had no reports of this rather troublesome side effect from America, where cortisone originated and has been so much more extensively used.

Apart from abscesses, tender indurations in the deep subcutaneous tissues, which are presumably of a similar nature, are not uncommon and would seem to be the result of local irritation, possibly of chemical origin. I have seen these also—but never an abscess—as the sequel of A C T H administration. Although structurally these two substances are in pure form very different, it may be that they sometimes contain impurities of similar type, and it is the employment of a larger bulk of cortisone than of A C T H which determines actual abscess formation.

The therapeutic moral would appear to be that where intramuscular injections of cortisone or A C T H are necessary, great care should be taken to ensure that the substance actually reaches the muscular layer, and is not discharged into the deep subcutaneous tissues In obese patients this will often necessitate the use of a longer needle than is normally employed

W S C COPEMAN

London W 1

RHESUS NOMENCLATURE

SIR,—An article by Renton and Stratton[1] starts "The following notation is used, for the sake of simplicity, in this paper $R_1 = CDe$, $R_0 = cDe$, $R' = Cde$, &c" In the same journal Lawler et al[2] use the following "short" symbols *rr* for *cde/cde*, R_0r for *cDe/cde*, R_0R_0 for *cDe/cDe*, &c These abbreviations are manifestly minor variations of Wiener's Rh-Hr nomenclature These investigators, therefore, are using two nomenclatures and resort to the Rh Hr nomenclature when it would otherwise be difficult to express themselves clearly The question arises why the British investigators continue to use C D E notations at all The original Rh-Hr notations, aside from having priority, are simple and unambiguous, and certainly one nomenclature is simpler than two

The chief criticism levelled by Race against Wiener's nomenclature is that the symbols are not sufficiently explicit—that is, that the symbols for the agglutinogens do not indicate all of the factors present in the agglutinogen Race[3] has prepared a table (table I) which details this objection The fallacy in Race's criticism is that the purpose of a symbol is to identify, and not to describe in full As a matter of fact, the more fully a symbol becomes descriptive the more unwieldy it becomes For example, in the diagram below are given the properties of the agglutinogens A_1 and A_2

Agglutinogen	*Reaction with anti A*	*Reaction with anti A_1*	*Reaction with anti O*
A_1	+	+	−
A_2	+	−	+

Since the fact that the designations A_1 and A_2 do not indicate the two principal partial antigens which each of the agglutinogens contain causes no difficulty to workers in the field, there is no reason why the symbols Rh_1 and Rh_2 should cause difficulty The fact is that they do not

On the other hand, to attempt to include all that is known about a subject in the symbols may lead to difficulties Firstly, it becomes necessary to change the symbols each time a new antiserum is discovered and as one's concept of the nature of the agglutinogen changes Secondly, when adhering unswervingly to the original preconceived ideas there develops a tendency to force the facts so that they conform to the nomenclature For example, in the article by Lawler et al there appeared the following two sentences "Antigens *C* and *c* are inherited as Mendelian characters and so are *E* and *e*, and *D* and *d* The antigens are inherited in threes, either *C* or *c*, and *D* or *d*, and *E* or *e*" In the first sentence the authors actually can make no statement in regard to the inheritance of *d* because they made no tests in any of their studies using anti-*d* serum The only documented report on *d* is the one by Haberman et al.,[4] and this has been challenged by Wiener[5] because he was unable to confirm their findings with samples of the patient's serum which were sent to him At any rate, if *d* does exist it seems strange that workers like Race, Mourant, Mollison, Levine, Simmons, Bessis, Diamond, and Wiener who have together tested many thousands of human sera containing abnormal antibodies, have been unable to obtain a reagent for this blood property, while so many other new properties recently announced have been immediately confirmed and reagents for them found In view of these considerations any nomenclature that includes a symbol for *d* or Hr_0 is misleading and therefore incorrect The second statement is also erroneous because the number of blood factors in an agglutinogen is not uniformly three but may vary between one and four, as table II shows,

TABLE I—RACE'S CRITIQUE OF THE Rh Hr NOMENCLATURE

Nomenclature		Criticism
Fisher	Wiener	
CDe	Rh_1 or Rh_0 ← = *C* ← = *D*	*e* ignored
cDE	Rh_2 or Rh_0'' ← = *E* ← = *D*	*c* ignored
cDe	Rh_0 ← = *D*	*c* and *e* ignored
cde	rh ← ? *d*	*c* and *e* ignored
Cde	rh ← = *C* ← ? *d*	*e* ignored
cdE	rh'' ← = *E* ← ? *d*	*c* ignored

The main objection to the C D-E notations is that they are based on a genetic theory that would allow for crossing over For this there is no support whatever, while there are ample data to support Wiener's theory of multiple alleles In fact, the paper by Lawler et al provides additional data supporting the theory of multiple alleles, and as the authors state in their conclusions, "No examples of crossing over have been found in the families tested in this unit, nor do we know of any certain examples found elsewhere The work

TABLE II—BLOOD FACTORS PRESENT IN THE Rh AGGLUTINOGENS

Wiener notations		Reaction with antisera						Fisher-Race notations	
Gene	Corresponding agglutinogen	rh C	rh^w C^w	rh'' E	Rh_0 D	hr c	hr'' e	Designation*	Error
r	rh	−	−	−	−	+	+	*cde*	*d* not demonstrated
r	rh	+	−	−	−	−	+	*Cde*	*d* not demonstrated
r''	rh^y	−	−	+	−	+	−	*cdE*	*d* not demonstrated
r''	rh^y	+	−	+	−	−	−	*CdE*	*d* not demonstrated
R^0	Rh_0	−	−	−	+	+	+	*cDe*	None
R^1	Rh_1	+	−	−	+	−	+	*CDe*	None
R^{1w}	Rh_1^w	+	+	−	+	−	+	C^wDe	*C* omitted four factors present
R^2	Rh_2	−	−	+	+	+	−	*cDE*	None
R^z	Rh_z	+	−	+	+	−	−	*CDE*	None
R^{1y}	Rh_1^y	+	−	−	+	+	−	c^rDe	Symbol does not indicate presence of *C* and *c*†
New rare agglutinogen of Race and Sanger		−	−	−	+	−	−	—*D*—	Contains only one factor

* The Fisher Race nomenclature does not distinguish between genes (chromosomes) and agglutinogens, nor between genotypes and phenotypes.

† Moreover this contradicts the Fisher-Race theory which precludes the presence of both *C* and *c* in the same chromosome and agglutinogen

---

[1] Renton P H Stratton F *Ann Eugen* 1950 15 13

[2] Lawler S D Bertenshaw D Sanger R., Race R. R. *Ibid*, p 258

[3] Race R R *Antonie van Leeuwenhoek* 1949 15 29

[4] Haberman S Hill J M Everist B W Davenport, J W jun *Blood* 1948 3 682

[5] Wiener, A S *Ibid* 1950 5 693

done by Dr Alexander Wiener's laboratory and in this unit has established with certainty the manner of inheritance of the allelomorphs of Rh

Brooklyn, New York. IRVING B WEXLER.

CORONARY DISEASE AND MODERN STRESS

SIR,—In manual workers mental activity is accompanied by bodily activity, and while the systolic pressure is raised the heart is well filled by the action of the muscles and valves in the veins and by the increased respiratory pumping action Thus the diastolic supply to the coronary vessels is maintained Mental activity, particularly with anxiety or stress of work in the sedentary professions, excites a rise of systolic pressure which, unaccompanied by muscular activity, does not produce that same maintenance of diastolic pressure which is needed for a good supply of blood to the heart by the coronary arteries This, I suggest, accounts for the far greater prevalence of angina pectoris and coronary thrombosis in busy mental workers than in manual workers To compensate for sedentary mental work I think the *Exercises in the Bath* worked out by Mr T R Togna[1] are of considerable value These exercises do not raise the systolic pressure and they increase the pulse rate very little, but they secure a good return of blood to the heart and high oxygen u e per pulse beat Patients with angina have used the exercises with success

Corton near Lowestoft LEONARD HILL

SIR,—May I offer a brief contribution to the problem of coronary disease in physicians and surgeons, mentioned by Dr Rentoul (March 10) and Dr Stewart (Dec 23)

Dunbar has drawn our attention to the factor of exposure The impression from observing heart disease and death from it is, according to her, an important stress agent in patients with relatives and close friends who have suffered from such disease Dunbar concludes from her considerable material that heredity acts only in conjunction with this psychological factor I have been for a long time occupied with the related problem of medical men who suppress the ordinary emotional reactions to the many illnesses they encounter Habit does not wholly eliminate anxiety responses, and these recurrent experiences together with responsibility for the patients may be a potent substitute for the close relationship referred to by Dunbar

London, W 1 S LOWY

WILL WE NEVER LEARN ?

SIR,—The subject of this provoking correspondence has always interested me, and I have worked out the mortality rates for gastrectomy at two provincial hospitals where I have been a registrar To continue with Mr MacLellan's metaphor (Feb 3), the pitches were not like Lord's (I have been a registrar spectator there too) but good county grounds nevertheless The mortality-rate for both hospitals combined over a period of three years (132 cases, 7 surgeons) was 13 5% Your correspondents must agree that this is pretty fast bowling A few bowled "slows" (gastro enterostomy), and there were one or two googlies (vagotomies), these had a much lower bowling average

The point I wish to emphasise is that the cause of this poor bowling average was not, in my estimation, that the bowlers were bad, but that they were rushed They bowled 8 ball overs in the time that a professional at Lord's would take to roll up his sleeve I am not referring necessarily to operating time but to time for investigation and preparation—time to think Far more important than the "have a go" mentality (Dr Brailsford, March 10) is the "what's the next case" attitude and the glance at the list and the theatre clock

Orthodox and better bowling will be achieved by improving the pitch, but this will take a long time as we all know An immediate partial solution to Sir Heneage's problem (March 3) lies, not in edicts, a full time service, and control, but in more bowlers The bowlers are there, twice the age of Tattersall, fully trained, waiting I would hazard a guess that the mortality for gastrectomy performed by senior surgical registrars is below the average for the country's consultants They are more careful—they have to be The trouble is that the present bowlers do not want any additions to the team—there will be fewer benefits, and the bonuses will become more infrequent Nor do the county committees wish to increase their staff, for financial reasons

Will Sir Heneage have the courage of the M C C and urge that more bowlers are sent out ?

F R.C.S

HEPATITIS FROM TATTOOING

SIR,—The letter from Dr Robertson in your issue of Jan 6 adds still more support to the suggestion that jaundice may be transmitted by inoculation during tattooing Dr H Still and I have described[1] four cases of jaundice which we thought were very probably acquired in this way

Our four patients all attended a certain tattooing den on Feb 5, 1949, and were tattooed in succession Each developed jaundice between June 17 and 29 the same year There was no infectious hepatitis prevalent at the time, and after full inquiry we could not resist the conclusion that the virus of serum hepatitis had been inoculated through the agency of the tattooing needle Dr Ballard F Smith had presumably not seen our article when he presented his paper,[2] but his conclusions were very similar to ours

Since our cases occurred we have made careful inquiries of all our jaundice patients, but have not again demonstrated this causal connection There can be little doubt, however, that there is a real danger of virus transmission during tattooing as usually performed, and stricter control over "artists" is long overdue

Halifax, Nova Scotia R HOWELL ROBERTS

NURSING INFECTIOUS DISEASES

SIR,—The belief that there is no longer a case for fever hospitals, which is widely held and is expressed by Mr Crabb in his letter of March 10, is one of the main obstacles to the recruitment of nurses for these hospitals The would-be nurse is advised that fever nursing is a thing of the past This view has been strengthened by the publication of a proposal to abolish the special certificate in fever nursing Thus, the high standard of nursing and nurse training which fever hospitals maintained is being undermined Yet the demand for their services, as the Emergency Bed Service could testify, remains greater than the fever hospitals at present functioning can satisfy

Despite Mr Crabb's final remark, general hospitals have very little accommodation suitable for infectious cases The extensive reconstruction needed to increase such accommodation is not likely to be undertaken for many years to come The general hospitals realise this, and not only refuse to admit patients suffering from many of the common infections but are anxious to transfer patients who develop such infections while in hospital Meanwhile, those who decry the value or necessity of fever hospitals bear a considerable part of the responsibility for the grave nursing position described by Dr Banks (Feb 3) and Dr Kennedy (Jan 20)

Waddon Hospital,
Croydon J J LINEHAN

---

[1] Togna, T R. Exercises in the Bath Pp 67 6s 6d. Obtainable from the author Tuscan Hotel London W 1

[1] Roberts R H Still H *Canad med Ass J* 1950 62, 75

[2] Smith B F *J Amer med. Ass* 1950, 144 1074

Parliament

Half-closed Shop

ON March 13 on the adjournment Miss FLORENCE HORSBRUGH moved a resolution regretting

> the decision of the Durham County Council in insisting on membership of an appropriate professional association or trade union as a condition of employment.

The council had passed this decision, she recalled, on Nov 1 On Nov 15, when Dr Charles Hill had raised the matter in the House the parliamentary secretary to the Ministry of Health, replying for the Government, had said, ‘ We regret the resolution passed by the Durham County Council." Letters had been sent from the Ministries of Health and Education to the council saying that the Government did not approve of coercion. The council replied that the resolution had been reaffirmed Consultations had then taken place between the Ministries and representatives of the council. The dismissals were not enforced on the appointed day, but the resolution had not yet been rescinded The *Schoolmaster*, the official organ of the National Union of Teachers, had stated that the council's policy was being implemented in another way When candidates were called for an interview they were asked whether they were members of a trade union Miss Horsbrugh cited one instance when five candidates for a headmastership had not answered the question, saying that they had been advised by their union not to do so The sixth candidate had answered and he had got the job

Mr W R. BLYTON moved an amendment, that the House

> while approving the attitude already adopted by His Majesty's Government, and being anxious not to interfere with the autonomy of local authorities, hopes that the discussions now proceeding between the Durham County Council and some of the associations concerned will lead to an amicable settlement of the points at issue.

He had been a staunch trade unionist all his life, and he preferred to describe the situation not as a closed shop but as an attempt to get a 100% trade-union membership He believed, however, that the job of the Durham County Council was that of administrators and not trade-union organisers. Action to force people into unions should come from the bottom and not from the top, and he therefore approved of the Government's attitude The Durham County Council had decided not to implement the disputed resolution, and he could not himself see it was a crime to ask a person if he was a member of a trade union.

Mr GEORGE TOMLINSON, Minister of Education, said he had made it clear to the council that though he approved of teachers joining a union or professional association he did not consider they should be coerced by the action of their employing authority The council had in fact not implemented the resolution they had passed, but it was said that did not matter because the resolution was still on the books. But there were thousands of resolutions still on the books of local authorities and nobody bothered about them It was the action taken of which we must take cognisance. He did not want to interfere with a local authority as to the way it carried out its duties. But unless the N U T and the Durham County Council could be got to come together circumstances might arise in which he would be compelled to issue a direction He did not know whether that might not be just a victory for pigheadedness at the expense of the children.

Dr CHARLES HILL said that whatever force the arguments put forward on grounds of convenience or practical difficulty might have had in the past, it was fundamentally wrong that any man should be compelled to join any organisation of any kind Where an important freedom was involved—whether in the field of religion or whether as a conscientious objection to military service—it was right that the majority should respect the minority Speaking as one who until some months ago was involved in collective bargaining on behalf of a not unimportant body, he believed, there was nothing that kept an organisation on its toes more than the right of members to resign. Again a good trade union might want the right to expel the unsuitable and unwanted member. Must that action carry loss of a man's livelihood? Asking candidates whether they belonged to a union was in principle the same as sacking an existing staff and asking them as a condition of re-employment to produce evidence of trade-union membership Before the House approved of the Government's attitude they should be told what it was The amendment was carried by 298 votes to 283

Tuberculosis a Prescribed Disease

In the House of Commons on March 14 Mr IAIN MACLEOD moved the annulment of the regulation prescribing tuberculosis as an industrial disease for nurses and other health workers[1] Before prescribing a disease the Minister must be satisfied that the disease ought to be treated as a risk of occupation, and that it can be presumed with reasonable certainty to be due to employment. Mr MacLeod questioned whether these conditions had been fulfilled. He also urged that regulations suggesting, as they did, that nurses had an additional chance of contracting tuberculosis by reason of their employment might adversely affect the recruitment of nurses On what evidence had these regulations been made? The Advisory Council, whose recommendations had presumably been accepted by the Minister, had said that few statistics were available What statistics there were, notably those contained in the report on the Prophit Tuberculosis Survey, indicated a higher incidence of tuberculosis in nurses in general hospitals than in nurses in sanatoria. Tuberculosis, Mr MacLeod pointed out, was being prescribed because it was a communicable disease Did not all other communicable diseases immediately come into consideration? Nurses in infectious diseases hospitals, for instance, had an additional risk. The Trades Union Congress had stated that in their opinion every disease which could be shown to be contracted by virtue of employment should be prescribed, and that view was supported independently by the Royal College of Physicians Mr MacLeod was sympathetic to this point of view, but it was, he said, the end of the Industrial Injuries conception as they had known it since 1897 Mr MacLeod said he did not propose to press the motion to a division, but he had thought it right to submit to the House the case against the regulations

Dr H B MORGAN said that the Trades Union Congress had been concerned with this matter for years. They had gone through it with a fine comb and they were perfectly satisfied that at present these regulations went as far as it was legitimately possible to go in protecting the interests of workers exposed to tuberculosis infection

Mr C J ALPORT asked what was the position of a wife looking after her husband. Could her husband employ her as an attendant? Were medical students also included in the definition of the schedule?

Mr BERNARD TAYLOR, parliamentary secretary to the Ministry of National Insurance, said he did not share the gloom or pessimism of those who opposed the regulations So far from being apologetic about them, the Government were proud to have had an opportunity of introducing them and were convinced that they would prove of benefit to nurses and others who came into contact with tuberculosis patients In the view of the Minister of National Insurance the report of the Advisory Council contained abundant evidence of an added risk among the nurses in the occupations mentioned. Even if there were only one case he claimed that that would be a complete justification for the regulations The sort of men and women who entered the nursing profession were not likely to be deterred by the knowledge that there may be certain risks attached The Government were satisfied that only those who were really at some special risk would be able to qualify for benefit The regulations were intended to cover ward maids, hospital laundry workers and tuberculosis visitors, but the occupation must be insurable under the Industrial Injuries Act The Ministry had arranged with the coöperation of the Health Departments that on every claim under the new regulations they would have specialist advice

Royal Commission on Divorce

Replying to a number of questions the Prime Minister announced on March 14 that he had decided to recommend the appointment of a Royal Commission to review

---

[1] See *Lancet* March 10, 1951 p. 573

University of Sheffield

On July 12 the honorary degree of LITT D will be conferred on Mr Geoffrey Keynes, F R C S, vice president of the Bibliographical Society of London

Royal College of Physicians of London

The Lumleian lectures will be delivered at the college, Pall Mall East, S W 1, on Tuesday, April 10, and Thursday, April 12, at 5 P M, by Sir Adolphe Abrahams, who is to speak on Physical Exercise—Its Clinical Associations

Royal College of Surgeons

At the annual dinner of the Faculty of Anæsthetists, held at the college on March 14, Mr A D Marston, the dean, expressed his appreciation of the encouragement and help given by the college to the faculty He was proposing The College, and he congratulated it on the "enthusiasm, initiative, and intelligence" it had shown in its coöperation with the other surgical corporations, both at home and in the Commonwealth in a scheme for reciprocity of primary fellowship examinations, and on its continued close collaboration with the British Postgraduate Medical Federation of the University of London He went on to remind his listeners that work on the new college buildings would soon begin, but that in spite of generous gifts money was still needed Responding for the college, Sir Cecil Wakeley, the president, remarked that it was the surgeons who were in debt to the anæsthetists, for, he said, the recent advances in surgery were largely due to increasing skill in the specialty He contrasted his first experience of anæsthesia as a patient—when he was given pure ether and "vomited for a week"—with a recent anæsthetic given him by Mr Marston Twenty five years ago it had been said that surgery had reached its zenith, but events had proved that one was never justified in saying this, he now looked forward to the time when surgeons would transplant whole hearts—with consequent reduction of the divorce rate Responses to the toast of The Guests, proposed by Dr Frankis Evans, were made by Mr D W Logan, M A, D PHIL, principal of the University of London, and by Sir Gordon Gordon Taylor who paid tribute to the "kindest" profession by whose efforts Great Britain had become the mecca of anæsthetists all over the world Dr I W Magill proposed The Dean, and Mr Marston replied

Royal Society

Brigadier J S K Boyd, M D, director of the Wellcome Laboratories of Tropical Medicine, and Dr A Neuberger, biochemist at the National Institute for Medical Research, have been elected to the fellowship The 25 new fellows also include Mr S J Folley, D SC, head of the department of physiology, National Institute for Research in Dairying, and Mr H R Ing, D PHIL, reader in pharmacological chemistry, University of Oxford

French Course on Gastro-enterology

A course on this subject will be held at the Hôpital Tenon, 4, rue de la Chine, Paris XXe, from May 21 to 26 The lectures will be given in French, but they are illustrated by radiographs Further particulars may be had from Dr Viguié, of the Laboratoire Marcel Brulé, at the hospital

Leeds Travelling Fellowships

The United Leeds Hospital Board have awarded travelling fellowships, each of the value of £1000, to Dr Gordon Fryers, senior registrar in the medical unit of the hospital, and to Dr J D Everall, tutor and senior registrar to the dermatological department Dr Fryers will spend nine months at the isotopes centre at Berkeley, California, and the remaining three months of his fellowship visiting other centres, including Boston and New York Dr Everall will spend his year in the department of dermatology at the Bellevue Medical Centre New York

Prescribing in the Isle of Man

In the Isle of Man a charge of 6*d* is normally recoverable by chemists for each prescription form Patients now exempted are children until they cease to be under full time instruction at school people incapable of work because of illness for the preceding six months, and those in receipt of old age pensions, pensions for blindness or other incapacity, and supplementary pensions Hospital patients and those at convalescent homes are also exempt The Health Services Board has promised to support doctors who feel that they cannot comply with unnecessary demands

Meeting of Scottish Registrars

The second annual general meeting of the Registrars' Group of the Western Region of Scotland will be held at Glasgow Royal Infirmary on Wednesday, March 28, at 7 30 P M

Diary of the Week

MARCH 25 TO 31

Tuesday, 27th

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Street, W C 2
5 P.M Dr Hugh Gordon Benign New Growths of the Skin

Wednesday, 28th

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place W 1
3 30 P M Prof Robert Cruickshank Control of Infectious Diseases

Thursday, 29th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields W C 2
5 P M Mr Arthur Naylor Brachial Neuritis with particular reference to Lesions of the Cervical Intervertebral Discs. (Hunterian lecture)
OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM
10 A M (Royal Society of Medicine, 1, Wimpole Street, W 1) Opening of three day congress Mr M H Whiting Surgical Treatment of Rodent Ulcers Near the Eye (Presidential Address)
ROYAL ARMY MEDICAL COLLEGE, Millbank, S W 1
5 P M Dr John Owston Rocket Propellants—Toxic Effects, Hazards, and First Aid
LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant, Liverpool, 3
8 P M Miss I Forshall, Mr P P Rickham Hirschsprung's Disease

Friday, 30th

ROYAL COLLEGE OF SURGEONS
3 45 P.M Dr L W Proger Additions to the Museum (Erasmus Wilson demonstration)
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W 1
8 P M Dr Wilson Rae Venereal Disease in the Colonies. Dr Robert Lees and Dr G L M McElligott will also speak
BRITISH TUBERCULOSIS ASSOCIATION AND YORKSHIRE TUBERCULOSIS SOCIETY
2 P M (General Infirmary, Leeds) Opening of joint 2-day meeting Mr P R Allison (Changing Viewpoint in Thoracic Surgery for Tuberculosis

Saturday, 31st

KENT PÆDIATRIC SOCIETY
11 30 A M (Farnborough Hospital Farnborough Kent) Dr F O MacCallum, Dr Simon Behrman Mr Franklin Symposium on Anterior Poliomyelitis

Births, Marriages, and Deaths

BIRTHS

ARMSTRONG—On March 10, in London the wife of Dr B P Armstrong—a son
CUTTS—On March 14, in London the wife of Dr Geoffrey Cutts—a son
FORBES—On March 13 at Canterbury the wife of Dr G B Forbes—a son
GILBERT—On March 11 at Ashtead, Surrey, the wife of Mr Roger Gilbert F R C S—a son
HUGO—On March 8, at Guildford the wife of Dr Richard Hugo—a son
JOLLY—On March 9, in London the wife of Dr Hugh Jolly—a son
LAIRD—On March 11 in Liverpool the wife of Dr Campbell Laird—a daughter
PURSER—On March 7 at Swanage Dorset the wife of Dr Stanley Purser—a son
SHAW—On March 6 the wife of Mr R F Shaw F R C S—a daughter
TATE—On March 11, in London the wife of Dr Norman Tate—a son
THOMAS—In March at Seattle U S A the wife of Dr L B Thomas—a daughter
WHITBY—On March 11 in London the wife of Dr James Whitby—a daughter

MARRIAGES

CLARKE—STEVENS—On March 10 at Hagley Worcs, John Alexander Grove Clarke M B, to Brenda Winifred Stevens M B
DAVENPORT—PARISH—On March 10 at Wilmslow, Cheshire, John Davenport M B to Cristine Mary Parish
GRAHAM STEWART—BISHOP—On March 14 at Nettleden Herts, Colin Woodward Graham Stewart F R C S to Gillian Mary Bishop

DEATHS

AVENT—On March 13 at Seaton, Devon, Arthur Avent, L R C P E
SMITH—On March 12 in Edinburgh Austin Nimmo Smith, M B Edin
WARD—On March 9 at Reading Berks Ernest Ward M B L, M R C S aged 87

AN EVALUATION OF PUBLIC-HEALTH MEASURES FOR THE CONTROL OF SYPHILIS

AN EPIDEMIOLOGICAL STUDY*

JOSEPH EARLE MOORE
M.D. Johns Hopkins

From the Venereal Disease Division of the Medical Clinic Johns Hopkins University and Hospital, Baltimore

SYPHILIS control in the modern sense, dates from 1905–10, and the fundamental discoveries of Schaudinn (*Treponema pallidum*), Wassermann, Neisser, and Bruck (a diagnostic test), and Ehrlich ('Salvarsan') Before 1910, and for lack of these basic scientific discoveries little or nothing could be, or was, done

In the intervening 40 years, all civilised countries have recognised the danger to public health and welfare imposed by syphilis, and each has engaged in programmes, comprehensive or partial, looking toward its control and, hopefully, to its eventual eradication Leadership in the development and application of such programmes was taken first in Scandinavia, and more recently, within the last 15 years, in the United States

Stimulated by recent advances in knowledge, many public-health administrators view the future with extreme optimism They believe that the application of existing knowledge will effect control of this disease and perhaps eventual eradication It is proposed here to review past experience, with a view to determining whether this optimism is well founded. To this end it is pertinent to examine (1) available data which reflect incidence of syphilis in human populations in the years prior to 1910, before scientific measures of control were applied (2) the principal factors which determine fluctuations in incidence and its trend during this period, (3) the extent to which these factors are still operative in the modern period since 1910, and (4) the additional effect of measures represented by advances in knowledge in the modern period.

The geographical areas and the time periods for which morbidity and mortality rates from syphilis are available are extremely limited Moreover, completely accurate information as to morbidity and mortality of the group of venereal diseases is prevented by the social implications of their method of transmission, and, in the case of syphilis at least, by its biological, often nearly symptomless, course Legal requirements as to reporting morbidity and mortality to the health authorities have differed widely in various countries in different parts of the same country, or from time to time within a particular community Epidemiological data are often confused by consolidation of the entire group of diseases because of their common mode of transmission, and without regard to separate infectious entities The trend of "venereal disease" incidence does not necessarily express the trend of incidence of a particular infection, since the rate of one may remain stationary, or even rise, while the rate of another falls—e.g., gonorrhœa as compared with syphilis

The Public-health Implications of Early versus Late Syphilis

For practical epidemiological purposes, syphilis is not one but two diseases One of these, early syphilis (i.e., the first 2 to 4 years), represents an acute infection Infectiousness is concentrated largely within the first year, diminishing rapidly thereafter so that by the end of the fourth year the risk of transmission from one adult to another has almost, if not entirely, disappeared The other, late syphilis (i.e., of more than 4 years' duration), is a public health problem comparable in importance to such non-infectious conditions as hypertension and cancer

It is necessary at the outset to distinguish clearly between the epidemiological terms "incidence" and "prevalence" An attack upon early syphilis should be calculated to break the chain of infectiousness, thereby reducing the *incidence* of fresh infections, and ultimately, within a *generation or more*, to reduce also the reservoir (i.e., *prevalence*) of late syphilis In the following discussion, major interest lies in incidence—the rate and extent of dissemination of syphilitic infection

The public-health objective may be clearly stated by changing only three words in the remarks of Frost (1937) on the control of tuberculosis

> 'It is not necessary that transmission be *immediately* and *completely* prevented. [Italics are Frost's] It is necessary only that the rate of transmission be held permanently below the level at which a given number of infection spreading (i.e., 'open') cases succeed in establishing an equivalent number (of 'open' cases) to carry on the succession If, in successive periods of time the number of infectious hosts is continuously reduced, the end result of this diminishing ratio if continued long enough must be extermination of the *treponeme of syphilis* [Italicised words are the three I have substituted.]

Unavoidably, however, a public-health attack is simultaneously directed at late syphilis as well—here without major influence upon incidence (in the epidemiological sense), but instead for the purpose of preventing or treating late complications and thereby minimising invalidism, death, and community cost

This elementary epidemiological recognition of the division of syphilis into two separate entities has been laggard in application to public health practice Where incidence and prevalence data have been collected, it has been customary to record all syphilis as a group, without distinction between its two epidemiological types In England and Wales, for example, figures as to incidence of early syphilis as such are available only since 1932, in the United States as a whole, only since 1941

There are exceptions to this epidemiological confusion in various countries and in certain small populations, notably military rather than civilian, though the entanglement is so serious as to give the epidemiologist pause in evaluating long term trends

EARLY DATA AS TO MORBIDITY AND MORTALITY

In civilian as opposed to military populations, there is therefore singularly little information as to trend of incidence of syphilis until very recent years It is known (Hirsch 1885, Bloch 1901), without statistical documentation that the infection spread in major epidemic fashion over Western Europe in the late 15th and early 16th centuries, and thereafter over the entire world; and that from time to time since there have been minor epidemics or major endemics (Scotland, mid-17th century, Scandinavia, early 18th century, Serbia, early 19th century)

It is also established, on reliable clinical testimony, though again without statistical proof, that the characteristics of the disease have undergone a profound change in the 450 years of its recognised history An often rapidly fatal infection has evolved into one of exquisite chronicity Malignant, destructive lesions of the skin, mucosæ and bones have been replaced by less obvious but more serious cardiovascular or nervous system involvement, or even by almost complete clinical latency There is indeed some evidence of a change in clinical character in the United States within the last thirty years. The incidence of early asymptomatic neurosyphilis'

---

* The Malcolm Morris lecture delivered at St Mary's Hospital, London, on Sept 21 1950 It is appearing also in the March issue of the *American Journal of Syphilis, Gonorrhœa and Venereal Diseases*

University of Sheffield

On July 12 the honorary degree of LITT D will be conferred on Mr Geoffrey Keynes, F R C S, vice president of the Bibliographical Society of London

Royal College of Physicians of London

The Lumleian lectures will be delivered at the college, Pall Mall East, S W 1, on Tuesday, April 10, and Thursday, April 12, at 5 P M, by Sir Adolphe Abrahams, who is to speak on Physical Exercise—Its Clinical Associations

Royal College of Surgeons

At the annual dinner of the Faculty of Anæsthetists, held at the college on March 14, Mr A D Marston, the dean, expressed his appreciation of the encouragement and help given by the college to the faculty He was proposing The College, and he congratulated it on the "enthusiasm, initiative, and intelligence" it had shown in its coöperation with the other surgical corporations, both at home and in the Commonwealth in a scheme for reciprocity of primary fellowship examinations, and on its continued close collaboration with the British Postgraduate Medical Federation of the University of London He went on to remind his listeners that work on the new college buildings would soon begin, but that in spite of generous gifts money was still needed Responding for the college, Sir Cecil Wakeley, the president, remarked that it was the surgeons who were in debt to the anæsthetists, for, he said, the recent advances in surgery were largely due to increasing skill in the specialty He contrasted his first experience of anæsthesia as a patient—when he was given pure ether and "vomited for a week"—with a recent anæsthetic given him by Mr Marston Twenty-five years ago it had been said that surgery had reached its zenith, but events had proved that one was never justified in saying this, he now looked forward to the time when surgeons would transplant whole hearts—with consequent reduction of the divorce rate Responses to the toast of The Guests, proposed by Dr Frankis Evans, were made by Mr D W Logan, M A., D PHIL, principal of the University of London, and by Sir Gordon Gordon Taylor who paid tribute to the "kindest" profession by whose efforts Great Britain had become the mecca of anæsthetists all over the world Dr I W Magill proposed The Dean, and Mr Marston replied

Royal Society

Brigadier J S K Boyd, M D, director of the Wellcome Laboratories of Tropical Medicine, and Dr A Neuberger, biochemist at the National Institute for Medical Research, have been elected to the fellowship The 25 new fellows also include Mr S J Folley, D SC, head of the department of physiology, National Institute for Research in Dairying, and Mr H R Ing, D.PHIL, reader in pharmacological chemistry, University of Oxford

French Course on Gastro-enterology

A course on this subject will be held at the Hôpital Tenon, 4, rue de la Chine, Paris XXe, from May 21 to 25 The lectures will be given in French, but they are illustrated by radiographs Further particulars may be had from Dr Viguie, of the Laboratoire Marcel Brule, at the hospital

Leeds Travelling Fellowships

The United Leeds Hospital Board have awarded travelling fellowships, each of the value of £1000, to Dr Gordon Fryers, senior registrar in the medical unit of the hospital, and to Dr J D Everall, tutor and senior registrar to the dermatological department Dr Fryers will spend nine months at the isotopes centre at Berkeley, California, and the remaining three months of his fellowship visiting other centres, including Boston and New York Dr Everall will spend his year in the department of dermatology at the Bellevue Medical Centre New York

Prescribing in the Isle of Man

In the Isle of Man a charge of 6*d* is normally recoverable by chemists for each prescription form Patients now exempted are children until they cease to be under full time instruction at school, people incapable of work because of illness for the preceding six months, and those in receipt of old age pensions, pensions for blindness or other incapacity, and supplementary pensions Hospital patients and those at convalescent homes are also exempt The Health Services Board has promised to support doctors who feel that they cannot comply with unnecessary demands

Meeting of Scottish Registrars

The second annual general meeting of the Registrars' Group of the Western Region of Scotland will be held at Glasgow Royal Infirmary on Wednesday, March 28, at 7 30 P M

Diary of the Week

MARCH 25 TO 31

Tuesday, 27th

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle street, W C 2
5 P.M Dr Hugh Gordon Benign New Growth of the Skin

Wednesday, 28th

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, [illegible], Portland Place W 1
3 30 P M Prof Robert Cruickshank Control of Infectious Diseases

Thursday, 29th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C 2
5 P M Mr Arthur Naylor Brachial Neuritis with particular reference to Lesions of the Cervical Intervertebral Disc (Hunterian lecture)

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM
10 A M (Royal Society of Medicine, 1 Wimpole Street, W 1) Opening of three day congress Mr M. H Whiting Surgical Treatment of Rodent-Ulcers Near the Eye (Presidential Address)

ROYAL ARMY MEDICAL COLLEGE, Millbank, S W 1
5 P M Dr John Owston Rocket Propellants—Toxic Effects, Hazards and First Aid

LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant, Liverpool, 3
8 P M Miss I Forshall Mr P P Rickham Hirschsprung's Disease

Friday, 30th

ROYAL COLLEGE OF SURGEONS
3 45 P.M Dr L W Proger Additions to the Museum. (Erasmus Wilson demonstration)

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11 Chandos Street, W 1
8 P M Dr Wilson Rae Venereal Disease in the Colonies. Dr Robert Lees and Dr G L M McElligott will also speak

BRITISH TUBERCULOSIS ASSOCIATION AND YORKSHIRE TUBERCULOSIS SOCIETY
2 P M (General Infirmary, Leeds) Opening of joint [illegible]-day meeting Mr P R Allison (Changing Viewpoint in Thoracic Surgery for Tuberculosis

Saturday, 31st

KENT PÆDIATRIC SOCIETY
11 30 A M (Farnborough Hospital Farnborough Kent) Dr F O MacCallum Dr Simon Behrman Mr Franklin Symposium on Anterior Poliomyelitis.

Births, Marriages, and Deaths

BIRTHS

ARMSTRONG —On March 10, in London the wife of Dr B P Armstrong—a son

CUTTS —On March 14 in London, the wife of Dr Geoffrey Cutts—a son

FORBES —On March 13, at Canterbury the wife of Dr G B Forbes—a son

GILBERT —On March 11 at Ashtead Surrey the wife of Mr Roger Gilbert, F R.C.S —a son

HUGO —On March 8, at Guildford, the wife of Dr Richard Hugo—a son

JOLLY —On March 9, in London the wife of Dr Hugh Jolly—a son.

LAIRD —On March 11 in Liverpool the wife of Dr Campbell Laird —a daughter

PURSER —On March 7 at Swanage Dorset the wife of Dr Stanley Purser—a son

SHAW —On March 6 the wife of Mr R E Shaw, F R.C.S —a daughter

TATE —On March 11, in London, the wife of Dr Norman Tate—a son

THOMAS —In March at Seattle U S A the wife of Dr L B Thomas—a daughter

WHITBY —On March 11 in London the wife of Dr James Whitby —a daughter

MARRIAGES

CLARKE—STEVENS —On March 10, at Hagley Worcs John Alexander Grove Clarke M B, to Brenda Winifred Stevens, M B.

DAVENPORT—PARISH —On March 10 at Wilmslow Cheshire, John Davenport M B, to Cristine Mary Parish

GRAHAM STEWART—BISHOP —On March 14 at Nettleden Herts Colin Woodward Graham Stewart F R C S, to Gillian Mary Bishop

DEATHS

AVENT —On March 13 at Seaton, Devon Arthur Avent L.R.C.P E

SMITH —On March 12, in Edinburgh Austin Nimmo Smith M.B Edin

WARD —On March 9, at Reading Berks Ernest Ward M B L., M R.C S aged 87

AN EVALUATION OF PUBLIC-HEALTH MEASURES FOR THE CONTROL OF SYPHILIS

AN EPIDEMIOLOGICAL STUDY*

JOSEPH EARLE MOORE
M.D Johns Hopkins

From the Venereal Disease Division of the Medical Clinic, Johns Hopkins University and Hospital, Baltimore

SYPHILIS control, in the modern sense, dates from 1905–10, and the fundamental discoveries of Schaudinn (*Treponema pallidum*), Wassermann, Neisser, and Bruck (a diagnostic test), and Ehrlich ('Salvarsan') Before 1910, and for lack of these basic scientific discoveries little or nothing could be, or was, done

In the intervening 40 years, all civilised countries have recognised the danger to public health and welfare imposed by syphilis, and each has engaged in programmes, comprehensive or partial, looking toward its control and, hopefully, to its eventual eradication Leadership in the development and application of such programmes was taken first in Scandinavia, and more recently, within the last 15 years, in the United States

Stimulated by recent advances in knowledge, many public health administrators view the future with extreme optimism They believe that the application of existing knowledge will effect control of this disease and perhaps eventual eradication It is proposed here to review past experience, with a view to determining whether this optimism is well founded To this end it is pertinent to examine (1) available data which reflect incidence of syphilis in human populations in the years prior to 1910 before scientific measures of control were applied, (2) the principal factors which determine fluctuations in incidence and its trend during this period, (3) the extent to which these factors are still operative in the modern period since 1910, and (4) the additional effect of measures represented by advances in knowledge in the modern period

The geographical areas and the time periods for which morbidity and mortality rates from syphilis are available are extremely limited Moreover, completely accurate information as to morbidity and mortality of the group of venereal diseases is prevented by the social implications of their method of transmission, and, in the case of syphilis at least, by its biological, often nearly symptomless course Legal requirements as to reporting morbidity and mortality to the health authorities have differed widely in various countries in different parts of the same country, or from time to time within a particular community Epidemiological data are often confused by consolidation of the entire group of diseases, because of their common mode of transmission, and without regard to separate infectious entities The trend of "venereal disease" incidence does not necessarily express the trend of incidence of a particular infection, since the rate of one may remain stationary, or even rise, while the rate of another falls—e g, gonorrhœa as compared with syphilis

The Public health Implications of Early versus Late Syphilis

For practical epidemiological purposes, syphilis is not one but two diseases One of these, early syphilis (i e, the first 2 to 4 years), represents an acute infection Infectiousness is concentrated largely within the first year, diminishing rapidly thereafter so that by the end of the fourth year the risk of transmission from one adult to another has almost, if not entirely, disappeared The other, late syphilis (i e, of more than 4 years' duration), is a public health problem comparable in importance to such non infectious conditions as hypertension and cancer

It is necessary at the outset to distinguish clearly between the epidemiological terms "incidence" and "prevalence." An attack upon early syphilis should be calculated to break the chain of infectiousness, thereby reducing the *incidence* of fresh infections, and ultimately, within a generation or more, to reduce also the reservoir (i.e, *prevalence*) of late syphilis In the following discussion, major interest lies in incidence—the rate and extent of dissemination of syphilitic infection

The public health objective may be clearly stated by changing only three words in the remarks of Frost (1937) on the control of tuberculosis

> 'It is not necessary that transmission be *immediately* and *completely* prevented [Italics are Frost s] It is necessary only that the rate of transmission be held permanently below the level at which a given number of infection spreading (i e, 'open') cases succeed in establishing an equivalent number (of 'open cases) to carry on the succession If in successive periods of time, the number of infectious hosts is continuously reduced, the end result of this diminishing ratio, if continued long enough, must be extermination of the *treponeme of syphilis*.' [Italicised words are the three I have substituted.]

Unavoidably, however, a public health attack is simultaneously directed at late syphilis as well—here without major influence upon incidence (in the epidemiological sense), but instead for the purpose of preventing or treating late complications and thereby minimising invalidism, death, and community cost

This elementary epidemiological recognition of the division of syphilis into two separate entities has been laggard in application to public-health practice Where incidence and prevalence data have been collected, it has been customary to record all syphilis as a group, without distinction between its two epidemiological types In England and Wales, for example, figures as to incidence of early syphilis as such are available only since 1932, in the United States as a whole, only since 1941

There are exceptions to this epidemiological confusion in various countries and in certain small populations, notably military rather than civilian, though the entanglement is so serious as to give the epidemiologist pause in evaluating long term trends

EARLY DATA AS TO MORBIDITY AND MORTALITY

In civilian as opposed to military populations, there is therefore singularly little information as to trend of incidence of syphilis until very recent years It is known (Hirsch 1885, Bloch 1901), without statistical documentation, that the infection spread in major epidemic fashion over Western Europe in the late 15th and early 16th centuries, and thereafter over the entire world, and that from time to time since there have been minor epidemics or major endemics (Scotland mid-17th century, Scandinavia, early 18th century, Serbia, early 19th century)

It is also established, on reliable clinical testimony, though again without statistical proof, that the characteristics of the disease have undergone a profound change in the 450 years of its recognised history An often rapidly fatal infection has evolved into one of exquisite chronicity Malignant, destructive lesions of the skin, mucosæ, and bones have been replaced by less obvious but more serious cardiovascular or nervous system involvement, or even by almost complete clinical latency There is indeed some evidence of a change in clinical character in the United States within the last thirty years The incidence of early asymptomatic neurosyphilis'

---

* The Malcolm Morris lecture delivered at St Mary s Hospital, London on Sept 21 1950 It is appearing also in the March issue of the *American Journal of Syphilis Gonorrhœa and Venereal Diseases*

6657

(abnormal spinal fluids in persons with primary or secondary syphilis), formerly 25–40%, has fallen to a current 5–15%

THE TREND OF INFECTION 1865–1910 AS REFLECTED BY MILITARY DATA

If civilian data are lacking, something may be learned of intermediate or long term trends from military population groups I have elsewhere attempted such a study (Moore 1951a), of which only brief excerpts are possible here

The *importance of syphilis to armies has been apparent* since the first 16th century epidemic in the army of Charles V Most of the major armies and navies of the world have morbidity data dating from the period 1865–80 These are recorded in detail by Haustein (1937) and Hinrichsen (1944, 1945) and for the United States Army by Siler (1943)

One must first inquire as to the extent to which military data may be used as an index of the incidence of syphilis in the civilian population from which military personnel are drawn or with which they are associated To employ them for this purpose, one should be cognisant of certain facts and assumptions which I have outlined in detail elsewhere (Moore 1951a) The evidence permits, I think, the tentative conclusion that both in peace and war time, the *military* incidence of fresh infections is at least a rough index to prevalence, and perhaps to incidence as well, in the civilian community in which the military command is stationed

Information is available for nine major armies of Western Europe, and for the United States In most of Europe, the period chosen was, after the Franco Prussian War of 1870, one of uninterrupted peace I shall here present detailed incidence curves for only three of the armies studied — Prussian, British, and United States These are shown in figs 1–3 In all is observed the same downward trend of incidence of syphilis

The percentage change in incidence of syphilis in these several armies during the last half of the 19th and first decade of the 20th centuries is summarised in fig 4 In all the armies studied, except the Austro Hungarian Russian, and Italian (in which there was an increase), there was a downward trend from the beginning of the period to its end, ranging from 38% in the Prussian to 80% in the British armies

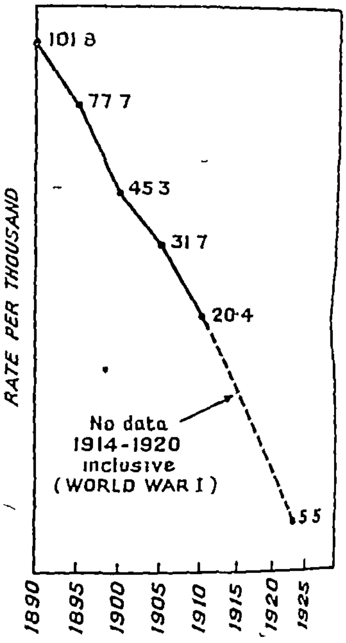


Fig 2—Incidence of syphilis (primary and secondary) in the British army (at home) 1890–1925 (Haustein 1937) Average strength of army about 100,000.

Note that while the *starting* base line incidence figure *varies in* different armies (Prussian about 30 per 1000, U S A about 70 per 1000, British about 100 per 1000) as shown in *figs 1, 2*, and 3, the shape of the falling curves of incidence is about the same

Note also that in the British army (at home), the *rate of fall* was continuous but *apparently not* accelerated in the *modern era* 1910–25

INFLUENCE OF WAR ON SYPHILIS INCIDENCE IN MILITARY POPULATIONS

Making all allowances for their partial unreliability, the foregoing data suggest strongly that in the period 1865–1910 there was a spontaneous decline in the incidence of fresh infections with syphilis in most of the armies of Western Europe and of the United States, and, by implication, in the civilian populations of the countries It is important to note that, excepting the United States, Russian, and Italian armies (the latter two engaged in the Russo Turkish War of 1877–78, the Russo Japanese War of 1904–05 and its concomitant and subsequent internal Russian revolution, and the Italian African adventures of 1887–1900) the other major armies were *at peace*

It is a commonplace, however, that in military populations (and in civilian as well) the incidence of syphilis rises in war time For two European armies, the belligerent French and the neighbouring neutral Dutch, this is well shown for *World War I by fig 5, from which is* to be noted not only the abrupt rise during hostilities, but also the equally abrupt post war fall to or even slightly below pre war levels

In fig 6 are shown, for the United States Army (limited to personnel stationed in the *continental* United States and excluding troops on foreign service), three decades of war and post war (Civil War, 1861–71, World War I 1914–22, World War II, 1939–49) Here, too, appear war or immediate post war peaks of incidence on each occasion, *falling within 4 years* to or below pre war levels

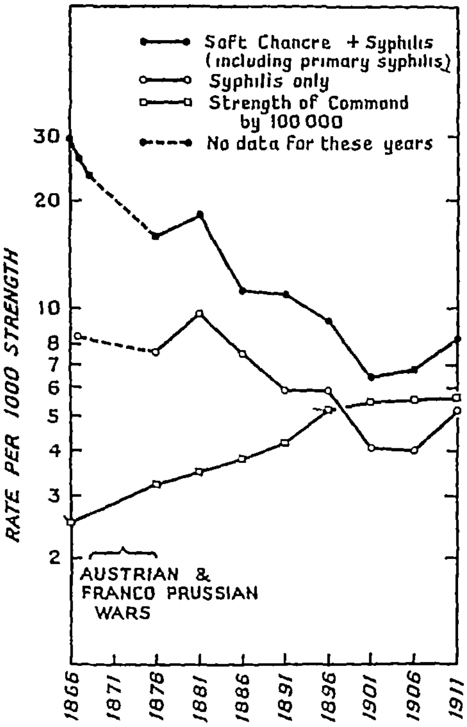


Fig 1—Incidence of syphilis in the Prussian army 1866–1913 (Haustein 1937)

In this and similar curves showing military rates I have shown the average incidence rate by quintades, in order to smooth minor fluctuations The average is based on the sum of the rate per 1000 strength for each of five successive years, divided of course by 5, *and the years* recorded on the base line of each chart represent the mid point of the quintade

An important difficulty in acceptance of pre 1910 military rates arises with regard to chancroid In certain armies (e g, the Prussian, according to Haustein), primary syphilis was at times or even regularly included during the pre laboratory period in question, under the diagnostic heading 'soft chancre with bubo' Where this is probably true, I have constructed separate curves for syphilis alone and for syphilis plus chancroid, which (except in two armies, Austro Hungarian and Italian) show remarkable parallelism For armies reporting primary and secondary syphilis as such these data alone have been used

These data offer a strong suggestion that the fall in incidence of syphilis observed in most major European armies and in the United States in the period 1865–1910 depends on the usually observed post-war fall in incidence, a phenomenon not directly related to syphilis control measures. This is further suggested by crude United States Army rates from 1820 to 1940, shown in fig 3. Here there is first a fall, probably representing the aftermath of the war of 1812 (if the data could be extrapolated backward), with rises and falls during and after each succeeding war.† One suspects that if European data were available from, say, 1750 to the present, an initial period of low incidence might have been replaced by fluctuating peaks of high incidence, dating from the major internal and external disturbances initiated by the French Revolution in 1789 and ending (temporarily) with the Franco Prussian War in 1871.

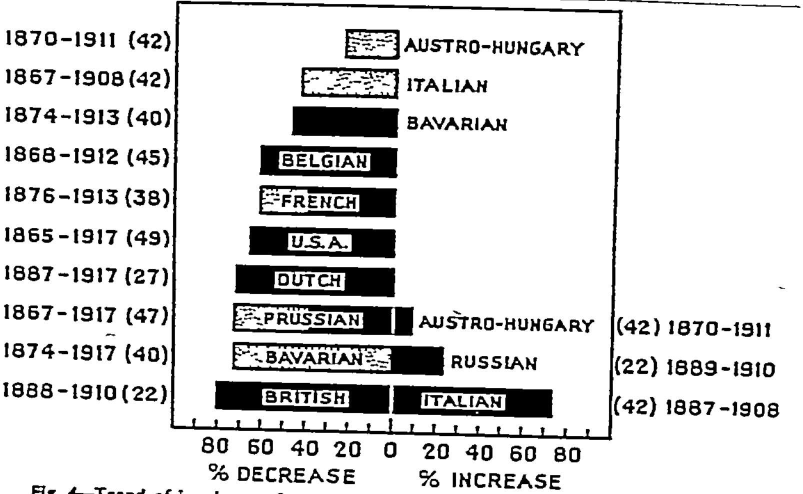


Fig 4—Trend of incidence of syphilis in major armies 1865–1913 (Haustein 1937)

In this chart the solid black blocks represent syphilis only, the stippled blocks syphilis plus chancroid (see text for explanation). For certain armies (Bavarian, Prussian, French, Italian, and Austro Hungarian), both sets of data are shown. In all except the Austro Hungarian and Italian armies, both rates fall in approximate parallel. For the two latter, the chancroid rate fell slightly but that for syphilis increased. Perhaps this phenomenon reflects both a higher incidence of chancroid in the Mediterranean basin than elsewhere in Europe (certainly true during World War II), and more early diagnostic confusion between syphilis and chancroid in these two armies than in others.

Note that during the period in question 1865–1913, and after the conclusion of the Franco Prussian War in 1871, all the countries here represented were at peace except Russia and Italy, each of which, engaged in war, showed a rise in incidence.

FACTORS POSSIBLY INFLUENCING THE PRE 1910 INCIDENCE OF SYPHILIS

In the absence of knowledge of prevention or of successful treatment methods of syphilis, the only pre 1910 method of control of syphilis attempted in most countries—and this half-heartedly and wholly unsuccessfully—was regulation or repression of prostitution.‡ As a method of syphilis control in civilian populations (perhaps of more value in military groups), this single effort was foredoomed to failure, since, at least in the United States, organised prostitution is not now and probably never has been, the largest factor in the transmission of syphilis.§ The feminine contact, especially in younger age groups, is usually the casual contact, and if prostitute at all, is often clandestine rather than the inmate of a brothel. The explanation of a falling syphilis rate in the last half of the 19th century must therefore be sought elsewhere.

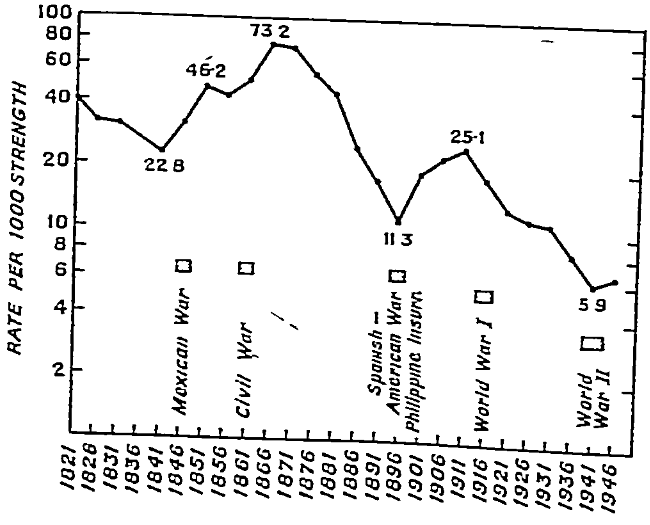


Fig. 3—Incidence of syphilis in U.S. Army at home and abroad 1820–1946 (based on data from Siler 1943)

Note first, in connection with the text argument of spontaneous decline the falling rate 1866–96, analogous to that shown in figs 1 and 2 for the Prussian and British armies. During this time period the U S Army had no troops on foreign service.

Note next in connection with the text argument on the effect of war on incidence of syphilis the fall in rate 1820–41 (the aftermath of the war of 1812) and the rises and subsequent falls centring around the Mexican War (1845–47), the Civil War (1861–65) the Spanish American Wars, and the Philippine Insurrection (1898–1908). The absence of a rise during World War I is due according to Siler to inadequate reporting from the A.E.F in France.

Was the Decline a Natural Phenomenon?

In a stimulating paragraph, Dubos (1950) implies an exciting possible parallel between the two major chronic infections, tuberculosis and syphilis:

> Not so long ago tuberculosis was the Great White Plague, the 'captain of all men of death' for the white race. In Boston, New York, Philadelphia and Charleston—in London, Paris and Berlin—all available statistics reveal tuberculosis mortality rates of 500 or higher per 100 000 inhabitants in the year 1850. Some time around 1860 the number of deaths from the disease began to decrease in Europe and North America, and it has continued to decrease ever since except for brief interruptions in the downward trend interruptions associated with two world wars. In 1947, tuberculosis mortality

---

† Excepting World War I where the figures are inaccurate because of the failure of reporting from the American Expeditionary Force in France (Siler 1943).

‡ The hospitalised quarantine of patients with early syphilis continued until their open lesions were healed, was practised in only a few countries (notably Norway) and cannot have been a factor in a general European decline.

§ This statement may not be true of other countries and other times. Guthe and Hume (see Vonderlehr 1939) lay stress on the importance of prostitution in the spread of syphilis, especially to military groups, and believe it to have been an important factor in civilian infections in France and Russia some decades ago.

(abnormal spinal fluids in persons with primary or secondary syphilis), formerly 25–40%, has fallen to a current 5–15%

THE TREND OF INFECTION 1865–1910 AS REFLECTED BY MILITARY DATA

If civilian data are lacking, something may be learned of intermediate or long term trends from military population groups I have elsewhere attempted such a study (Moore 1951a), of which only brief excerpts are possible here

The importance of syphilis to armies has been apparent since the first 16th century epidemic in the army of Charles V Most of the major armies and navies of the world have morbidity data dating from the period 1865–80 These are recorded in detail by Haustein (1937) and Hinrichsen (1944, 1945) and for the United States Army by Siler (1943)

One must first inquire as to the extent to which military data may be used as an index of the incidence of syphilis in the civilian population from which military personnel are drawn or with which they are associated. To employ them for this purpose, one should be cognisant of certain facts and assumptions which I have outlined in detail elsewhere (Moore 1951a) The evidence permits, I think, the tentative conclusion that both in peace and war time, the military incidence of fresh infections is at least a rough index to prevalence, and perhaps to incidence as well, in the civilian community in which the military command is stationed

Information is available for nine major armies of Western Europe, and for the United States In most of Europe, the period chosen was, after the Franco Prussian War of 1870, one of uninterrupted peace I shall here present detailed incidence curves for only three of the armies studied — Prussian, British, and United States These are shown in figs 1–3 In all is observed the same downward trend of incidence of syphilis

The percentage change in incidence of syphilis in these several armies during the last half of the 19th and first decade of the 20th centuries is summarised in fig 4 In all the armies studied, except the Austro Hungarian Russian, and Italian (in which there was an increase), there was a downward trend from the beginning of the period to its end, ranging from 38% in the Prussian to 80% in the British armies

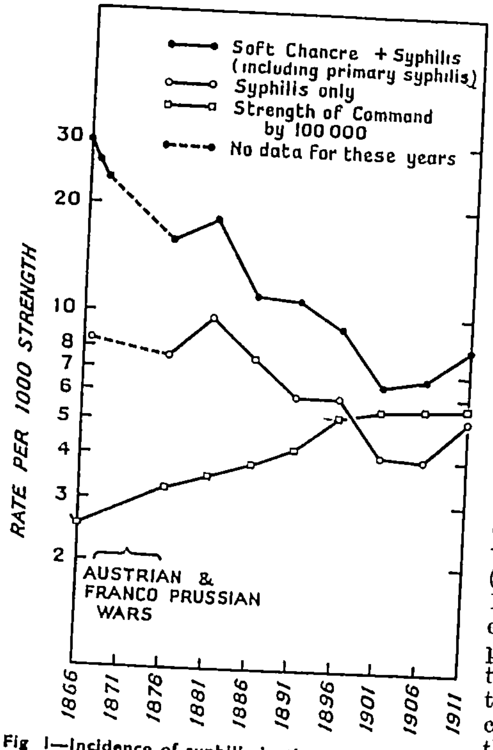


Fig 1—Incidence of syphilis in the Prussian army 1866–1913 (Haustein 1937)

In this and similar curves showing military rates, I have shown the average incidence rate by quintades, in order to smooth minor fluctuations The average is based on the sum of the rate per 1000 strength for each of five successive years, divided of course by 5, and the years recorded on the base line of each chart represent the mid point of the quintade

An important difficulty in acceptance of pre 1910 military rates arises with regard to chancroid In certain armies (e g, the Prussian, according to Haustein), primary syphilis was at times or even regularly included, during the pre laboratory period in question, under the diagnostic heading "soft chancre with bubo" Where this is probably true, I have constructed separate curves for syphilis alone and for syphilis plus chancroid, which (except in two armies, Austro Hungarian and Italian) show remarkable parallelism For armies reporting primary and secondary syphilis as such these data alone have been used

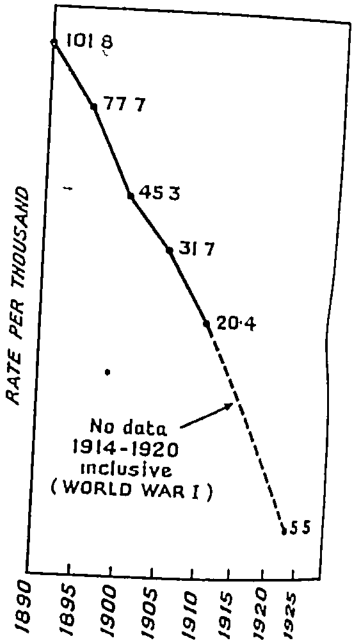


Fig 2—Incidence of syphilis (primary and secondary) in the British army (at home) 1890–1925 (Haustein 1937) Average strength of army about 100,000.

Note that while the starting base line incidence figure varies in different armies (Prussian about 30 per 1000, U S A about 70 per 1000, British about 100 per 1000) as shown in figs 1, 2, and 3, the shape of the falling curves of incidence is about the same

Note also that in the British army (at home), the rate of fall was continuous but apparently not accelerated in the modern era 1910–25

INFLUENCE OF WAR ON SYPHILIS INCIDENCE IN MILITARY POPULATIONS

Making all allowances for their partial unreliability, the foregoing data suggest strongly that in the period 1865–1910 there was a spontaneous decline in the incidence of fresh infections with syphilis in most of the armies of Western Europe and of the United States, and, by implication, in the civilian populations of these countries It is important to note that, excepting the United States, Russian, and Italian armies (the latter two engaged in the Russo Turkish War of 1877–78, the Russo Japanese War of 1904–05 and its concomitant and subsequent internal Russian revolution, and the Italian African adventures of 1887–1900) the other major armies were at peace

It is a commonplace, however, that in military populations (and in civilian as well) the incidence of syphilis rises in war time For two European armies, the belligerent French and the neighbouring neutral Dutch, this is well shown for World War I by fig 5, from which is to be noted not only the abrupt rise during hostilities, but also the equally abrupt post war fall to or even slightly below pre war levels

In fig 6 are shown, for the United States Army (limited to personnel stationed in the continental United States and excluding troops on foreign service), three decades of war and post war (Civil War, 1861–71, World War I 1914–22, World War II, 1939–49) Here, too, appear war or immediate post war peaks of incidence on each occasion, falling within 4 years to or below pre war levels

These data offer a strong suggestion that the fall in incidence of syphilis observed in most major European armies and in the United States in the period 1865–1910 depends on the usually observed post-war fall in incidence, a phenomenon not directly related to syphilis control measures This is further suggested by crude United States Army rates from 1820 to 1940, shown in fig 3 Here there is first a fall, probably representing the aftermath of the war of 1812 (if the data could be extrapolated backward), with rises and falls during and after each succeeding war † One suspects that if European data were available from, say, 1750 to the present, an initial period of low incidence might have been replaced by fluctuating peaks of high incidence, dating from the major internal and external disturbances initiated by the French Revolution in 1789 and ending (temporarily) with the Franco-Prussian War in 1871

FACTORS POSSIBLY INFLUENCING THE PRE 1910 INCIDENCE OF SYPHILIS

In the absence of knowledge of prevention or of successful treatment methods of syphilis, the only pre-1910 method of control of syphilis attempted in most countries—and this half heartedly and wholly unsuccessfully—was regulation or repression of prostitution ‡ As a method of syphilis control in civilian populations (perhaps of more value in military groups), this single effort was foredoomed to failure, since, at least in the United States, organised prostitution is not now, and probably never has been the largest factor in the transmission of syphilis § The feminine contact, especially in younger age groups, is usually the casual contact, and if prostitute at all, is often clandestine rather than the inmate of a brothel The explanation of a falling syphilis rate in the last half of the 19th century must therefore be sought elsewhere

Was the Decline a Natural Phenomenon ?

In a stimulating paragraph, Dubos (1950) implies an exciting possible parallel between the two major chronic infections, tuberculosis and syphilis

> Not so long ago, tuberculosis was the Great White Plague, the 'captain of all men of death' for the white race In Boston New York, Philadelphia, and Charleston —in London, Paris and Berlin—all available statistics reveal tuberculosis mortality rates of 500 or higher per 100 000 inhabitants in the year 1850 Some time around 1860, the number of deaths from the disease began to decrease in Europe and North America and it has continued to decrease ever since except for brief interruptions in the downward trend, interruptions associated with two world wars In 1947, tuberculosis mortality

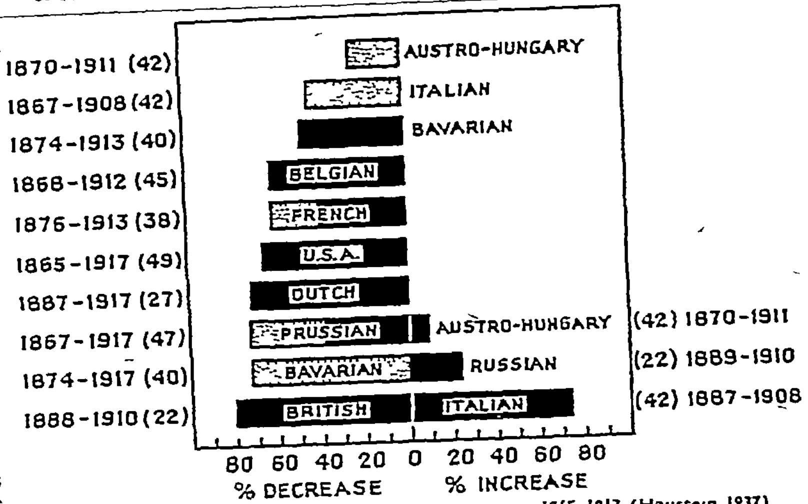


Fig. 4—Trend of incidence of syphilis in major armies 1865–1913 (Haustein 1937)

In this chart, the solid black blocks represent syphilis only, the stippled blocks syphilis plus chancroid (see text for explanation) For certain armies (Bavarian, Prussian French, Italian, and Austro Hungarian), both sets of data are shown. In all except the Austro Hungarian and Italian armies, both rates fall in approximate parallel For the two latter, the chancroid rate fell slightly but that for syphilis increased Perhaps this phenomenon reflects both a higher incidence of chancroid in the Mediterranean basin than elsewhere in Europe (certainly true during World War II) and more early diagnostic confusion between syphilis and chancroid in these two armies than in others

Note that during the period in question 1865–1913, and after the conclusion of the Franco Prussian War in 1871, all the countries here represented were at peace except Russia and Italy, each of which engaged in war, showed a rise in incidence

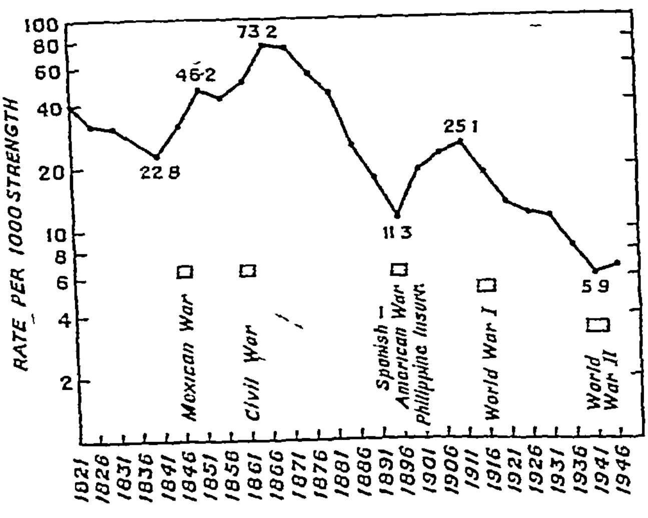


Fig. 3—Incidence of syphilis in U.S Army at home and abroad, 1820–1946 (based on data from Siler 1943)

Note first, in connection with the text argument of spontaneous decline, the falling rate 1866–98 analogous to that shown in figs 1 and 2 for the Prussian and British armies During this time period, the U.S Army had no troops on foreign service

Note next in connection with the text argument on the effect of war on incidence of syphilis, the fall in rate 1820–41 (the aftermath of the war of 1812), and the rises and subsequent falls centring around the Mexican War (1845–47), the Civil War (1861–65) the Spanish American Wars, and the Philippine Insurrection (1898–1908) The absence of a rise during World War I is due, according to Siler to inadequate reporting from the A.E.F in France rates were below 40 per 100,000 population in several countries and were still decreasing Thus, in many places, the toll of deaths due to tuberculosis had decreased more than tenfold in less than a century, a spectacular event that has excited endless discussions among students of public health The decrease began before the discovery of the tubercle bacillus, long before there were available any specific methods of prevention or cure Western civilization is slowly, but perhaps not surely, gaining in its fight over tuberculosis, without being too certain of the circumstances to which it owes its success For equally mysterious reasons scarlet fever is on the wane, fifty years ago a frequent cause of death it is to day a relatively mild disease [As to syphilis] Western civilization took the disease in stride and learned to live with it Indeed, the contagion may have made European culture burn with a brighter light, if it be true, as claimed by certain medical writers, that a correlation exists between syphilis and genius ”

---

† Excepting World War I where the figures are inaccurate, because of the failure of reporting from the American Expeditionary Force in France (Siler 1943)

‡ The hospitalised quarantine of patients with early syphilis continued until their open lesions were healed, was practised in only a few countries (notably Norway) and cannot have been a factor in a general European decline

§ This statement may not be true of other countries and other times Guthe and Hume (see Vonderlehr 1939) lay stress on the importance of prostitution in the spread of syphilis especially to military groups, and believe it to have been an important factor in civilian infections in France and Russia some decades ago

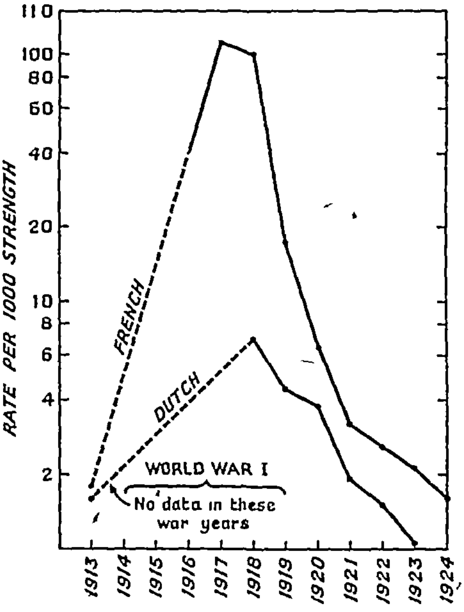


Fig 5—Rise in incidence of early syphilis in a belligerent (French) and neutral (Dutch) European army during World War I (Haustein 1937) Dutch army, all early syphilis, French army, primary' syphilis.

Inherent in this fascinating suggestion is the implication that some degree of change in host parasite relationship has developed in those civilised and syphilised populations which have been subjected to the influence of the infection for 450 years Whether, in turn, this depends on mutations and changes in virulence of the parasite, or on some degree of developing racial immunity in the host, or on both, are speculative questions impossible of proof, and too complicated for discussion here

Was the Decline Related to Improvement in Socio economic Conditions?

Here we begin to be on somewhat firmer ground It has long been known that the morbidity and mortality of syphilis, as of tuberculosis, are related to socio economic conditions—poverty, overcrowding due to poor housing, lack of recreational facilities, and the like One of the first studies is a report from the Registrar General in which (fig 7) mortality from syphilis plus paresis, tabes dorsalis, and aneurysm in persons 20–65 years of age in 1930–32 is related to five broad occupational groups (Registrar General 1938) There is a consistent rise with decreasing socio economic status

Schamberg (1945) has made ingenious use of data provided by Usilton et al (1945) concerning the prevalence of syphilis (positive serological tests) among United States male selectees of World War II aged 18–37, and in relating this to tuberculosis mortality in the United States by broad socio economic groups The data, scale adjusted for better comparability, are shown in fig 8 There is a sharp increase both in morbidity of syphilis and mortality of tuberculosis with lowering socio economic status Among unskilled labourers, the prevalence of syphilis is three times as high, and the mortality of tuberculosis fourteen times as high as among professional workers (i e, physicians, attorneys, teachers, architects, &c)

The relationship of syphilitic infection with socio-economic status is clarified further by the data of Kinsey et al (1948) on the sexual behaviour of 5300 white United States males There is reason to believe that the information they provide is applicable, at least in broad general principle, to males in any Western civilisation Exposure to the possibility of syphilitic infection through non marital sexual intercourse varies directly with educational level and occupational class, as may be seen from fig 9 (The data are “ double entry,” based on both the parental class in which the subject originated and the ultimate class into which he independently migrated The relative frequencies of non marital intercourse shown are for young males, aged 16–20, but the same relative positions of frequency hold good for all ages) Potential risk of infection with syphilis (if each episode of non marital intercourse is accepted as a risk) is about ten times greater in persons whose education is limited to primary or even secondary school than in those of college or university level, and about sixteen times greater among unskilled labourers than among professional men Moreover, as Kinsey points out, males of low educational and economic groups are much more liable to exposure with many, rather than few, partners, and the many partners are more likely to be drawn from female groups, including prostitutes, who themselves receive many, rather than

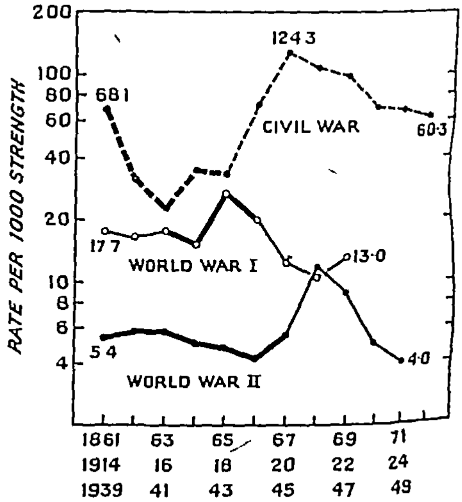


Fig 6—Incidence of early syphilis in the U.S Army at home (troops overseas excluded) during three widely separated decades surrounding three major wars (Surgeon-General, U.S. army) Figures for World War I include cases existing prior to service. Those for World War II exclude such cases.

Note that during the Civil War and World War II, the rise was post war, rather than during mobilisation and/or hostilities, for unexplained reasons, the World War I rise was in an actual combat year Note also, in each case, the fall in rate to or below pre war level within a quintade after the peak

Finally, as pertinent to the effect of modern control measures, note that the starting base line in 1861 was approximately 68 per 1000 strength, in 1914, 17 per 1000, and in 1939, 5 4 per 1000 Note further that the rates of decline after World Wars I and II are substantially steeper than after the Civil War, but that the 1946–49 decline is identical in shape to that of 1918–21 suggesting that penicillin has perhaps provided no special advantage

Compare this curve for World War II (limited to the U S Army at home) with that of fig 17 (entire U S Army, including troops overseas) The rise in troops at home was only from 4 2 to 11 5 per 1000 strength for the army as a whole from 5 8 to 54 per 1000 This comparison strengthens the suggestion that the incidence of syphilis in a military command may be related to that in the immediately surrounding civilian population few, males The infectious risk is thus many times multiplied.

These and other data, directly linking the incidence and prevalence of syphilis to low educational and socio-economic status, suggest the possibility that the decline in syphilis in Western Europe and the United States in the period 1865–1910 was related, in whole or in part, to gradual improvement in both educational and general economic conditions during this period and that any further decline since 1910 may also, at least in part, be so attributed. To some extent, this is certainly true

Special Influence of War and Population Instability on the 1865–1910 Decline

It has been many times shown, and I have emphasised the fact here, that the incidence of fresh infections with syphilis always rises in a country engaged in war, and also in neighbouring or even non neighbouring neutral countries The same phenomenon is observable in periods of serious internal political or economic unrest The war-time rise is always followed by a post war decline, which, within variable periods, brings incidence to or below pre-war level.

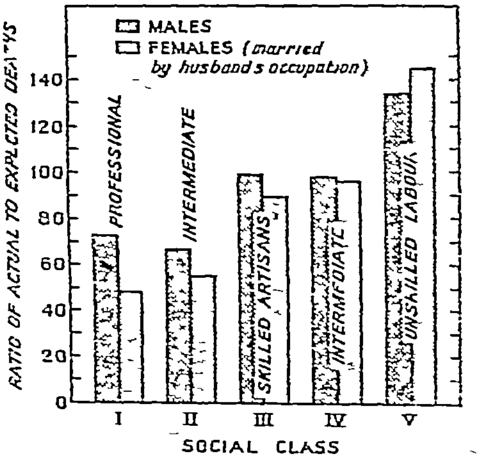


Fig 7—Relation of socio-economic status to the mortality of syphilis in England and Wales 1930–32 (Registrar-General 1938) Ratio of actual to expected deaths (syphilis tabes paresis and aneurysm) by social class ages 20–65

The factor common to war and internal political or economic unrest is population instability Large numbers of males in military service, and of males and females in war industry, are dislocated from their homes Often constantly on the move, they are likewise dislocated from their customary sexual partners marital or non marital There is reason to believe (Kinsey et al. 1948) that individual sexual behaviour, in terms of frequency of sexual intercourse, varies little whether a given population group is stable or unstable, at home or away from home. For purposes of illustration, one may assume that at home the average young United States male, with an average intercourse frequency of 1 2 per week (Kinsey), has his customary 62 contacts per year with one or a few regular partners Away from home, and constantly moving from one locale to another, he may still achieve the same number of contacts, but, as he is temporarily divorced from family and friends, the female partners are of necessity many rather than few, casual rather than regular, and themselves more likely to be exposed to contact with many, rather than few, men The infection risk is thereby enormously multiplied

With demobilisation of armies, and shift from unstable war time to peace time industry, relative population stability is once more restored, regular sexual contact with a few close associates replaces casual contact with many, risk of infection decreases, and the incidence of syphilis falls

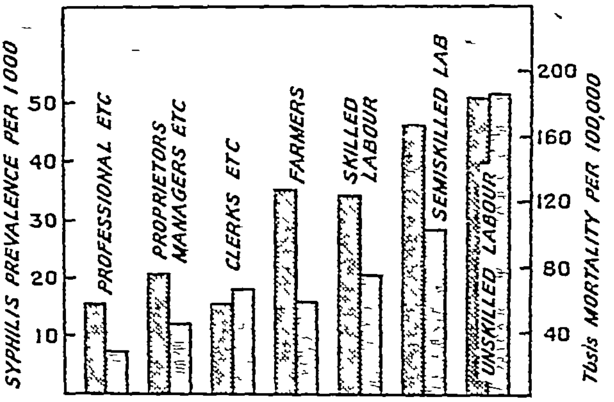


Fig 8—Relation of socio-economic status to the prevalence of syphilis and mortality of tuberculosis (from data gathered by Schamberg 1945)

Indeed, this factor of population stability is almost certainly operative in peace-time as well, and it largely explains the fact that in countries with little internal population shift (e g, Scandinavia, which is also specially distinguished by relatively high educational and socio economic standards), incidence and prevalence of syphilis have always been low as compared with rapidly growing countries (e g., the United States), where migratory labour has been, and still is, an important social phenomenon

TREND OF INCIDENCE OF SYPHILIS SINCE 1910 IN CIVILIAN AND MILITARY POPULATIONS

With 1910 we enter a period in which civilian, as well as military, data begin to become available, and in which, moreover, scientific methods for the control of syphilis began to be applied with ever increasing vigour. It should therefore be possible to determine whether modern methods of syphilis control are of value, and perhaps even to estimate which of them has had greatest effect

Trend of Infection in Civilian Scandinavia

In Denmark and Norway, and to a lesser extent in Sweden and Finland, the trend of syphilis morbidity is known, with apparently a high degree of accuracy, since about the mid-19th century (Clarke 1936, Guthe 1945) The data from Copenhagen, shown in fig 10, may be taken as an example. Here are shown the total number of cases of acquired syphilis reported from 1877 to 1944 Having in mind the absence of effective control measures before 1910, and the probable gradual influence of a

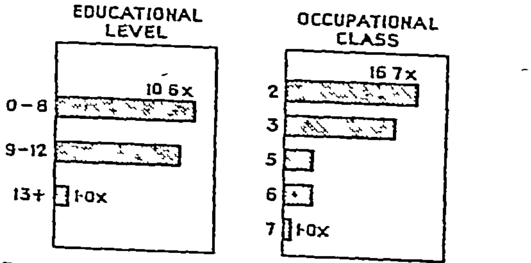


Fig 9—Frequency of extramarital sexual intercourse in males of varying educational level and occupational class (socio-economic status) Reproduced by permission from Kinsey et al. (1948)

Under Educational Level, the figures 0–8 represent persons whose education is limited to primary school level, 9–12 to secondary school, 13 — college or university Occupational Classes represent gradations between unskilled labour (2) and professional groups (7)

Frequencies are relative to the unit 1 0x.

vigorous control campaign beginning in Denmark and Sweden at about that date, one is struck by the relative stability of the Copenhagen curve from 1877 to 1919 (within a fluctuant range of 277–683 per 100,000 population) Beginning in 1919, there was a precipitous decline in incidence in Copenhagen (and also in Sweden, as is shown in fig 11), from a peak of 527 to an average low level of 30–40 per 100,000 population in 1932–42 With the German occupation of Denmark in World War II, the rate rose abruptly to or above its previously recorded peak, and only began to fall once more in 1947

Before accepting the premise that the Danish and Swedish declines in incidence were due to their vigorous control programmes, the cautious epidemiologist will note that both in Norway and in England and Wales, each of which countries followed the Danish and Swedish example only to the extent of an educational programme for the laity and provision of free treatment for all who wished to receive it, there was also a fall in incidence after World War I In Oslo (fig 12) the decline was from 360 per 100,000 population in 1919 to 30 per 100,000 in 1933 (Clarke 1936) In England and Wales (fig 13), there was also an apparent downward trend in incidence from 1918 to 1939 (from a peak of 42,805 cases in 1920 to a low of 11,319 cases in 1940), though the fall was neither so abrupt nor so complete as in Scandinavia In Britain, too, there was a sharp rise, especially in fresh infections, coincident with the outbreak of World War II

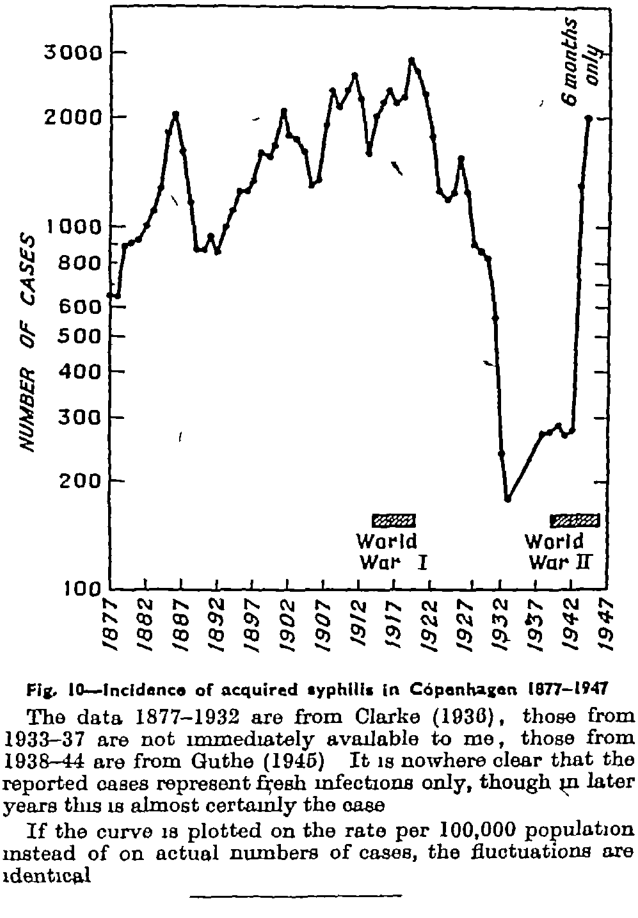


Fig. 10—Incidence of acquired syphilis in Copenhagen 1877–1947

The data 1877–1932 are from Clarke (1936), those from 1933–37 are not immediately available to me, those from 1938–44 are from Guthe (1945) It is nowhere clear that the reported cases represent fresh infections only, though in later years this is almost certainly the case

If the curve is plotted on the rate per 100,000 population instead of on actual numbers of cases, the fluctuations are identical

Parenthetically, there was a simultaneous and nearly parallel fall in the incidence of congenital syphilis in Copenhagen (fig 14), where the control programme was vigorous and in England and Wales (fig 15), where it was not

A similar but less well documented decline in incidence of fresh infections with syphilis also occurred in other countries of Western Europe in the period 1919–40 This was perhaps due in part to sociological changes affecting sex habits following World War I, in part to acceleration by control programmes

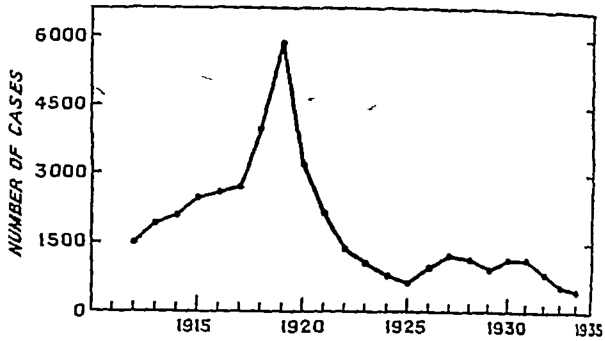


Fig 11—Incidence of syphilis in Sweden 1912–35 (Clarke 1936)

The control programme here was as vigorous as in Denmark Note that the rise during World War I was proportionately much greater than in Copenhagen, but the post-war fall was equally swift

Nevertheless, and disregarding the evidence from other countries, the remarkable decline in Denmark and Sweden, observed to a greater extent than elsewhere in the civilised world, was naturally attributed to the detailed plan of venereal disease control in these countries, which has been so well described by Clarke (1936) and many others The Scandinavian plans have served as the basis for similar and even more extended programmes in other nations, notably the United States

THE UNITED STATES SYPHILIS CONTROL PROGRAMME, WITH PARTICULAR REFERENCE TO THE DECLINE SINCE WORLD WAR II

Although the Armed Services of the United States possessed vigorous control programmes in both world wars, and to a considerably less extent in the interval between them, a nation-wide effort at control was inaugurated only in 1936 by Thomas Parran, then surgeon general, United States Public Health Service (Parran 1936, 1937) His efforts led to the passage by the Congress of the National Venereal Disease Control Act in 1938, to the continuing appropriation of Federal funds for this purpose, and to the stimulation of similar appropriations by State and local communities. For the first year of operation, the Federal appropriation was $3 million, gradually increased to or above its current annual level of about $16 million It is estimated that the total United States expenditure (Federal, State, and local) over the past 13 years for civilian venereal disease

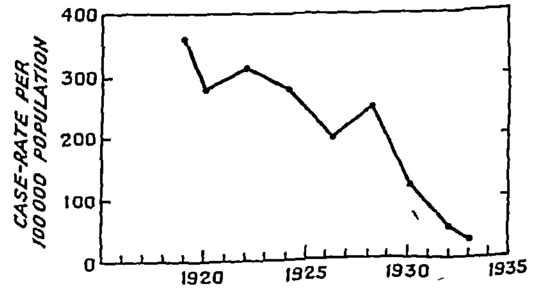


Fig 12—Incidence of syphilis in Norway 1919–33 (Clarke 1936)

In Norway, as in England and Wales (see fig 13), the control programme was much less vigorous than in Denmark and Sweden, but in these two countries, the incidence of syphilis also declined In Norway the rate of fall was not so abrupt as elsewhere in Scandinavia but the end low point in 1933 was about the same control is in excess of $350 million, when the Armed Services are included, the figure probably exceeds $450 million.

The United States venereal disease control programme is primarily directed against syphilis, hopefully but less enthusiastically against gonorrhœa and chancroid, and hardly at all against the lesser venereal infections. Implemented in the United States by the establishment of special venereal disease control divisions in Federal, State, and local health departments and in the Armed Services, it is based on six major avenues of attack. Pursued with varying intensity, these are

1 Methods planned to reduce the number of potentially infectious contacts by modification of human behaviour—i.e., an attack on the 'vector' of venereal disease sexual promiscuity

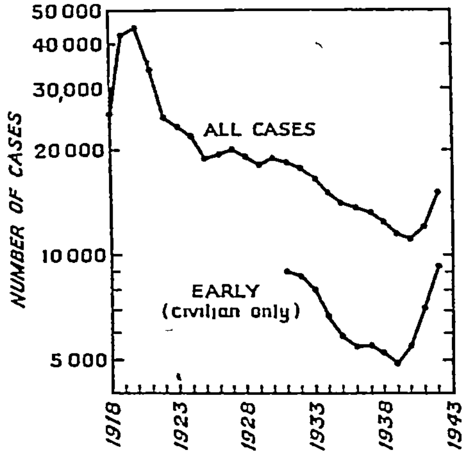


Fig. 13—Incidence of syphilis in England and Wales 1918–42 (Ministry of Health). Cases of syphilis dealt with for the first time at treatment centres.

In the absence of a system of notification, these data are not comparable with Scandinavian figures. Treatment centre statistics vary with economic conditions and are only a rough index to community status.

Note that until 1931, the curve is based on all syphilis, early and late and is therefore inaccurate both as to incidence and prevalence especially since there was no organised programme of case finding. Nevertheless it may be guessed that there was a decline in incidence, which, though starting from a far higher base-line in 1918 than that in Scandinavia was perhaps roughly parallel with the Norwegian decline.

- A. Religious appeals
- B Education of the population both as to sex and venereal disease (of young people in schools, of the public at large, of military personnel, and by various techniques including posters, pamphlets lectures press radio, and motion pictures)
- C Improved housing (relief of overcrowding)
- D The provision of improved recreational facilities for youth.
- E Law enforcement in repression of organised and clandestine prostitution and of facilitators thereof
- F Efforts at the rehabilitation of promiscuous girls (similar efforts in males are conspicuous by their absence)
- G Punishment for the acquisition of venereal disease (especially in the Armed Forces)

2 Methods planned to reduce the probability of infection if exposure occurs

- A. Mechanical chemical, and chemotherapeutic prophylaxis

3 Methods planned to improve the diagnosis and treatment of infected persons.

- A. Improved undergraduate and postgraduate medical education.
- B Improved methods of laboratory diagnosis

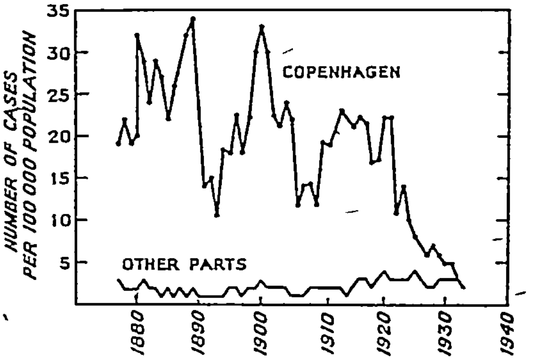


Fig 14—Incidence of congenital syphilis in Denmark 1878–1933 (Clarke 1936)

- C Improved methods of the use of chemotherapeutic agents and the introduction of new ones

4 Methods planned to promote diagnosis and treatment

- A. Increase in the number of serodiagnostic laboratories and their ready availability to physicians without cost to the patient
- B Increase in the number, and improvement in the calibre, of treatment centres, and their ready accessibility without, or at minimum, cost to the patient

5 Methods to increase the number of infected persons brought under treatment and to hold them there until completion (case finding and case holding)

- A. Mass blood-testing
- B The epidemiological approach to the discovery of new cases by examination of familial and sexual contacts of infected persons
- C Intensive efforts at case holding, to ensure that the maximum number of patients are treated "past the point of infectiousness" or "adequately for cure."

6 Medical research

THE RESULTS OF SYPHILIS CONTROL IN THE UNITED STATES

Incidence of Early Syphilis

Only since 1941 are there data from the entire United States concerning the number of cases of early syphilis in the civilian population, reported to the United States Public Health Service through State and territorial health departments. In earlier years, and then only incompletely after 1919, syphilis was reported without a breakdown between fresh infections and late syphilis. The picture 1941–49 is presented in fig 16, in which are shown the rates per 1000 population. Three curves are presented (*a*) for "open lesion" (i e, primary and secondary) early syphilis, (*b*) for early latent syphilis, and (*c*) a summation of these two (By administrative

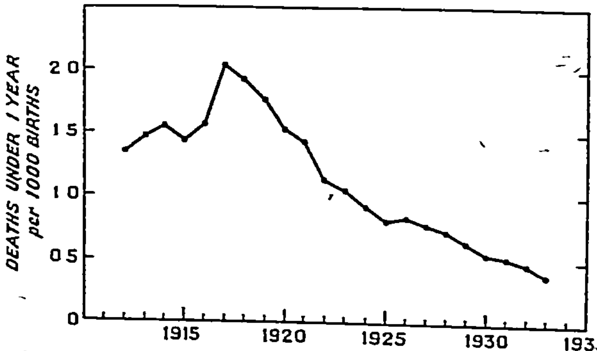


Fig. 15—Mortality-rate of congenital syphilis in England and Wales 1912–33 (Clarke 1936)

Note that the scale here (per 1000 live births) is not comparable to the Danish scale of fig 14 (per 100 000 population), but the same downward trend is apparent, in spite of less vigorous control measures vigorous control campaign beginning in Denmark and Sweden at about that date, one is struck by the relative stability of the Copenhagen curve from 1877 to 1919 (within a fluctuant range of 277–683 per 100,000 population). Beginning in 1919, there was a precipitous decline in incidence in Copenhagen (and also in Sweden, as is shown in fig. 11), from a peak of 527 to an average low level of 30–40 per 100,000 population in 1932–42. With the German occupation of Denmark in World War II, the rate rose abruptly to or above its previously recorded peak, and only began to fall once more in 1947.

Before accepting the premise that the Danish and Swedish declines in incidence were due to their vigorous control programmes, the cautious epidemiologist will note that both in Norway and in England and Wales, each of which countries followed the Danish and Swedish example only to the extent of an educational programme for the laity and provision of free treatment for all who wished to receive it, there was also a fall in incidence after World War I. In Oslo (fig. 12) the decline was from 360 per 100,000 population in 1919 to 30 per 100,000 in 1933 (Clarke 1936). In England and Wales (fig. 13), there was also an apparent downward trend in incidence from 1918 to 1939 (from a peak of 42,805 cases in 1920 to a low of 11,319 cases in 1940), though the fall was neither so abrupt nor so complete as in Scandinavia. In Britain, too, there was a sharp rise, especially in fresh infections, coincident with the outbreak of World War II.

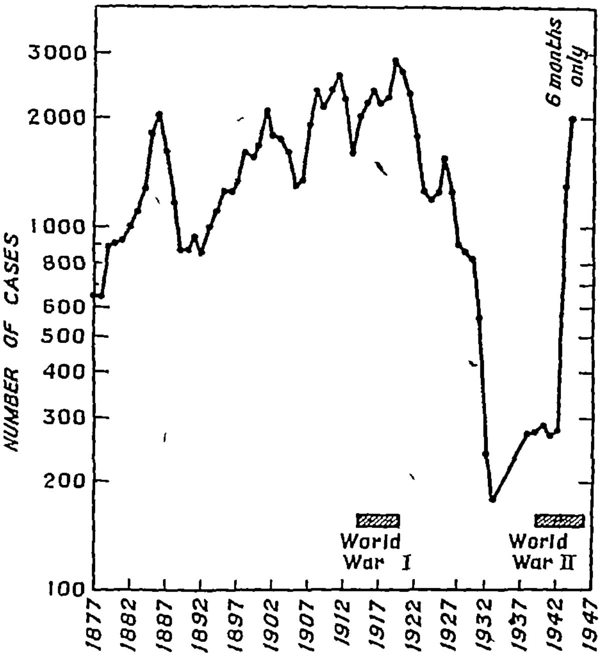


Fig. 10—Incidence of acquired syphilis in Copenhagen 1877–1947.

The data 1877–1932 are from Clarke (1936), those from 1933–37 are not immediately available to me, those from 1938–44 are from Guthe (1945). It is nowhere clear that the reported cases represent fresh infections only, though in later years this is almost certainly the case.

If the curve is plotted on the rate per 100 000 population instead of on actual numbers of cases, the fluctuations are identical.

Parenthetically, there was a simultaneous and nearly parallel fall in the incidence of congenital syphilis in Copenhagen (fig. 14), where the control programme was vigorous, and in England and Wales (fig. 15), where it was not.

A similar but less well documented decline in incidence of fresh infections with syphilis also occurred in other countries of Western Europe in the period 1919–40. This was perhaps due in part to sociological changes affecting sex habits following World War I, in part to acceleration by control programmes.

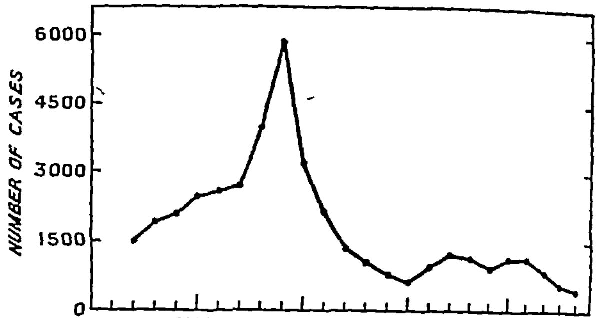


Fig. 11—Incidence of syphilis in Sweden 1912–35 (Clarke 1936).

The control programme here was as vigorous as in Denmark. Note that the rise during World War I was proportionately much greater than in Copenhagen, but the post-war fall was equally swift.

Nevertheless, and disregarding the evidence from other countries, the remarkable decline in Denmark and Sweden, observed to a greater extent than elsewhere in the civilised world, was naturally attributed to the detailed plan of venereal disease control in these countries, which has been so well described by Clarke (1936) and many others. The Scandinavian plans have served as the basis for similar and even more extended programmes in other nations, notably the United States.

THE UNITED STATES SYPHILIS CONTROL PROGRAMME, WITH PARTICULAR REFERENCE TO THE DECLINE SINCE WORLD WAR II

Although the Armed Services of the United States possessed vigorous control programmes in both world wars, and to a considerably less extent in the interval between them, a nation-wide effort at control was inaugurated only in 1936 by Thomas Parran, then surgeon general, United States Public Health Service (Parran 1936, 1937). His efforts led to the passage by the Congress of the National Venereal Disease Control Act in 1938, to the continuing appropriation of Federal funds for this purpose, and to the stimulation of similar appropriations by State and local communities. For the first year of operation, the Federal appropriation was $3 million, gradually increased to or above its current annual level of about $16 million. It is estimated that the total United States expenditure (Federal, State, and local) over the past 13 years for civilian venereal disease

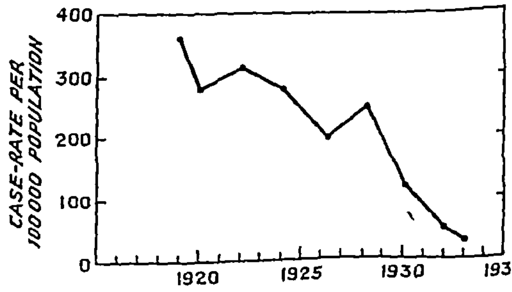


Fig. 12—Incidence of syphilis in Norway 1919–33 (Clarke 1936).

In Norway, as in England and Wales (see fig. 13), the control programme was much less vigorous than in Denmark and Sweden, but in these two countries, the incidence of syphilis also declined. In Norway, the rate of fall was not so abrupt as elsewhere in Scandinavia, but the end low point in 1933 was about the same.

control is in excess of $350 million, when the Armed Services are included, the figure probably exceeds $450 million

The United States venereal disease control programme is primarily directed against syphilis, hopefully but less enthusiastically against gonorrhœa and chancroid, and hardly at all against the lesser venereal infections Implemented in the United States by the establishment of special venereal disease control divisions in Federal, State, and local health departments and in the Armed Services, it is based on six major avenues of attack Pursued with varying intensity, these are

1 Methods planned to reduce the number of potentially infectious contacts by modification of human behaviour—i.e., an attack on the 'vector' of venereal disease sexual promiscuity

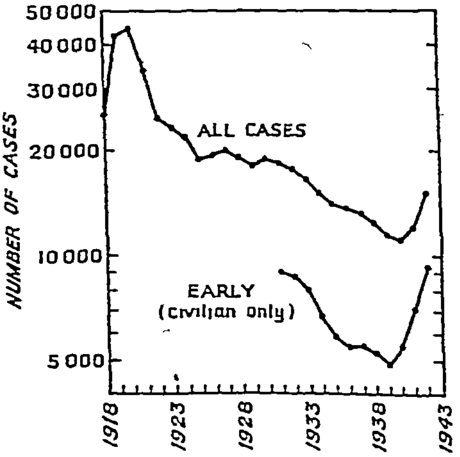


Fig. 13—Incidence of syphilis in England and Wales 1918–42 (Ministry of Health) Cases of syphilis dealt with for the first time at treatment centres.

In the absence of a system of notification, these data are not comparable with Scandinavian figures Treatment centre statistics vary with economic conditions and are only a rough index to community status

Note that until 1931, the curve is based on all syphilis, early and late and is therefore inaccurate both as to incidence and prevalence, especially since there was no organised programme of case finding Nevertheless it may be guessed that there was a decline in incidence, which, though starting from a far higher base-line in 1918 than that in Scandinavia was perhaps roughly parallel with the Norwegian decline

---

A. Religious appeals

B Education of the population, both as to sex and venereal disease (of young people in schools of the public at large of military personnel and by various techniques including posters pamphlets, lectures, press, radio, and motion pictures)

C Improved housing (relief of overcrowding)

D The provision of improved recreational facilities for youth.

E Law enforcement in repression of organised and clandestine prostitution and of facilitators thereof

F Efforts at the rehabilitation of promiscuous girls (similar efforts in males are conspicuous by their absence)

G Punishment for the acquisition of venereal disease (especially in the Armed Forces)

2 Methods planned to reduce the probability of infection if exposure occurs

A Mechanical chemical, and chemotherapeutic prophylaxis

3 Methods planned to improve the diagnosis and treatment of infected persons.

A. Improved undergraduate and postgraduate medical education.

B Improved methods of laboratory diagnosis

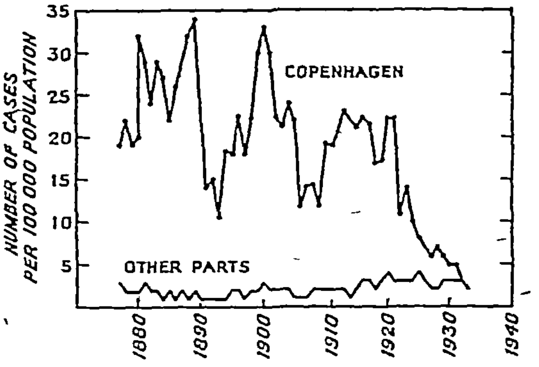


Fig 14—Incidence of congenital syphilis in Denmark 1878–1933 (Clarke 1936)

C Improved methods of the use of chemotherapeutic agents and the introduction of new ones

4 Methods planned to promote diagnosis and treatment

A. Increase in the number of serodiagnostic laboratories and their ready availability to physicians without cost to the patient

B Increase in the number and improvement in the calibre, of treatment centres and their ready accessibility without, or at minimum, cost to the patient

5 Methods to increase the number of infected persons brought under treatment and to hold them there until completion (case finding and case holding)

A. Mass blood testing

B The epidemiological approach to the discovery of new cases by examination of familial and sexual contacts of infected persons

C Intensive efforts at case holding, to ensure that the maximum number of patients are treated "past the point of infectiousness" or adequately for cure."

6 Medical research

THE RESULTS OF SYPHILIS CONTROL IN THE UNITED STATES

Incidence of Early Syphilis

Only since 1941 are there data from the entire United States concerning the number of cases of early syphilis in the civilian population, reported to the United States Public Health Service through State and territorial health departments In earlier years, and then only incompletely after 1919, syphilis was reported without a breakdown between fresh infections and late syphilis. The picture 1941–49 is presented in fig 16, in which are shown the rates per 1000 population. Three curves are presented (*a*) for "open lesion" (i e, primary and secondary) early syphilis (*b*) for early latent syphilis, and (*c*) a summation of these two (By administrative

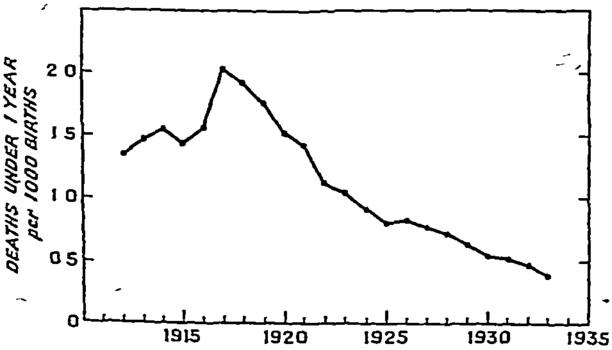


Fig. 15—Mortality-rate of congenital syphilis in England and Wales 1912–33 (Clarke 1936)

Note that the scale here (per 1000 live births) is not comparable to the Danish scale of fig 14 (per 100 000 population) but the same downward trend is apparent, in spite of less vigorous control measures vigorous control campaign beginning in Denmark and Sweden at about that date, one is struck by the relative stability of the Copenhagen curve from 1877 to 1919 (within a fluctuant range of 277–683 per 100,000 population) Beginning in 1919, there was a precipitous decline in incidence in Copenhagen (and also in Sweden, as is shown in fig 11), from a peak of 527 to an average low level of 30–40 per 100,000 population in 1932–42 With the German occupation of Denmark in World War II, the rate rose abruptly to or above its previously recorded peak, and only began to fall once more in 1947

Before accepting the premise that the Danish and Swedish declines in incidence were due to their vigorous control programmes, the cautious epidemiologist will note that both in Norway and in England and Wales, each of which countries followed the Danish and Swedish example only to the extent of an educational programme for the laity and provision of free treatment for all who wished to receive it, there was also a fall in incidence after World War I In Oslo (fig 12) the decline was from 360 per 100,000 population in 1919 to 30 per 100,000 in 1933 (Clarke 1936) In England and Wales (fig 13), there was also an apparent downward trend in incidence from 1918 to 1939 (from a peak of 42,805 cases in 1920 to a low of 11,319 cases in 1940), though the fall was neither so abrupt nor so complete as in Scandinavia In Britain, too, there was a sharp rise, especially in fresh infections, coincident with the outbreak of World War II

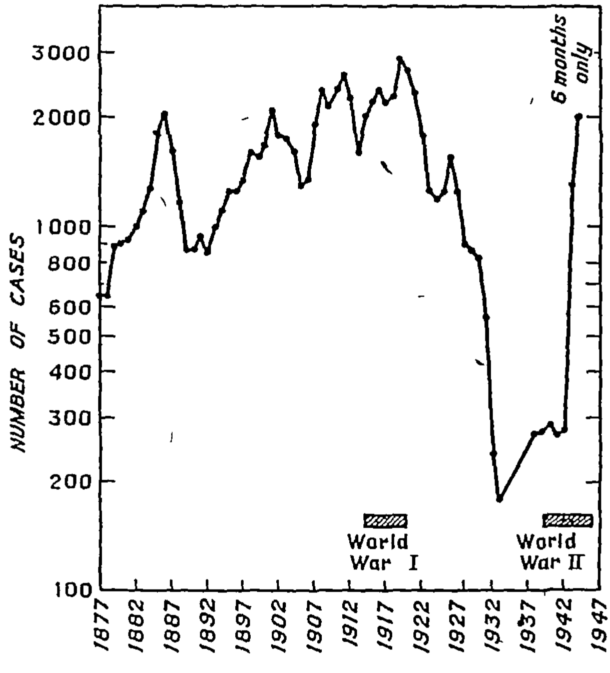


Fig 10—Incidence of acquired syphilis in Copenhagen 1877–1947

The data 1877–1932 are from Clarke (1936), those from 1933–37 are not immediately available to me, those from 1938–44 are from Guthe (1945) It is nowhere clear that the reported cases represent fresh infections only, though in later years this is almost certainly the case

If the curve is plotted on the rate per 100,000 population instead of on actual numbers of cases, the fluctuations are identical

Parenthetically, there was a simultaneous and nearly parallel fall in the incidence of congenital syphilis in Copenhagen (fig 14), where the control programme was vigorous, and in England and Wales (fig 15), where it was not

A similar but less well documented decline in incidence of fresh infections with syphilis also occurred in other countries of Western Europe in the period 1919–40 This was perhaps due in part to sociological changes affecting sex habits following World War I, in part to acceleration by control programmes

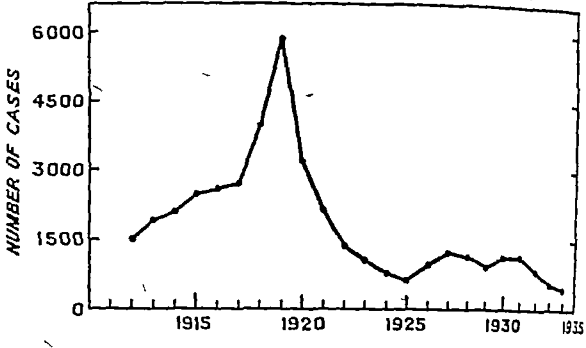


Fig 11—Incidence of syphilis in Sweden 1912–35 (Clarke 1936)

The control programme here was as vigorous as in Denmark Note that the rise during World War I was proportionately much greater than in Copenhagen, but the post-war fall was equally swift

Nevertheless, and disregarding the evidence from other countries, the remarkable decline in Denmark and Sweden, observed to a greater extent than elsewhere in the civilised world, was naturally attributed to the detailed plan of venereal disease control in these countries, which has been so well described by Clarke (1936) and many others The Scandinavian plans have served as the basis for similar and even more extended programmes in other nations, notably the United States

THE UNITED STATES SYPHILIS CONTROL PROGRAMME, WITH PARTICULAR REFERENCE TO THE DECLINE SINCE WORLD WAR II

Although the Armed Services of the United States possessed vigorous control programmes in both world wars, and to a considerably less extent in the interval between them, a nation-wide effort at control was inaugurated only in 1936 by Thomas Parran, then surgeon general, United States Public Health Service (Parran 1936, 1937) His efforts led to the passage by the Congress of the National Venereal Disease Control Act in 1938, to the continuing appropriation of Federal funds for this purpose, and to the stimulation of similar appropriations by State and local communities. For the first year of operation, the Federal appropriation was $3 million, gradually increased to or above its current annual level of about $16 million It is estimated that the total United States expenditure (Federal, State, and local) over the past 13 years for civilian venereal-disease

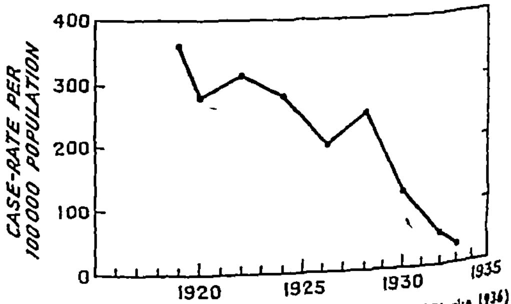


Fig 12—Incidence of syphilis in Norway 1919–33 (Clarke 1936)

In Norway, as in England and Wales (see fig 13), the control programme was much less vigorous than in Denmark and Sweden, but in these two countries, the incidence of syphilis also declined In Norway, the rate of fall was not so abrupt as elsewhere in Scandinavia, but the end low point in 1933 was about the same ntrol is in excess of $350 million, when the Armed rvices are included, the figure probably exceeds 50 million

The United States venereal-disease control programme primarily directed against syphilis, hopefully but less thusiastically against gonorrhœa and chancroid, and rdly at all against the lesser venereal infections nplemented in the United States by the establishment special venereal-disease control divisions in Federal, ate, and local health departments and in the Armed ervices, it is based on six major avenues of attack ursued with varying intensity, these are

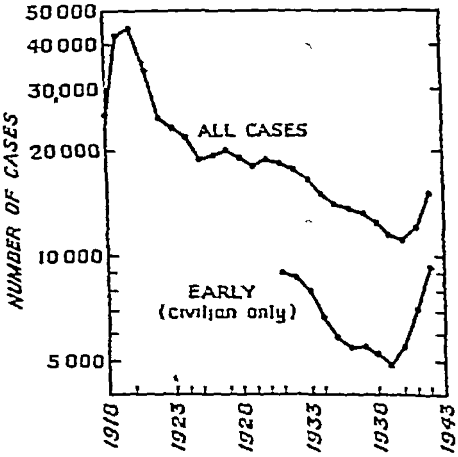


Fig. 13—Incidence of syphilis in England and Wales 1918–42 (Ministry of Health) Cases of syphilis dealt with for the first time at treatment centres.

In the absence of a system of notification, these data are not comparable with Scandinavian figures Treatment centre statistics vary with economic conditions and are only a rough index to community status.

Note that until 1931 the curve is based on all syphilis, early and late and is therefore inaccurate both as to incidence and prevalence especially since there was no organised programme of case finding Nevertheless it may be guessed that there was a decline in incidence, which, though starting from a far higher base-line in 1918 than that in Scandinavia was perhaps roughly parallel with the Norwegian decline

1 Methods planned to reduce the number of potentially fectious contacts by modification of human behaviour—i.e., an attack on the "vector" of venereal disease sexual promiscuity

- A. Religious appeals.
- B Education of the population, both as to sex and venereal disease (of young people in schools, of the public at large of military personnel, and by various techniques including posters pamphlets, lectures, press, radio, and motion pictures)
- C. Improved housing (relief of overcrowding)
- D The provision of improved recreational facilities for youth.
- E Law enforcement, in repression of organised and clandestine prostitution and of facilitators thereof.
- F Efforts at the rehabilitation of promiscuous girls (similar efforts in males are conspicuous by their absence)
- G Punishment for the acquisition of venereal disease (especially in the Armed Forces)

2. Methods planned to reduce the probability of infection if exposure occurs

- A. Mechanical, chemical, and chemotherapeutic prophylaxis.

3 Methods planned to improve the diagnosis and treatment of infected persons.

- A. Improved under-graduate and postgraduate medical education.
- B Improved methods of laboratory diagnosis

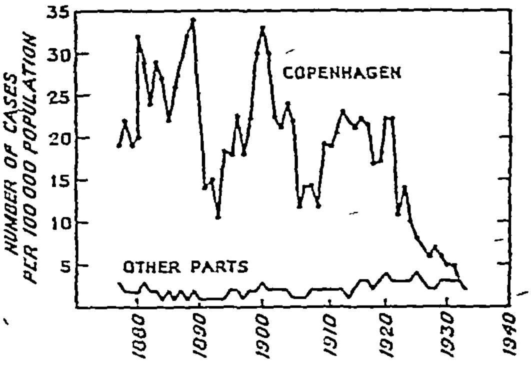


Fig 14—Incidence of congenital syphilis in Denmark 1878–1933 (Clarke 1936)

- C Improved methods of the use of chemotherapeutic agents and the introduction of new ones.

4 Methods planned to promote diagnosis and treatment

- A. Increase in the number of serodiagnostic laboratories and their ready availability to physicians without cost to the patient
- B Increase in the number and improvement in the calibre of treatment centres, and their ready accessibility without or at minimum, cost to the patient

5 Methods to increase the number of infected persons brought under treatment and to hold them there until completion (case finding and case holding)

- A. Mass blood testing
- B The epidemiological approach to the discovery of new cases by examination of familial and sexual contacts of infected persons
- C Intensive efforts at case holding, to ensure that the maximum number of patients are treated "past the point of infectiousness or adequately for cure"

6 Medical research.

THE RESULTS OF SYPHILIS CONTROL IN THE UNITED STATES

Incidence of Early Syphilis

Only since 1941 are there data from the entire United States concerning the number of cases of early syphilis in the civilian population reported to the United States Public Health Service through State and territorial health departments In earlier years, and then only incompletely after 1919, syphilis was reported without a breakdown between fresh infections and late syphilis. The picture 1941–49 is presented in fig 16, in which are shown the rates per 1000 population. Three curves are presented (*a*) for "open lesion" (i.e, primary and secondary) early syphilis, (*b*) for early latent syphilis, and (*c*) a summation of these two (By administrative

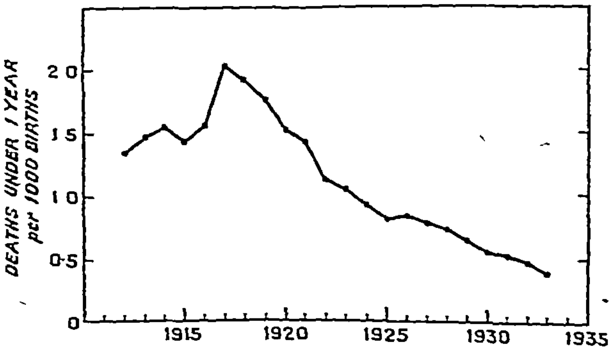


Fig. 15—Mortality-rate of congenital syphilis in England and Wales 1912–33 (Clarke 1936)

Note that the scale here (per 1000 live births) is not comparable to the Danish scale of fig 14 (per 100 000 population) but the same downward trend is apparent, in spite of less vigorous control measures decision, the term "early latent" syphilis is applied to those patients who give a reasonably clear cut history of infection within 4 years, or, as is usually the case, with history lacking, to persons under the age of 25 who are found to be seropositive)

In the 9 year period covered by fig 16, there were reported 730,700 cases of primary and secondary syphilis, and 1,020,000 cases of early latent syphilis —an annual average respectively of 81,200 and 113,300

A point of epidemiological importance to be deduced from the data of fig 16 is that more than one half (actually about 60%) of persons infected with early syphilis do not come under medical care at the time of recognisable infectious lesions, and this in spite of intensive efforts at case finding The reasons for this have been shown (Spoto and Iskrant 1949) to depend in part (at least 35%) on the relatively silent, trivial, and insignificant lesions of early syphilis, which are unrecognised or misinterpreted by the patient or his physician, and in larger part to the patient's ignorance or fear

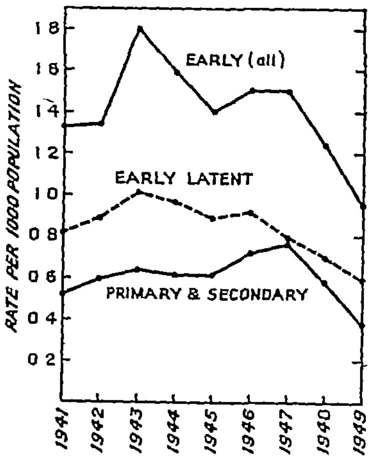


Fig 16—Incidence of early syphilis in U.S civilians 1941–49

Data as to incidence of early syphilis are not available in the United States before 1941 For a discussion of these curves, see text

The demonstrable fact that in the United States, and presumably in other countries as well, more than half of recently infected persons do not reach medical attention during the period of their maximum infectiousness for others is a serious, though not necessarily an insuperable, obstacle to the complete control of the disease Steps to be taken to remedy the situation lie clearly, as will be shown, in increased emphasis on case finding and on lay and medical education

Fig 16 shows also that there was a rise in the incidence of primary and secondary syphilis from 1941 to 1947, especially notable in the two immediate post war years, followed by a decline beginning in late 1947 which has been continuous since From the peak 1947 level, discovery rates have fallen by 34%, from the 1941 base line (if it is a base line) by 16% The decline continued through the first half of 1950 (detailed figures not yet available)

In Fig 17 are shown comparable curves for all early syphilis in the civilian United States population, and for all reported syphilis (mostly early syphilis, since pre existing infection in men inducted into military service is excluded) in the United States Army at home and overseas for the years 1941–49 The scale differs, since the Army rate, among young males, is from five to fifteen times the rate among civilians of both sexes and all ages The sharp post war rise from 1944 to 1947 is much more obvious in the military group, largely because of the inclusion of cases in troops on foreign service, as is the abruptness of the decline since 1947

The fall in incidence rate of early syphilis has attracted much attention within the past 18 months, first as to whether it is a genuine phenomenon, and if so, as to its cause Of these points, more later

THE DISCOVERY OF LATE SYPHILIS

A by product of attempted control of the incidence of early syphilis is the discovery of the prevalence of late syphilis, and the probable effect of this on mortality The rapid increase in the discovery rate of syphilis as a whole (not early syphilis) after 1936, which marked the inception of the control campaign in the United States (and the passage—in Connecticut—of the first of the premarital blood testing laws, which, with similar prenatal laws, now apply in 39 of the 48 States) is shown in fig 18 This rise is a direct reflection of mass blood testing The number of persons newly discovered probably to have syphilis by this procedure can be estimated only, but in the last 12 years must exceed 2 million That most of these had late, rather than early, infections is relatively unimportant, since the application of treatment to these long established cases has almost certainly been a major factor in the reduction, presently to be discussed, in infant and adult mortality rates and in admissions to mental hospitals That the previously undiscovered reservoir of late syphilis in the United States is probably diminishing is further suggested by the curves of fig 19, from 1941 to mid 1949 The discovery rate of late syphilis reached its peak in 1943 (blood testing of all selective service registrants), then fell abruptly, and has levelled off since mid-1947

MORTALITY FROM SYPHILIS

The most careful study of mortality of recent record is that of Kahn and Iskrant (1948) These authors present trends in the United States, beginning with 1933, the first year in which the whole country was included in the vital statistics registration area. The curves are based upon tabulation of death certificates by the National Office of Vital Statistics As deaths due to

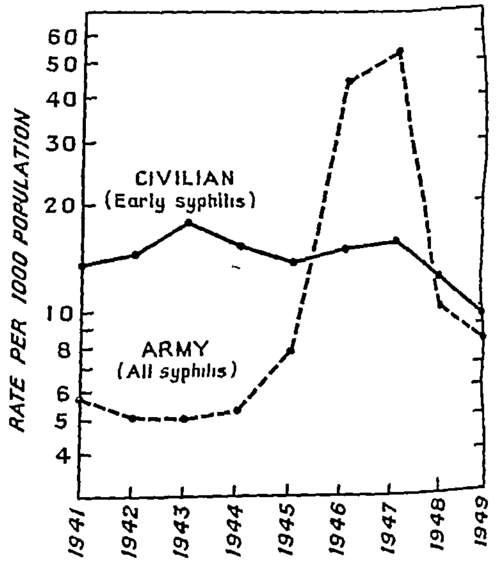


Fig 17—Military versus civilian incidence of early syphilis in the United States 1941–49 (Surgeon-General, U.S Army, U.S. Public Health Service)

The U S army rate includes all syphilis, latent and late as well as early, but since inductees (cases existing prior to service) are excluded, 90+% of all cases represent fresh infections

That the military rate is about 10 times the civilian rate is based on the selected population of the former (all young males) as contrasted with the inclusion of both sexes and all ages in the latter

Much of the sharp post-war military increase is accounted for by the fact that overseas troops, as well as those at home, are included Compare this curve with that of fig 6, which includes only the U S Army in the continental United States

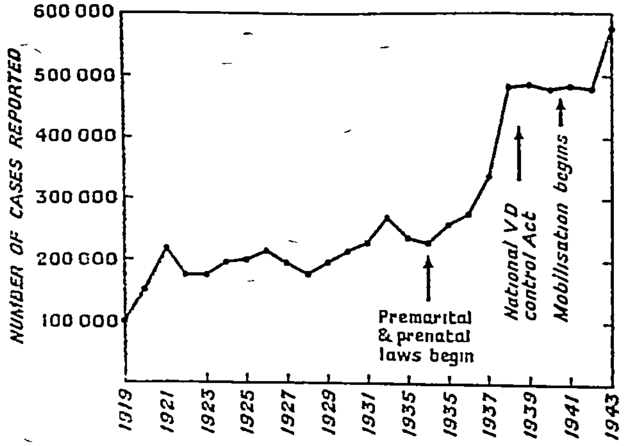


Fig 18—Effect of mass blood testing on the discovery rate of syphilis. All cases reported to U.S. Public Health Service (excluding military cases 1941–43)

Mass blood testing was stimulated, in medical agencies and in industry, as early as 1934, but it began in earnest with the rapid passage of compulsory premarital and prenatal blood testing laws in 1936, and with the routine use of blood tests by selective service in 1941.

---

syphilis, the authors include all those in which this disease was recorded by name as the primary cause, plus all those due to paresis, tabes dorsalis, and aneurysm (this latter only since 1939). The death rate so computed is minimal, since it omits all deaths from cardiovascular or neurosyphilis other than the three particularly named or from syphilis of other organs unless syphilis was specifically recorded (e.g., hepatitis). It must be emphasised that these recent death rates are in part a reflection of the incidence of syphilis some two decades earlier and in part a reflection of the effectiveness of modern treatment in preventing death from syphilis.

Kahn and Iskrant recognise the inadequacy, deliberate or unconscious, of reporting syphilis as a cause of death, but say:

> 'It seems probable that during this 13 year period, physicians have become more able and more willing to report syphilis as a cause of death, rather than less able and less willing to do so. Thus, the downward trend in syphilis rates during the last 9 years is considered to be indicative of real decreases rather than of poorer reporting.'

These data have been now brought through 1948 (United States Public Health Service 1950) with total mortality for 1949 estimated, and are graphically shown in fig. 20. Separate curves are shown for total mortality from syphilis and for paresis, tabes dorsalis, and aneurysm. Each curve, in order to show comparative trends, starts at its approximate peak as of 1933 (except for aneurysm, which was first recorded as a separate cause of death in 1939), percentage figures per 100,000 adjusted on the ordinate. The mortality from syphilis as a whole began a definite fall in 1938, the year of passage of the National Venereal Disease Control Act. Kahn and Iskrant believe that the downward trend in over all mortality is "highly reliable, since known factors (ageing of the population and redefinition of aneurysm) and probable improved reporting by physicians have all exerted an upward force on the rate during this period."

By an ingenious computation, Kahn and Iskrant estimate further that in 1933 the white population of the United States lost 290,000 years of life from the mortality due to syphilis, whereas by 1944 (allowing for the differences in life tables), this had been reduced to 201,000—a saving of 89,000 life years!

The over all mortality curve from syphilis in adults is further compared in fig. 21 with those for infant mortality from syphilis per 1000 live births, and for admission rates to mental hospitals due to syphilis per 100,000 population. The trend in all is downwards, that for infant mortality the most precipitous.

Although the death-rate from syphilis is apparently decreasing in the United States, it is emphasised (United States Public Health Service 1947) that in 1944 (at a level of 11.3 per 100,000 population) there were still more recorded deaths from this cause than from all the following diseases combined: poliomyelitis, rheumatic fever (probably excluding rheumatic heart disease, though not so specified), malaria, diphtheria, acute bacterial meningitis, typhoid and paratyphoid fevers, pertussis, scarlet fever, puerperal septicæmia, and dysentery (whether including the group of infant diarrhœa not specified). Moreover, Aufranc (1951) points out, that in spite of these declines, there were still, in 1949, among the American people, 14,000 infantile infections, and 6000 psychiatric hospital admissions due to syphilis.

EVALUATION OF COMPONENT PARTS OF A SYPHILIS CONTROL PROGRAMME

The Venereal Disease Division of the United States Public Health Service has prepared or stimulated many studies of the efficacy and relative cost of particular control measures. Holding other factors so far as possible equal, a public health experiment can be varied so as to permit at least a short term "spot" estimate of its usefulness. I have elsewhere (Moore 1951b) considered the available evidence in some detail, and will repeat only brief conclusions here.

Most of *the methods planned to reduce potentially infectious contacts* (*group I above*) represent community, rather than primarily medical or public health, effort. Some of these (religious appeals, elevation of general educational, socio economic, and recreational standards) are long-term rather than short-term and are largely intangible of measurement. Specific education of the public as to syphilis is difficult of evaluation but demonstrably effective and essential, even though expensive. Repression of prostitution is of some, but not decisive, value, especially for civilian populations. Punishment is useless and actually harmful.

Methods to reduce probability of infection if exposure occurs—i.e., prophylaxis—require a brief word. Chemical prophylaxis, as used in military practice for 40 years,

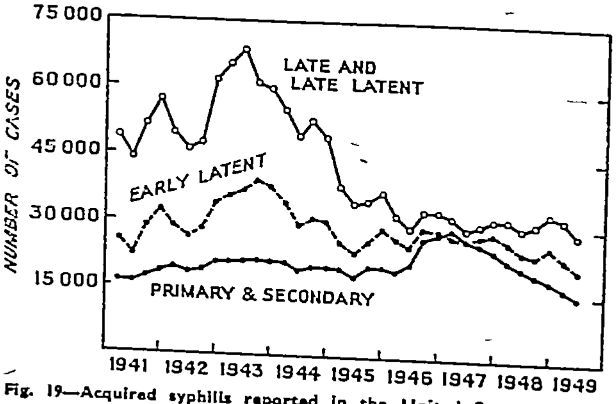


Fig. 19—Acquired syphilis reported in the United States 1941–49. Known military cases excluded.

Note the peaks of late, late latent and early latent syphilis in 1943. These are for the most part cases discovered by mass blood testing. The fall in late syphilis since 1943 suggests that the reservoir of previously undiscovered cases may be diminishing.

It is difficult to explain why the curve for early latent syphilis has not paralleled the downward trend of manifest early syphilis since early 1947.

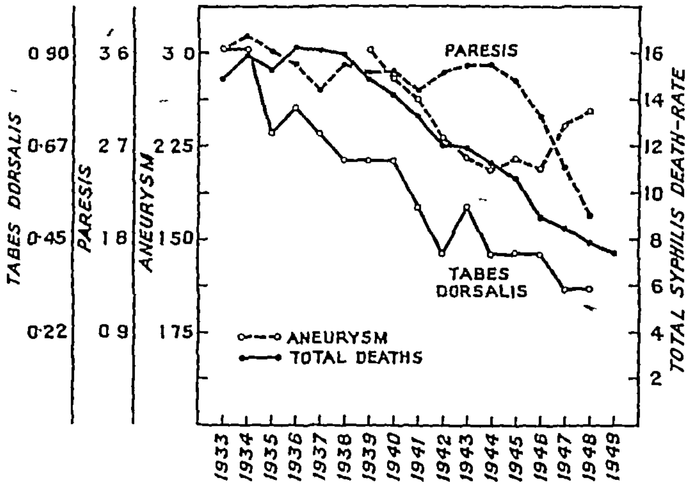


Fig 20—Reported mortality from acquired syphilis in the United States 1933–49 (curves adapted from U S Public Health Service 1947, 1950) Each curve is per 100,000 population, the ordinate percentages adjusted so that all curves start at about the same point.

See text for description There are curious discrepancies between the curves for, for example, tabes dorsalis, paresis, and aneurysm The fall in tabes deaths began in 1934, that in paresis not until a decade later Both of these have been continuous, while the curve for aneurysm, after an initial fall, seems to be rising again

is not applicable in civilian life, and is in any case nearly worthless and should be abandoned Mechanical condom prophylaxis is certainly of value, but its effect cannot be measured Penicillin prophylaxis by the oral route is effective against gonorrhœa, but not yet shown to be applicable to syphilis In civilian as opposed to military populations, any form of prophylaxis is a weak reed to lean upon

Methods to improve diagnosis and treatment of infected persons are of major importance In the United States, medical education as to syphilis, both undergraduate and postgraduate, has greatly improved in the last two decades New and improved methods of serodiagnosis have been introduced—e g, cardiolipin antigen, the discovery of treponemal immobilising antibody Performance of serological tests has been immeasurably bettered by national and local serological surveys New chemotherapeutic methods—at first, improved schemes of use of arsenic and bismuth, and since 1943, the introduction of antibiotics (especially penicillin, but also including 'Aureomycin,' chloramphenicol, and 'Terramycin')—have completely revolutionised the treatment of syphilis

PENICILLIN IN SYPHILIS CONTROL

A special word as to *penicillin* is necessary This drug proved to be effective in syphilis in 1943, had been adopted by the United States Armed Services by late 1944, and was in sufficient supply to become a factor in civilian life by 1946 It has provided a rapid, safe, and inexpensive method of treatment, so much more efficient in mass practice than arsenic and bismuth that these latter drugs have been practically abandoned in the United States It is now established that in primary and secondary syphilis, considered together, the "cure" rate is 80–85% at the end of 3 years, provided the drug is administered in such a manner as to produce a continuous detectable blood level for about 10 days The scheme of treatment does not seem greatly to matter if this requirement is fulfilled Since treatment is quick, safe, non toxic, almost completely painless and inexpensive and causes little loss of time all patients complete treatment For the individual patient the chance of cure is somewhat less, and the risk of infectious relapse and/or reinfection somewhat greater, than if he receives 6 months continuous metal chemotherapy, including 40 injections of arsenoxide and 20 of bismuth For the mass of patients, however, the over all chance of cure is greater, since in pre penicillin United States civilian practice few patients had the optimum amount of metal chemotherapy

In respect of penicillin treatment of early syphilis, however, there is an important unsolved public health problem of infectiousness The cumulative incidence of infectious relapse and/or reinfection (which cannot be clearly differentiated) is at least 10% with any satisfactory system of penicillin treatment so far devised This compares with an incidence of 1 75% (Sternberg and Leifer 1947) in a large series of patients treated semi intensively with 26 weeks' 'Mapharsen' bismuth in the United States Army The issue is raised as to whether the total man days of potential infectiousness due to relapse and/or reinfection after penicillin treatment may not actually be greater than after metal chemotherapy (assuming, of course, which is not the case, that all patients actually completed the desired amount of the latter) If it were not for the troublesome 10% incidence of relapse and/or reinfection, one might expect the general use of penicillin to be reflected in a break in the chain of infection, and a lowering of incidence rate Indeed, this explanation of the recent fall in incidence has been advanced in the United States It has been seriously said, verbally if not in print, that penicillin is the final answer, to be shortly effective in eradicating syphilis altogether or relegating it to the minor status of typhoid fever As yet, however, the epidemiologist is unprepared to accept this glowing optimism He must examine the rest of the evidence

In the United States, *methods to increase the availability of diagnostic and treatment facilities* have been outstandingly successful, and it is for this phase of the programme that most of the syphilis control dollar has been spent It is now possible for an infected person anywhere in the United States to receive comparatively

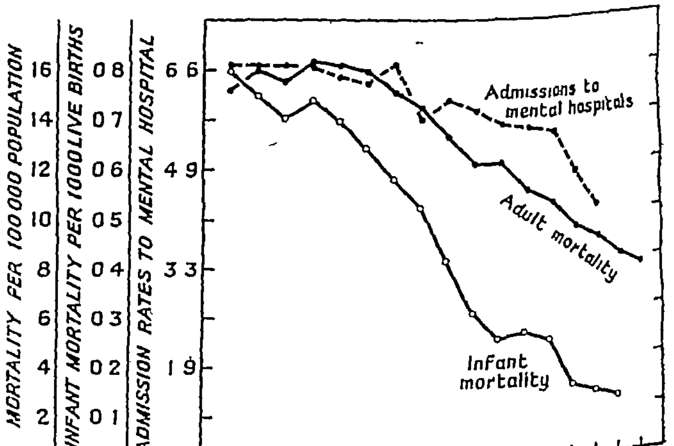


Fig 21—Comparison of adult and infant mortality from syphilis and of admissions to mental hospitals for syphilitic psychosis, in the United States 1933–49 (adapted from U S Public Health Service 1947, 1950)

These curves are adjusted in scale to an identical 100% starting point The declines may be interpreted as a by product of the syphilis control programme, and as the result of discovery of late rather than early syphilis, with prevention of complications and death by treatment

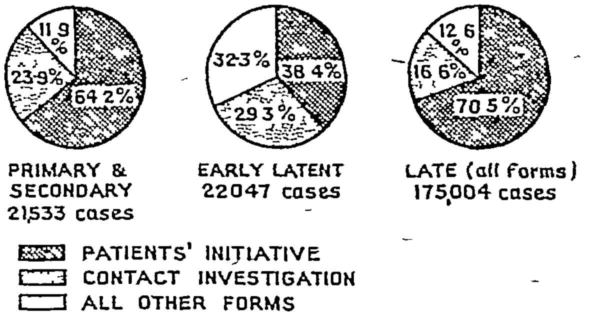


Fig 22—Value of contact investigation in the discovery of syphilis, especially early syphilis in the United States. Showing how previously untreated patients reached medical care (July, 1946 to December 1947) Based on data from 16 States Chicago, St. Louis and New York City

expert diagnostic and therapeutic service at no cost

Methods to increase the number of infected persons brought under treatment (*case finding*) are of great interest and importance to American observers *Mass blood testing*, by custom, regulation, or law, is a development of the last 15 years, and is almost peculiar to the United States It may be estimated that some 50 million Americans have been routinely tested, in medical practice, in industry, in the Armed Services, and in premarital or prenatal tests

An important objection to mass blood testing lies in its non specificity Technical and biological false-positive reactions are frequent, and in certain United States population groups probably represent nearly half of the positive tests discovered. Moreover, the yield of early infectious syphilis is low, and for the purpose of interrupting the chain of infectiousness the method is inefficiently expensive These objections are more than counterbalanced, however, by the discovery of at least a large part of the huge reservoir of late syphilis, by the resultant fall in mortality, and by the educational value of the method

The most significant United States contribution to syphilis control lies in the widespread application of the *epidemiological approach to case finding* To enlightened syphilologists, responsibility for the patient with syphilis has never ended with the patient himself Always it has included the urgent questions "From whom did you contract syphilis?", "To whom may you have given it?" The first demonstration of its value on a nation wide scale, however, proceeds from United States experience of the past 15 years The voluminous literature on the point is well summarised by two brief articles

The first of these, without authorship, emanates from the Venereal Disease Division (United States Public Health Service 1948) An analysis is made of the reasons which brought more than 200,000 previously untreated patients to clinics in widely scattered and wholly representative areas of the United States covering 16 States plus the large cities of Chicago, St Louis, and New York, for the period July, 1946, to December, 1947 The data are graphically presented in fig 22 Of 21,533 cases of primary and secondary (i e, open lesion) syphilis, 64% reported on their own initiative, 24% were individually sought for and found as the sexual contacts of other infected persons, and 12% came for other reasons (usually routine serological discovery) Only 38% of 22,000 patients with early latent (i e, potentially infectious) syphilis came to medical care on their own initiative, 29% because of contact investigation, and 32% for other reasons Of 175,000 cases with late syphilis, 16 6% were brought to care by contact investigation These are imposing numbers

Bauer (1949) adds statistical confirmation of a different sort For each voluntary admission of a patient with early infectious syphilis in 15 areas of the United States, investigators obtained identifiable data as to an average of 2 52 persons exposed but not yet examined, discovered on examination 0 75 persons infected with syphilis, and found 0 19 persons with actual "open lesion" infectious syphilis These are cases which otherwise would fail to come under medical care at all, or at least not until the lapse of years

Each such person with early syphilis discovered and brought under treatment constitutes a fresh break in the chain of infection, which should lead, if continued long enough, to the gradual control of syphilis

DECLINE IN MORBIDITY AND MORTALITY

Is there Evidence of a Decline since 1910?

On the basis of accurate civilian data, the question as to fall in incidence cannot yet be satisfactorily answered except in Scandinavia, and partially in Britain Military information may be added, however In the United States Army, the pre war base line in 1861 was about 68 per 1000 strength, in 1914, 17 per 1000, and in 1941, about 5 per 1000 (see fig 6) Combining this and other military data with Scandinavian and British civilian experience, one may tentatively conclude that the incidence of syphilis in Western Europe and the United States has fallen significantly below its pre 1910 level; and is probably still declining Moreover, although exact figures are lacking to document the statement, it is highly probable that the rate of decline has been greater since 1918 than previously

Mortality in adults has certainly declined in the past 15 years, and in some countries infant mortality appears to be approaching the vanishing point

That the accelerated decline in morbidity did not begin for about 8–10 years after the great discoveries of 1905–10 is accounted for by the inevitable lag in their world-wide application, and by the rise in incidence attributable to World War I It was interrupted temporarily by a similar rise during and after World War II, but has now been resumed.

A fall in mortality did not become apparent, at least in the United States, for nearly a generation after the introduction of metal chemotherapy This delay is certainly due to continuing deaths in the period 1910–38 of patients wholly untreated, or given mercury only, or inadequate arsenic

It is permissible, I believe, to attribute declining morbidity (since 1918) and mortality (since 1938) to the application of modern control methods, especially effective treatment, to millions of persons Nevertheless, a cautionary word should be added that most of these declines occurred during the era of metal chemotherapy (prior to 1946), and there is as yet no convincing evidence to indicate that the rate of decline has been further accelerated in the few years since the introduction of penicillin

Has the Decline been More Abrupt in Countries with Elaborate Control Programmes?

Here there is less firm ground Some of the evidence given above suggests that a fall in incidence occurred, to some degree or perhaps even to the same degree, in countries which, for many of the years since 1910, did little or nothing except to use modern drugs in infected applicants (e g, Norway, Britain) as in countries with more elaborate programmes (e g, Denmark, Sweden, the United States) Available information is too scanty and too short-term to provide an answer

Has the Decline been Sufficient to Promise Eventual Complete Control?

Here the answer, up to the outbreak of World War II, is certainly "No," since that war resulted (as have

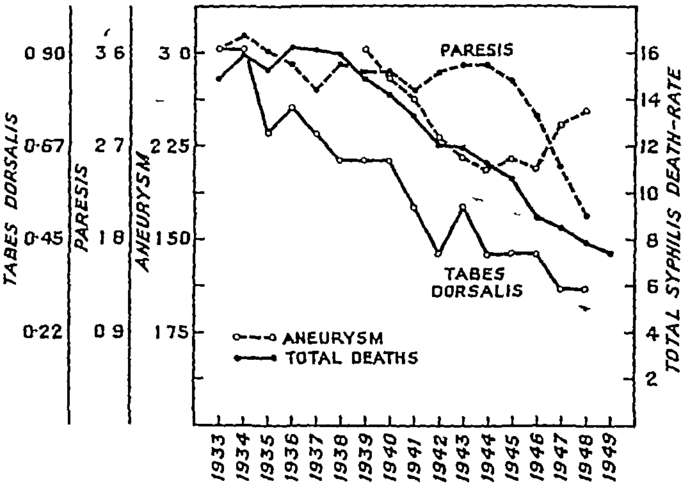


Fig 20—Reported mortality from acquired syphilis in the United States 1933–49 (curves adapted from U.S Public Health Service 1947, 1950) Each curve is per 100,000 population the ordinate percentages adjusted so that all curves start at about the same point.

See text for description There are curious discrepancies between the curves for, for example, tabes dorsalis, paresis, and aneurysm The fall in tabes deaths began in 1934, that in paresis not until a decade later Both of these have been continuous, while the curve for aneurysm, after an initial fall, seems to be rising again

is not applicable in civilian life, and is in any case nearly worthless and should be abandoned Mechanical condom prophylaxis is certainly of value, but its effect cannot be measured Penicillin prophylaxis by the oral route is effective against gonorrhœa, but not yet shown to be applicable to syphilis In civilian as opposed to military populations, any form of prophylaxis is a weak reed to lean upon

Methods to improve diagnosis and treatment of infected persons are of major importance In the United States, medical education as to syphilis, both undergraduate and postgraduate, has greatly improved in the last two decades New and improved methods of serodiagnosis have been introduced—e g, cardiolipin antigen, the discovery of treponemal immobilising antibody Performance of serological tests has been immeasurably bettered by national and local serological surveys New chemotherapeutic methods—at first, improved schemes of use of arsenic and bismuth, and since 1943, the introduction of antibiotics (especially penicillin, but also including 'Aureomycin,' chloramphenicol, and 'Terramycin')—have completely revolutionised the treatment of syphilis

PENICILLIN IN SYPHILIS CONTROL

A special word as to *penicillin* is necessary This drug proved to be effective in syphilis in 1943, had been adopted by the United States Armed Services by late 1944, and was in sufficient supply to become a factor in civilian life by 1946 It has provided a rapid, safe, and inexpensive method of treatment, so much more efficient in mass practice than arsenic and bismuth that these latter drugs have been practically abandoned in the United States It is now established that in primary and secondary syphilis, considered together, the "cure" rate is 80–85% at the end of 3 years, provided the drug is administered in such a manner as to produce a continuous detectable blood level for about 10 days The scheme of treatment does not seem greatly to matter if this requirement is fulfilled Since treatment is quick, safe, non toxic, almost completely painless and inexpensive and causes little loss of time all patients complete treatment For the individual patient the chance of cure is somewhat less, and the risk of infectious relapse and/or reinfection somewhat greater, than if he receives 6 months continuous metal chemotherapy, including 40 injections of arsenoxide and 20 of bismuth. For the mass of patients, however, the over all chance of cure is greater, since in pre penicillin United States civilian practice few patients had the optimum amount of metal chemotherapy

In respect of penicillin treatment of early syphilis, however, there is an important unsolved public health problem of infectiousness The cumulative incidence of infectious relapse and/or reinfection (which cannot be clearly differentiated) is at least 10% with any satisfactory system of penicillin treatment so far devised This compares with an incidence of 17·5% (Sternberg and Leifer 1947) in a large series of patients treated semi intensively with 26 weeks' 'Mapharsen' bismuth in the United States Army The issue is raised as to whether the total man days of potential infectiousness due to relapse and/or reinfection after penicillin treatment may not actually be greater than after metal chemotherapy (assuming, of course, which is not the case, that all patients actually completed the desired amount of the latter) If it were not for the troublesome 10% incidence of relapse and/or reinfection, one might expect the general use of penicillin to be reflected in a break in the chain of infection, and a lowering of incidence rate Indeed, this explanation of the recent fall in incidence has been advanced in the United States It has been seriously said, verbally if not in print, that penicillin is the final answer, to be shortly effective in eradicating syphilis altogether or relegating it to the minor status of typhoid fever As yet, however, the epidemiologist is unprepared to accept this glowing optimism He must examine the rest of the evidence

In the United States, *methods to increase the availability of diagnostic and treatment facilities* have been outstandingly successful, and it is for this phase of the programme that most of the syphilis control dollar has been spent It is now possible for an infected person anywhere in the United States to receive comparatively

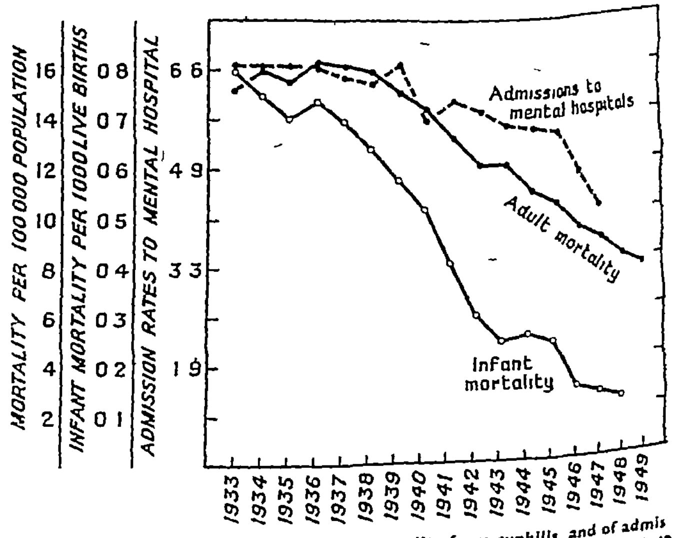


Fig 21—Comparison of adult and infant mortality from syphilis and of admissions to mental hospitals for syphilitic psychosis, in the United States 1933–49 (adapted from U.S Public Health Service 1947, 1950)

These curves are adjusted in scale to an identical 100% starting-point The declines may be interpreted as a by product of the syphilis control programme, and as the result of discovery of late syphilis rather than early syphilis, with prevention of complications and death by treatment

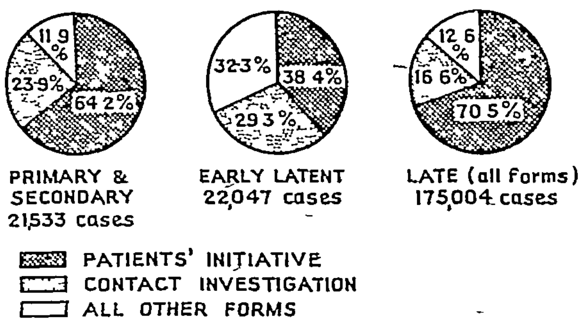


Fig. 22—Value of contact investigation in the discovery of syphilis, especially early syphilis, in the United States. Showing how previously untreated patients reached medical care (July, 1946, to December 1947). Based on data from 16 States, Chicago, St. Louis and New York City.

expert diagnostic and therapeutic service at no cost.

Methods to increase the number of infected persons brought under treatment (*case finding*) are of great interest and importance to American observers. *Mass blood-testing*, by custom, regulation, or law, is a development of the last 15 years, and is almost peculiar to the United States. It may be estimated that some 50 million Americans have been routinely tested, in medical practice, in industry, in the Armed Services, and in premarital or prenatal tests.

An important objection to mass blood testing lies in its non specificity. Technical and biological false-positive reactions are frequent, and in certain United States population groups probably represent nearly half of the positive tests discovered. Moreover, the yield of early infectious syphilis is low, and for the purpose of interrupting the chain of infectiousness the method is inefficiently expensive. These objections are more than counterbalanced, however, by the discovery of at least a large part of the huge reservoir of late syphilis, by the resultant fall in mortality, and by the educational value of the method.

The most significant United States contribution to syphilis control lies in the widespread application of the *epidemiological approach to case finding*. To enlightened syphilologists, responsibility for the patient with syphilis has never ended with the patient himself. Always it has included the urgent questions "From whom did you contract syphilis?", "To whom may you have given it?" The first demonstration of its value on a nation wide scale, however, proceeds from United States experience of the past 15 years. The voluminous literature on the point is well summarised by two brief articles.

The first of these, without authorship, emanates from the Venereal Disease Division (United States Public Health Service 1948). An analysis is made of the reasons which brought more than 200,000 previously untreated patients to clinics in widely scattered and wholly representative areas of the United States covering 16 States plus the large cities of Chicago, St. Louis, and New York, for the period July, 1946, to December, 1947. The data are graphically presented in fig. 22. Of 21,533 cases of primary and secondary (i.e., open lesion) syphilis, 64% reported on their own initiative, 24% were individually sought for and found as the sexual contacts of other infected persons, and 12% came for other reasons (usually routine serological discovery). Only 38% of 22,000 patients with early latent (i.e., potentially infectious) syphilis came to medical care on their own initiative, 29% because of contact investigation, and 32% for other reasons. Of 175,000 cases with late syphilis, 16.6% were brought to care by contact investigation. These are imposing numbers.

Bauer (1949) adds statistical confirmation of a different sort. For each voluntary admission of a patient with early infectious syphilis in 15 areas of the United States, investigators obtained identifiable data as to an average of 2.52 persons exposed but not yet examined, discovered on examination 0.75 persons infected with syphilis, and found 0.19 persons with actual "open lesion" infectious syphilis. These are cases which otherwise would fail to come under medical care at all, or at least not until the lapse of years.

Each such person with early syphilis discovered and brought under treatment constitutes a fresh break in the chain of infection, which should lead, if continued long enough, to the gradual control of syphilis.

DECLINE IN MORBIDITY AND MORTALITY

Is there Evidence of a Decline since 1910?

On the basis of accurate civilian data, the question as to fall in incidence cannot yet be satisfactorily answered except in Scandinavia, and partially in Britain. Military information may be added, however. In the United States Army, the pre war base-line in 1861 was about 68 per 1000 strength, in 1914, 17 per 1000, and in 1941, about 5 per 1000 (see fig. 6). Combining this and other military data with Scandinavian and British civilian experience, one may tentatively conclude that the incidence of syphilis in Western Europe and the United States has fallen significantly below its pre 1910 level; and is probably still declining. Moreover, although exact figures are lacking to document the statement, it is highly probable that the rate of decline has been greater since 1918 than previously.

Mortality in adults has certainly declined in the past 15 years, and in some countries infant mortality appears to be approaching the vanishing point.

That the accelerated decline in morbidity did not begin for about 8–10 years after the great discoveries of 1905–10 is accounted for by the inevitable lag in their world wide application, and by the rise in incidence attributable to World War I. It was interrupted temporarily by a similar rise during and after World War II, but has now been resumed.

A fall in mortality did not become apparent, at least in the United States, for nearly a generation after the introduction of metal chemotherapy. This delay is certainly due to continuing deaths in the period 1910–38 of patients wholly untreated, or given mercury only, or inadequate arsenic.

It is permissible, I believe, to attribute declining morbidity (since 1918) and mortality (since 1938) to the application of modern control methods, especially effective treatment, to millions of persons. Nevertheless, a cautionary word should be added that most of these declines occurred during the era of metal chemotherapy (prior to 1946), and there is as yet no convincing evidence to indicate that the rate of decline has been further accelerated in the few years since the introduction of penicillin.

Has the Decline been More Abrupt in Countries with Elaborate Control Programmes?

Here there is less firm ground. Some of the evidence given above suggests that a fall in incidence occurred, to some degree or perhaps even to the same degree, in countries which, for many of the years since 1910, did little or nothing except to use modern drugs in infected applicants (e.g., Norway, Britain) as in countries with more elaborate programmes (e.g., Denmark, Sweden, the United States). Available information is too scanty and too short term to provide an answer.

Has the Decline been Sufficient to Promise Eventual Complete Control?

Here the answer, up to the outbreak of World War II, is certainly "No," since that war resulted (as have

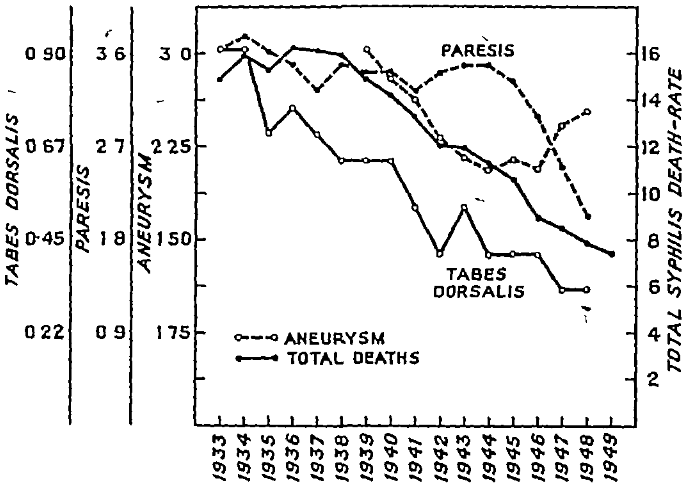


Fig 20—Reported mortality from acquired syphilis in the United States 1933–49 (curves adapted from U S Public Health Service 1947, 1950) Each curve is per 100 000 population, the ordinate percentages adjusted so that all curves start at about the same point.

See text for description There are curious discrepancies between the curves for, for example, tabes dorsalis, paresis, and aneurysm The fall in tabes deaths began in 1934, that in paresis not until a decade later Both of these have been continuous, while the curve for aneurysm, after an initial fall, seems to be rising again

is not applicable in civilian life, and is in any case nearly worthless and should be abandoned Mechanical condom prophylaxis is certainly of value, but its effect cannot be measured Penicillin prophylaxis by the oral route is effective against gonorrhœa, but not yet shown to be applicable to syphilis In civilian as opposed to military populations, any form of prophylaxis is a weak reed to lean upon

Methods to improve diagnosis and treatment of infected persons are of major importance In the United States, medical education as to syphilis, both undergraduate and postgraduate, has greatly improved in the last two decades New and improved methods of serodiagnosis have been introduced—e g, cardiolipin antigen, the discovery of treponemal immobilising antibody Performance of serological tests has been immeasurably bettered by national and local serological surveys New chemotherapeutic methods—at first, improved schemes of use of arsenic and bismuth, and since 1943, the introduction of antibiotics (especially penicillin, but also including 'Aureomycin,' chloramphenicol, and 'Terramycin')—have completely revolutionised the treatment of syphilis

PENICILLIN IN SYPHILIS CONTROL

A special word as to *penicillin* is necessary This drug proved to be effective in syphilis in 1943, had been adopted by the United States Armed Services by late 1944, and was in sufficient supply to become a factor in civilian life by 1946 It has provided a rapid, safe, and inexpensive method of treatment, so much more efficient in mass practice than arsenic and bismuth that these latter drugs have been practically abandoned in the United States It is now established that in primary and secondary syphilis, considered together, the "cure" rate is 80–85% at the end of 3 years, provided the drug is administered in such a manner as to produce a continuous detectable blood level for about 10 days The scheme of treatment does not seem greatly to matter if this requirement is fulfilled Since treatment is quick, safe, non toxic, almost completely painless and inexpensive and causes little loss of time all patients complete treatment For the individual patient the chance of cure is somewhat less, and the risk of infectious relapse and/or reinfection somewhat greater, than if he receives 6 months continuous metal chemotherapy, including 40 injections of arsenoxide and 20 of bismuth For the mass of patients, however, the over all chance of cure is greater, since in pre penicillin United States civilian practice few patients had the optimum amount of metal chemotherapy

In respect of penicillin treatment of early syphilis, however, there is an important unsolved public health problem of infectiousness The cumulative incidence of infectious relapse and/or reinfection (which cannot be clearly differentiated) is at least 10% with any satisfactory system of penicillin treatment so far devised This compares with an incidence of 1 75% (Sternberg and Leifer 1947) in a large series of patients treated semi-intensively with 26 weeks' 'Mapharsen' bismuth in the United States Army The issue is raised as to whether the total man days of potential infectiousness due to relapse and/or reinfection after penicillin treatment may not actually be greater than after metal chemotherapy (assuming, of course, which is not the case, that all patients actually completed the desired amount of the latter) If it were not for the troublesome 10% incidence of relapse and/or reinfection, one might expect the general use of penicillin to be reflected in a break in the chain of infection, and a lowering of incidence rate Indeed, this explanation of the recent fall in incidence has been advanced in the United States It has been seriously said, verbally if not in print, that penicillin is the final answer, to be shortly effective in eradicating syphilis altogether or relegating it to the minor status of typhoid fever As yet, however, the epidemiologist is unprepared to accept this glowing optimism He must examine the rest of the evidence

In the United States, *methods to increase the availability of diagnostic and treatment facilities* have been outstandingly successful, and it is for this phase of the programme that most of the syphilis control dollar has been spent It is now possible for an infected person anywhere in the United States to receive comparatively

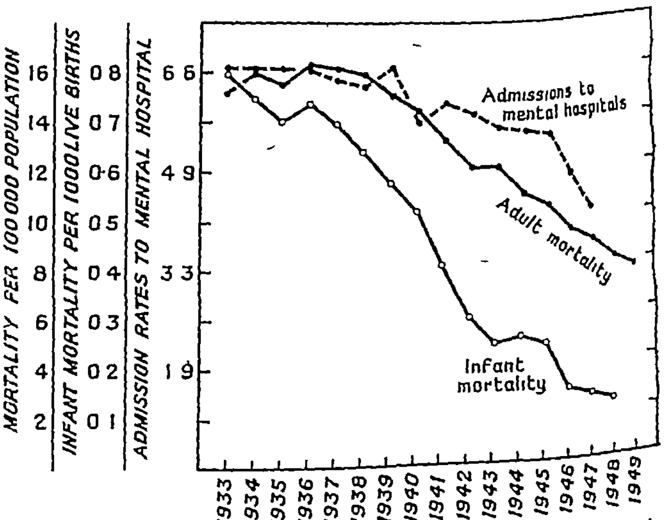


Fig 21—Comparison of adult and infant mortality from syphilis and of admissions to mental hospitals for syphilitic psychosis, in the United States 1933–49 (adapted from U.S Public Health Service 1947 1950)

These curves are adjusted in scale to an identical 100% starting point The declines may be interpreted as a by product of the syphilis control programme, and as the result of discovery of late syphilis rather than early syphilis, with prevention of complications and death by treatment developed through further medical research, is a more promising approach.

REFERENCES

Aufranc W H (1951) Are Venereal Diseases Disappearing? (in the press)
Bauer T J (1949) *J vener Dis Inform.* 30 339
Bloch I (1901) Der Ursprung der Syphilis. Jena.
Clarke, C W (1936) *Amer J Syph.* 20 7
Dubos J (1950) Louis Pasteur Free Lance of Science Boston p 294
Eagle H (1939) *Amer J Syph* 23 712
Frost W H. (1937) *Amer J publ Hlth* 27, 759
Guthe T (1945) *Amer J Syph* 29 351
Haustein H (1937) in Handbuch der Haut- und Geschlechtskrankheiten vol XXII p 228
Hinrichsen J (1944) *Amer J Syph.* 28 736
— (1945) *Ibid* 29 50 229
Hirsch A (1885) Handbook of Geographical and Historical Pathology London vol 2, p 59
Kahn H A. Iskrant A. P (1948) *J vener Dis Inform.* 29 193
Kinsey A. C Pomeroy W B Martin C E (1948) Sexual Behaviour in the Human Male. Philadelphia and London
Moore J E (1939) *Amer J Syph.* 23 701
— (1951a) Morbidity of Syphilis in Armies as a Possible Guide to Civilian Incidence (in the press).
— (1951b) Efficacy of Individual Components of a Syphilis Control Program (in the press)
Parran T (1936) *Survey Graphic* July abstracted in *Readers' Digest* July
— (1937) Shadow on the Land Syphilis. New York.
Registrar-General (1935) Decennial Supplement England and Wales 1931. Part IIa. Occupational Mortality
Schamberg I L (1945) *Amer J Syph* 29 529
Siler J F. (1943) *Army med Bull.* no 67 p 1
Spoto J S Iskrant A P (1949) *J vener Dis Inform* 30 140
Sternberg T H Leifer W (1947) *Amer J Syph* 31 124
United States Public Health Service (1947) *J vener Dis Inform* 28 17
— (1948) *Ibid* 29 190
— (1950) *Ibid* 31 123.
Usilton L J Bruyere, P T Bruyere M. C (1945) *Ibid* 26 216
Vonderlehr R. A. (1939) *Amer J Syph* 23 692

INTRAMEDULLARY NAILING IN RECENT FRACTURES OF THE FEMORAL SHAFT

G C LLOYD-ROBERTS
M.B Camb , F.R C.S
SENIOR REGISTRAR, ORTHOPÆDIC DEPARTMENT,
ST PETER'S HOSPITAL, CHERTSEY

ON the Continent intramedullary nailing is a well-recognised and widely practised method of treatment for fractures of the femoral shaft, and a copious literature has accumulated Very few reports, however, have appeared in England Fraenkel (1948) described cases he observed while on a visit to Kiel, Chance (1949) reviewed a personal series in a paper read before the British Orthopædic Association, and McKee (1948) reported unfavourably on his experience of three cases in which he had used trifin nails. Watson Jones et al. (1950) in a long article in the *Journal of Bone and Joint Surgery* have reviewed the difficulties and complications of this method. It therefore seems advisable to review the results obtained in twenty cases at this hospital.

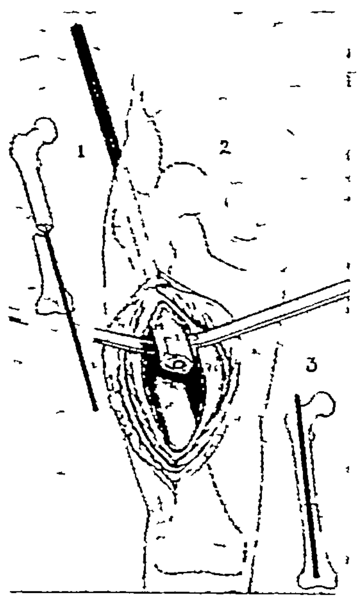
It must be emphasised that intramedullary nailing presents no new principle in the treatment of fractures Hey Groves (1918–19) applied the technique experimentally, Lambotte (1913) treated fractures of the clavicle in this manner, and Lambrinudi (1940) the ulna It has an established position in certain fractures of the metacarpals and phalanges For fractures of the shaft of the femur it is the logical sequel to the acceptance of Smith Petersen's intramedullary fixation of fractures of the femoral neck. Long Smith-Petersen nails within the medullary cavity of the shaft were used in the treatment of subtrochanteric fractures by B H Burns in 1938 and G K McKee in 1940 (personal communications)

Küntscher (1940) must receive full credit for establishing the method His contribution delivered before the Berlin Surgical Congress although for the most part coldly received, was followed by a renewal of interest in the principle, and consequently Böhler's (1948) monograph describes in detail the experiences of the Viennese school and includes a considerable bibliography

In the United States the method, though gaining in popularity, cannot yet be described as the standard treatment for fractures of the shaft of the femur Several notable papers have, however, been published, including Haebler's (1949) review of 118 cases

MATERIAL

Experience at this hospital of intramedullary nailing of the femoral shaft comprises 37 cases, but in 17 the operation was performed for mal union, non union, or limb shortening Only the remaining 20 cases, in which nailing was used as the primary definitive treatment, are considered here The length of time that elapsed between fracture and operation was a matter of hours in 7 cases, and days in 9 The remaining 4 cases were operated on within two weeks of injury In 1 case the fracture was compound, and in 3 others it was complicated by fractures of the bones of the lower leg on the same side. The ages of the patients ranged from 17 to 85



Intramedullary nailing 1 nail about to be inserted into proximal fragment of femur 2, nail driven through proximal fragment 3 nail driven into distal fragment.

OPERATION

The method used involves exposure of the fracture and insertion of the nail under direct vision We have not tried the closed method which entails manipulative reduction under X-ray control and the passage of the nail from the trochanteric region of the femur by indirect means We prefer to expose the fracture and pass the nail under direct vision (see figure), feeling that the theoretical advantages of the closed method are outweighed by the longer time it takes and by some inevitable loss of precision Furthermore Burns early experienced difficulties in finding the precise spot on the neck of the femur for introduction of the nail from above This led to his return in 1943 to the older method of Hey Groves in which the nail is inserted through the fracture site The closed method is, however, more in favour among Continental surgeons who have been denied until recently the advantages of antibiotics

The figure illustrates the principle of the operation but a few points require special emphasis

Before the operation is begun, the distance from the tip of the great trochanter to the knee joint is measured on the normal side U-shaped nails of various diameters are selected measuring 4 cm less than this measurement The fracture is exposed by an anterolateral approach in most cases, but fractures of the subtrochanteric region are more easily dealt with through a lateral approach. The incision should extend more generously over the proximal fragment than over the distal. When the fracture has been exposed, the proximal fragment must be delivered into the wound so that the medullary cavity presents at the surface A nail is selected whose diameter fits snugly the medullary cavity at its narrowest point The nail is hammered upwards through the proximal fragment until it is felt to penetrate the cortex of the basal part of the neck of the femur medial to the great trochanter At this stage it will be an advantage to adduct the limb as far as possible before driving the nail into the subcutaneous tissue of the buttock, so that other wars) in what can only be described as a fresh epidemic of syphilis in Europe and the United States From the end of World War II, it is yet far too soon, probably at least by a decade, to determine whether the presently occurring decline represents only a return of population stability, or a continuing acceleration due to the increasing application of control measures, especially penicillin

The 1910–50 trend of incidence of syphilis is certainly influenced by the factors operative before 1910, especially slow improvement in socio economic conditions, and fluctuations in population stability The gradual decline probably initiated in the mid 19th century has apparently been accelerated by modern public health control measures But this acceleration is not yet sufficiently significant (unless in Scandinavia) to promise eventual complete control in any country, nor to set a time limit within which that desired goal may be reached Certainly it is not enough to justify complacent relaxation of effort or a decrease in the expenditure of public funds Premature satisfaction with accomplishment is dangerous

In one direction, the expenditure of additional money seems essential—i e , the gathering of reliable information on the incidence and prevalence of syphilis in various countries The discussion of this paper makes abundantly clear the difficulty of estimating the effect of a control programme or of any of its components for lack of such data For individual countries and for the World Health Organisation, Guthe and Hume emphasise this in saying " One of the main needs is the establishment of uniform reporting procedures and nomenclature throughout the world Reports should be available currently and analysis of the reports should also proceed on a reasonably current basis in order to provide useful information to the nations of the world " (Vonderlehr 1939) The mathematician finds it impossible to solve a problem unless provided with the basic figures

Will a Control Programme based on Present Knowledge be Effective in Global Eradication?

In a global sense, certain infections may be eradicated entirely in one country while they flourish in another With syphilis, as with tuberculosis, this is improbable Improved transportation methods facilitate population exchange While endemic areas of syphilis exist anywhere in the world, it is unlikely that any country will locally so reduce the importance of the infection as to avoid a few smouldering endemic foci of its own, and a new epidemic with a new cause of population instability It is, therefore, pertinent to inquire into the possible global eradication of syphilis with the means at present to hand

The cost of syphilis control, on the basis of United States and Scandinavian programmes, is sufficiently high as to make it difficult to envisage their applicability in some densely populated but less prosperous countries which presently have a high rate of incidence and prevalence—e g , China, India If this be true—if in turn the continued existence of the infection in one country constitutes a potential public health danger to another, no matter how successful the latter may have been in stable peace time years—how best can we approach the problem on a global basis ?

MEDICAL RESEARCH IN THE CONTROL OF SYPHILIS

I have deliberately left till last any consideration of an all important method of syphilis control, *medical research* In 1939 there was presented in the United States a symposium on unsolved problems as to syphilis (Vonderlehr 1939, Moore 1939, Eagle 1939) The questions posed then remain largely unanswered 11 years later Some of the many gaps in knowledge have not only fundamental biological but also very practical epidemiological importance Virulent *T pallidum* has never been successfully grown on artificial media This is the very cornerstone of further progress Until it is successfully accomplished, we shall remain ignorant of the chemistry of the organism, its growth requirements, its life-cycle, and the possible infectivity of non spiral forms, the explanation for its extraordinary predilection for certain tissues in man, the factors underlying immunity and allergy, the development of a genuinely specific diagnostic test, and the fascinating possibility of mass immunisation.

The solution of these and other practical problems depends upon financial support of medical research, with a large proportion of the syphilis control dollar for this purpose than has heretofore been available even in the United States Emphasis should be on fundamental rather than on applied investigation, since on the unsolved fundamental problems outlined above depends the development of effective immunisation.

If immunisation proved to be possible, then—and perhaps not until then—will there be surely within grasp a financially feasible method of global relegation of the great pox to the present level of oblivion now achieved for smallpox

SUMMARY AND CONCLUSIONS

1 The evaluation of a public health programme for the control of syphilis depends on accurate epidemiological figures as to morbidity and mortality, from which trends may be estimated

Reliable information on these points is not available in any country before the mid 19th century From about 1865 to 1940, it may be had for civilian population groups from Scandinavia only , but it is available, with varying degress of validity, for military population groups from several countries of Western Europe and the United States After 1940, data as to trends among civilians begin to accumulate in the United States

2 Since the scientific discoveries of 1905–10, the public health control of syphilis has been potentially possible. Trends from 1910 to the present may therefore be compared with those in the roughly equal time-period 1865–1910, when, for lack of this knowledge, control efforts were largely futile

3 In both of these periods, pre 1910 and post 1910, there can be no doubt that war or internal unrest is accompanied, in any country involved, by an increase in morbidity followed by a post war decrease

4 Military data strongly suggest that from 1865 to 1910 there was a decline in the incidence of syphilis in most countries of Western Europe and in the United States

5 The factors possibly contributing to this decline are (*a*) a natural phenomenon of infectious disease, with modifications of the host parasite relationship, (*b*) a general improvement in socio economic conditions in Western civilisation , and (*c*) relative population stability after a long period of instability

6 These same long term influences have also operated since 1910

7 Since 1910, there has been a further decline in the incidence of syphilis in Western Europe and the United States , and at a probably accelerated rate The acceleration may be attributed to modern public health control measures, especially the application of effective treatment to millions of infected persons, and of programmes designed to increase the number of such persons brought to treatment As a by effect of these efforts, mortality has probably declined more rapidly than morbidity

8 The possible effect of penicillin in further accelerating the decline in incidence cannot be measured for at least another decade

9 The present decline is not yet sufficient (unless in Scandinavia) to promise eventual complete control in any country, to permit the relaxation of control efforts, or to set a time limit on achievement of the desired goal

10 Global control is unlikely with the methods at present available Mass immunisation, if this can be

eveloped through further medical research, is a more romising approach

REFERENCES

ufranc W H. (1951) Are Venereal Diseases Disappearing? (In the press)
Bauer T J (1949) *J vener Dis Inform.* 30 339
Bloch I. (1901) Der Ursprung der Syphilis. Jena.
Clarke, C. W (1936) *Amer J Syph.* 20 7
Dubos J (1950) Louis Pasteur Free Lance of Science Boston p 294
Eagle H. (1939) *Amer J Syph* 23 712
Frost, W H (1937) *Amer J publ Hlth* 27, 759
Guthe T (1945) *Amer J Syph.* 29 381
Haustein, H. (1937) in Handbuch der Haut und Geschlechtskrankheiten vol XXII p. 223
Hinrichsen J (1944) *Amer J Syph.* 28 736
— (1945) *Ibid* 29 80 229
Hirsch A (1885) Handbook of Geographical and Historical Pathology London vol. 2 p 59
Kahn H A. Iskrant, A. P (1948) *J vener Dis Inform* 29 193
Kinsey A. C Pomeroy W B Martin C E (1948) Sexual Behaviour in the Human Male. Philadelphia and London
Moore J E (1939) *Amer J Syph.* 23 701
— (1951a) Morbidity of Syphilis in Armies as a Possible Guide to Civilian Incidence (in the press)
— (1951b) Efficacy of Individual Components of a Syphilis Control Program (in the press).
Parran T (1936) *Survey Graphic,* July abstracted in *Readers' Digest* July
— (1937) Shadow on the Land Syphilis New York.
Registrar-General (1938) Decennial Supplement England and Wales 1931 Part IIa. Occupational Mortality
Schamberg I. L (1945) *Amer J Syph* 29 529
Siler J F. (1943) *Army med. Bull.* no 67 p 1
Spoto J S Iskrant A P (1949) *J vener Dis. Inform* 30 140
Sternberg T H Leifer W (1947) *Amer J Syph* 31 124.
United States Public Health Service (1947) *J vener Dis Inform* 28 17
— (1948) *Ibid* 29 190
— (1950) *Ibid* 31 123
Usilton, L J Bruyere P T Bruyere M. C (1945) *Ibid* 26 216
Vonderlehr, R. A. (1939) *Amer J Syph* 23 692

INTRAMEDULLARY NAILING IN RECENT FRACTURES OF THE FEMORAL SHAFT

G C Lloyd-Roberts
M.B Camb, F.R C S

SENIOR REGISTRAR, ORTHOPÆDIC DEPARTMENT,
ST PETER'S HOSPITAL, CHERTSEY

On the Continent intramedullary nailing is a well-recognised and widely practised method of treatment for fractures of the femoral shaft, and a copious literature has accumulated Very few reports, however, have appeared in England Fraenkel (1948) described cases he observed while on a visit to Kiel, Chance (1949) reviewed a personal series in a paper read before the British Orthopædic Association and McKee (1948) reported unfavourably on his experience of three cases in which he had used trifin nails. Watson-Jones et al. (1950) in a long article in the *Journal of Bone and Joint Surgery* have reviewed the difficulties and complications of this method It therefore seems advisable to review the results obtained in twenty cases at this hospital.

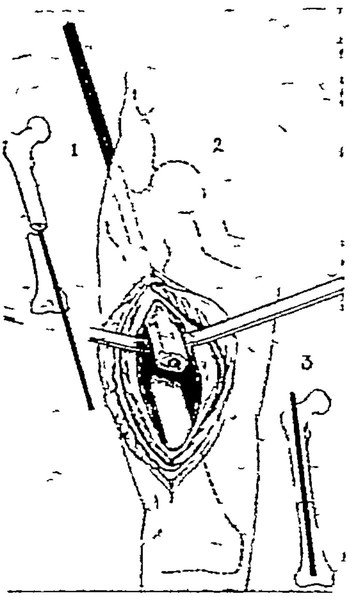
It must be emphasised that intramedullary nailing presents no new principle in the treatment of fractures Hey Groves (1918–19) applied the technique experimentally, Lambotte (1913) treated fractures of the clavicle in this manner, and Lambrinudi (1940) the ulna It has an established position in certain fractures of the metacarpals and phalanges For fractures of the shaft of the femur it is the logical sequel to the acceptance of Smith Petersen's intramedullary fixation of fractures of the femoral neck. Long Smith Petersen nails within the medullary cavity of the shaft were used in the treatment of subtrochanteric fractures by B H Burns in 1938 and G K McKee in 1940 (personal communications)

Küntscher (1940) must receive full credit for establishing the method His contribution delivered before the Berlin Surgical Congress although for the most part coldly received, was followed by a renewal of interest in the principle, and consequently Böhler's (1948) monograph describes in detail the experiences of the Viennese school and includes a considerable bibliography

In the United States the method, though gaining in popularity, cannot yet be described as the standard treatment for fractures of the shaft of the femur Several notable papers have, however, been published, including Haebler's (1949) review of 118 cases

MATERIAL

Experience at this hospital of intramedullary nailing of the femoral shaft comprises 37 cases, but in 17 the operation was performed for mal union, non union, or limb shortening Only the remaining 20 cases, in which nailing was used as the primary definitive treatment, are considered here The length of time that elapsed between fracture and operation was a matter of hours in 7 cases, and days in 9 The remaining 4 cases were operated on within two weeks of injury In 1 case the fracture was compound, and in 3 others it was complicated by fractures of the bones of the lower leg on the same side The ages of the patients ranged from 17 to 85



Intramedullary nailing 1 nail about to be inserted into proximal fragment of femur 2, nail driven through proximal fragment 3, nail driven into distal fragment.

OPERATION

The method used involves exposure of the fracture and insertion of the nail under direct vision We have not tried the closed method which entails manipulative reduction under X-ray control and the passage of the nail from the trochanteric region of the femur by indirect means. We prefer to expose the fracture and pass the nail under direct vision (see figure), feeling that the theoretical advantages of the closed method are outweighed by the longer time it takes and by some inevitable loss of precision Furthermore Burns early experienced difficulties in finding the precise spot on the neck of the femur for introduction of the nail from above This led to his return in 1943 to the older method of Hey Groves in which the nail is inserted through the fracture site The closed method is, however, more in favour among Continental surgeons who have been denied until recently the advantages of antibiotics

The figure illustrates the principle of the operation but a few points require special emphasis

Before the operation is begun, the distance from the tip of the great trochanter to the knee joint is measured on the normal side U-shaped nails of various diameters are selected measuring 4 cm less than this measurement The fracture is exposed by an anterolateral approach in most cases, but fractures of the subtrochanteric region are more easily dealt with through a lateral approach. The incision should extend more generously over the proximal fragment than over the distal When the fracture has been exposed, the proximal fragment must be delivered into the wound so that the medullary cavity presents at the surface A nail is selected whose diameter fits snugly the medullary cavity at its narrowest point The nail is hammered upwards through the proximal fragment until it is felt to penetrate the cortex of the basal part of the neck of the femur medial to the great trochanter At this stage it will be an advantage to adduct the limb as far as possible before driving the nail into the subcutaneous tissue of the buttock, so that other wars) in what can only be described as a fresh epidemic of syphilis in Europe and the United States From the end of World War II, it is yet far too soon, probably at least by a decade, to determine whether the presently occurring decline represents only a return of population stability, or a continuing acceleration due to the increasing application of control measures, especially penicillin

The 1910–50 trend of incidence of syphilis is certainly influenced by the factors operative before 1910, especially slow improvement in socio economic conditions, and fluctuations in population stability The gradual decline probably initiated in the mid 19th century has apparently been accelerated by modern public health control measures But this acceleration is not yet sufficiently significant (unless in Scandinavia) to promise eventual complete control in any country, nor to set a time limit within which that desired goal may be reached Certainly it is not enough to justify complacent relaxation of effort or a decrease in the expenditure of public funds Premature satisfaction with accomplishment is dangerous

In one direction, the expenditure of additional money seems essential—i e , the gathering of reliable information on the incidence and prevalence of syphilis in various countries The discussion of this paper makes abundantly clear the difficulty of estimating the effect of a control programme or of any of its components for lack of such data For individual countries and for the World Health Organisation, Guthe and Hume emphasise this in saying "One of the main needs is the establishment of uniform reporting procedures and nomenclature throughout the world Reports should be available currently and analysis of the reports should also proceed on a reasonably current basis in order to provide useful information to the nations of the world" (Vonderlehr 1939) The mathematician finds it impossible to solve a problem unless provided with the basic figures

Will a Control Programme based on Present Knowledge be Effective in Global Eradication?

In a global sense, certain infections may be eradicated entirely in one country while they flourish in another With syphilis, as with tuberculosis, this is improbable Improved transportation methods facilitate population exchange While endemic areas of syphilis exist anywhere in the world, it is unlikely that any country will locally so reduce the importance of the infection as to avoid a few smouldering endemic foci of its own, and a new epidemic with a new cause of population instability It is, therefore, pertinent to inquire into the possible global eradication of syphilis with the means at present to hand

The cost of syphilis control, on the basis of United States and Scandinavian programmes, is sufficiently high as to make it difficult to envisage their applicability in some densely populated but less prosperous countries which presently have a high rate of incidence and prevalence—e g , China, India If this be true—if in turn the continued existence of the infection in one country constitutes a potential public health danger to another, no matter how successful the latter may have been in stable peace time years—how best can we approach the problem on a global basis?

MEDICAL RESEARCH IN THE CONTROL OF SYPHILIS

I have deliberately left till last any consideration of an all important method of syphilis control, *medical research* In 1939 there was presented in the United States a symposium on unsolved problems as to syphilis (Vonderlehr 1939, Moore 1939, Eagle 1939) The questions posed then remain largely unanswered 11 years later Some of the many gaps in knowledge have not only fundamental biological but also very practical epidemiological importance Virulent *T pallidum* has never been successfully grown on artificial media This is the very cornerstone of further progress Until it is successfully accomplished, we shall remain ignorant of the chemistry of the organism, its growth requirements, its life-cycle, and the possible infectivity of non spiral forms, the explanation for its extraordinary predilection for certain tissues in man, the factors underlying immunity and allergy, the development of a genuinely specific diagnostic test, and the fascinating possibility of mass immunisation.

The solution of these and other practical problems depends upon financial support of medical research, with a large proportion of the syphilis control dollar for this purpose than has heretofore been available, even in the United States Emphasis should be on fundamental rather than on applied investigation, since on the unsolved fundamental problems outlined above depends the development of effective immunisation

If immunisation proved to be possible, then—and perhaps not until then—will there be surely within grasp a financially feasible method of global relegation of the great pox to the present level of oblivion now achieved for smallpox

SUMMARY AND CONCLUSIONS

1 The evaluation of a public health programme for the control of syphilis depends on accurate epidemiological figures as to morbidity and mortality, from which trends may be estimated

Reliable information on these points is not available in any country before the mid 19th century From about 1865 to 1940, it may be had for civilian population groups from Scandinavia only , but it is available, with varying degrees of validity, for military population groups from several countries of Western Europe and the United States After 1940, data as to trends among civilians begin to accumulate in the United States

2 Since the scientific discoveries of 1905–10, the public health control of syphilis has been potentially possible. Trends from 1910 to the present may therefore be compared with those in the roughly equal time period 1865–1910, when, for lack of this knowledge, control efforts were largely futile

3 In both of these periods, pre 1910 and post 1910, there can be no doubt that war or internal unrest is accompanied, in any country involved, by an increase in morbidity followed by a post war decrease

4 Military data strongly suggest that from 1865 to 1910 there was a decline in the incidence of syphilis in most countries of Western Europe and in the United States

5 The factors possibly contributing to this decline are (*a*) a natural phenomenon of infectious disease, with modifications of the host parasite relationship , (*b*) a general improvement in socio economic conditions in Western civilisation , and (*c*) relative population stability after a long period of instability

6 These same long term influences have also operated since 1910

7 Since 1910, there has been a further decline in the incidence of syphilis in Western Europe and the United States , and at a probably accelerated rate The acceleration may be attributed to modern public health control measures, especially the application of effective treatment to millions of infected persons, and of programmes designed to increase the number of such persons brought to treatment As a by effect of these efforts, mortality has probably declined more rapidly than morbidity

8 The possible effect of penicillin in further accelerating the decline in incidence cannot be measured for at least another decade

9 The present decline is not yet sufficient (unless in Scandinavia) to promise eventual complete control in any country, to permit the relaxation of control efforts, or to set a time limit on achievement of the desired goal.

10 Global control is unlikely with the methods at present available Mass immunisation, if this can be

in nailed fractures produces little callus between the cortices involved in the fracture. Union depends mainly on callus laid down peripherally. This was a constant finding in our series. It has been suggested that pressure of the nail in the medullary cavity is responsible (Fitts et al. 1949).

As the time of "bony union" I have therefore taken the point at which unprotected weight bearing without sticks or splintage is allowed. This corresponds functionally to the stage of consolidation in fractures treated by closed methods.

The average time between injury and the removal of all protection was 17.2 weeks. This compares favourably with the 23 weeks required to reach the same stage in a group of femoral fractures treated without internal fixation in this hospital.

The absence of late bending at the fracture site in any case taking full weight confirms that functional consolidation had indeed taken place.

Complications

The 1 death from causes unassociated with the operation has been mentioned. There were no cases of septic bone, non-union, or fat embolism. Superficial sepsis occurred in the buttock wound in 1 case; this is potentially a weak point in the technique and has been mentioned above.

Three cases require particular consideration.

Case 3.—A man with a fracture of the upper third of the femur was found to have bent his nail during the period of partial weight-bearing. He was one of the early cases (1945), and it is now evident that the nail used was too short. The angulation of the femur is not gross, and when the patient was last seen five years later he had 1 in. of shortening but a full range of movement. He is following his pre war trade as a bricklayer.

Case 4.—A man was discharged from hospital bearing partial weight six weeks after nailing of a transverse middle third fracture. Next day he fell on to a concrete floor and bent his nail at the site of fracture. He was readmitted, and true alignment was restored by traction. This was possible because the distal fragment could be moved on the pin in the splayed-out lower end of the bone. The final result is excellent, but the pin will probably have to be left in situ.

Case 5.—An uncoöperative schizophrenic had an oblique fracture at the junction of the middle and lower thirds of the femur. After operation he could not be restrained, and as early as two weeks later he was walking round his room without any support. The site and obliquity of the fracture, coupled with early unprotected weight bearing have led to early bony union with 20° of angulation at the fracture site and a secondary genu valgum. Further surgery may be necessary.

In summary, therefore the complications which have arisen have, apart from one exceptional case, had no influence upon the final result.

REMOVAL OF NAIL

The nail should be removed when firm consolidation has taken place. This can be very easily done through a small incision over the buttock and with an extractor which resembles a crochet hook and fits the slot made in the end of the nail for this purpose. The nail is removed because a bursa often forms round the protruding tip and causes pain when the patient sits down, and because the permanent retention of so large a piece of metal within the medulla may have its own dangers.

SUMMARY

Intramedullary nailing in 20 cases of fracture of the femoral shaft is reviewed. The operation and its indications are described. Return of function and bony union are good. A few complications are described.

I am very grateful to Mr B. H. Burns and Mr R. H. Young under whose care the patients were treated at St. Peter's Hospital, Chertsey (Botleys Park), for permission to review their cases, and for their assistance in the preparation of this report. My thanks are also due to Miss Zita Stead for the illustration.

REFERENCES

Böhler L (1948) Medullary Nailing of Küntscher London
Chance A (1949) *J Bone Jt Surg* 31B 135
Fitts W T jun. Roberts B Spoont, S I Ritter W W (1949) *Surg Gynec. Obstet.* 89, 609
Fraenkel G J (1948) *Lancet*, ii 337
Groves E W H (1918–19) *Brit J Surg* 6 203
Haebler C (1949) *Nav med Bull. Wash* 49 423 626 831 1033
Küntscher G (1940) *Arch klin-Chir* 200 443
Lambotte A. (1913) Chirurgie opératoire des fractures. Paris
Lambrinudi C (1940) *Proc R Soc Med* 33, 153
McKee G K. (1948) *Lancet* ii 511
Watson Jones R., et al. (1950) *J Bone Jt Surg* 32B, 694

DIPHTHERIA ANTITOXIN IN CORD-BLOOD

SURVEY OF SAMPLES FROM 15 AREAS OF BRITISH ISLES

MOLLIE BARR
M.Sc. Lond., A.R.I.C

A. T. GLENNY
B.Sc. Lond., F.R.S.

H. J. PARISH
M.D. Edin., F.R.C.P.E.

From the Wellcome Research Laboratories, Beckenham

In a study of factors involved in the active immunisation of young babies against diphtheria Barr et al. (1950) found that, when the level of passive maternally conferred antitoxin in babies was below 0.04 unit per ml. at the time of the first injection of prophylactic (0.5 ml. of A.P.T.), there was no interference with active immunisation, whereas titres of 0.1 unit per ml., or more, caused interference with the first dose of A.P.T.

Barr et al. (1949) showed that it was possible to calculate from the antitoxic titres of the cord-blood, the age at which any baby could be injected with prophylactic without interference from passive antitoxin. Barr et al. (1950) calculated that over 80% of a population of 200 babies born in South-East London would be satisfactorily immunised if they received the first dose of 0.5 ml. of A.P.T. at the age of 3 months. They suggested that antitoxin titrations on a limited number of cord-blood samples from different districts would give a good idea of the immunity state of the newborn, and that methods of immunisation could be derived therefrom which would be most satisfactory for most of the babies.

This paper gives analyses of values of cord-blood samples from fifteen areas of the British Isles—Aberdeen, Birmingham, Cardiff, Castleford, Cork, Coventry, Dumfries, Glasgow, Leeds, three districts of London, Rochdale, Stratford on-Avon, and West Bromwich. The statistical analyses were done by one of us (M. B.). The values recorded are those of a relatively large age group, most of the mothers being aged 20–35, but some being older or younger. They cannot be regarded as a fair sample of the general population, because most of the samples were obtained from urban areas. The figures give a picture of the immunity state at present, and may change considerably in future years according to the trend of immunisation and the presence or absence of epidemics.

The techniques adopted for taking the cord-blood samples and estimating the antitoxin levels were those described by Barr et al. (1949). They found that the distributions of values of 100 samples from each of two socially similar districts of South-East London were not significantly different. In the present investigation of cord-blood from different districts a sample of 100 has therefore been studied, although from one large industrial town two consecutive samples of 100 were compared, and confirmed that the number tested constituted an adequate statistical sample.

The results of this comparison are shown in table I, the antitoxic values being arranged in five groups. I the second wound made over the emerging point of the nail will be placed as far laterally as possible The proximal end of the nail is then driven out through the skin until the distal end is flush with the level of the fracture (The use of a second incision and the passage of the nail through the skin is a theoretically weak point in the technique We have had a minor complication attributable to this) The fracture is now reduced under direct vision and held in the reduced position while the nail is driven across the fracture into the distal fragment to its full extent The aim should be to leave as small a length of the nail as possible projecting above the trochanter The full introduction of the nail will be found simpler if an assistant applies traction to the leg while the nail is being hammered into position The incisions are both closed, and the patient is returned to bed without any other form of fixation whatever

INDICATIONS

Although the present series is small, we feel that we now have sufficient experience of the method to differentiate between those cases in which intramedullary nailing may be used with benefit and those in which it is contra indicated

We have come to regard nailing as the method of choice for fractures between and including the subtrochanteric region and the junction of the middle and lower thirds of the shaft, unless they are extensively comminuted or other local or general factors preclude operation Fractures of the lower third cannot be effectively maintained in the position obtained at operation without additional external fixation or traction This, by preventing early unhampered movement of both the patient and his limb, neutralises the advantages of intramedullary nailing

Failure to maintain reduction in low fractures is due to two factors (1) the short length of nail that can be passed distal to the fracture cannot prevent angulation and may lose contact with the distal fragment if any upward riding of the nail as a whole takes place, and (2) the disproportion between the diameter of the nail and the flared out medullary cavity prevents firm contact between the nail and the cortical bone in a circumferential plane at the level of the fracture

The danger of causing severe damage to the bone by secondary splitting due to the impact of the nail has discouraged us from using the method in comminuted fractures Further, comminution of the proximal fragment prevents the elevation of this fragment into the wound—an essential step in the operation

In addition to the broad indications outlined above there are two types of case in which we feel that nailing has a particular application

(1) In fractures of the femoral shaft complicated by fracture of the tibia and fibula on the same side, where the operation is combined with internal fixation of the tibial fracture We believe that this notoriously difficult problem is best treated in this way An obstinately stiff knee need not be the price the patient must pay for a reconstructed limb, his postoperative régime does not involve restriction of movement

Case 1 —A boy, aged 19, had a motor accident and sustained a transverse fracture of the middle third of his right femur and a transverse fracture of his right tibia, with a large butterfly third fragment Operation three hours later consisted in intramedullary nailing of the femur and plating of the tibia No further fixation was considered necessary at any time Six weeks later the patient was up and about on crutches, having control of the limb and knee flexion to 70° He was accordingly discharged to his home and attended as an outpatient At nineteen weeks he had a full range of knee movement and was walking without protection, his fractures being in anatomical position.

(2) By removing the necessity to restrict movement, and by reducing the period of recumbency, intramedullary nailing minimises the problems which arise in treating old people

Case 2 —A woman, aged 85, fell from her bed two months after a nailing operation for a fractured neck of femur and sustained a subtrochanteric fracture through the level at which the pin had been inserted Five days later intramedullary nailing was done and the Smith Petersen nail was removed The transcervical fracture was stable enough to require no further treatment The postoperative course was uneventful, and the patient was allowed up in a chair two weeks after the operation At four weeks she got about with two sticks, and at ten weeks she walked without protection. Six months after the operation the fracture was soundly united and she walked well with one stick. In spite of her two operations she still retained 120° of knee flexion—10° less than on her normal side

RESULTS

Of the 20 patients under review, 1 died six weeks after the operation, from cerebral hæmorrhage, 3 cases are too recent for assessment, and 2 in subjects of Paget's disease are also excluded There remain 14 cases for analysis

Our earliest case treated in this way has now been followed for more than six years, 5 for more than three years, and 6 for a year or more Results are reviewed in terms of functional restoration, bony union, and complications

Return of Function

The postoperative régime allows the patient to move about freely in bed from the start It is our impression that this not only reduces his discomfort but also favours rapid return of mental well being Nursing is much easier and the risk of deep venous thrombosis is less.

We allow the patients to walk with crutches without weight bearing when the wound is healed and when they can lift the leg off the bed The average delay before these two criteria are satisfied has been 3 3 weeks This is an important step in that it allows more purposeful active movement of the knee joint and thus reduces the extent and duration of the reactionary œdema

Partial weight bearing is encouraged at a time which depends on various factors Local conditions peculiar to the fracture—i e, its degree of obliquity and level—and associated injuries, especially of the leg bones on the same side, will influence this decision Especially favourable cases—i e, transverse fractures of the middle third—have taken weight at four weeks and rapidly graduated to unprotected weight bearing at six weeks In spite of this early weight bearing we have not seen displacement in these transverse fractures This is probably due to the fact that the nail obtains its greatest grip at this level On the other hand, a patient with an ipsolateral tibial fracture did not bear weight until eighteen weeks had elapsed

The average time taken to achieve partial weight bearing was 8 5 weeks, this is the stage at which most of these patients are discharged from hospital

The restoration of function to the knee joint, always of moment in this injury, has been studied in some detail. When they were discharged from medical supervision 11 patients had achieved full flexion at the knee Of the remainder, 2 are untraced and 1 has only 90° of flexion

Although these end results are gratifying, I want to emphasise again the speed with which function is re established in these cases Early weight bearing allows early discharge from hospital and rapid rehabilitation, and this is, we believe, achieved without prejudice to the final result

Bony Union

The stability afforded by a well fitting nail prevents assessment of union by traditional clinical methods Radiography is also of doubtful value, because union in nailed fractures produces little callus between the cortices involved in the fracture Union depends mainly on callus laid down peripherally This was a constant finding in our series. It has been suggested that pressure of the nail in the medullary cavity is responsible (Fitts et al. 1949)

As the time of "bony union" I have therefore taken the point at which unprotected weight bearing without sticks or splintage is allowed This corresponds functionally to the stage of consolidation in fractures treated by closed methods

The average time between injury and the removal of all protection was 17 2 weeks This compares favourably with the 23 weeks required to reach the same stage in a group of femoral fractures treated without internal fixation in this hospital

The absence of late bending at the fracture site in any case taking full weight confirms that functional consolidation had indeed taken place

Complications

The 1 death from causes unassociated with the operation has been mentioned There were no cases of septic bone, non-union, or fat emboli Superficial sepsis occurred in the buttock wound in 1 case this is potentially a weak point in the technique and has been mentioned above

Three cases require particular consideration

Case 3 —A man with a fracture of the upper third of the femur was found to have bent his nail during the period of partial weight-bearing He was one of the early cases (1945), and it is now evident that the nail used was too short The angulation of the femur is not gross, and when the patient was last seen five years later he had 1 in. of shortening but a full range of movement He is following his pre war trade as a bricklayer

Case 4 —A man was discharged from hospital bearing partial weight six weeks after nailing of a transverse middle third fracture Next day he fell on to a concrete floor and bent his nail at the site of fracture He was readmitted, and true alignment was restored by traction. This was possible because the distal fragment could be moved on the pin in the splayed-out lower end of the bone The final result is excellent, but the pin will probably have to be left in situ.

Case 5 —An uncoöperative schizophrenic had an oblique fracture at the junction of the middle and lower thirds of the femur After operation he could not be restrained, and as early as two weeks later he was walking round his room without any support The site and obliquity of the fracture, coupled with early unprotected weight bearing, have led to early bony union with 20° of angulation at the fracture site and a secondary genu valgum. Further surgery may be necessary

In summary, therefore, the complications which have arisen have, apart from one exceptional case, had no influence upon the final result

REMOVAL OF NAIL

The nail should be removed when firm consolidation has taken place This can be very easily done through a small incision over the buttock and with an extractor which resembles a crochet hook and fits the slot made in the end of the nail for this purpose The nail is removed because a bursa often forms round the protruding tip and causes pain when the patient sits down, and because the permanent retention of so large a piece of metal within the medulla may have its own dangers

SUMMARY

Intramedullary nailing in 20 cases of fracture of the femoral shaft is reviewed The operation and its indications are described Return of function and bony union are good A few complications are described

I am very grateful to Mr B H. Burns and Mr R H. Young, under whose care the patients were treated at St Peter's Hospital, Chertsey (Botleys Park) for permission to review their cases, and for their assistance in the preparation of this report My thanks are also due to Miss Zita Stead for the illustration.

REFERENCES

Böhler L (1948) Medullary Nailing of Küntscher London
Chance A (1949) *J Bone Jt Surg* 31B 135
Fitts W T jun Roberts B Spoont, S I, Ritter W W (1949) *Surg Gynec Obstet* 89, 609
Fraenkel G J (1945) *Lancet* ii 387
Groves E W H (1916–19) *Brit J Surg* 6 203
Haebler C (1949) *Nav med Bull. Wash* 49 423 626 831 1033
Küntscher G. (1940) *Arch klin Chir* 200 443
Lambotte A. (1913) Chirurgie opératoire des fractures. Paris
Lambrinudi C (1940) *Proc R. Soc. Med* 33 153.
McKee G K. (1948) *Lancet* ii 511
Watson Jones R., et al. (1950) *J Bone Jt Surg* 32B, 694

DIPHTHERIA ANTITOXIN IN CORD-BLOOD

SURVEY OF SAMPLES FROM 15 AREAS OF BRITISH ISLES

MOLLIE BARR
M.Sc Lond., A.R.I.C

A T GLENNY
B Sc Lond., F.R S

H J PARISH
M.D Edin., F.R C.P.E.

From the Wellcome Research Laboratories, Beckenham

In a study of factors involved in the active immunisation of young babies against diphtheria Barr et al. (1950) found that, when the level of passive maternally conferred antitoxin in babies was below 0 04 unit per ml at the time of the first injection of prophylactic (0 5 ml of A.P T), there was no interference with active immunisation, whereas titres of 0·1 unit per ml., or more, caused interference with the first dose of A.P T

Barr et al. (1949) showed that it was possible to calculate from the antitoxic titres of the cord-blood, the age at which any baby could be injected with prophylactic without interference from passive antitoxin Barr et al. (1950) calculated that over 80% of a population of 200 babies born in South East London would be satisfactorily immunised if they received the first dose of 0·5 ml. of A.P T at the age of 3 months They suggested that antitoxin titrations on a limited number of cord-blood samples from different districts would give a good idea of the immunity state of the newborn, and that methods of immunisation could be derived therefrom which would be most satisfactory for most of the babies

This paper gives analyses of values of cord-blood samples from fifteen areas of the British Isles—Aberdeen, Birmingham, Cardiff, Castleford, Cork, Coventry, Dumfries, Glasgow, Leeds, three districts of London, Rochdale, Stratford on-Avon, and West Bromwich The statistical analyses were done by one of us (M B) The values recorded are those of a relatively large age group, most of the mothers being aged 20–35, but some being older or younger They cannot be regarded as a fair sample of the general population, because most of the samples were obtained from urban areas The figures give a picture of the immunity state at present, and may change considerably in future years according to the trend of immunisation and the presence or absence of epidemics

The techniques adopted for taking the cord blood samples and estimating the antitoxin levels were those described by Barr et al (1949) They found that the distributions of values of 100 samples from each of two socially similar districts of South East London were not significantly different In the present investigation of cord blood from different districts a sample of 100 has therefore been studied, although from one large industrial town two consecutive samples of 100 were compared, and confirmed that the number tested constituted an adequate statistical sample

The results of this comparison are shown in table I the antitoxic values being arranged in five groups I

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02, 0 04	17	19	36
0 1, 0 2 0 5	23	30	53
1 0, 2 0, 5 0	10	8	18
Total	100	100	200

$\chi^2 = 2\ 568$ 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant ($\chi^2 = 64\ 29$ 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml or higher are rare, only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al (1950), who compared the staphylococcal antitoxic titres of serum from cord-blood, and mothers' and infants' blood

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml , this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

$\chi^2 = 15\ 685$ 10 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant ($\chi^2 = 8\ 005$ 4 D F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al for the South East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	522
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	180
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1,500

$\chi^2 = 148\ 305$ 56 D F P = <0 01

TABLE V—APPROXIMATE SCHICK-POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

Age (weeks)	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (37·6%)
	Number of babies with titres below 0·04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (51·7%)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1260 (84·4%)
26	96	98	98	95	96	98	98	98	99	98	96	93	96	89	97	1445 (96·3%)
34	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (99·1%)

shown in table III These districts are represented as C, D, E, H, and M in table II, but the sequence is not as stated above There is no significant difference between the distributions of values of blood samples from these areas, and the differences between districts C and M are not significant when compared alone, except for the numbers with and without detectable antitoxin

Comparisons have also been made between samples from the London area and from these same five provincial towns, and table IV shows that the differences in distribution are highly significant The analysis shows that the number of samples with less than 0·01 unit per ml is below expectation in the London series, the number between 0·01 and 0·2 exceeds expectation, while the number of high value samples, above 0·5 unit, is approximately equal to the expected number The differences between the distributions are even greater if the West London samples (Queen Charlotte's Hospital) are excluded for the latter are statistically comparable with the provincial samples ($\chi^2 = 4.019$ 4 D.F P = 0·41)

It is unfortunately impossible to make any comparison between strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas

TABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml)	Percentage of samples from		Total no of samples
	London	Industrial towns	
Under 0·001	28·0	35·8	263
0·001–0·004	5·0	9·4	62
0·01–0·04	22·0	15·6	144
0·1 0·2	29·0	21·6	195
0·5 and over	16·0	17·6	136
Total	300	500	800

$\chi^2 = 16.914$ 4 D F P = <0·01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times Of a small number of samples received from a rural area, however and not included in table II few contained any detectable antitoxin

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population It is possible that many of the mothers were not then residing in the area affected by the epidemic The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information There is no reason to suppose that the information from these towns was less reliable than that from the other 8 There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts The wide age group covered would necessitate the examination of very large numbers of samples.

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S E London) with antitoxic values below the Schick level were significantly different, the numbers in these areas that could be satisfactorily immunised at the age of 3 months, however, were not significantly different

Table V gives the approximate Schick-positive rates of the mothers in each of the fifteen districts of this survey For this purpose all with cord blood values under 0·004 unit per ml. have been recorded as Schick-positive, and those with values of 0·004 unit or higher as Schick-negative The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out probably they provide a slightly lower estimate, in view of the higher titre of cord blood Very considerable differences, which are clearly highly significant, exist between the approximate Schick-positive rates in the fifteen districts ($\chi^2 = 73.718$ 14 D.F P = <0·001) The figures range from 23 in district O to 62 in district A, with an average of 37·6 It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P.T at birth and at the age of 3, 6, and 8 months, these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0·04 unit per ml. at these ages Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A, these differences are highly significant ($\chi^2 = 38.097$ 14 D.F P = <0·001) A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0·05 At the age of 6 months 96·3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present

It is abundantly clear from table V that, as noted before (Barr 1950), little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01, 0 02 0 04	17	19	36
0 1 0 2, 0 5	23	30	53
1 0, 2 0, 5 0	10	8	18
Total	100	100	200

χ^2 = 2 508   4 D F   P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant (χ^2 = 64 29 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml. or higher are rare, only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al. (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al. (1950), who compared the staphylococcal antitoxic titres of serum from cord blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml , this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	O	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1, 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

χ^2 = 15 685   16 D F   P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant (χ^2 = 8 005 4 D.F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al for the South East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	522
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	3	5	4	8	8	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	186
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

χ^2 = 148 305   56 D F   P = <0 01

TABLE V—APPROXIMATE SCHICK-POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (37·6%)
Age reeks)	Number of babies with titres below 0·04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (51·7%)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1266 (84·4%)
26	96	98	98	95	96	98	98	98	99	98	96	93	96	89	97	1445 (96·3%)
34	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (99·1%)

own in table III These districts are represented as D, E, H, and M in table II, but the sequence is not stated above There is no significant difference tween the distributions of values of blood samples om these areas, and the differences between districts and M are not significant when compared alone, except r the numbers with and without detectable antitoxin

Comparisons have also been made between samples om the London area and from these same five provincial wns, and table IV shows that the differences in distriution are highly significant The analysis shows that e number of samples with less than 0·01 unit per ml. below expectation in the London series, the number etween 0·01 and 0·2 exceeds expectation, while the umber of high-value samples, above 0·5 unit, is approxiately equal to the expected number The differences etween the distributions are even greater if the West ondon samples (Queen Charlotte's Hospital) are excluded or the latter are statistically comparable with the rovincial samples (χ^2 = 4·019 4 D F P = 0·41)

It is unfortunately impossible to make any comparison etween strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas

ABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD-BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml)	Percentage of samples from		Total no of samples
	London	Industrial towns	
Under 0·001	25·0	35·8	263
0·001–0·004	5·0	9·4	62
0·01–0·04	22·0	15·6	144
0·1 0·2	29·0	21·6	195
0·5 and over	16·0	17·6	136
Total	300	500	800

χ^2 = 16·914 4 D.F P = <0·01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times Of a small number of samples received from a rural area, however, and not included in table II few contained any detectable antitoxin.

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population It is possible that many of the mothers were not then residing in the area affected by the epidemic The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information There is no reason to suppose that the information from these towns was less reliable than that from the other 8 There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts The wide age group covered would necessitate the examination of very large numbers of samples

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S.E London) with antitoxic values below the Schick level were significantly different, the numbers in these areas that could be satisfactorily immunised at the age of 3 months however, were not significantly different

Table V gives the approximate Schick-positive rates of the mothers in each of the fifteen districts of this survey For this purpose all with cord-blood values under 0·004 unit per ml. have been recorded as Schick-positive, and those with values of 0·004 unit or higher as Schick-negative The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out probably they provide a slightly lower estimate, in view of the higher titre of cord-blood Very considerable differences, which are clearly highly significant, exist between the approximate Schick positive rates in the fifteen districts (χ^2 = 73·718 14 D.F P = <0·001) The figures range from 23 in district O to 62 in district A, with an average of 37·6 It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P.T at birth and at the age of 3, 6, and 8 months, these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0·04 unit per ml. at these ages Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A, these differences are highly significant (χ^2 = 38·097 14 D.F P = <0·001) A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0·05 At the age of 6 months 96·3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present

It is abundantly clear from table V that, as noted before (Barr 1950), little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02 0 04	17	19	36
0 1 0 2 0 5	23	30	53
1 0, 2 0 5 0	10	8	18
Total	100	100	200

χ^2 = 2 568 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant (χ^2 = 64 29 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml or higher are rare, only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al (1950), who compared the staphylococcal antitoxic titres of serum from cord blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml , this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	[illegible]
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	[illegible]
Total	100	100	100	100	100	500

χ^2 = 15 685 16 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al. (1949) found that the distributions of values in samples from two districts of South East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant (χ^2 = 8 005 4 D.F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al. for the South East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	532
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	186
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

χ^2 = 148 305 56 D F P = <0 01

TABLE V—APPROXIMATE SCHICK-POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

Age (weeks)	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (*37 6%*)
	Number of babies with titres below 0 04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (*51 7%*)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1266 (*84 4%*)
26	96	98	98	95	96	98	98	98	99	98	96	93	96	89	97	1445 (*96 3%*)
34	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (*99 1%*)

shown in table III These districts are represented as C, D, E, H, and M in table II, but the sequence is not as stated above There is no significant difference between the distributions of values of blood samples from these areas, and the differences between districts C and M are not significant when compared alone, except for the numbers with and without detectable antitoxin

Comparisons have also been made between samples from the London area and from these same five provincial towns, and table IV shows that the differences in distribution are highly significant The analysis shows that the number of samples with less than 0·01 unit per ml. is below expectation in the London series, the number between 0 01 and 0 2 exceeds expectation, while the number of high-value samples, above 0·5 unit, is approximately equal to the expected number The differences between the distributions are even greater if the West London samples (Queen Charlotte's Hospital) are excluded for the latter are statistically comparable with the provincial samples ($\chi^2 = 4\ 019$ 4 D.F P = 0 41)

It is unfortunately impossible to make any comparison between strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas

TABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD-BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml)	Percentage of samples from		Total no of samples
	London	Industrial towns	
Under 0 001	28·0	35 8	263
0 001–0 004	5 0	9 4	62
0·01–0 04	22 0	15 6	144
0 1 0 2	29·0	21 6	195
0 5 and over	16 0	17·6	136
Total	300	500	800

$\chi^2 = 16\ 914$ 4 D.F P = <0·01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times Of a small number of samples received from a rural area, however, and not included in table II few contained any detectable antitoxin

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population It is possible that many of the mothers were not then residing in the area affected by the epidemic The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information There is no reason to suppose that the information from these towns was less reliable than that from the other 8 There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts The wide age group covered would necessitate the examination of very large numbers of samples

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S.E London) with antitoxic values below the Schick level were significantly different, the numbers in these areas that could be satisfactorily immunised at the age of 3 months however, were not significantly different

Table V gives the approximate Schick-positive rates of the mothers in each of the fifteen districts of this survey For this purpose all with cord-blood values under 0 004 unit per ml. have been recorded as Schick-positive, and those with values of 0 004 unit or higher as Schick negative The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out probably they provide a slightly lower estimate in view of the higher titre of cord blood Very considerable differences, which are clearly highly significant, exist between the approximate Schick-positive rates in the fifteen districts ($\chi^2 = 73\ 718$ 14 D.F P = <0·001) The figures range from 23 in district O to 62 in district A, with an average of 37 6 It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P.T at birth and at the age of 3, 6, and 8 months, these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0 04 unit per ml. at these ages Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A, these differences are highly significant ($\chi^2 = 38\ 097$ 14 D.F P = <0 001) A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0·05 At the age of 6 months 96 3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present

It is abundantly clear from table V that, as noted before (Barr 1950) little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02 0 04	17	19	36
0 1 0 2, 0 5	23	30	53
1 0 2 0, 5 0	10	8	18
Total	100	100	200

$\chi^2 = 2\ 568$ 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant ($\chi^2 = 64\ 29$ 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml or higher are rare, only 5 of the 1500 samples (0 33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al. (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al. (1950), who compared the staphylococcal antitoxic titres of serum from cord blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml , this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

$\chi^2 = 15\ 685$ 10 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South-East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant ($\chi^2 = 8\ 005$ 4 D F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al. for the South-East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	632
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	180
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

$\chi^2 = 148\ 305$ 56 D F P = <0 01

TABLE V—APPROXIMATE SCHICK-POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

Age (weeks)	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (*37 6%*)
	Number of babies with titres below 0 04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (*51 7%*)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1266 (*84 4%*)
26	96	98	98	95	96	98	98	98	99	98	96	93	96	89	97	1445 (*96 3%*)
34	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (*99 1%*)

shown in table III These districts are represented as C, D, E, H, and M in table II, but the sequence is not as stated above There is no significant difference between the distributions of values of blood samples from these areas, and the differences between districts C and M are not significant when compared alone, except for the numbers with and without detectable antitoxin

Comparisons have also been made between samples from the London area and from these same five provincial towns, and table IV shows that the differences in distribution are highly significant The analysis shows that the number of samples with less than 0·01 unit per ml is below expectation in the London series, the number between 0 01 and 0 2 exceeds expectation, while the number of high value samples, above 0 5 unit, is approximately equal to the expected number The differences between the distributions are even greater if the West London samples (Queen Charlotte's Hospital) are excluded for the latter are statistically comparable with the provincial samples ($\chi^2 = 4\ 019$ 4 D F P = 0 41)

It is unfortunately impossible to make any comparison between strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas

TABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml)	Percentage of samples from		Total no of samples
	London	Industrial towns	
Under 0 001	28 0	35 8	263
0 001–0 004	5 0	9·4	62
0·01–0 04	22 0	15 6	144
0 1 0 2	29 0	21 6	195
0 5 and over	16 0	17 6	136
Total	300	500	800

$\chi^2 = 16\ 914$ 4 D F P = <0 01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times Of a small number of samples received from a rural area, however, and not included in table II few contained any detectable antitoxin

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population It is possible that many of the mothers were not then residing in the area affected by the epidemic The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information There is no reason to suppose that the information from these towns was less reliable than that from the other 8 There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts The wide age group covered would necessitate the examination of very large numbers of samples

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S E London) with antitoxic values below the Schick level were significantly different, the numbers in these areas that could be satisfactorily immunised at the age of 3 months, however, were not significantly different

Table V gives the approximate Schick positive rates of the mothers in each of the fifteen districts of this survey For this purpose all with cord-blood values under 0 004 unit per ml have been recorded as Schick-positive, and those with values of 0 004 unit or higher as Schick negative The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out probably they provide a slightly lower estimate, in view of the higher titre of cord blood Very considerable differences, which are clearly highly significant, exist between the approximate Schick positive rates in the fifteen districts ($\chi^2 = 73\ 718$ 14 D F P = <0 001) The figures range from 23 in district O to 62 in district A, with an average of 37 6 It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P T at birth and at the age of 3, 6, and 8 months, these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0 04 unit per ml at these ages Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A, these differences are highly significant ($\chi^2 = 38\ 097$ 14 D.F P = <0 001) A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0 05 At the age of 6 months 96 3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present

It is abundantly clear from table V that, as noted before (Barr 1950), little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02 0 04	17	19	36
0 1 0 2, 0 5	23	30	53
1 0 2 0, 5 0	10	8	18
Total	100	100	200

χ^2 = 2 563 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant (χ^2 = 64 29 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml or higher are rare, only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al. (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al. (1950), who compared the staphylococcal antitoxic titres of serum from cord blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml, this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

χ^2 = 15 685 16 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant (χ^2 = 8 005 4 D F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al for the South-East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	522
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	186
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

χ^2 = 148 305 56 D F P = <0 01

TABLE V—APPROXIMATE SCHICK-POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

Age (weeks)	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (37 6%)
	Number of babies with titres below 0 04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (51 7%)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1266 (84 4%)
26	96	98	98	95	96	98	98	98	99	98	96	93	96	89	97	1445 (96 3%)
34 –	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (99 1%)

shown in table III These districts are represented as C, D, E, H, and M in table II, but the sequence is not as stated above There is no significant difference between the distributions of values of blood samples from these areas, and the differences between districts C and M are not significant when compared alone, except for the numbers with and without detectable antitoxin

Comparisons have also been made between samples from the London area and from these same five provincial towns, and table IV shows that the differences in distribution are highly significant The analysis shows that the number of samples with less than 0·01 unit per ml is below expectation in the London series, the number between 0 01 and 0 2 exceeds expectation, while the number of high value samples, above 0 5 unit, is approximately equal to the expected number The differences between the distributions are even greater if the West London samples (Queen Charlotte's Hospital) are excluded for the latter are statistically comparable with the provincial samples (χ^2 = 4 019 4 D F P = 0 41)

It is unfortunately impossible to make any comparison between strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas.

TABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml)	Percentage of samples from		Total no of samples
	London	Industrial towns	
Under 0 001	28 0	35 8	263
0 001–0 004	5 0	9·4	62
0 01–0 04	22 0	15 6	144
0 1 0 2	29 0	21 6	195
0 5 and over	16 0	17 6	136
Total	300	500	800

χ^2 = 16 914 4 D F P = <0 01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times Of a small number of samples received from a rural area, however, and not included in table II few contained any detectable antitoxin

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population It is possible that many of the mothers were not then residing in the area affected by the epidemic The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information There is no reason to suppose that the information from these towns was less reliable than that from the other 8 There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts The wide age group covered would necessitate the examination of very large numbers of samples

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S E London) with antitoxic values below the Schick level were *significantly different*, the numbers in these areas that could be satisfactorily immunised at the age of 3 months, however, were not significantly different

Table V gives the approximate Schick positive rates of the mothers in each of the fifteen districts of this survey For this purpose all with cord-blood values under 0 004 unit per ml have been recorded as Schick-positive, and those with values of 0 004 unit or higher as Schick negative The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out probably they provide a slightly lower estimate, in view of the higher titre of cord blood Very considerable differences, which are clearly highly significant, exist between the approximate Schick positive rates in the fifteen districts (χ^2 = 73 718 14 D.F P = <0 001) The figures range from 23 in district O to 62 in district A, with an average of 37 6 It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P T at birth and at the age of 3, 6, and 8 months, these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0 04 unit per ml at these ages Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A, these differences are highly significant (χ^2 = 38 097 14 D.F P = <0 001) A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0 05 At the age of 6 months 96 3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present

It is abundantly clear from table V that, as noted before (Barr 1950), little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02 0 04	17	19	36
0 1 0 2 0 5	23	30	53
1 0, 2 0, 5 0	10	8	18
Total	100	100	200

χ^2 = 2 568 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant (χ^2 = 64 29 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml or higher are rare, only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al. (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al (1950), who compared the staphylococcal antitoxic titres of serum from cord blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml, this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

χ^2 = 15 685 16 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South-East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples. The differences found were not significant (χ^2 = 8 005 4 D F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al. for the South East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	522
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	16	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	186
0 5	3	4	5	9	9	10	9	10	7	8	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

χ^2 = 148 305 56 D F P = <0 01

TABLE V—APPROXIMATE SCHICK POSITIVE RATES OF MOTHERS, COMPARED WITH NUMBERS OF BABIES IN EACH AREA THAT COULD SATISFACTORILY START IMMUNISATION AT VARIOUS AGES

Age (weeks)	Approximate Schick positive rates of mothers in area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
	62	56	48	42	44	38	36	36	32	34	29	30	25	29	23	564 (*37.6%*)
	Number of babies with titres below 0.04 unit per ml															
0	80	68	62	61	57	45	53	53	42	50	36	38	43	41	37	766 (*51.7%*)
13	93	90	88	81	84	85	87	82	91	90	85	83	77	70	80	1266 (*84.4%*)
26	96	98	98	95	96	98	98	98	90	98	96	93	96	89	97	1445 (*96.3%*)
34	100	99	99	99	99	100	99	100	100	100	100	97	99	95	100	1486 (*99.1%*)

shown in table III. These districts are represented as C, D, E, H, and M in table II, but the sequence is not as stated above. There is no significant difference between the distributions of values of blood samples from these areas, and the differences between districts C and M are not significant when compared alone, except for the numbers with and without detectable antitoxin.

Comparisons have also been made between samples from the London area and from these same five provincial towns, and table IV shows that the differences in distribution are highly significant. The analysis shows that the number of samples with less than 0.01 unit per ml is below expectation in the London series; the number between 0.01 and 0.2 exceeds expectation; while the number of high value samples, above 0.5 unit, is approximately equal to the expected number. The differences between the distributions are even greater if the West London samples (Queen Charlotte's Hospital) are excluded for the latter are statistically comparable with the provincial samples ($\chi^2 = 4.019$ 4 D.F. P = 0.41).

It is unfortunately impossible to make any comparison between strictly rural and urban districts, because many of the towns included in the survey receive patients from outlying rural areas.

TABLE IV—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES AMONG CORD BLOOD SAMPLES FROM LONDON AND FIVE INDUSTRIAL TOWNS IN THE PROVINCES

Antitoxic value (unit per ml.)	Percentage of samples from		Total no. of samples
	London	Industrial towns	
Under 0.001	28.0	35.8	263
0.001–0.004	5.0	9.4	62
0.01–0.04	22.0	15.6	144
0.1–0.2	29.0	21.6	195
0.5 and over	16.0	17.6	136
Total	300	500	800

$\chi^2 = 16.914$ 4 D.F. P = <0.01

Possibly differences which may have existed in the past between the antitoxic values of people from rural and urban districts are now reduced to some extent because of the greater movements of the population in recent times. Of a small number of samples received from a rural area, however, and not included in table II few contained any detectable antitoxin.

EFFECT OF EPIDEMICS

Certain towns included in this survey have experienced severe epidemics within the last twenty years. The distribution of antitoxic values from these areas does not differ from those of similar towns which have not experienced such epidemics. This may possibly be explained by the long lapse of time between the epidemics and the sampling of the population. It is possible that many of the mothers were not then residing in the area affected by the epidemic. The percentage of mothers in each of two such towns, who stated that they had had diphtheria, was less than half those in 6 out of 8 other districts returning information. There is no reason to suppose that the information from these towns was less reliable than that from the other 8. There are insufficient figures from immunised mothers for any conclusions to be drawn as to the relative success of methods of immunisation in different districts. The wide age group covered would necessitate the examination of very large numbers of samples.

AGE AT WHICH IMMUNISATION COULD BE STARTED

It has already been shown (Barr 1950) that the numbers of babies born in Coventry and Southwark (S.E. London) with antitoxic values below the Schick level were significantly different; the numbers in these areas that could be satisfactorily immunised at the age of 3 months, however, were not significantly different.

Table V gives the approximate Schick positive rates of the mothers in each of the fifteen districts of this survey. For this purpose all with cord blood values under 0.004 unit per ml. have been recorded as Schick-positive, and those with values of 0.004 unit or higher as Schick negative. The figures therefore give only a fair approximation to the result which would have been obtained had the Schick test actually been carried out; probably they provide a slightly lower estimate, in view of the higher titre of cord blood. Very considerable differences, which are clearly highly significant, exist between the approximate Schick positive rates in the fifteen districts ($\chi^2 = 73.718$ 14 D.F. P = <0.001). The figures range from 23 in district O to 62 in district A, with an average of 37.6. It will be seen that the order of the figures from A to O is roughly, but not exactly, the same as that in table II, where the number of samples with no detectable antitoxin is given.

Table V also shows the numbers of babies that could be satisfactorily immunised if they received their first dose of A.P.T. at birth and at the age of 3, 6, and 8 months; these figures were obtained by calculation and represent the numbers whose level of maternally conferred antitoxin would have fallen below 0.04 unit per ml. at these ages. Very considerable differences exist between the numbers that could be immunised at birth, and the average number is just over 50% for the 1500 samples. At the age of 3 months the differences are greatly reduced, ranging from 70 in district O to 93 in district A; these differences are highly significant ($\chi^2 = 38.097$ 14 D.F. P = <0.001). A study of the table shows that the greatest deviation from the mean is provided by district N, and, if this figure is omitted from the analysis, the value of P becomes 0.05. At the age of 6 months 96.3% of the babies could be successfully immunised (though only 89% in district N), and little is gained by further delaying the first dose of prophylactic until the age of 8 months, officially recommended at present.

It is abundantly clear from table V that, as noted before (Barr 1950), little useful information as to when immunisation can be started in a population is provided

TABLE I—COMPARISON OF DISTRIBUTION OF ANTITOXIC VALUES IN TWO CONSECUTIVE SERIES EACH OF 100 CORD BLOOD SAMPLES FROM THE SAME TOWN

Antitoxic values (units per ml)	No of cord blood samples		
	Series 1	Series 2	Total
Under 0 001	41	32	73
0 001 0 002 0 004	9	11	20
0 01 0 02 0 04	17	19	36
0 1, 0 2, 0 5	23	30	53
1 0 2 0 5 0	10	8	18
Total	100	100	200

$\chi^{2} = 2\ 568$ 4 D F P = 0 635

will be seen that there was no significant difference in distribution between the two series, and a high value of P (0 635) was obtained It was therefore concluded that a sample of 100 is adequate for statistical comparisons

DISTRIBUTION OF VALUES

Table II shows in detail the distribution of values from all fifteen districts investigated These have been arranged in order according to the numbers with no detectable antitoxin, and the districts have been named from A to O to preserve anonymity The numbers with less than 0 001 unit per ml range from 59 in district A to 21 in district O, with an average of 34 8 The differences between the numbers with and without detectable antitoxin are highly significant ($\chi^{2} = 64\ 29$ 14 D F P = < 0 001) A comparison of the general distribution of values, arranged in groups as indicated by the brackets in column 1 of table II, shows that the differences are highly significant (see foot of table II) The chief points of difference lie in the numbers with no detectable antitoxin, and to a lesser degree in those with over 0 1 unit per ml District N provided an abnormally large number of high values, 20% being 1 unit or higher 11 samples from M and 10 from D contained 1 unit or more, but only 2 samples of such value were obtained from district I Barr (1950) has already shown that the number of samples with no detectable antitoxin in any population may give no indication of the mean value or the scatter of the remainder Table II shows that the number of high values, over 0 5 or 1 unit, is unrelated to the values of the rest of the population It is clear that some difficulty would be encountered in formulating a simple scheme of immunisation for district N, owing to the large scatter of values and the number of high titres found in this population It should be noted that the only sample with a value of over 20 units was obtained from that district Table II shows that values of 10 units per ml. or higher are rare , only 5 of the 1500 samples (0·33%) reached or exceeded this figure Slightly lower values would have been expected had the blood samples been taken from the mothers, because Barr et al (1949) found that the antitoxic content of cord blood was usually appreciably higher and might be double that of the mother's blood taken during labour This observation has recently been confirmed by Murray et al (1950), who compared the staphylococcal antitoxic titres of serum from cord-blood, and mothers' and infants' blood.

The main peaking in value in the distributions shown in table II occurs over the range 0 04, 0 1, 0 2, 0 5 unit, but in several cases there is a suggestion of a lower peak, usually at 0 004 unit per ml , this is especially evident in districts D and M

TABLE III—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD BLOOD SAMPLES FROM FIVE INDUSTRIAL TOWNS

Antitoxic value (unit per ml)	No of samples from district					Total
	C	D	E	H	M	
Under 0 001	42	41	37	34	25	179
0 01–0 004	10	9	10	8	10	47
0 01–0 04	17	17	16	13	15	78
0 1 0 2	19	14	21	27	27	108
0 5 and over	12	19	16	18	23	88
Total	100	100	100	100	100	500

$\chi^{2} = 15\ 685$ 16 D F P = 0 48

COMPARISON OF VALUES FROM VARIOUS AREAS

As we have already stated, Barr et al (1949) found that the distributions of values in samples from two districts of South East London were not significantly different A third district of London has now been investigated, 100 samples from Queen Charlotte's Hospital being examined, and a comparison has been made between these three series of samples The differences found were not significant ($\chi^{2} = 8\ 005$ 4 D F P = 0 093), the value of P was considerably lower however than that obtained by Barr et al. for the South-East London samples The chief difference between the districts lay in the smaller number of low values (under 0 01) in the South East London series

A comparison has been made between five industrial towns in the provinces—Birmingham, Coventry, Leeds, Rochdale, and West Bromwich—and the results are

TABLE II—DISTRIBUTION OF ANTITOXIC VALUES AMONG SERIES OF 100 CORD-BLOOD SAMPLES TAKEN FROM 15 AREAS OF BRITISH ISLES

Antitoxic values (units per ml)	No of samples from area															Total
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
Under 0 001	59	51	42	41	37	36	34	34	31	30	29	28	25	24	21	522
0 001	1	1	2	0	3	0	0	1	0	2	0	1	0	1	2	14
0 002	2	4	4	1	4	2	2	1	1	2	0	1	0	4	0	28
0 004	7	3	4	8	3	1	6	6	0	7	2	2	10	3	3	65
0 01	3	3	4	6	5	2	4	5	3	2	3	1	4	1	5	51
0 02	8	6	6	5	5	4	7	6	7	7	2	5	4	8	6	86
0 04	3	9	7	6	6	12	12	2	15	8	16	15	7	10	11	139
0 1	6	11	8	6	10	11	11	12	15	11	17	16	14	12	15	175
0 2	4	2	11	8	11	17	11	15	19	21	16	14	13	7	17	186
0 5	3	4	5	9	9	10	9	10	7	6	8	8	12	10	14	124
1 0	0	4	5	5	3	3	2	6	1	2	3	2	7	9	3	55
2 0	4	1	1	4	3	2	1	2	1	2	4	4	3	6	3	41
5 0	0	1	1	1	0	0	0	0	0	0	0	2	1	3	0	9
10 0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	0	4
20 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1500

$\chi^{2} = 148\ 305$ 56 D F P = <0 01

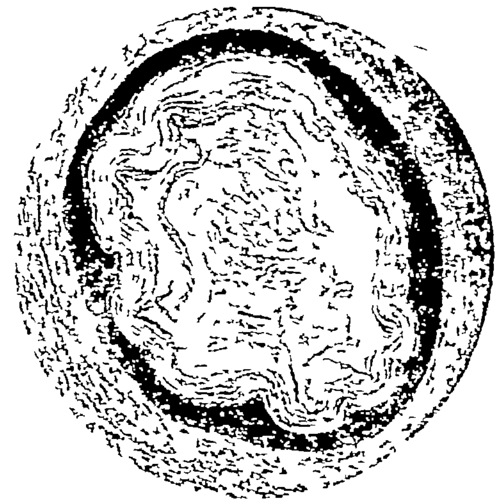


Fig 2—Cyst lined by squamous epithelium and containing concentric layers of keratin

ÆTIOLOGY

It appears therefore that the condition is one in which surface epithelium is displaced into the corium either in the form of single cells or cell nests, or by the invagination of the whole skin The result is the production of non specific inflammatory tissue and of implantation epidermoid cysts

The underlying cause is the piston action of the artificial leg Each time weight is put on the limb the stump is pushed into it and sustains pressure from the upper rim, mainly on its anterior and medial edge When the weight is taken off the leg, the pressure is released This oft repeated pressure and release presumably causes some displacement of the skin, and epithelium may be pushed inwards into the corium

Much has been written on epidermoid cysts following trauma either single (Le Fort 1894, Hartley 1896, King 1933 Yachnin and Summerill 1941, Ewing 1942, Pohlmann and Wachstein 1944, Stabb 1891), or repeated (King 1933) The cysts associated with artificial limbs have hitherto been regarded as sebaceous adenomata, but they should be recognised as post traumatic epidermoid cysts

CASE NOTES

Case 1 —Mrs A aged 34 Bilateral amputations above the knees after a railway accident in 1946 Started to wear artificial limbs in 1947 Three or four months later developed small painful lumps in the adductor regions, which improved with rest The lumps tended to become more painful and more evident in hot weather The local discomfort increased when the patient lost weight by dieting and the limbs fitted more loosely When examined in 1949 she had shotty thickening of the skin in the adductor regions of the thighs in a transverse direction corresponding to the level of the rims of the artificial legs Sections show the histological pictures described above

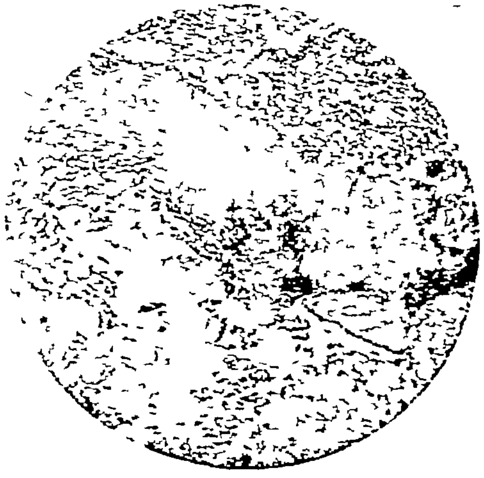


Fig 3—Fragment of skin epithelium lying free in the midst of chronic inflammatory cells.

Case 2 —Mrs B, aged 23 At 8 years the right leg was amputated above the knee following osteomyelitis She had an artificial limb soon afterwards, and eleven years later developed one small lump in the adductor region, "which remained uninfected for one year" This ultimately became infected and developed a discharging sinus Since then has had numerous lumps and the whole area is so painful that she cannot wear a prosthesis Examination showed thickening of the skin in the adductor region of the right leg in which small shotty nodules could be palpated (fig 1) Between the nodules the tissue appeared normal There was a well healed oblique scar, the site of previous operative removal of tissue Sections showed the typical histological picture

Case 3 —Mr C aged 47 Amputation of left leg above the knee twenty years ago Developed small lumps in the adductor region of the left leg fourteen months after starting to wear an artificial limb Lumps painful, and seemed to grow more in warm weather Had to discontinue wearing the limb for periods of two or three weeks at intervals of three or four months to allow the lumps to "settle" The area affected gradually became larger and at the time of examination the patient had been unable to wear the leg for eighteen months Thickening and lumpiness were evident in the adductor region of the thigh in a line corresponding with the upper edge of the artificial limb There were several painful lumps with reddened skin over them and discharging sinuses, from which pus could be expressed The pus was sterile on culture and the cellular components were polymorphs and scanty epithelial cells Histological appearances were as described.

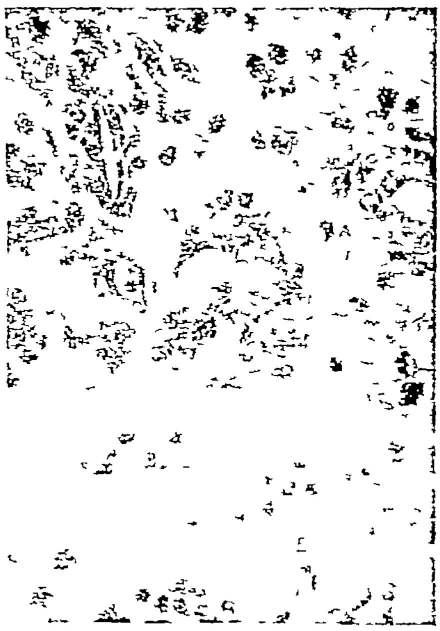


Fig 4—Chronic granulation tissue showing large giant-cell enclosing cornified epithelial cell

Case 4 —Mr D, aged 50 Amputation of right leg above the knee in first world war Developed lumps in the right adductor region which later became painful and formed discharging sinuses Unable to wear limb for six months Histological appearances characteristic.

Case 5 —Mr E, aged 29 Amputation above the left knee following compound fracture Developed lumps in the adductor region, which were painful and worse in hot weather They subsided with rest At the time of examination the patient was unable to wear his artificial leg Histological appearances characteristic

SUMMARY

Cases are described in which patients wearing the type of artificial leg usual in this country have developed a skin lesion in the adductor region of the thigh by the results of Schick testing For instance, in district B about 56% of babies were born with antitoxic values below the Schick level compared with 32% in district I, at the age of 3 months 90% of babies in B and 91% in I could receive their first dose of prophylactic In referring to successful immunisation the criteria of Barr et al (1950) have been adopted They obtained, in babies about 2 months after the second dose of A P T, normally distributed antitoxic values with a mean of about 0 2 unit per ml

SUMMARY

Titrations for diphtheria antitoxin have been made on 100 samples of cord blood from each of fifteen districts of the British Isles Highly significant differences exist between the distributions of values of samples from the various areas

Statistically comparable distributions were obtained from five industrial towns in the provinces, but these were significantly different from those of the London area

Very considerable differences existed between the approximate Schick positive rates and the number of high values in the various areas These differences could not be explained by earlier epidemics or methods of immunisation, the interval elapsing since serious epidemics is probably too great to exert any influence at present

The Schick test would give little useful information as to when immunisation could be started in the babies with expectation of success

We are greatly indebted to the following collaborators for supplying the samples of cord blood and for much valuable information Prof D Baird, Dr H J Rae, and Dr J Smith in Aberdeen, Dr J Hallum and Dr J McGarrity in Birmingham, Dr Scott Thomson in Cardiff, Dr J Paterson in Castleford, Dr J C Saunders in Cork, Mr H R Duval and Dr J F Galpine in Coventry, Dr J Bruce Dewar in Dumfries, Dr T Anderson and Dr E Hutton Brown in Glasgow, Prof A M Claye in Leeds, Dr K J Randall in S E London, Dr J Murray in W London, Dr J Innes in Rochdale, Dr E S Thomas in Stratford on Avon, and Dr J Tudor Lewis in West Bromwich Without their interest and coöperation the investigation could not have been made

REFERENCES

Barr M (1950) *Lancet* i 1110
— Glenny A T Randall, K J (1949) *Ibid* ii, 324
— — — (1950) *Ibid*, i 6
Murray J, Calman, R M Lepine A (1950) *Ibid*, ii 14

POST-TRAUMATIC EPIDERMOID CYSTS

FREIDA YOUNG
M B Lond, D C P
PATHOLOGIST, WILLESDEN GENERAL HOSPITAL, LATE
PATHOLOGIST, EAST HAM MEMORIAL HOSPITAL

THERE seems to be only one reference in the literature to epidermoid cysts in amputation stumps (Ministry of Pensions 1939) yet the condition is one which causes considerable inconvenience and financial loss to the patient, and much concern to those interested in his welfare

In a typical case the cysts first appear when the patient has worn an artificial limb for some months or years—usually after an above knee amputation Small lumps then develop in the skin of the adductor region of the thigh along the upper edge of the prosthesis In the early stages they disappear when the stump is rested, but in time they may become larger and more numerous the skin breaks down, "pus" is discharged, and the discharging sinus may become chronic The skin in the affected region often becomes pigmented (fig 1) At this stage it is impossible to wear the prosthesis, and the patient either becomes bedridden or takes to a crutch

No entirely satisfactory treatment has yet been devised, but attempts have been made to relieve the condition by excision of the affected area

PATHOLOGY

The specimens received from the surgeons consist of an elliptical pigmented piece of skin with underlying tissues On cutting through such a specimen at right angles to the skin surface one sees small round areas which appear to be abscesses, some with central softening There are also some round zones, outlined in the formol fixed tissue by a thin white line Microscopical examination shows zones of non specific inflammatory tissue composed of lymphocytes, plasma cells, and polymorphs, surrounded by young capillaries and fibroblasts or fibrous tissue Foreign body giant cells are always present and may be collected into follicles, some of which have a central cavity containing amorphous eosinophilic material There are also small cystic spaces lined with stratified squamous epithelium, these contain no hairs or sweat glands, and usually no dermal papillæ, and they are filled with concentric layers of keratin (fig 2) Some of the cysts are surrounded by, or are in close contact with, the inflammatory cells Most of them are microscopic in size, but some are large enough to be seen with the naked eye, and their lining of skin then appears as a thin white line

In some places there are fragments of readily recognisable skin epithelium in the chronic inflammatory tissue (fig 3) We were anxious to discover the contents of the slit like vacuoles in many of the foreign body giant cells and of the cystic spaces in which some of them lie However, neither polariscopic examination, nor staining with Scharlach R or Nile blue sulphate, or by the Golodetz, Windaus, or Schultz techniques (Mallory 1938) showed the presence of anisotropic material or of any fatty substance.

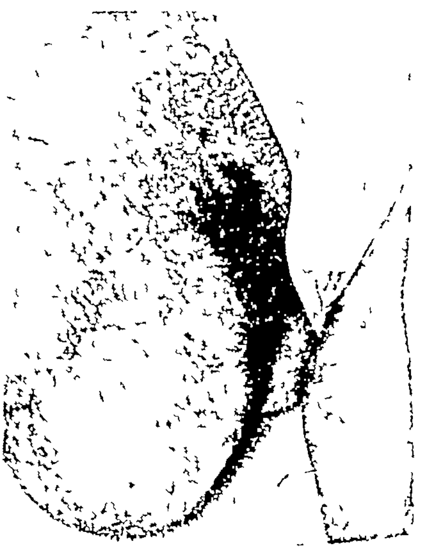


Fig 1—Amputation stump showing pigmented skin and sinuses and nodules along upper antero medial line of apposition of prosthesis.

Among the chronic inflammatory cells are scattered a few large rounded cells with small nuclei which closely resemble cornified epithelial cells Using Papanicolaou's water blue stain (Papanicolaou 1933) it was found that these cells stain as cornified epithelial cells, and with Mallory's aniline blue collagen stain (Mallory 1938) they take on the same crimson colour as cornified skin epithelium Examination with these stains shows that some of the giant cells contain fragments of similar material, and fig 4 shows a giant cell within which a complete epithelial cell can be identified No fragments of collagen (Pullinger 1942) could be demonstrated in these cells

The "pus" obtained from the discharging sinus contains not only polymorphs but also squamous epithelial cells No single infective organism has been identified inoculated on to the chorioallantois of developing chick embryos, but only ill defined lesions developed after 3 days' incubation, and further egg passage was negative The remainder of the fluid was rubbed into linear scarifications on the loin of a sheep The animal developed a typical infection with the formation of vesicles along the line of scarification on the 4th day Smears made from the base of one vesicle on the 6th day after inoculation were stained by Gutstein's method These showed large numbers of minute particles of identical size and appearance, and many of them were associated with damaged host cells A typical field is shown in fig 2, and the particles are indistinguishable from those seen in stained smears made from the base of vesicles in cases of smallpox Smears of the same material stained by Gram did not reveal any bacteria

Histological examination of sections from the edge of one vesicle showed epithelial proliferation and reticular degeneration, but inclusion bodies were not found Material from these lesions was also inoculated into eggs, but the virus did not produce lesions after the first egg passage

Cross immunity Experiments

To confirm the identity of the human strain of virus, reciprocal cross immunity experiments were carried out in sheep with this strain and a known laboratory strain of C P D virus

Immunity Afforded by Human Strain —A sheep (3216) which had recovered from a widespread infection of the abdomen and thigh with the human virus was reinoculated on one thigh 18 days later with serial dilutions of 1/100 1/1000, 1/5000, 1/10,000, and 1/50 000 of the homologous virus, and on the other thigh with similar dilutions of the stock sheep strain (U F 1) A control sheep (3231) received the U.F 1 virus and the activity of the human strain was checked later in sheep 3240 There was no reaction in the protected sheep to either virus even with the 1/100 dilution The control animal (3231) showed typical lesions which were moderate at dilutions of 1/100 to 1/10,000 and slight at 1/50 000

Immunity Afforded by the Sheep Strain —Sheep 3231 which had recovered from infection with strain U.F 1 was reinoculated 29 days later with dilutions of the two viruses as outlined above The activity of the ovine strain had already been demonstrated the human strain was checked in control sheep 3240 Sheep 3231 was completely immune to both strains while sheep 3240 was fully susceptible

These cross immunity experiments demonstrate that the strain of virus recovered from the patient was immunologically indistinguishable from a standard strain of the virus of ovine contagious pustular dermatitis

DISCUSSION

The laboratory findings in this case confirmed a clinical diagnosis of infection with the virus of contagious pustular dermatitis One of us (G M L) has seen a considerable number of such infections in farm workers, and a clinical account of these will be published elsewhere The disease is well known among Australian sheep shearers, who have occasionally refused to handle infected flocks because of the likelihood of developing lesions on the hands and arms While a history of contact with infected sheep is a help in diagnosis, the possibility of infection with cowpox virus and certain bacterial infections must also be kept in mind Most laboratories have not the facilities to undertake the tests on sheep described here though these are at present the only certain means of diagnosis However, a full bacteriological examination would be useful, as would microscopic examination of smears made on glass slides from scrapings taken from the base of early lesions Culture of the material on the chorioallantois of the developing hen's egg should serve to distinguish between infection caused by cowpox and by C P D virus Cowpox virus produces typical lesions on the chorioallantois whereas C P D virus either fails to take or dies out rapidly on passage Serological methods of diagnosing human infection would be useful but we know little of their value Glover (1932) showed that the sera of hyperimmune sheep contained complement fixing antibodies and that weak reactions could be obtained from the sera of recovered natural cases in sheep Blakemore et al (1948) have also shown that agglutination takes place with patient's serum and washed elementary body suspensions Several cases of orf among butchers and other city workers have recently come to our notice, and various laboratory methods of diagnosis are now being investigated Until a simple test is available the clinical diagnosis of human infections with C P D virus will often go unconfirmed

SUMMARY

A case of natural transmission of the virus of ovine contagious pustular dermatitis to man is described The diagnosis was confirmed by infecting a sheep with the human material and by cross immunity tests

REFERENCES

Aynaud M (1923) *Ann Inst Pasteur*, **37** 498
Blakemore F Abdussalam M Goldsmith W N (1948) *Brit J Derm* **60** 404
Carne H R Wickham N Whitten W K Lockley R P (1946) *Aust J Sci* **9**, 73
Glover R E (1928) *J comp Path* **41** 318
— (1932) Report of Director of Institute of Animal Pathology Cambridge
Newsom I E Cross F (1934) *J Amer vet med Ass* **84** 799
Peterkin G A G (1937) *Brit J Derm Syph* **49** 492

EXPERIMENTAL NYSTAGMUS

R C Browne
M A, D M Oxfd, M R C P
NUFFIELD PROFESSOR OF INDUSTRIAL HEALTH IN THE UNIVERSITY OF DURHAM

The origin of coalminers' nystagmus has never been satisfactorily explained Some hold that it is primarily psychoneurotic (*Lancet* 1940, Halliday 1943) whereas others suggest that the chief cause is using the eye at levels of illumination below the threshold of perception by the cones, with the result that the fine normal scanning movements of the retina are grossly exaggerated because the macula is in effect blind and the eye has only peripheral vision at these low intensities of light (Ferguson 1943, Davson 1949)

One of the consequences of this conflict of opinion is that both doctors and pit managers tend to consider miners with nystagmus as "neurotic," while the victim and his workmates consider that he is "finished" The demonstration that darkness produces nystagmus in animals with visual apparatus analogous to that of man is therefore important

A cat's eye is similar to a man's in that the retina has both rods for seeing in "the dark" and cones for seeing at higher intensities of light, but there are proportionately fewer cones and relatively more rods to suit the cat's nocturnal habits The cat uses both eyes at once, and so strong is its urge towards binocular vision that, if the extrinsic eye muscles are detached from the eyeball and reattached in the wrong places, binocular vision is reinstituted in a few days (Walls 1942) In man half the fibres in the optic nerves do not cross in the chiasma, but in the cat about a third do not The nocturnal cat has a reflector, the tapetum, at the back of its rods and cones to increase their sensitivity, whereas in man, working at higher intensities of light by day, a pigmented "backing" in the choroid cuts down the scatter of the brighter light The visual systems of cat and man are therefore much alike both need and have binocular vision, the cat for accurate judgment of range and position when stalking and seizing its prey, and man for manipulation The differences between them are due to the different ranges of intensity of light under which the two species usually live

HUMAN INFECTION WITH THE VIRUS OF CONTAGIOUS PUSTULAR DERMATITIS

G M Lloyd
M R C S
GENERAL PRACTITIONER, ROSS ON WYE

A Macdonald
M A, M D Aberd
READER IN BACTERIOLOGY, UNIVERSITY OF LIVERPOOL

R E Glover
M A Camb, B Sc Lond, F R C V S
PROFESSOR OF VETERINARY PATHOLOGY, UNIVERSITY OF LIVERPOOL

Contagious pustular dermatitis, or orf, is an infectious disease of sheep which is common in most sheep raising areas of this and other countries Affected animals develop a vesiculopapular eruption usually confined to the lips and surrounding tissue, but, in the severe form, lesions may also be present on the oral mucosa and on various other non wool bearing parts of the body The disease is prevalent in spring and summer and weaned lambs up to a year old are highly susceptible Aynaud (1923) showed that the disease is caused by a virus and this was confirmed by Glover (1928), who transmitted the infection with Berkefeld V filtrates of scrapings from infected animals to normal lambs Glover also showed by cross immunity tests that different sheep strains were immunologically identical

Veterinary surgeons and some physicians have long suspected that human infection was possible with the virus of contagious pustular dermatitis (C P D), but in most reported cases the evidence is circumstantial Thus Peterkin (1937) described five cases, but he did not demonstrate virus in the human lesions In the U S A, however Newsom and Cross (1934) transmitted infection from a human case to sheep but did not confirm its nature In Australia, Carne et al (1946) described three cases in which the nature of the lesions was investigated by infecting normal sheep from human material and by cross immunity tests There can be little doubt about the diagnosis in the patient described by Blakemore et al (1948) who transmitted the infection from a sheep to a human volunteer In most of these cases the lesions were on the skin of the hands or arms

The present case was confirmed by laboratory tests and is described not only because the site of the lesion was unusual, but also because there is reason to believe that human infections are less often recognised than their distribution and frequency warrant

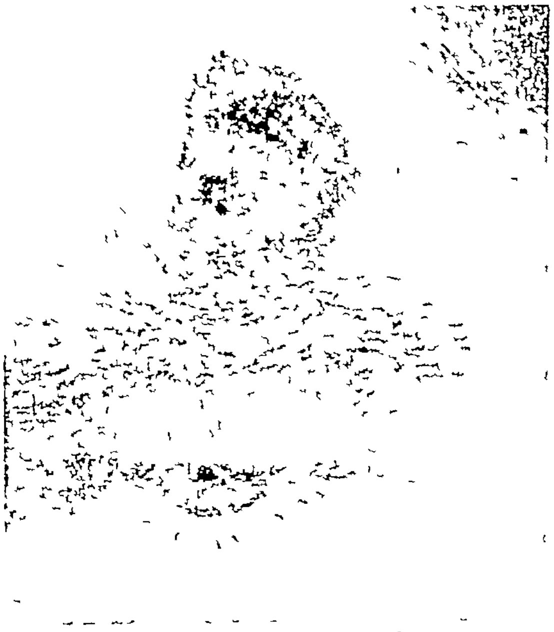


Fig 1—Lesion on brow caused by the virus of contagious pustular dermatitis

CLINICAL ACCOUNT

A pupil farmer, aged 21, worked on a lowland mixed farm but had recently helped in sheep rearing The flock was not known to be infected with orf, but the disease was subsequently confirmed by a veterinary colleague Early in August, 1950, the patient complained of a small vesicular swelling on the left side of the brow, which had started some days previously as a small red papule Within 48 hours the surface had flattened and increased in area During the next three days it grew to about $^1/_2$ in in diameter and the surface of the vesicle thickened The patient said there had been no escape of fluid, and at this stage material was collected with sterile precautions by Dr W H J Baker, pathologist, Public Health Laboratory Service, Hereford, and sent to the department of bacteriology at Liverpool University

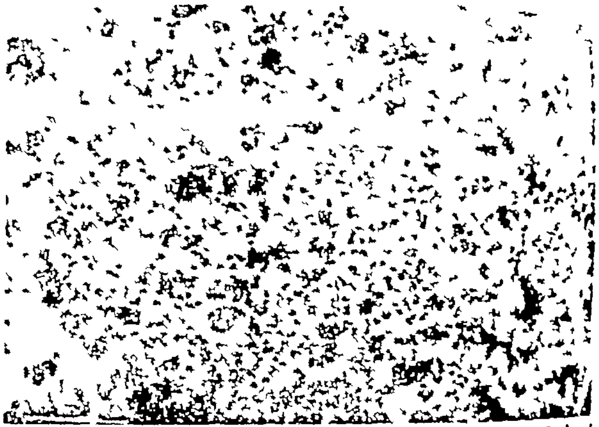


Fig 2—Elementary bodies in smear from C.P D lesion. Stained Gutstein (× 1500)

The lesion was essentially a flat topped vesicle with raised indurated edges and containing a clear exudate Later it became pustular but by this time it had been opened and there was opportunity for secondary invasion The patient then developed pre auricular adenitis There was little constitutional upset though orbital œdema produced a mild headache He was apyrexial when first seen, but after the lesion became pustular he had an occasional temperature of 99°F Thereafter an eschar was rapidly formed and the adjacent œdema decreased The photograph (fig 1) was taken 8 days after his first attendance at the surgery The eschar was difficult to remove and appeared to be embedded in an excessive growth of epithelial tissue The underlying ulcer showed raised edges and a granulomatous border

Two weeks after collecting the fluid for examination the œdema and induration had subsided but the scar and gross scaling were still prominent Two months after the original examination the affected part of the brow showed hyperæmia and desquamation but no evidence of scarring

At first the lesion caused some irritation but it became painless as it increased in size There was no history of minor injury to the brow before it developed

LABORATORY INVESTIGATIONS

Smears on glass slides of the serous fluid within the lesion, and a part of tissue from the edge of the lesion were available for examination The smears were stained by Gutstein's method but the specimens contained much cell debris and it was not possible to say whether or not virus was present The piece of tissue was ground in a mortar with powdered glass and extracted in a small volume of broth saline The supernatant fluid from the ground tissue suspension was cultured on blood agar Because of a scanty growth of *Staphylococcus albus* 50 units of penicillin per ml were added before further tests were undertaken Some of this fluid was then inoculated on to the chorioallantois of developing chick embryos, but only ill-defined lesions developed after 3 days' incubation, and further egg passage was negative. The remainder of the fluid was rubbed into linear scarifications on the loin of a sheep. The animal developed a typical infection with the formation of vesicles along the line of scarification on the 4th day. Smears made from the base of one vesicle on the 6th day after inoculation were stained by Gutstein's method. These showed large numbers of minute particles of identical size and appearance, and many of them were associated with damaged host cells. A typical field is shown in fig. 2, and the particles are indistinguishable from those seen in stained smears made from the base of vesicles in cases of smallpox. Smears of the same material stained by Gram did not reveal any bacteria.

Histological examination of sections from the edge of one vesicle showed epithelial proliferation and reticular degeneration, but inclusion bodies were not found. Material from these lesions was also inoculated into eggs, but the virus did not produce lesions after the first egg passage.

Cross-immunity Experiments

To confirm the identity of the human strain of virus, reciprocal cross-immunity experiments were carried out in sheep with this strain and a known laboratory strain of C.P.D. virus.

Immunity Afforded by Human Strain.—A sheep (3216) which had recovered from a widespread infection of the abdomen and thigh with the human virus was reinoculated on one thigh 18 days later with serial dilutions of 1/100, 1/1000, 1/5000, 1/10,000, and 1/50,000 of the homologous virus, and on the other thigh with similar dilutions of the stock sheep strain (U.F. 1). A control sheep (3231) received the U.F. 1 virus, and the activity of the human strain was checked later in sheep 3240. There was no reaction in the protected sheep to either virus even with the 1/100 dilution. The control animal (3231) showed typical lesions which were moderate at dilutions of 1/100 to 1/10,000 and slight at 1/50,000.

Immunity Afforded by the Sheep Strain.—Sheep 3231 which had recovered from infection with strain U.F. 1 was reinoculated 29 days later with dilutions of the two viruses as outlined above. The activity of the ovine strain had already been demonstrated; the human strain was checked in control sheep 3240. Sheep 3231 was completely immune to both strains, while sheep 3240 was fully susceptible.

These cross-immunity experiments demonstrate that the strain of virus recovered from the patient was immunologically indistinguishable from a standard strain of the virus of ovine contagious pustular dermatitis.

DISCUSSION

The laboratory findings in this case confirmed a clinical diagnosis of infection with the virus of contagious pustular dermatitis. One of us (G. M. L.) has seen a considerable number of such infections in farm workers, and a clinical account of these will be published elsewhere. The disease is well known among Australian sheep-shearers, who have occasionally refused to handle infected flocks because of the likelihood of developing lesions on the hands and arms. While a history of contact with infected sheep is a help in diagnosis, the possibility of infection with cowpox virus and certain bacterial infections must also be kept in mind. Most laboratories have not the facilities to undertake the tests on sheep described here, though these are at present the only certain means of diagnosis. However, a full bacteriological examination would be useful, as would microscopic examination of smears made on glass slides from scrapings taken from the base of early lesions. Culture of the material on the chorioallantois of the developing hen's egg should serve to distinguish between infection caused by cowpox and by C.P.D. virus. Cowpox virus produces typical lesions on the chorioallantois, whereas C.P.D. virus either fails to take or dies out rapidly on passage. Serological methods of diagnosing human infection would be useful, but we know little of their value. Glover (1932) showed that the sera of hyperimmune sheep contained complement-fixing antibodies and that weak reactions could be obtained from the sera of recovered natural cases in sheep. Blakemore et al. (1948) have also shown that agglutination takes place with patient's serum and washed elementary-body suspensions. Several cases of orf among butchers and other city workers have recently come to our notice, and various laboratory methods of diagnosis are now being investigated. Until a simple test is available the clinical diagnosis of human infections with C.P.D. virus will often go unconfirmed.

SUMMARY

A case of natural transmission of the virus of ovine contagious pustular dermatitis to man is described. The diagnosis was confirmed by infecting a sheep with the human material and by cross-immunity tests.

REFERENCES

Aynaud, M. (1923) *Ann. Inst. Pasteur*, 37, 498.
Blakemore, F., Abdussalam, M., Goldsmith, W. N. (1948) *Brit. J. Derm.* 60, 404.
Carne, H. R., Wickham, N., Whitten, W. K., Lockley, R. P. (1946) *Aust. J. Sci.* 9, 73.
Glover, R. E. (1928) *J. comp. Path.* 41, 318.
— (1932) *Report of Director of Institute of Animal Pathology, Cambridge.*
Newsom, I. E., Cross, F. (1934) *J. Amer. vet. med. Ass.* 84, 799.
Peterkin, G. A. G. (1937) *Brit. J. Derm. Syph.* 49, 492.

EXPERIMENTAL NYSTAGMUS

R. C. Browne
M.A., D.M. Oxfd, M.R.C.P.
NUFFIELD PROFESSOR OF INDUSTRIAL HEALTH IN THE UNIVERSITY OF DURHAM

The origin of coalminers' nystagmus has never been satisfactorily explained. Some hold that it is primarily psychoneurotic (*Lancet* 1940, Halliday 1943), whereas others suggest that the chief cause is using the eye at levels of illumination below the threshold of perception by the cones, with the result that the fine normal scanning movements of the retina are grossly exaggerated because the macula is in effect blind and the eye has only peripheral vision at these low intensities of light (Ferguson 1943, Davson 1949).

One of the consequences of this conflict of opinion is that both doctors and pit managers tend to consider miners with nystagmus as "neurotic," while the victim and his workmates consider that he is "finished." The demonstration that darkness produces nystagmus in animals with visual apparatus analogous to that of man is therefore important.

A cat's eye is similar to a man's in that the retina has both rods for seeing in "the dark" and cones for seeing at higher intensities of light; but there are proportionately fewer cones and relatively more rods to suit the cat's nocturnal habits. The cat uses both eyes at once, and so strong is its urge towards binocular vision that if the extrinsic eye muscles are detached from the eyeball and reattached in the wrong places, binocular vision is reinstituted in a few days (Walls 1942). In man half the fibres in the optic nerves do not cross in the chiasma, but in the cat about a third do not. The nocturnal cat has a reflector, the tapetum, at the back of its rods and cones to increase their sensitivity, whereas in man, working at higher intensities of light by day, a pigmented "backing" in the choroid cuts down the scatter of the brighter light. The visual systems of cat and man are therefore much alike; both need and have binocular vision, the cat for accurate judgment of range and position when stalking and seizing its prey, and man for manipulation. The differences between them are due to the different ranges of intensity of light under which the two species usually live.

HUMAN INFECTION WITH THE VIRUS OF CONTAGIOUS PUSTULAR DERMATITIS

G M Lloyd
M R C S
GENERAL PRACTITIONER, ROSS ON WYE

A Macdonald
M A , M D Aberd
READER IN BACTERIOLOGY, UNIVERSITY OF LIVERPOOL

R E Glover
M A Camb , B Sc Lond , F R C V S
PROFESSOR OF VETERINARY PATHOLOGY, UNIVERSITY OF LIVERPOOL

Contagious pustular *dermatitis, or orf,* is an infectious disease of sheep which is common in most sheep raising areas of this and other countries Affected animals develop a vesiculopapular eruption usually confined to the lips and surrounding tissue, but, in the severe form, lesions may also be present on the oral mucosa and on various other non wool bearing parts of the body The disease is prevalent in spring *and summer* and weaned lambs up to a year old are highly susceptible Aynaud (1923) showed that the disease is caused by a virus and this was confirmed by Glover (1928), who transmitted the infection with Berkefeld V filtrates of scrapings from infected *animals to* normal lambs Glover also showed by cross immunity tests that different sheep strains were immunologically identical

Veterinary surgeons and some physicians have long suspected that human infection was possible with the virus of contagious pustular dermatitis (C P D), but in most reported cases the evidence is circumstantial Thus Peterkin (1937) described five cases, but he did not demonstrate virus in the human lesions In the U S A , however Newsom and Cross (1934) transmitted *infection* from a human case to sheep but did not confirm its nature *In Australia,* Carne et al (1946) described three cases in which the nature of the lesions was *investigated* by *infecting* normal sheep from human material and by cross immunity tests There can be little doubt about the diagnosis in the *patient described by* Blakemore et al (1948) who transmitted the infection from a sheep to a human volunteer In most of these cases the lesions were *on the skin of the hands* or arms

The present case was confirmed by laboratory tests and is *described not only* because the site of the lesion was unusual, but also because there is reason to believe that human infections are less often recognised than their distribution and frequency warrant

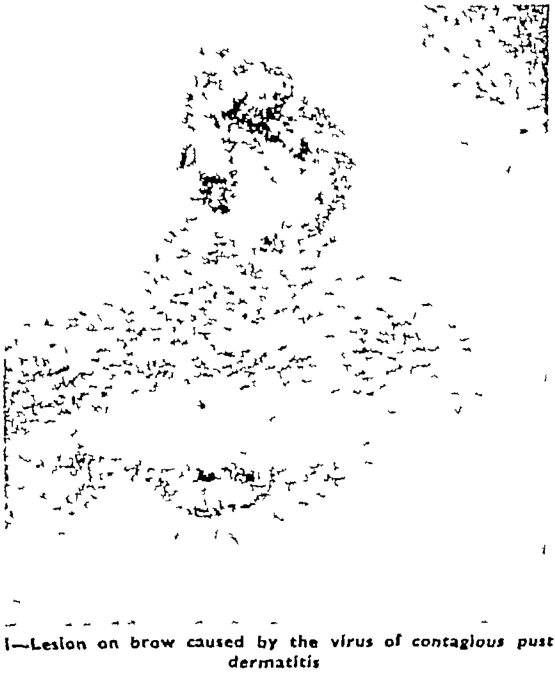


Fig 1—Lesion on brow caused by the virus of *contagious pustular dermatitis*

CLINICAL ACCOUNT

A pupil farmer, aged 21, worked on a lowland mixed farm but had recently helped in sheep rearing The flock was not known to be infected with orf, but the disease was subsequently confirmed by a veterinary colleague Early in August, 1950, the patient complained of a small vesicular swelling on the left side of the brow, which had started some days previously as a small red papule Within 48 hours the surface had flattened and increased in area During the next three days *it grew* to about $^1/_2$ in in diameter and the surface *of the vesicle thickened* The patient said there had been no escape of fluid , and at this stage material was collected with sterile precautions by Dr W H J Baker, pathologist, Public Health Laboratory Service, Hereford, and sent to the department of bacteriology at Liverpool University

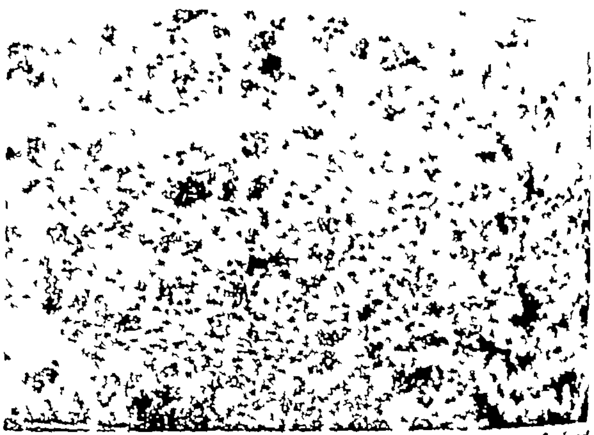


Fig 2—Elementary bodies in smear from C P D lesion Stained Gutstein (× 1500)

The lesion was *essentially a flat-topped* vesicle with raised indurated edges and containing a clear exudate Later it became pustular but by this time it had been opened and there was opportunity for secondary invasion The patient then *developed pre auricular* adenitis There was little constitutional upset though orbital œdema produced a mild headache He was apyrexial when first seen, but after the lesion became pustular he had an occasional temperature of 99°F Thereafter an eschar was rapidly formed and the adjacent œdema decreased The photograph (fig 1) was taken 8 days after his first attendance at the surgery The eschar was difficult to remove and appeared to be embedded in an excessive growth of epithelial tissue The underlying ulcer showed raised edges and a granulomatous border

Two weeks after collecting the fluid for examination the œdema and induration had subsided but the scar and gross scaling were still prominent Two months after the original examination the affected part of the brow showed hyperæmia and desquamation but no evidence of scarring

At first the lesion caused some irritation but it became painless as it increased in size There was no history of minor injury to the brow before it developed

LABORATORY INVESTIGATIONS

Smears on glass slides of the serous fluid within the lesion, and a part of tissue from the edge of the lesion, were available for examination The smears were stained by Gutstein's method but the specimens contained much cell debris and it was not possible to say whether or not virus was present The piece of tissue was ground in a mortar with powdered glass and extracted in a small volume of broth saline The supernatant fluid from the ground tissue suspension was cultured *on blood* agar Because of a scanty growth of *Staphylococcus albus* 50 units of penicillin per ml were *added before* further tests were undertaken Some *of this fluid* was then inoculated on to the chorioallantois of developing chick embryos, but only ill defined lesions developed after 3 days' incubation, and further egg passage was negative The remainder of the fluid was rubbed into linear scarifications on the loin of a sheep The animal developed a typical infection with the formation of vesicles along the line of scarification on the 4th day Smears made from the base of one vesicle on the 6th day after inoculation were stained by Gutstein's method These showed large numbers of minute particles of identical size and appearance, and many of them were associated with damaged host cells A typical field is shown in fig 2, and the particles are indistinguishable from those seen in stained smears made from the base of vesicles in cases of smallpox Smears of the same material stained by Gram did not reveal any bacteria

Histological examination of sections from the edge of one vesicle showed epithelial proliferation and reticular degeneration, but inclusion bodies were not found Material from these lesions was also inoculated into eggs, but the virus did not produce lesions after the first egg passage

Cross immunity Experiments

To confirm the identity of the human strain of virus, reciprocal cross immunity experiments were carried out in sheep with this strain and a known laboratory strain of C P D virus

Immunity Afforded by Human Strain—A sheep (3216) which had recovered from a widespread infection of the abdomen and thigh with the human virus was reinoculated on one thigh 18 days later with serial dilutions of 1/100 1/1000, 1/5000, 1/10 000, and 1/50,000 of the homologous virus and on the other thigh with similar dilutions of the stock sheep strain (U F 1) A control sheep (3231) received the U F 1 virus and the activity of the human strain was checked later in sheep 3240 There was no reaction in the protected sheep to either virus even with the 1/100 dilution The control animal (3231) showed typical lesions which were moderate at dilutions of 1/100 to 1/10 000 and slight at 1/50 000

Immunity Afforded by the Sheep Strain—Sheep 3231 which had recovered from infection with strain U.F 1 was reinoculated 29 days later with dilutions of the two viruses as outlined above The activity of the ovine strain had already been demonstrated the human strain was checked in control sheep 3240 Sheep 3231 was completely immune to both strains while sheep 3240 was fully susceptible

These cross immunity experiments demonstrate that the strain of virus recovered from the patient was immunologically indistinguishable from a standard strain of the virus of ovine contagious pustular dermatitis

DISCUSSION

The laboratory findings in this case confirmed a clinical diagnosis of infection with the virus of contagious pustular dermatitis One of us (G M L) has seen a considerable number of such infections in farm workers, and a clinical account of these will be published elsewhere The disease is well known among Australian sheep shearers, who have occasionally refused to handle infected flocks because of the likelihood of developing lesions on the hands and arms While a history of contact with infected sheep is a help in diagnosis, the possibility of infection with cowpox virus and certain bacterial infections must also be kept in mind Most laboratories have not the facilities to undertake the tests on sheep described here though these are at present the only certain means of diagnosis However, a full bacteriological examination would be useful, as would microscopic examination of smears made on glass slides from scrapings taken from the base of early lesions Culture of the material on the chorioallantois of the developing hen's egg should serve to distinguish between infection caused by cowpox and by C P D virus Cowpox virus produces typical lesions on the chorioallantois where is C P D virus either fails to take or dies out rapidly on passage Serological methods of diagnosing human infection would be useful but we know little of their value Glover (1932) showed that the sera of hyperimmune sheep contained complement fixing antibodies and that weak reactions could be obtained from the sera of recovered natural cases in sheep Blakemore et al (1948) have also shown that agglutination takes place with patient's serum and washed elementary-body suspensions Several cases of orf among butchers and other city workers have recently come to our notice, and various laboratory methods of diagnosis are now being investigated Until a simple test is available the clinical diagnosis of human infections with C P D virus will often go unconfirmed

SUMMARY

A case of natural transmission of the virus of ovine contagious pustular dermatitis to man is described The diagnosis was confirmed by infecting a sheep with the human material and by cross immunity tests

REFERENCES

Aynaud M (1923) *Ann Inst Pasteur*, 37 498
Blakemore F Abdussalam M Goldsmith W N (1948) *Brit J Derm* 60 404
Carne H R Wickham N Whitten W K Lockley R P (1946) *Aust J Sci* 9 73
Glover, R E (1928) *J comp Path* 41 318
— (1932) Report of Director of Institute of Animal Pathology, Cambridge
Newsom I E Cross F (1934) *J Amer vet med Ass* 84, 799
Peterkin G A G (1937) *Brit J Derm Syph* 49 492

EXPERIMENTAL NYSTAGMUS

R C BROWNE
M.A, D.M Oxfd, M.R C P
NUFFIELD PROFESSOR OF INDUSTRIAL HEALTH IN THE UNIVERSITY OF DURHAM

THE origin of coalminers' nystagmus has never been satisfactorily explained Some hold that it is primarily psychoneurotic (*Lancet* 1940, Halliday 1943) whereas others suggest that the chief cause is using the eye at levels of illumination below the threshold of perception by the cones, with the result that the fine normal scanning movements of the retina are grossly exaggerated because the macula is in effect blind and the eye has only peripheral vision at these low intensities of light (Ferguson 1943, Davson 1949)

One of the consequences of this conflict of opinion is that both doctors and pit managers tend to consider miners with nystagmus as "neurotic," while the victim and his workmates consider that he is "finished" The demonstration that darkness produces nystagmus in animals with visual apparatus analogous to that of man is therefore important

A cat's eye is similar to a man's in that the retina has both rods for seeing in "the dark" and cones for seeing at higher intensities of light, but there are proportionately fewer cones and relatively more rods to suit the cat's nocturnal habits The cat uses both eyes at once, and so strong is its urge towards binocular vision that, if the extrinsic eye muscles are detached from the eyeball and reattached in the wrong places, binocular vision is reinstituted in a few days (Walls 1942) In man half the fibres in the optic nerves do not cross in the chiasma, but in the cat about a third do not The nocturnal cat has a reflector, the tapetum, at the back of its rods and cones to increase their sensitivity, whereas in man, working at higher intensities of light by day, a pigmented "backing" in the choroid cuts down the scatter of the brighter light The visual systems of cat and man are therefore much alike both need and have binocular vision, the cat for accurate judgment of range and position when stalking and seizing its prey, and man for manipulation The differences between them are due to the different ranges of intensity of light under which the two species usually live

HUMAN INFECTION WITH THE VIRUS OF CONTAGIOUS PUSTULAR DERMATITIS

G M Lloyd
M R C S
GENERAL PRACTITIONER, ROSS ON WYE

A Macdonald
M A , M D Aberd
READER IN BACTERIOLOGY, UNIVERSITY OF LIVERPOOL

R E Glover
M A Camb , B Sc Lond , F R C V S
PROFESSOR OF VETERINARY PATHOLOGY, UNIVERSITY OF LIVERPOOL

Contagious pustular dermatitis, or orf, is an infectious disease of sheep which is common in most sheep raising areas of this and other countries Affected animals develop a vesiculopapular eruption usually confined to the lips and surrounding tissue, but, in the severe form, lesions may also be present on the oral mucosa and on various other non wool bearing parts of the body The disease is prevalent in spring and summer and weaned lambs up to a year old are highly susceptible Aynaud (1923) showed that the disease is caused by a virus and this was confirmed by Glover (1928), who transmitted the infection with Berkefeld V filtrates of scrapings from infected animals to normal lambs Glover also showed by cross immunity tests that different sheep strains were immunologically identical

Veterinary surgeons and some physicians have long suspected that human infection was possible with the virus of contagious pustular dermatitis (C P D), but in most reported cases the evidence is circumstantial Thus Peterkin (1937) described five cases, but he did not demonstrate virus in the human lesions In the U S A , however Newsom and Cross (1934) transmitted infection from a human case to sheep but did not confirm its nature In Australia, Carne et al (1946) described three cases in which the nature of the lesions was investigated by infecting normal sheep from human material and by cross immunity tests There can be little doubt about the diagnosis in the patient described by Blakemore et al (1948) who transmitted the infection from a sheep to a human volunteer In most of these cases the lesions were on the skin of the hands or arms

The present case was confirmed by laboratory tests and is described not only because the site of the lesion was unusual, but also because there is reason to believe that human infections are less often recognised than their distribution and frequency warrant

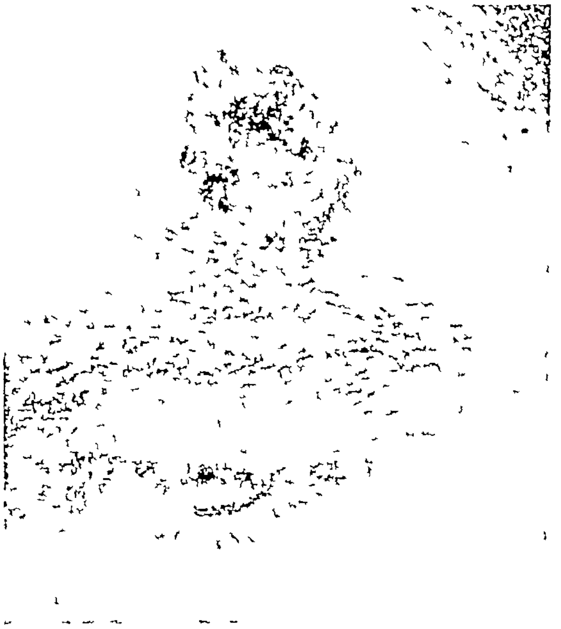


Fig 1—Lesion on brow caused by the virus of contagious pustular dermatitis

CLINICAL ACCOUNT

A pupil farmer, aged 21, worked on a lowland mixed farm but had recently helped in sheep rearing The flock was not known to be infected with orf, but the disease was subsequently confirmed by a veterinary colleague Early in August, 1950, the patient complained of a small vesicular swelling on the left side of the brow, which had started some days previously as a small red papule Within 48 hours the surface had flattened and increased in area During the next three days it grew to about $^1/_2$ in in diameter and the surface of the vesicle thickened The patient said there had been no escape of fluid, and at this stage material was collected with sterile precautions by Dr W H J Baker, pathologist, Public Health Laboratory Service, Hereford, and sent to the department of bacteriology at Liverpool University

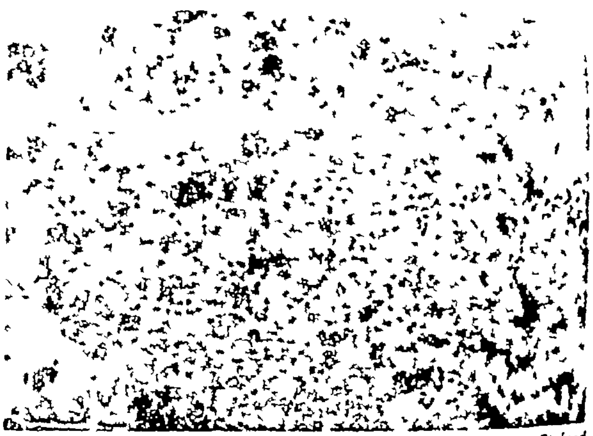


Fig 2—Elementary bodies in smear from C P D lesion Stained Gutstein (× 1500)

The lesion was essentially a flat topped vesicle with raised indurated edges and containing a clear exudate Later it became pustular but by this time it had been opened and there was opportunity for secondary invasion The patient then developed pre auricular adenitis There was little constitutional upset though orbital œdema produced a mild headache He was apyrexial when first seen, but after the lesion became pustular he had an occasional temperature of 99°F Thereafter an eschar was rapidly formed and the adjacent œdema decreased The photograph (fig 1) was taken 8 days after his first attendance at the surgery The eschar was difficult to remove and appeared to be embedded in an excessive growth of epithelial tissue The underlying ulcer showed raised edges and a granulomatous border

Two weeks after collecting the fluid for examination the œdema and induration had subsided but the scar and gross scaling were still prominent Two months after the original examination the affected part of the brow showed hyperæmia and desquamation but no evidence of scarring

At first the lesion caused some irritation but it became painless as it increased in size There was no history of minor injury to the brow before it developed

LABORATORY INVESTIGATIONS

Smears on glass slides of the serous fluid within the lesion, and a part of tissue from the edge of the lesion, were available for examination The smears were stained by Gutstein's method but the specimens contained much cell debris and it was not possible to say whether or not virus was present The piece of tissue was ground in a mortar with powdered glass and extracted in a small volume of broth saline The supernatant fluid from the ground tissue suspension was cultured on blood agar Because of a scanty growth of *Staphylococcus albus* 50 units of penicillin per ml were added before further tests were undertaken Some of this fluid was then

Brockman et al (1950) have described the synthesis and isolation in crystalline form, and the empirical formula, of a substance which they have produced from folic acid and which appears to have the same biological properties as those described for citrovorum factor derived from liver In 1949 Bond et al. reported the isolation from liver of a substance which they named 'folinic acid," and which is probably the same as the citrovorum factor

A leading article in THE LANCET (1951) gives an excellent account of the historical aspects of these discoveries and the evidence for their relation to each other It also mentions the therapeutic response to folic acid of a megaloblastic anæmia induced in monkeys by dietary deficiency, and expresses the hope that reports on its action in human megaloblastic anæmia should soon be to hand. This preliminary report is accordingly submitted for publication

MATERIAL

The citrovorum factor used in this investigation was a product of biological origin kindly supplied to us by Dr T H Jukes, of Lederle Laboratories, Inc , Pearl River, N Y It was free from vitamin B_{12} and folic acid, and was prepared for parenteral administration in ampoules containing 20 million units of microbiological activity per ml It has recently been shown (Brockman et al. 1950) that about 0 15–0 20 mμg of the synthetic citrovorum factor corresponds to one "unit" of the biological product, and hence each millilitre of the preparation supplied to us contained the equivalent of approximately 3–4 mg of the synthetic citrovorum factor

METHOD

Three patients with addisonian pernicious anæmia were chosen In each case the dietary history was good , there was no diarrhœa , the test-meal showed histamine fast achlorhydria , and the marrow was megaloblastic

After a control period, during which there was no evidence of remission, the patients were given, respectively, 20, 40, and 80 million units of citrovorum factor in a single intramuscular injection, and the hæmatological response was followed for two weeks

The results are shown in the accompanying table It is evident that there was a slight hæmatological response in case 1 receiving 20 million units, and in case 2 where 40 million units was given and a good hæmatological response in case 3 where 80 million units was given A corresponding improvement in the state of well-being also occurred in case 3

DISCUSSION

These results suggest that provided a large enough dose is given, the *L citrovorum* factor will produce a hæmatological and clinical response in pernicious anæmia Since 80 million units of the citrovorum factor derived from biological sources contains the equivalent of approximately 12–16 mg of synthetic citrovorum factor, it would appear that the therapeutic dose in milligrammes of folic acid and citrovorum factor are of the same order This is to be contrasted with the therapeutically active dosage of vitamin B_{12}, which is measured in microgrammes rather than milligrammes

It is now known that the citrovorum factor can replace folic acid as a growth factor for *Streptococcus fæcalis* It is also known that the content of folic acid in refined liver extracts is of the order of a few micro grammes or less This figure represents not only the folic acid content but also the amount of *L citrovorum* factor in the liver extracts Accordingly it is certain that the activity of refined liver extract in the treatment of pernicious anæmia is not related to its content of either of these substances but to its content of vitamin B_{12}. The work of Nichol and Welch (1950) suggests that the *L citrovorum* factor may be the derivative of pteroylglutamic acid actually responsible for the continuation of normoblastic blood formation

SUMMARY

Three cases of addisonian pernicious anæmia have been treated with 20, 40, and 80 million biological units of citrovorum factor Only when 80 million units was given was a satisfactory response obtained

REFERENCES

Bond T J Bardos T J Sibley M Shive, W (1949) *J Amer chem Soc* 71 3852
Brockman J A jun Roth B Broquist, H P Hultquist M E. Smith J M jun Fahrenbach M. J Cosulich D B Parker R. P Stokstad E L R. Jukes T H (1950) *Ibid* 72 4325
Lancet (1951) Leading article 1 623
Lyman C M Prescott J M (1949) *J biol Chem* 178 523
Nichol C A Welch A D (1950) *Proc Soc exp Biol., N Y* 74 403
Sauberlich H E Baumann C A (1948) *J biol. Chem* 176, 165
Scheid H E Schweigert B S (1950) *Ibid*, 185 1

L S P DAVIDSON
M.D Edin. F.R C.P E F.R C.P
Professor of Medicine

R H GIRDWOOD
F.R C.P.E , M.R C.P
Lecturer in Medicine

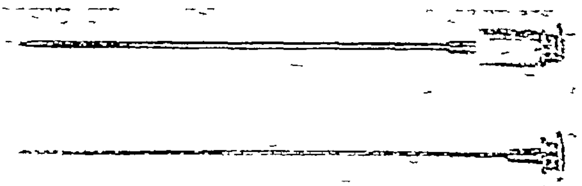
University of Edinburgh.

New Inventions

TROCHAR AND CANNULA FOR TAPPING LATERAL VENTRICLE

TAPPING the lateral ventricles is now an established procedure for both diagnostic and therapeutic purposes. Where it is necessary to drill a burr-hole in the skull the dura is usually nicked with a tenotomy knife and the ventricle tapped with a blunt-ended brain cannula In infants, however the ventricle can be reached without trephining the skull through the lateral corner of the anterior fontanelle The instrument here described has been designed for use in infants and for repeated ventricular tapping in older children in whom the skin over a previous burr-hole has healed

As this procedure is usually performed, the operator either incises skin and dura with a scalpel before inserting a brain cannula or more simply uses a lumbar-puncture needle for traversing skin, meninges, and brain substance The second method is not without risk because the sharp needle may cut through an intracerebral blood-vessel



The instrument illustrated consists of a fine cannula which may be fitted with a trochar or with a blunt obturator The Pannett s mount, which is Record fitting, is keyed to ensure that the trochar or obturator fits closely and does not rotate The end of the cannula is tapered slightly to make a smooth surface with the trochar or obturator, which just protrudes The instrument, which is graduated in centimetres from the distal end is made in two sizes 17 and 19 S W G , both 3 inches long (excluding mount)

Technique.—With the trochar in position the cannula is inserted through the skin and cautiously pushed onwards until the dura is pierced This is easily felt by the operator who then removes the trochar and replaces it with the blunt obturator before traversing the brain itself.

Our thanks are due to Mr A. W Woodhead of the Hospital for Sick Children, Great Ormond Street, who made the prototype and to Mr W A S Whittlesey of St Mary s Hospital for his help in designing the model here described The cannula is made by Messrs. Willen Bros , of 44 New Cavendish Street London, W 1

I A. B CATHIE, M.D Lond.
J P M TIZARD, B.M Oxfd, M.R C P
The Hospital for Sick Children Great Ormond Street,
and St Mary's Hospital Medical School London.

OSCILLATION OF THE EYES OF KITTENS KEPT IN THE DARK

Cat no	Litter no	Age (weeks)	Weeks in dark		Weeks to recover
			Before oscillations	No oscillations	
A	1	6	4		1
B			4		1
C			7		1
D	2	4	Died		
E			4		Died
F				8	Died

METHOD AND RESULTS

Three black kittens, aged 6 weeks, and three tabbies, aged 4 weeks, were placed in a completely dark room and observed every week with an ophthalmoscope Six brown rats and six black and white rabbits were treated in the same way None of the animals had oscillating eyes before being put in the dark, but oscillations were noted in three of the kittens after 4 weeks in the dark, and in a fourth after 7 weeks (see table) One kitten had no oscillations after 8 weeks in the dark In the black kittens (litter 1) the oscillations were rotary and there was a synchronous tremor of the head The oscillations were exaggerated on looking up and to the sides, comparable to what is noticed in coalminers' nystagmus On being put back into daylight all the kittens in litter 1 recovered within a week, but litter 2 died of an intercurrent infection before the experiment was finished A close up cinematograph film of the oscillating eyes of kittens A and B was taken, and again of kitten B when its eyes had recovered None of the rats or rabbits showed oscillations even after 7 months in the dark

DISCUSSION

The Miners' Nystagmus Committee (1922) cited Ohm (1916) as having kept three puppies and two kittens in a dark cellar and as finding nystagmus in all of them after an interval of 10–48 days This observation seems never to have been confirmed or definitely demonstrated since then Ohm, at that date, could only use a mechanical recording method, in which a lever pressed directly on the eyeball and drew a tracing on a kymograph drum He also found that light had a "calming" influence on the oscillations The present pilot experiment confirms and records this fundamental observation

Riesen (1947, 1950) produced nystagmus in chimpanzees, which have a visual apparatus almost identical to that of man, by rearing them in the dark from birth before they had time to develop binocular vision One of his chimpanzees developed an external squint, and another an internal squint, comparable to the convergence so often seen in coalminers' nystagmus One chimpanzee had attacks of nystagmus when it was excited, closely comparable to a patient recently seen who complained of the oscillations "when he was vexed" Riesen's final experiment was to put a chimpanzee, aged 7 months (when it had developed its full visual functions), into the dark, and it too developed nystagmus and became unable to recognise surrounding objects This perhaps suggests that coalminers' nystagmus may well be a partial disuse atrophy of the visual function from lack of light Moreover Browne and others (1950) have shown that coalminers with nystagmus differ very little from those without it, and that the psychological symptoms are the result, rather than the cause, of the disability

SUMMARY

Four out of six kittens developed rotary nystagmus after being kept in the dark 4–7 weeks Three of the four recovered after being in daylight for a week

A close up cinematograph film recorded the results

These findings confirm the results of experiments made by Ohm (1916) on puppies and by Riesen (1947, 1950) on chimpanzees

They suggest that coalminers' nystagmus may be a type of disuse atrophy of the visual apparatus

Acknowledgments are due to the National Coal Board for a grant towards the expense of this work.

REFERENCES

Browne R C, Beck I F, Saint, E G, McCallum, R I (1950) *Brit J Ophthal* 34 601
Davson H (1949) Physiology of the Eye London.
Ferguson W J W (1943) *Brit J phys Med* 6, 40
Halliday J L (1943) *Psychosomat Med* 5, 71
Lancet (1940) i 468
Miners Nystagmus Committee (1922) *Spec. Rep med Res Coun., Lond* no 65, p 47
Ohm J (1916) *Z Augenheilk* 36, 198
Riesen A H (1947) *Science* 106 107
— (1950) *Scientific American* 183, 16
Walls, G L (1942) The Vertebrate Eye Michigan.

Preliminary Communication

TREATMENT OF PERNICIOUS ANÆMIA WITH LEUCONOSTOC CITROVORUM FACTOR

In recent years there have been numerous reports about the activity of pteroylglutamic acid (folic acid) and of vitamin B_{12} in the treatment of the megaloblastic anæmias The purpose of this paper is to report on the hæmopoietic activity in pernicious anæmia of yet another factor that has been isolated from liver

Sauberlich and Baumann (1948) showed that certain natural materials, including liver, liver extracts, and yeast extracts, contain a growth factor for the streptococcus—*Leuconostoc citrovorum* This factor, which they called the "citrovorum factor," differs from vitamin B_{12} in that it can be separated from the latter by electrolysis (Lyman and Prescott 1949), and because pure vitamin B_{12} will not stimulate the growth of *L citrovorum* (Scheid and Schweigert 1950) It also differs from folic acid in certain *growth promoting* activities for bacteria (Sauberlich and Baumann 1948)

RESPONSE TO CITROVORUM FACTOR

Case no	Sex	Age (years)	Day	Hb (g per 100 ml)	R B C (millions per c mm)	Reticulocytes (%)	Sternal marrow	Treatment (million units of citrovorum factor intramuscularly)
1	F	60	0	9 9	2 63	1 8	Megaloblastic	20
			2			1 4		
			3			1 8		
			4			2 4		
			5			4 1		
			6			4 5		
			7	10 1	2 51	1 8		
			9				Megaloblastic	
			11	11 2	2 95	< 1		
			14	11 1	3 05	< 1		
2	M	64	0	6 1	1 73	1 2	Megaloblastic	40
			1			1 1		
			2			1 1		
			3			1 2		
			4			3 1		
			5			3 8		
			6			4 8		
			9	6 2	1 77	< 1		
			10				Nuclear condensation of megaloblasts	
			14	6 8	1 93	< 1		
3	F	54	0	6 5	1 61	1 0	Megaloblastic	80
			2			< 1		
			3	6 4	1 58	5 0		
			4			5 2		
			5			7 6		
			6	8 7	2 11	7 0	Normoblastic	
			7			5 1		
			8			2 3		
			10	9 9	2 75	1 2		
			14	9 8	2 66	< 1		

Brockman et al. (1950) have described the synthesis and isolation in crystalline form, and the empirical formula, of a substance which they have produced from folic acid and which appears to have the same biological properties as those described for citrovorum factor derived from liver In 1949 Bond et al reported the isolation from liver of a substance which they named 'folinic acid," and which is probably the same as the citrovorum factor

A leading article in THE LANCET (1951) gives an excellent account of the historical aspects of these discoveries and the evidence for their relation to each other It also mentions the therapeutic response to folic acid of a megaloblastic anæmia induced in monkeys by dietary deficiency, and expresses the hope that reports on its action in human megaloblastic anæmia should soon be to hand This preliminary report is accordingly submitted for publication

MATERIAL

The citrovorum factor used in this investigation was a product of biological origin kindly supplied to us by Dr T H Jukes, of Lederle Laboratories, Inc , Pearl River, N Y It was free from vitamin B_{12} and folic acid, and was prepared for parenteral administration in ampoules containing 20 million units of microbiological activity per ml It has recently been shown (Brockman et al. 1950) that about 0 15–0 20 mμg of the synthetic citrovorum factor corresponds to one "unit" of the biological product, and hence each millilitre of the preparation supplied to us contained the equivalent of approximately 3–4 mg of the synthetic citrovorum factor

METHOD

Three patients with addisonian pernicious anæmia were chosen In each case the dietary history was good , there was no diarrhœa , the test meal showed histamine fast achlorhydria , and the marrow was megaloblastic

After a control period, during which there was no evidence of remission, the patients were given, respectively, 20, 40, and 80 million units of citrovorum factor in a single intramuscular injection, and the hæmatological response was followed for two weeks

The results are shown in the accompanying table It is evident that there was a slight hæmatological response in case 1 receiving 20 million units, and in case 2 where 40 million units was given and a good hæmatological response in case 3 where 80 million units was given A corresponding improvement in the state of well-being also occurred in case 3

DISCUSSION

These results suggest that, provided a large enough dose is given, the *L citrovorum* factor will produce a hæmatological and clinical response in pernicious anæmia Since 80 million units of the citrovorum factor derived from biological sources contains the equivalent of approximately 12–16 mg of synthetic citrovorum factor, it would appear that the therapeutic dose in milligrammes of folic acid and citrovorum factor are of the same order This is to be contrasted with the therapeutically active dosage of vitamin B_{12}, which is measured in microgrammes rather than milligrammes

It is now known that the citrovorum factor can replace folic acid as a growth factor for *Streptococcus fæcalis* It is also known that the content of folic acid in refined liver extracts is of the order of a few microgrammes or less This figure represents not only the folic acid content but also the amount of *L citrovorum* factor in the liver extracts Accordingly it is certain that the activity of refined liver extract in the treatment of pernicious anæmia is not related to its content of either of these substances but to its content of vitamin B_{12} The work of Nichol and Welch (1950) suggests that the *L citrovorum* factor may be the derivative of pteroyl glutamic acid actually responsible for the continuation of normoblastic blood formation

SUMMARY

Three cases of addisonian pernicious anæmia have been treated with 20, 40, and 80 million biological units of citrovorum factor Only when 80 million units was given was a satisfactory response obtained

REFERENCES

Bond T J Bardos T J Sibley M Shive, W (1949) *J Amer chem Soc* 71 3852
Brockman J A jun Roth, B Broquist, H P Hultquist M E Smith J M jun Fahrenbach, M. J Cosulich D B Parker R P Stokstad E L R , Jukes T H (1950) *Ibid* 72 4325
Lancet (1951) Leading article i 623
Lyman C M Prescott J M. (1949) *J biol. Chem* 178, 523
Nichol C A Welch, A D (1950) *Proc Soc exp Biol N Y* 74 403
Sauberlich, H E Baumann C A (1948) *J biol. Chem.* 176, 165
Scheid H E Schweigert B S (1950) *Ibid*, 185 1

L S P DAVIDSON
M D Edin , F.R C.P E F.R C.P
Professor of Medicine

R H GIRDWOOD
F.R C.P.E , M R C.P
Lecturer in Medicine

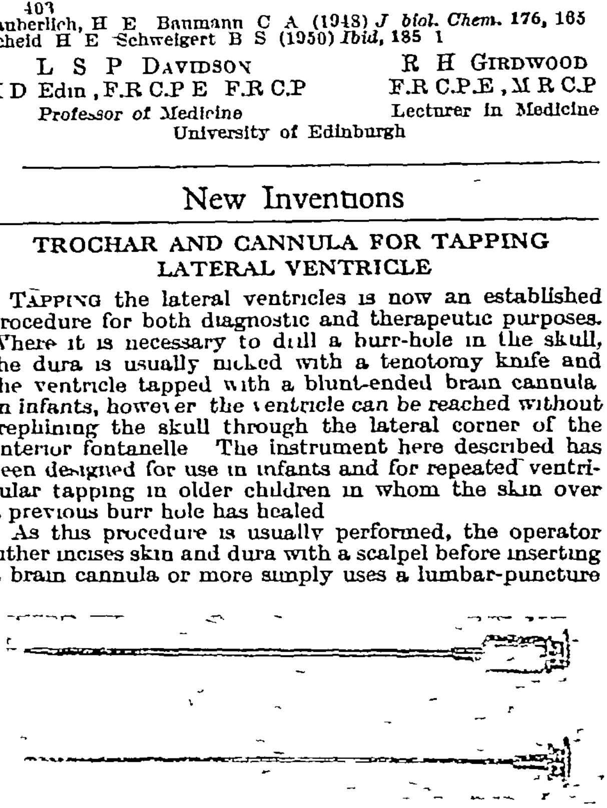
University of Edinburgh

New Inventions

TROCHAR AND CANNULA FOR TAPPING LATERAL VENTRICLE

TAPPING the lateral ventricles is now an established procedure for both diagnostic and therapeutic purposes. Where it is necessary to drill a burr-hole in the skull, the dura is usually nicked with a tenotomy knife and the ventricle tapped with a blunt-ended brain cannula In infants, however the ventricle can be reached without trephining the skull through the lateral corner of the anterior fontanelle The instrument here described has been designed for use in infants and for repeated ventricular tapping in older children in whom the skin over a previous burr hole has healed

As this procedure is usually performed, the operator either incises skin and dura with a scalpel before inserting a brain cannula or more simply uses a lumbar-puncture needle for traversing skin, meninges, and brain substance The second method is not without risk because the sharp needle may cut through an intracerebral blood-vessel



The instrument illustrated consists of a fine cannula which may be fitted with a trochar or with a blunt obturator The Pannett's mount, which is Record fitting, is keyed to ensure that the trochar or obturator fits closely and does not rotate The end of the cannula is tapered slightly to make a smooth surface with the trochar or obturator, which just protrudes The instrument, which is graduated in centimetres from the distal end, is made in two sizes, 17 and 19 S W G , both 3 inches long (excluding mount)

Technique.—With the trochar in position the cannula is inserted through the skin and cautiously pushed onwards until the dura is pierced This is easily felt by the operator who then removes the trochar and replaces it with the blunt obturator before traversing the brain itself

Our thanks are due to Mr A W Woodhead, of the Hospital for Sick Children, Great Ormond Street, who made the prototype, and to Mr W A S Whittlesey of St Mary's Hospital for his help in designing the model here described The cannula is made by Messrs Willen Bros , of 44 New Cavendish Street, London W 1

I A. B CATHIE, M D Lond.
J P M TIZARD, B M Oxfd, M.R C P
The Hospital for Sick Children Great Ormond Street, and St Mary's Hospital Medical School London

OSCILLATION OF THE EYES OF KITTENS KEPT IN THE DARK

Cat no	Litter no	Age (weeks)	Weeks in dark		Weeks to recover
			Before oscillations	No oscillations	
A	1	6	4		1
B			4		1
C			7		1
D	2	4	Died		
E			4		Died
F				8	Died

METHOD AND RESULTS

Three black kittens, aged 6 weeks, and three tabbies, aged 4 weeks, were placed in a completely dark room and observed every week with an ophthalmoscope Six brown rats and six black and white rabbits were treated in the same way None of the animals had oscillating eyes before being put in the dark, but oscillations were noted in three of the kittens after 4 weeks in the dark, and in a fourth after 7 weeks (see table) One kitten had no oscillations after 8 weeks in the dark In the black kittens (litter 1) the oscillations were rotary and there was a synchronous tremor of the head The oscillations were exaggerated on looking up and to the sides, comparable to what is noticed in coalminers' nystagmus On being put back into daylight all the kittens in litter 1 recovered within a week, but litter 2 died of an intercurrent infection before the experiment was finished A close up cinematograph film of the oscillating eyes of kittens A and B was taken, and again of kitten B when its eyes had recovered None of the rats or rabbits showed oscillations even after 7 months in the dark

DISCUSSION

The Miners' Nystagmus Committee (1922) cited Ohm (1916) as having kept three puppies and two kittens in a dark cellar and as finding nystagmus in all of them after an interval of 10–48 days This observation seems never to have been confirmed or definitely demonstrated since then Ohm, at that date, could only use a mechanical recording method, in which a lever pressed directly on the eyeball and drew a tracing on a kymograph drum He also found that light had a "calming" influence on the oscillations The present pilot experiment confirms and records this fundamental observation

Riesen (1947, 1950) produced nystagmus in chimpanzees, which have a visual apparatus almost identical to that of man, by rearing them in the dark from birth before they had time to develop binocular vision One of his chimpanzees developed an external squint, and another an internal squint, comparable to the convergence so often seen in coalminers' nystagmus One chimpanzee had attacks of nystagmus when it was excited, closely comparable to a patient recently seen who complained of the oscillations "when he was vexed" Riesen's final experiment was to put a chimpanzee, aged 7 months (when it had developed its full visual functions), into the dark, and it too developed nystagmus and became unable to recognise surrounding objects This perhaps suggests that coalminers' nystagmus may well be a partial disuse atrophy of the visual function from lack of light Moreover Browne and others (1950) have shown that coalminers with nystagmus differ very little from those without it, and that the psychological symptoms are the result, rather than the cause, of the disability

SUMMARY

Four out of six kittens developed rotary nystagmus after being kept in the dark 4–7 weeks Three of the four recovered after being in daylight for a week

A close up cinematograph film recorded the results

These findings confirm the results of experiments made by Ohm (1916) on puppies and by Riesen (1947, 1950) on chimpanzees

They suggest that coalminers' nystagmus may be a type of disuse atrophy of the visual apparatus

Acknowledgments are due to the National Coal Board for a grant towards the expense of this work.

REFERENCES

Browne R C, Beck I F, Saint, E G, McCallum, R I (19 *Brit J Ophthal* 34 601
Davson H (1949) Physiology of the Eye London
Ferguson W J W (1943) *Brit J phys Med.* 6, 40
Halliday J L (1943) *Psychosomat Med* 5, 71
Lancet (1940) i 468
Miners Nystagmus Committee (1922) *Spec Rep med Res. Coun., Lond* no 65, p 47
Ohm, J (1916) *Z Augenheilk* 36, 198
Riesen A H (1947) *Science* 106 107
— (1950) *Scientific American*, 183, 16
Walls, G L (1942) The Vertebrate Eye Michigan

Preliminary Communication

TREATMENT OF PERNICIOUS ANÆMIA WITH LEUCONOSTOC CITROVORUM FACTOR

IN recent years there have been numerous reports about the activity of pteroylglutamic acid (folic acid) and of vitamin B_{12} in the treatment of the megaloblastic anæmias The purpose of this paper is to report on the hæmopoietic activity in pernicious anæmia of yet another factor that has been isolated from liver

Sauberlich and Baumann (1948) showed that certain natural materials, including liver, liver extracts, and yeast extracts, contain a growth factor for the streptococcus—*Leuconostoc citrovorum* This factor, which they called the "citrovorum factor," differs from vitamin B_{12} in that it can be separated from the latter by electrolysis (Lyman and Prescott 1949), and because pure vitamin B_{12} will not stimulate the growth of *L citrovorum* (Scheid and Schweigert 1950) It also differs from folic acid in certain growth promoting activities for bacteria (Sauberlich and Baumann 1948)

RESPONSE TO CITROVORUM FACTOR

Case no	Sex	Age (years)	Day	Hb (g per 100 ml)	R B C (millions per c mm)	Reticulocytes (%)	Sternal marrow	Treatment (million units of citrovorum factor intramuscularly)
1	F	60	0	9 9	2 63	1 8	Megaloblastic	20
			2			1 4		
			3			1·8		
			4			2 4		
			5			4 1		
			6			4 5		
			7	10 1	2 51	1 8	Megaloblastic	
			9					
			11	11 2	2 95	<1		
			14	11 4	3 05	<1		
2	M	64	0	6 1	1 73	1 2	Megaloblastic	40
			1			1 1		
			2			1 1		
			3			1 2		
			4			3 1		
			5			3 8		
			6			4 8		
			9	6 2	1 77	<1		
			10				Nuclear condensation of megaloblasts	
			14	6 8	1 93	<1		
3	F	54	0	6 5	1 61	1 0	Megaloblastic	80
			2			<1		
			3	6 4	1 58	5 0		
			4			5 2		
			5			7 6		
			6	8 7	2 44	7 0	Normoblastic	
			7			5 1		
			8			2 3		
			10	9 9	2 75	1 2		
			14	9 8	2 60	<1		

THE LANCET

LONDON SATURDAY, MARCH 31, 1951

Penicillin Dosage

THE ultimate aim of antibiotic therapy is to cure the patient as quickly and comfortably as possible The planning of treatment may present no difficulties, but in serious cases it often calls for close liaison between clinician and pathologist, and for some understanding of drug actions and the defence mechanisms of the tissues To treat every case with the latest antibiotic is an impressive but unjustifiably costly practice, nor should one look on one drug as "the best" for pneumonia, another for meningitis, and a third for cystitis—the action of antibiotics is specific for infecting micro organisms, not for clinical syndromes However, in an acute infection a day's delay in starting treatment may mean irreparable damage, so antibiotic treatment should be started as soon as the material needed for isolating the infecting organism has been collected When the pathogen has been identified and its drug sensitivity determined, the clinician applies his knowledge of therapeutics to these findings to obtain the best results Some drugs, like the sulphonamides and perhaps the newer antibiotics, are more bacteriostatic than bactericidal, treatment with these should therefore be continued long enough to allow the host's tissues to play their full part in overcoming the infection, though not unnecessarily long because of the risk of sensitisation and other drug reactions Penicillin and streptomycin are known to be bactericidal in optimal concentrations, and they are therefore particularly useful drugs when the host's reaction is poor, as in the bronchopneumonias of the very young and the very old

Most antibiotics are effective only against bacterial cells that are actively growing, and some relapses have been ascribed to the survival of resting organisms —"persisters," as BIGGER calls them—which begin to multiply again when the course of antibiotic is finished. For this and other reasons, some authorities advocate the administration of penicillin, in a dosage or preparation which will produce a high intermittent blood-penicillin level rather than a low sustained one The merits of the two procedures were compared, on the basis of laboratory work, by EAGLE[1] and MARSHALL,[2] and they are admirably summarised by BEYER[3] in his new book on the pharmacology of penicillin. EAGLE and his colleagues[4] contend, from their findings in experimental streptococcal, pneumococcal and syphilitic infections in rabbits and mice, that the factor on which the therapeutic activity of penicillin mainly depends is the aggregate time, not necessarily continuous, during which a bactericidal level exists in the blood But the concentration of penicillin in the infected lesion may not bear any close relation to the blood level, for the drug passes more slowly into inflamed than into normal tissue and the drug concentration attained in inflamed tissue is usually lower than the blood level, moreover, if the lesion is poorly vascularised or walled off by a fibrinous barrier, as in bacterial endocarditis and staphylococcal abscesses, the blood-level will have to be many times the minimum effective in-vitro level before enough of the drug will seep into the lesion to produce a bactericidal concentration We must remember, too, that the laboratory test measures the *bacteriostatic* concentration, which for penicillin may be well below the *bactericidal* level required to destroy bacteria in infected tissues The concentration of penicillin to which an organism has been exposed and the duration of that exposure affect the time required for the bacteria to recover both in vitro and in vivo Any attempts to estimate the interval that may safely be allowed between doses of penicillin must take into account the wide differences in the rate of multiplication of bacteria (20–30 minutes for the pyogenic cocci, and 18–24 hours for the tubercle bacillus and *Treponema pallidum*), the variable time required by different bacteria to recover from the toxic effects of penicillin, and the variable number of organisms to be destroyed.

Such considerations do not necessarily justify the massive dosage of penicillin that has become routine practice today, for, provided the drug has ready access to the lesion, a serum level only two to four times that required to kill micro organisms at the maximum rate in vitro will be equally effective in vivo, and though massive dosage may multiply this serum level by several hundred it will not accelerate the rate of killing On the other hand, a daily dose of procaine penicillin which maintains a fairly constant low blood-level may not produce a concentration of penicillin in the diseased tissues high enough or for long enough to be bactericidal in staphylococcal pyæmia or more chronic infections like subacute bacterial endocarditis and actinomycosis Even fortification with crystalline penicillin may not help unless it is given in very large doses, because its action is too evanescent There is, however, good experimental and clinical evidence that intermittent penicillin therapy with infrequent doses is effective in various infections, and on this evidence greater use might be made of penicillin by mouth, given on an empty stomach twice a day in amounts 5–10 times the parenteral dose This method is suitable for adults as well as for babies and older children,[5] and it is particularly convenient in general practice, its wider adoption would save doctors' and nurses' time and hospital beds, besides lessening the patient's discomfort Penicillin's toxicity is low, but it retains some allergenic propensity even when purified, and for this reason the clinician may prefer a brief but unstinting dosage to a more sparing and protracted one The best way to save expense is by re educating the young doctor and some of his senior colleagues in the value of sulphonamides, keeping the more expensive antibiotics for conditions which really demand them A note on p 750 shows how costly these drugs can be

---

[1] Eagle H *Ann. intern Med* 1948, 28 260

[2] Marshall E K. *Bull Johns Hopk Hosp* 1948 82 403

[3] Pharmacological Basis of Penicillin Therapy By KARL H BEYER, M D F.A C.P director of pharmacological research Medical Research Division Sharp and Dohme Inc Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 214 32s 6d

[4] Eagle H Fleischman R Musselman A D *Amer J Med* 1950 9 280

[5] Bunn P Caldwell E R Adair C Lepper, M., Dowling H *J Amer med Ass* 1950 144 1540

Reviews of Books

The Abnormal Pneumoencephalogram

LEO M DAVIDOFF, M D, clinical professor of neuro surgery, New York University, BERNARD S EPSTEIN, M.D, associate radiologist, The Jewish Hospital of Brooklyn, N Y London Henry Kimpton 1950 Pp 506 £5 5*s*

THIS book is the sequel promised in *The Normal Encephalogram* which Professor Davidoff wrote in collaboration with Dr Cornelius Dyke, whose early death in 1943 caused postponement of the projected book on air studies of the abnormal brain Dr Bernard Epstein has joined Professor Davidoff on the neuroradiological side, and the volume has been much enlarged by comparison with what was originally proposed It will certainly become a standard reference work, and the large amount of case-material will interest neurologists and neurosurgeons as well as radiologists

Through analysis of the changes in outline produced by space occupying lesions in various sites, the authors proceed to consideration of the changes caused by atrophic and other lesions of the brain and meninges Each chapter is divided into a brief clinical survey, a thorough survey of previous literature, some well presented and well illustrated case material, and a summary of findings with a discussion on differential diagnosis

The radiographic technique employed seems to rely on relatively complete replacement of cerebrospinal fluid by air, in that many of their illustrations show projections obtained with the head in the lateral position In some cases projections with the head in the brow up or brow down position, using the technique described by Lysholm, might have demonstrated the lesions more convincingly, particularly in the chapters on the temporal horn and on neoplasms of the corpus callosum In the chapter on neoplasms of the lateral ventricles there is a failure to differentiate clearly between neoplasm arising from the ventricular wall and the invading neoplasm, and the films reproduced to illustrate agenesis of the corpus callosum might have been better These, however are small defects in a book which is a worthy companion to its forerunner

The Cytologic Diagnosis of Cancer

Staff of the Vincent Memorial Hospital, Department of Gynecology, Harvard Medical School Philadelphia and London W B Saunders 1950 Pp 229 33*s*

THIS book, devoted to the diagnosis of cancer by smear techniques, using the method of Papanicolaou, describes fully the applications of the method to cells exfoliated from various mucous membranes, or present in serous exudates Nearly half the volume is concerned with the female genital tract, and this section is profusely illustrated, in atlas form, with different combinations of photographs and drawings (some in colour) accompanied by diagrammatic keys These illustrations demonstrate clearly the different types of cells encountered in normal and pathological conditions of the genital tract The remaining chapters deal more briefly with the respiratory tract, stomach, pleural and peritoneal fluids, and urinary tract, including the prostate Even with such aids as this it cannot be concluded that accurate diagnosis by the Papanicolaou technique is achieved save by long-continued observation and experience, but for those who are resolved to embark on this hazardous enterprise this book should be indispensable

A Surgeon's Fight to Rebuild Men

FRED ALBEE, M D London Robert Hale 1950 Pp 270 15*s*

DR Albee's account of his fight is addressed to the general public in terms which they can well understand It is a story of success, related by the author with gusto and becoming modesty He tells how even his childhood experiences were turned to good account His grandfather, at work in the orchard, taught the little boy the first principles of successful grafting Before he was ten years old he had made for himself a tiny water driven rotary saw, the forerunner of the famous Albee bone mill to which can be fitted the tools used in the precise shaping and adaptation of the bone graft—saws drills, die cutters, chisels, and files Before he was forty he was invited to demonstrate his instrument at the 17th conference of the International Association of Medicine and Surgery, held in London in 1913 In two great wars he perfected his methods, relying always, as he explains, on the phenomenal power of bone to regenerate The most slender graft, in a long bone, if successfully implanted, will always grow to that thickness which is necessary to bear the strain to which it is subjected

Successful results in orthopædic surgery are visible not only to the delighted patient but to the eye of every onlooker The photograph, before and after, proclaims the marvel even to the uninitiated Perhaps only the *plastic surgeon of the face enjoys an* equal share of public appreciation Workers in both these fields are apt to find themselves more than ordinarily liable to be hailed as miracle-workers and as benefactors of humanity, but in Dr Albee's case the claim will not be disputed

The Enzymes

Chemistry and Mechanism of Action Vol I, part 1 Editors JAMES B SUMNER, Laboratory of Enzyme Chemistry, Cornell University, New York, KARL MYRBÄCK, Institute for Organic Chemistry and Biochemistry, *University of Stockholm* New York Academic Press 1950 Pp 724 $13 50

THIS treatise, the scope of which is correctly described by the publishers as 'encyclopædic," will appear in four parts, of which this is the first Since C Oppenheimer's *Die Fermente*, published 25 years ago, nothing like this book has appeared The work of 78 leading specialists is to be incorporated in the four parts, and the whole *subject—not only* recent advances—will be covered This first part contains an introduction to enzymology, in eight general chapters, and three fascinating long sections—on enzymes in relation to genes viruses, hormones, vitamins, and chemotherapy, on the *cytochemical foundations of enzyme* chemistry, and on enzymatic adaptation—in which recent activity is well surveyed L Massart contributes a chapter on enzyme inhibition, and J R Marrack, of the London Hospital, an excellent review of enzymes and immunology Chapters on special enzymes cover esterases, cholinesterase, sulphatases, invertase, glucosidases, and glucuronidase, and end with an informative review of amylases by K Myrbäck and G Neumüller The book will undoubtedly become a standard reference work.

Collected Papers on Psychoanalysis

ELLA FREEMAN SHARPE Editor MARJORIE BRIERLEY London Hogarth Press and Institute of Psychoanalysis 1950 Pp 280 21*s*

MISS Sharpe was a gifted expositor of psycho analysis, as this collection shows The papers fall into three groups on technique, on theory, and on literary interpretation The seven lectures on technical matters are lucid and obviously based on much experience Studies of sublimation in art and science, and the development of metaphor as an outcome of the control of bodily orifices, lead the reader into territory which, if he is not a psycho analyst, he may well view with sceptical eye, especially when he meets a familiar phrase seemingly misquoted or misheard (as in 'I wouldn't touch her with a branched pole') More in keeping with Miss Sharpe's gifts and earlier training are the literary studies with which the book ends These examine the imagery of Francis Thompson's poetry, the impatience which Hamlet shows (in contrast to the procrastination commonly stressed) in his character and behaviour, and some inferences about Shakespeare's life which can be drawn from *King Lear* by an alert and ingenious psycho analyst

---

A Doctor Remembers (London Seeley Service & Co 1950 Pp 288 12*s* 6*d*)—*Many an* elderly reader, taking up Dr E A Barton's autobiography, will wish he could have had it by him when he was a young doctor The whole of his medical life might have been altered No one could be a more frank and reliable guide than Dr Barton for the fifth year student or the houseman—though not everybody will agree with his views on euthanasia Kindliness, charity, wit, and humour fill his pages no rushing the patient to the operating theatre , *ohne Hast, ohne Rast, immer langsam voran* is a good dictum Plain (' scout ") radiographs of the abdomen, with the patient supine and erect, should invariably be taken These will demonstrate the cæcum, which serves as the wind sock—the guide to the surgical line of approach—and also clinches the diagnosis of large bowel obstruction The volvulus will be clearly outlined , and the small intestine obstruction will be evident in the parallel loops and multiple fluid pools Moreover, as Mr RODNEY SMITH emphasised, in many cases the ileocæcal valve holds, forming a closed obstruction loop which only operation can relieve , when this valve is incompetent, ballooning of the small intestine is evident on the radiograph The surgeon may then be tempted to introduce a Miller-Abbott tube, but every speaker agreed that this may lose valuable time , for the tube cannot decompress the large bowel and its passage through the pylorus is unpredictable Passage of a Ryle tube is always necessary, and the anæsthetist must take precautions against regurgitation Fluid replacement is called for, as Mr H E LOCKHART-MUMMERY remarked , but this therapy has to be tempered with fine judgment, particularly in the old Awareness of the hazards of intravenous therapy is now more acute (It has been well declared that more people have been drowned on the banks of the Thames than in it) The saline content of the urine is a sensitive indicator of salt need, and should become a standard ward test Mr E W GRAHAME recommended that if the chloride test is positive, 0·45% saline should be infused, and this should be followed with plasma or even blood.

As to the surgical procedure, opinion differed little Cæcostomy, blind or otherwise, was regarded as less satisfactory than transverse colon loop colostomy, preferably through a transverse abdominal incision This affords more effective rapid decompression , and the more complete defunctioning ' is a great advantage in the subsequent stage of resection Some wag, talking of visceroptosis, has suggested that " where a man wears his guts is his own business " , but in large-bowel obstruction it is very much the surgeon's concern Fat patients very often have short mesenteries , and, as Mr H R THOMPSON said, the obstructed colon, tethered by its mesentery, expands between the leaves, shortening it even more Delivery of such a colostomy to the surface may thus be difficult or impossible , and the surgeon is sometimes forced to do a cæcostomy This may be difficult If spilling is to be avoided, the bowel should be punctured with a fine needle and then cleared with trochar-puncture suction, after suitable packing and purse string suture , satisfactory decompression will be achieved only with drainage through a large tube and exteriorisation of the bowel. Cæcostomy may also be advisable for growths of the splenic flexure , for in the subsequent resection the surgeon is not handicapped by an otherwise fixed transverse colon Even the obstructing transverse colon growth is probably better handled in this way than by immediate resection on an area of œdematous mesentery Pelvic colon colostomy is to be avoided , it embarrasses the surgeon in any subsequent resection

Should the abdomen be gently explored at the same time? Obviously the surgeon will be guided by the amount of bowel distension Professor MORLEY suggested that with the anæsthetist's use of muscle relaxants (spinal anæsthetics are hazardous) this was now often possible , and it provided the surgeon with reasonable information for planning further procedures Mr RODNEY SMITH, however, felt that this procedure was dangerous, and from the patient's angle often merely morbid curiosity Mr LOCKHART-MUMMERY, who described a study of some 90 case-records collected from five different hospitals, gave examples showing that what seemed an inoperable growth on palpation by this method was often merely due to secondary inflammatory changes Even with secondary growths in the liver, most surgeons now endeavour to remove subsequently the primary growth , and these patients often live for three years in relative comfort [4] Immediate resection and anastomosis, as any surgical tyro knows, has no place in this type of surgery The Paul-Mikulicz procedure though it has a deservedly good reputation in mild subacute obstruction, should not be undertaken here , for it does not safely afford the necessary wide mobilisation of the bowel. Obstruction of the right colon, it was also generally agreed, is preferably dealt with by lateral ileocolic anastomosis rather than ileostomy, which might lead to skin excoriation and a distressing convalescence Such anastomosis needs very fine close stitching if leakage is to be avoided , the anastomosis should be placed some twelve inches from the ileocæcal valve and joined to the mid transverse colon. Primary hemicolectomy is occasionally permissible , Professor MORLEY recommends in addition E G MUIR's manœuvre of passing a drainage tube through the colon end and via the stoma into the ileum

In the immediate aftercare the electrolyte balance will need attention. House-surgeons to whom drips are delegated should be warned , for otherwise they will not tiptoe as the experienced surgeon does, appreciating more fully the complex physiological issues Increased significance is now attached to the potassium ion [5] , and Mr GRAHAME pointed out that the potassium values were high in these cases, probably owing to circulatory failure and associated renal insufficiency The effects of parenteral potassium on the myocardium may be serious, so at least three conditions must be met there must be a daily urinary output of over 750 ml , and each day an electrocardiogram must be taken and the serum potassium level recorded [6] Three weeks seems to be ample time for resolution of the colon œdema and ulceration, and for the wall blood supply to become fit for resection of the bowel End-to end anastomosis is to be preferred, though there is room for personal choice The so called aseptic anastomosis, as Professor MORLEY emphasised, is of no particular advantage at this stage The method of closing colostomies needs further thought by the surgeon This may be a difficult procedure, with occasional deaths The present practice of enterotome-crushing of the spur in the Paul Mikulicz procedure is surely an anachronism Closure of large numbers of colostomies in the belly wounds of war has convinced many surgeons that excision of the

---

[4] Garlock J H Klein S H *Arch Surg* 1949, 59 1289

[5] Elman R Semmer R A Weichselbaum T E Owen J G York, R W *Ann Surg* 1949 130 703 Moore F D *J Amer med Ass* 1949 141 646 Randall H T Habif D V Lockwood, J S Werner S C *Surgery* 1949 26 341

[6] Marks L J *Ann Surg* 1950 132 20

Treatment of Depression

IF, among the many who attended the discussion on depression at the Royal Society of Medicine on March 13, there was anyone who came to see the psychological and somatological schools of psychiatry in open combat, he must have been disappointed Since 1936 Dr Clifford Scott, the representative of psycho analysis, has treated selected patients with affective psychoses by the methods of Freudian analysis but in such cases he still regards this treatment as experimental and full of difficulties and dangers Moreover, during analysis he has observed faints, drowsiness, amnesia, attacks of rage and furor, and sudden suicidal urges—in short, symptoms reminiscent of epilepsy, pointing, he thinks, to an instinctive yearning by the patient for " shock " and convulsive treatment He also found that previous convulsive treatment was helpful to the progress of analytical procedure The number of beneficial results he could quote from psycho analysis alone, was not impressive, but his critical and persistent endeavour to unravel the psychopathology of melancholia in the footsteps of Abraham command respect

Dr Scott was preceded by Dr W Mayer Gross, who began by pointing out the change in therapeutic approach to the affective psychoses within the last fifteen years, through the introduction of convulsive therapy He thought it necessary, however, to recapitulate long established measures Some of these, such as the avoidance of suicidal risks, have in a modified form become more important with the new treatment, others, such as the combating of anorexia, loss of weight, and constipation—formerly the most hazardous tasks in treating depression—hardly present any problem nowadays Depressive illness is still often mistaken for physical disease, and the patient may be treated for gastro intestinal complaints, anæmia, pulmonary tuberculosis, or malignant disease But even if the patient's bodily health is greatly impaired during lengthy investigations before he sees a psychiatrist, once the diagnosis is made a few convulsions will restore all bodily functions, including sleep, before the psychological effect becomes very obvious Wisely used, electrically induced convulsion treatment can transform the outlook of a depressive attack, and the most common mistake, according to Dr Mayer Gross, is its excessive and indiscriminate use Of all the affective syndromes, involutional depression derives most benefit from convulsion treatment A series of 100 depressive patients over the age of forty, without earlier history of depression, were followed up for two to nine years after being treated at Crichton Royal between 1940 and 1947 At the time of the follow up, 72 were fully recovered, 6 socially recovered, and 11 home invalids, only 3 had had to remain in hospital all the time There had been 8 deaths, 2 by suicide In an equal group of younger manic depressive patients with definite recurrent attacks, the response to convulsive therapy was not so definite, but, despite a larger proportion of relapses, a shortening of suffering and of hospital care was usually apparent The rhythm of the illness and the number of attacks was, however, not influenced by the convulsive treatment

In the general discussion great interest was shown in the type of case that totally or partially resists convulsion therapy Most speakers agreed on its failure in younger patients in whom severe anxiety is associated with depression Opinion was divided on its suitability in reactive depression—i.e, in patients with an acute or chronic conflict situation probably responsible for the depressive illness Dr G Garmany, the third opener, who dealt mainly with the important use of electric convulsions in outpatient clinics, illustrated his points with some statistics from Westminster Hospital He found the treatment worth while and efficient in reactive depressions, provided the premorbid personality was stable and not of a psychopathic type Little was said about leucotomy in depressive states except for some cautionary counsel that it may destroy the delicate emotional responses which are the great asset of the cyclothymic patient Only for those cases of manic depression in which psychotic attacks follow one another so quickly that the patient has to stay permanently in hospital, is operative treatment indicated, and less damaging and more exactly localised neurosurgical techniques should be sought for such cases

Carcinomatous Obstruction of the Colon

MEDICINE is advancing so swiftly at so many points that any slower progress seems disappointing The mortality from acute obstruction of the colon due to malignant disease is a good example of this slower tempo In the '30s the operative mortality was about 30%, and since then, despite antibiotics, intestinal antiseptics, and other innovations, it has fallen only to some 18–20% By contrast, the mortality of operations on uncomplicated carcinoma of the colon has fallen strikingly The figures of Allen et al[1] indicate a fall from 17 5% to under 2%, and indeed it is reasonably contended that " barring accidents , the surgeon may be reasonably confident that his patient will survive such uncomplicated colon resection "[2]

At the Royal Society of Medicine on March 7, Prof John Morley, opening a discussion on large bowel obstruction due to malignant disease, urged the need for clear instructions to registrars, who are most commonly required to cope with this emergency Nevertheless the greatest skill may not suffice, for obstruction of this sort is often a late complication, and the patient may arrive with the bowel already perforated, moreover many of these patients have what Samuel Johnson termed the most incurable of all diseases—old age Obstruction does not usually come without warning, diarrhœa, with mucus in the stools, and colicky pain drive most patients into seeking advice Occasionally, however, as Mr Rodney Smith pointed out, the doctor may be deceived by the complaint of right sided abdominal pain, due to cæcal distension or mobility of a distended sigmoid loop[3] In 90% of cases the obstruction—usually of the ' napkin ring " type—is in the left colon, and involvement of the right colon nearly always indicates an advanced growth There must be

---

1 Allen W A Welch C E Donaldson G A *Ann Surg* 1947 126 19

2 Pemberton J de J *Proc Mayo Clin* 1947, 22 561

3 Lyons A S *Ann Surg* 1948 127 398

no rushing the patient to the operating-theatre, *ohne Hast, ohne Rast, immer langsam voran* is a good dictum Plain (' scout ") radiographs of the abdomen, with the patient supine and erect, should invariably be taken These will demonstrate the cæcum, which serves as the wind-sock—the guide to the surgical line of approach—and also clinches the diagnosis of large bowel obstruction The volvulus will be clearly outlined, and the small intestine obstruction will be evident in the parallel loops and multiple fluid pools Moreover, as Mr RODNEY SMITH emphasised, in many cases the ileocæcal valve holds, forming a closed obstruction loop which only operation can relieve, when this valve is incompetent, ballooning of the small intestine is evident on the radiograph The surgeon may then be tempted to introduce a Miller Abbott tube, but every speaker agreed that this may lose valuable time, for the tube cannot decompress the large bowel, and its passage through the pylorus is unpredictable Passage of a Ryle tube is always necessary, and the anæsthetist must take precautions against regurgitation Fluid replacement is called for, as Mr H E LOCKHART-MUMMERY remarked, but this therapy has to be tempered with fine judgment, particularly in the old Awareness of the hazards of intravenous therapy is now more acute (It has been well declared that more people have been drowned on the banks of the Thames than in it) The saline content of the urine is a sensitive indicator of salt need, and should become a standard ward test Mr E W GRAHAME recommended that if the chloride test is positive, 0 45% saline should be infused, and this should be followed with plasma or even blood

As to the surgical procedure, opinion differed little Cæcostomy, blind or otherwise, was regarded as less satisfactory than transverse colon loop colostomy, preferably through a transverse abdominal incision This affords more effective rapid decompression, and the more complete " defunctioning " is a great advantage in the subsequent stage of resection Some wag, talking of visceroptosis, has suggested that " where a man wears his guts is his own business ", but in large bowel obstruction it is very much the surgeon's concern Fat patients very often have short mesenteries, and, as Mr H R THOMPSON said, the obstructed colon, tethered by its mesentery, expands between the leaves, shortening it even more Delivery of such a colostomy to the surface may thus be difficult or impossible, and the surgeon is sometimes forced to do a cæcostomy This may be difficult If spilling is to be avoided, the bowel should be punctured with a fine needle and then cleared with trochar puncture suction, after suitable packing and purse string suture, satisfactory decompression will be achieved only with drainage through a large tube and exteriorisation of the bowel Cæcostomy may also be advisable for growths of the splenic flexure, for in the subsequent resection the surgeon is not handicapped by an otherwise fixed transverse colon Even the obstructing transverse colon growth is probably better handled in this way than by immediate resection on an area of œdematous mesentery Pelvic colon colostomy is to be avoided, it embarrasses the surgeon in any subsequent resection

Should the abdomen be gently explored at the same time [2] Obviously the surgeon will be guided by the amount of bowel distension Professor MORLEY suggested that with the anæsthetist's use of muscle relaxants (spinal anæsthetics are hazardous) this was now often possible, and it provided the surgeon with reasonable information for planning further procedures Mr RODNEY SMITH, however, felt that this procedure was dangerous, and from the patient's angle often merely morbid curiosity Mr LOCKHART MUMMERY, who described a study of some 90 case records collected from five different hospitals, gave examples showing that what seemed an inoperable growth on palpation by this method was often merely due to secondary inflammatory changes Even with secondary growths in the liver, most surgeons now endeavour to remove subsequently the primary growth, and these patients often live for three years in relative comfort [4] Immediate resection and anastomosis, as any surgical tyro knows, has no place in this type of surgery The Paul-Mikulicz procedure though it has a deservedly good reputation in mild subacute obstruction, should not be undertaken here, for it does not safely afford the necessary wide mobilisation of the bowel Obstruction of the right colon, it was also generally agreed, is preferably dealt with by lateral ileocolic anastomosis rather than ileostomy, which might lead to skin excoriation and a distressing convalescence Such anastomosis needs very fine close stitching if leakage is to be avoided, the anastomosis should be placed some twelve inches from the ileocæcal valve and joined to the mid transverse colon Primary hemicolectomy is occasionally permissible, Professor MORLEY recommends in addition E G MUIR's manœuvre of passing a drainage tube through the colon end and via the stoma into the ileum

In the immediate aftercare the electrolyte balance will need attention. House surgeons to whom drips are delegated should be warned, for otherwise they will not tiptoe as the experienced surgeon does, appreciating more fully the complex physiological issues Increased significance is now attached to the potassium ion [5], and Mr GRAHAME pointed out that the potassium values were high in these cases, probably owing to circulatory failure and associated renal insufficiency The effects of parenteral potassium on the myocardium may be serious, so at least three conditions must be met there must be a daily urinary output of over 750 ml, and each day an electrocardiogram must be taken and the serum-potassium level recorded [6] Three weeks seems to be ample time for resolution of the colon œdema and ulceration, and for the wall blood supply to become fit for resection of the bowel End to end anastomosis is to be preferred, though there is room for personal choice The so called aseptic anastomosis, as Professor MORLEY emphasised, is of no particular advantage at this stage The method of closing colostomies needs further thought by the surgeon This may be a difficult procedure, with occasional deaths The present practice of enterotome crushing of the spur in the Paul Mikulicz procedure is surely an anachronism Closure of large numbers of colostomies in the belly wounds of war has convinced many surgeons that excision of the

---

[4] Garlock J H Klein S H *Arch Surg* 1949 **59** 1289

[5] Elman R Semmer R A Welchselbaum T E Owen J G York R W *Ann Surg* 1949 **130** 703 Moore F D *J Amer med Ass* 1949 **141** 646 Randall H T, Habif D V Lockwood J S Werner S C *Surgery* 1949 **26** 341

[6] Marks L J *Ann Surg* 1950 **132** 20

Treatment of Depression

If, among the many who attended the discussion on depression at the Royal Society of Medicine on March 13, there was anyone who came to see the psychological and somatological schools of psychiatry in open combat, he must have been disappointed Since 1936 Dr Clifford Scott, the representative of psycho analysis, has treated selected patients with affective psychoses by the methods of Freudian analysis, but in such cases he still regards this treatment as experimental and full of difficulties and dangers Moreover, during analysis he has observed faints, drowsiness, amnesia, attacks of rage and furor, and sudden suicidal urges—in short, symptoms reminiscent of epilepsy, pointing, he thinks, to an instinctive yearning by the patient for " shock " and convulsive treatment He also found that previous convulsive treatment was helpful to the progress of analytical procedure The number of beneficial results he could quote from psycho analysis alone, was not impressive, but his critical and persistent endeavour to unravel the psychopathology of melancholia in the footsteps of Abraham command respect

Dr Scott was preceded by Dr W Mayer Gross, who began by pointing out the change in therapeutic approach to the affective psychoses within the last fifteen years, through the introduction of convulsive therapy He thought it necessary, however, to recapitulate long established measures Some of these, such as the avoidance of suicidal risks, have in a modified form become more important with the new treatment, others, such as the combating of anorexia, loss of weight, and constipation—formerly the most hazardous tasks in treating depression—hardly present any problem nowadays Depressive illness is still often mistaken for physical disease, and the patient may be treated for gastro intestinal complaints, anæmia, pulmonary tuberculosis, or malignant disease But even if the patient's bodily health is greatly impaired during lengthy investigations before he sees a psychiatrist, once the diagnosis is made a few convulsions will restore all bodily functions, including sleep, before the psychological effect becomes very obvious Wisely used, electrically induced convulsion treatment can transform the outlook of a depressive attack, and the most common mistake, according to Dr Mayer-Gross, is its excessive and indiscriminate use Of all the affective syndromes, involutional depression derives most benefit from convulsion treatment A series of 100 depressive patients over the age of forty, without earlier history of depression, were followed up for two to nine years after being treated at Crichton Royal between 1940 and 1947 At the time of the follow up, 72 were fully recovered, 6 socially recovered, and 11 home invalids, only 3 had had to remain in hospital all the time There had been 8 deaths, 2 by suicide In an equal group of younger manic depressive patients with definite recurrent attacks, the response to convulsive therapy was not so definite, but, despite a larger proportion of relapses, a shortening of suffering and of hospital care was usually apparent The rhythm of the illness and the number of attacks was, however, not influenced by the convulsive treatment

In the general discussion great interest was shown in the type of case that totally or partially resists convulsion therapy Most speakers agreed on its failure in younger patients in whom severe anxiety is associated with depression Opinion was divided on its suitability in reactive depression—i.e, in patients with an acute or chronic conflict situation probably responsible for the depressive illness Dr G Garmany, the third opener, who dealt mainly with the important use of electric convulsions in outpatient clinics, illustrated his points with some statistics from Westminster Hospital He found the treatment worth while and efficient in reactive depressions, provided the premorbid personality was stable and not of a psychopathic type Little was said about leucotomy in depressive states except for some cautionary counsel that it may destroy the delicate emotional responses which are the great asset of the cyclothymic patient Only for those cases of manic depression in which psychotic attacks follow one another so quickly that the patient has to stay permanently in hospital, is operative treatment indicated, and less damaging and more exactly localised neurosurgical techniques should be sought for such cases

Carcinomatous Obstruction of the Colon

Medicine is advancing so swiftly at so many points that any slower progress seems disappointing The mortality from acute obstruction of the colon due to malignant disease is a good example of this slower tempo In the '30s the operative mortality was about 30%, and since then, despite antibiotics, intestinal antiseptics, and other innovations, it has fallen only to some 18–20% By contrast, the mortality of operations on uncomplicated carcinoma of the colon has fallen strikingly The figures of Allen et al.[1] indicate a fall from 17 5% to under 2%, and indeed it is reasonably contended that " barring accidents the surgeon may be reasonably confident that his patient will survive such uncomplicated colon resection "[2]

At the Royal Society of Medicine on March 7, Prof John Morley, opening a discussion on large bowel obstruction due to malignant disease, urged the need for clear instructions to registrars, who are most commonly required to cope with this emergency Nevertheless the greatest skill may not suffice, for obstruction of this sort is often a late complication, and the patient may arrive with the bowel already perforated, moreover many of these patients have what Samuel Johnson termed the most incurable of all diseases—old age Obstruction does not usually come without warning, diarrhœa, with mucus in the stools, and colicky pain drive most patients into seeking advice Occasionally, however, as Mr Rodney Smith pointed out, the doctor may be deceived by the complaint of right-sided abdominal pain, due to cæcal distension or mobility of a distended sigmoid loop[3] In 90% of cases the obstruction—usually of the " napkin ring " type—is in the left colon, and involvement of the right colon nearly always indicates an advanced growth There must be no rushing the patient to the operating-theatre , *ohne Hast, ohne Rast, immer langsam voran* is a good dictum Plain (' scout ") radiographs of the abdomen, with the patient supine and erect, should invariably be taken These will demonstrate the cæcum, which serves as the wind sock—the guide to the surgical line of approach—and also clinches the diagnosis of large bowel obstruction The volvulus will be clearly outlined , and the small intestine obstruction will be evident in the parallel loops and multiple fluid pools Moreover, as Mr **RODNEY SMITH** emphasised, in many cases the ileocæcal valve holds, forming a closed obstruction loop which only operation can relieve , when this valve is incompetent, ballooning of the small intestine is evident on the radiograph The surgeon may then be tempted to introduce a Miller-Abbott tube, but every speaker agreed that this may lose valuable time , for the tube cannot decompress the large bowel, and its passage through the pylorus is unpredictable Passage of a Ryle tube is always necessary, and the anæsthetist must take precautions against regurgitation Fluid replacement is called for, as Mr H E **LOCKHART-MUMMERY** remarked , but this therapy has to be tempered with fine judgment, particularly in the old Awareness of the hazards of intravenous therapy is now more acute (It has been well declared that more people have been drowned on the banks of the Thames than in it) The saline content of the urine is a sensitive indicator of salt need, and should become a standard ward test Mr E W **GRAHAME** recommended that if the chloride test is positive, 0 45% saline should be infused, and this should be followed with plasma or even blood

---

[1] Allen W A Welch C E Donaldson G A Ann Surg 1947, 126 19

[2] Pemberton J de J Proc Mayo Clin 1947, 22 561

[3] Lyons A S Ann Surg 1948 127 398

As to the surgical procedure, opinion differed little Cæcostomy, blind or otherwise, was regarded as less satisfactory than transverse colon loop colostomy, preferably through a transverse abdominal incision This affords more effective rapid decompression , and the more complete ' defunctioning " is a great advantage in the subsequent stage of resection Some wag, talking of visceroptosis, has suggested that " where a man wears his guts is his own business " , but in large-bowel obstruction it is very much the surgeon's concern Fat patients very often have short mesenteries , and, as Mr H R **THOMPSON** said, the obstructed colon, tethered by its mesentery, expands between the leaves, shortening it even more Delivery of such a colostomy to the surface may thus be difficult or impossible , and the surgeon is sometimes forced to do a cæcostomy This may be difficult If spilling is to be avoided, the bowel should be punctured with a fine needle and then cleared with trochar puncture suction, after suitable packing and purse string suture , satisfactory decompression will be achieved only with drainage through a large tube and exteriorisation of the bowel Cæcostomy may also be advisable for growths of the splenic flexure , for in the subsequent resection the surgeon is not handicapped by an otherwise fixed transverse colon Even the obstructing transverse colon growth is probably better handled in this way than by immediate resection on an area of œdematous mesentery Pelvic colon colostomy is to be avoided , it embarrasses the surgeon in any subsequent resection

Should the abdomen be gently explored at the same time ? Obviously the surgeon will be guided by the amount of bowel distension Professor **MORLEY** suggested that with the anæsthetist's use of muscle relaxants (spinal anæsthetics are hazardous) this was now often possible , and it provided the surgeon with reasonable information for planning further procedures Mr **RODNEY SMITH**, however, felt that this procedure was dangerous, and from the patient's angle often merely morbid curiosity Mr **LOCKHART MUMMERY**, who described a study of some 90 case-records collected from five different hospitals, gave examples showing that what seemed an inoperable growth on palpation by this method was often merely due to secondary inflammatory changes Even with secondary growths in the liver, most surgeons now endeavour to remove subsequently the primary growth , and these patients often live for three years in relative comfort [4] Immediate resection and anastomosis, as any surgical tyro knows, has no place in this type of surgery The Paul-Mikulicz procedure though it has a deservedly good reputation in mild subacute obstruction, should not be undertaken here , for it does not safely afford the necessary wide mobilisation of the bowel Obstruction of the right colon, it was also generally agreed, is preferably dealt with by lateral ileocolic anastomosis rather than ileostomy, which might lead to skin excoriation and a distressing convalescence Such anastomosis needs very fine close stitching if leakage is to be avoided , the anastomosis should be placed some twelve inches from the ileocæcal valve and joined to the mid transverse colon Primary hemicolectomy is occasionally permissible , Professor **MORLEY** recommends in addition E G **MUIR**'s manœuvre of passing a drainage tube through the colon end and via the stoma into the ileum

In the immediate aftercare the electrolyte balance will need attention. House-surgeons to whom drips are delegated should be warned , for otherwise they will not tiptoe as the experienced surgeon does, appreciating more fully the complex physiological issues Increased significance is now attached to the potassium ion [5] , and Mr **GRAHAME** pointed out that the potassium values were high in these cases, probably owing to circulatory failure and associated renal insufficiency The effects of parenteral potassium on the myocardium may be serious, so at least three conditions must be met there must be a daily urinary output of over 750 ml , and each day an electrocardiogram must be taken and the serum potassium level recorded [6] Three weeks seems to be ample time for resolution of the colon œdema and ulceration, and for the wall blood supply to become fit for resection of the bowel End-to end anastomosis is to be preferred, though there is room for personal choice The so called aseptic anastomosis, as Professor **MORLEY** emphasised, is of no particular advantage at this stage The method of closing colostomies needs further thought by the surgeon This may be a difficult procedure, with occasional deaths The present practice of enterotome crushing of the spur in the Paul-Mikulicz procedure is surely an anachronism Closure of large numbers of colostomies in the belly wounds of war has convinced many surgeons that excision of the

---

[4] Garlock J H Klein S H *Arch Surg* 1949 59 1289

[5] Elman R Semmer R A Welchselbaum T E Owen J G
York R W *Ann Surg* 1949, 130 703 Moore F D *J Amer*
med Ass 1949 141 646 Randall H T Habif D V
Lockwood J S Werner S C *Surgery*, 1949 26, 341

[6] Marks L J *Ann Surg* 1950 132 20

Treatment of Depression

IF, among the many who attended the discussion on depression at the Royal Society of Medicine on March 13, there was anyone who came to see the psychological and somatological schools of psychiatry in open combat, he must have been disappointed Since 1936 Dr CLIFFORD SCOTT, the representative of psycho analysis, has treated selected patients with affective psychoses by the methods of Freudian analysis , but in such cases he still regards this treatment as experimental and full of difficulties and dangers Moreover, during analysis he has observed faints, drowsiness, amnesia, attacks of rage and furor, and sudden suicidal urges—in short, symptoms reminiscent of epilepsy, pointing, he thinks, to an instinctive yearning by the patient for " shock " and convulsive treatment He also found that previous convulsive treatment was helpful to the progress of analytical procedure The number of beneficial results he could quote from psycho analysis alone, was not impressive , but his critical and persistent endeavour to unravel the psychopathology of melancholia in the footsteps of ABRAHAM command respect

Dr SCOTT was preceded by Dr W MAYER GROSS, who began by pointing out the change in therapeutic approach to the affective psychoses within the last fifteen years, through the introduction of convulsive therapy He thought it necessary, however, to recapitulate long established measures Some of these, such as the avoidance of suicidal risks, have in a modified form become more important with the new treatment , others, such as the combating of anorexia, loss of weight, and constipation—formerly the most hazardous tasks in treating depression—hardly present any problem nowadays Depressive illness is still often mistaken for physical disease , and the patient may be treated for gastro intestinal complaints, anæmia, pulmonary tuberculosis, or malignant disease But even if the patient s bodily health is greatly impaired during lengthy investigations before he sees a psychiatrist, once the diagnosis is made a few convulsions will restore all bodily functions, including sleep, before the psychological effect becomes very obvious Wisely used, electrically induced convulsion treatment can transform the outlook of a depressive attack , and the most common mistake, according to Dr MAYER GROSS, is its excessive and indiscriminate use Of all the affective syndromes, involutional depression derives most benefit from convulsion treatment A series of 100 depressive patients over the age of forty, without earlier history of depression, were followed up for two to nine years after being treated at Crichton Royal between 1940 and 1947 At the time of the follow up, 72 were fully recovered, 6 socially recovered, and 11 home invalids , only 3 had had to remain in hospital all the time There had been 8 deaths, 2 by suicide In an equal group of younger manic depressive patients with definite recurrent attacks, the response to convulsive therapy was not so definite , but, despite a larger proportion of relapses, a shortening of suffering and of hospital care was usually apparent The rhythm of the illness and the number of attacks was, however, not influenced by the convulsive treatment

In the general discussion great interest was shown in the type of case that totally or partially resists convulsion therapy Most speakers agreed on its failure in younger patients in whom severe anxiety is associated with depression Opinion was divided on its suitability in reactive depression—i.e , in patients with an acute or chronic conflict situation probably responsible for the depressive illness Dr G GARMANY, the third opener, who dealt mainly with the important use of electric convulsions in outpatient clinics, illustrated his points with some statistics from Westminster Hospital He found the treatment worth while and efficient in reactive depressions, provided the premorbid personality was stable and not of a psychopathic type Little was said about leucotomy in depressive states except for some cautionary counsel that it may destroy the delicate emotional responses which are the great asset of the cyclothymic patient Only for those cases of manic depression in which psychotic attacks follow one another so quickly that the patient has to stay permanently in hospital, is operative treatment indicated , and less damaging and more exactly localised neurosurgical techniques should be sought for such cases

Carcinomatous Obstruction of the Colon

MEDICINE is advancing so swiftly at so many points that any slower progress seems disappointing The mortality from acute obstruction of the colon due to malignant disease is a good example of this slower tempo In the '30s the operative mortality was about 30% , and since then, despite antibiotics, intestinal antiseptics, and other innovations, it has fallen only to some 18–20% By contrast, the mortality of operations on uncomplicated carcinoma of the colon has fallen strikingly The figures of ALLEN et al.[1] indicate a fall from 17 5% to under 2% , and indeed it is reasonably contended that ' barring accidents the surgeon may be reasonably confident that his patient will survive such uncomplicated colon resection [2]

At the Royal Society of Medicine on March 7, Prof JOHN MORLEY, opening a discussion on large bowel obstruction due to malignant disease, urged the need for clear instructions to registrars, who are most commonly required to cope with this emergency Nevertheless the greatest skill may not suffice, for obstruction of this sort is often a late complication, and the patient may arrive with the bowel already perforated , moreover many of these patients have what SAMUEL JOHNSON termed the most incurable of all diseases—old age Obstruction does not usually come without warning , diarrhœa, with mucus in the stools, and colicky pain drive most patients into seeking advice Occasionally, however, as Mr RODNEY SMITH pointed out, the doctor may be deceived by the complaint of right sided abdominal pain, due to cæcal distension or mobility of a distended sigmoid loop [3] In 90% of cases the obstruction—usually of the ' napkin ring " type—is in the left colon , and involvement of the right colon nearly always indicates an advanced growth There must be

---

1 Allen W A Welch C E Donaldson G A *Ann Surg* 194 126 19

2 Pemberton J de J *Proc Mayo Clin* 1947, 22 361

3 Lyons A S *Ann Surg* 1948 127 398

no rushing the patient to the operating-theatre , *ohne Hast, ohne Rast, immer langsam voran* is a good dictum Plain (' scout ") radiographs of the abdomen, with the patient supine and erect, should invariably be taken These will demonstrate the cæcum, which serves as the wind-sock—the guide to the surgical line of approach—and also clinches the diagnosis of large bowel obstruction The volvulus will be clearly outlined , and the small intestine obstruction will be evident in the parallel loops and multiple fluid pools Moreover, as Mr RODNEY SMITH emphasised, in many cases the ileocæcal valve holds, forming a closed obstruction loop which only operation can relieve , when this valve is incompetent, ballooning of the small intestine is evident on the radiograph The surgeon may then be tempted to introduce a Miller Abbott tube, but every speaker agreed that this may lose valuable time , for the tube cannot decompress the large bowel, and its passage through the pylorus is unpredictable Passage of a Ryle tube is always necessary, and the anæsthetist must take precautions against regurgitation. Fluid replacement is called for, as Mr H E LOCKHART-MUMMERY remarked , but this therapy has to be tempered with fine judgment, particularly in the old Awareness of the hazards of intravenous therapy is now more acute (It has been well declared that more people have been drowned on the banks of the Thames than in it) The saline content of the urine is a sensitive indicator of salt need, and should become a standard ward-test Mr E W GRAHAME recommended that if the chloride test is positive, 0 45% saline should be infused, and this should be followed with plasma or even blood

As to the surgical procedure, opinion differed little Cæcostomy, blind or otherwise, was regarded as less satisfactory than transverse colon loop colostomy, preferably through a transverse abdominal incision This affords more effective rapid decompression , and the more complete ' defunctioning " is a great advantage in the subsequent stage of resection Some wag, talking of visceroptosis, has suggested that " where a man wears his guts is his own business " , but in large bowel obstruction it is very much the surgeon s concern Fat patients very often have short mesenteries , and, as Mr H R THOMPSON said, the obstructed colon, tethered by its mesentery, expands between the leaves, shortening it even more Delivery of such a colostomy to the surface may thus be difficult or impossible and the surgeon is sometimes forced to do a cæcostomy This may be difficult If spilling is to be avoided, the bowel should be punctured with a fine needle and then cleared with trochar puncture suction, after suitable packing and purse string suture , satisfactory decompression will be achieved only with drainage through a large tube and exteriorisation of the bowel. Cæcostomy may also be advisable for growths of the splenic flexure , for in the subsequent resection the surgeon is not handicapped by an otherwise fixed transverse colon Even the obstructing transverse colon growth is probably better handled in this way than by immediate resection on an area of œdematous mesentery Pelvic colon colostomy is to be avoided , it embarrasses the surgeon in any subsequent resection

Should the abdomen be gently explored at the same time ? Obviously the surgeon will be guided by the amount of bowel distension Professor MORLEY suggested that with the anæsthetist s use of muscle relaxants (spinal anæsthetics are hazardous) this was now often possible , and it provided the surgeon with reasonable information for planning further procedures Mr RODNEY SMITH, however, felt that this procedure was dangerous, and from the patient's angle often merely morbid curiosity Mr LOCKHART-MUMMERY, who described a study of some 90 case records collected from five different hospitals, gave examples showing that what seemed an inoperable growth on palpation by this method was often merely due to secondary inflammatory changes Even with secondary growths in the liver, most surgeons now endeavour to remove subsequently the primary growth , and these patients often live for three years in relative comfort [4] Immediate resection and anastomosis, as any surgical tyro knows, has no place in this type of surgery The Paul-Mikulicz procedure though it has a deservedly good reputation in mild subacute obstruction, should not be undertaken here , for it does not safely afford the necessary wide mobilisation of the bowel Obstruction of the right colon, it was also generally agreed, is preferably dealt with by lateral ileocolic anastomosis rather than ileostomy, which might lead to skin excoriation and a distressing convalescence Such anastomosis needs very fine close stitching if leakage is to be avoided , the anastomosis should be placed some twelve inches from the ileocæcal valve and joined to the mid transverse colon Primary hemicolectomy is occasionally permissible , Professor MORLEY recommends in addition E G MUIR's manœuvre of passing a drainage tube through the colon end and via the stoma into the ileum

In the immediate aftercare the electrolyte balance will need attention. House-surgeons to whom drips are delegated should be warned , for otherwise they will not tiptoe as the experienced surgeon does, appreciating more fully the complex physiological issues Increased significance is now attached to the potassium ion [5] , and Mr GRAHAME pointed out that the potassium values were high in these cases, probably owing to circulatory failure and associated renal insufficiency The effects of parenteral potassium on the myocardium may be serious, so at least three conditions must be met there must be a daily urinary output of over 750 ml , and each day an electrocardiogram must be taken and the serum potassium level recorded [6] Three weeks seems to be ample time for resolution of the colon œdema and ulceration, and for the wall blood-supply to become fit for resection of the bowel End to end anastomosis is to be preferred, though there is room for personal choice The so called aseptic anastomosis, as Professor MORLEY emphasised, is of no particular advantage at this stage The method of closing colostomies needs further thought by the surgeon This may be a difficult procedure, with occasional deaths The present practice of enterotome crushing of the spur in the Paul Mikulicz procedure is surely an anachronism Closure of large numbers of colostomies in the belly wounds of war has convinced many surgeons that excision of the

---

[4] Garlock J H Klein S H *Arch Surg* 1949 59 1289

[5] Elman R Semmer R A Weichselbaum T E, Owen, J G, York R W *Ann Surg* 1949 130 703. Moore F D *J Amer med Ass* 1949 141 646 Randall H T Habif D V Lockwood, J S Werner S C *Surgery* 1949 26 341

[6] Marks L J *Ann Surg* 1950 132 20

Treatment of Depression

If, among the many who attended the discussion on depression at the Royal Society of Medicine on March 13, there was anyone who came to see the psychological and somatological schools of psychiatry in open combat, he must have been disappointed. Since 1936 Dr CLIFFORD SCOTT, the representative of psycho-analysis, has treated selected patients with affective psychoses by the methods of Freudian analysis; but in such cases he still regards this treatment as experimental and full of difficulties and dangers. Moreover, during analysis he has observed faints, drowsiness, amnesia, attacks of rage and furor, and sudden suicidal urges—in short, symptoms reminiscent of epilepsy, pointing, he thinks, to an instinctive yearning by the patient for "shock" and convulsive treatment. He also found that previous convulsive treatment was helpful to the progress of analytical procedure. The number of beneficial results he could quote from psycho-analysis alone, was not impressive; but his critical and persistent endeavour to unravel the psychopathology of melancholia in the footsteps of ABRAHAM command respect.

Dr SCOTT was preceded by Dr W. MAYER-GROSS, who began by pointing out the change in therapeutic approach to the affective psychoses within the last fifteen years, through the introduction of convulsive therapy. He thought it necessary, however, to recapitulate long-established measures. Some of these, such as the avoidance of suicidal risks, have in a modified form become more important with the new treatment; others, such as the combating of anorexia, loss of weight, and constipation—formerly the most hazardous tasks in treating depression—hardly present any problem nowadays. Depressive illness is still often mistaken for physical disease, and the patient may be treated for gastro-intestinal complaints, anæmia, pulmonary tuberculosis, or malignant disease. But even if the patient's bodily health is greatly impaired during lengthy investigations before he sees a psychiatrist, once the diagnosis is made a few convulsions will restore all bodily functions, including sleep, before the psychological effect becomes very obvious. Wisely used, electrically induced convulsion treatment can transform the outlook of a depressive attack; and the most common mistake, according to Dr MAYER-GROSS, is its excessive and indiscriminate use. Of all the affective syndromes involutional depression derives most benefit from convulsion treatment. A series of 100 depressive patients over the age of forty, without earlier history of depression, were followed up for two to nine years after being treated at Crichton Royal between 1940 and 1947. At the time of the follow-up, 72 were fully recovered, 6 socially recovered, and 11 home invalids; only 3 had had to remain in hospital all the time. There had been 8 deaths, 2 by suicide. In an equal group of younger manic-depressive patients with definite recurrent attacks, the response to convulsive therapy was not so definite; but, despite a larger proportion of relapses, a shortening of suffering and of hospital care was usually apparent. The rhythm of the illness and the number of attacks was, however, not influenced by the convulsive treatment.

In the general discussion great interest was shown in the type of case that totally or partially resists convulsion therapy. Most speakers agreed on its failure in younger patients in whom severe anxiety is associated with depression. Opinion was divided on its suitability in reactive depression—i.e., in patients with an acute or chronic conflict situation probably responsible for the depressive illness. Dr G. GARMANY, the third opener, who dealt mainly with the important use of electric convulsions in outpatient clinics, illustrated his points with some statistics from Westminster Hospital. He found the treatment worth while and efficient in reactive depressions, provided the premorbid personality was stable and not of a psychopathic type. Little was said about leucotomy in depressive states except for some cautionary counsel that it may destroy the delicate emotional responses which are the great asset of the cyclothymic patient. Only for those cases of manic depression in which psychotic attacks follow one another so quickly that the patient has to stay permanently in hospital, is operative treatment indicated; and less damaging and more exactly localised neurosurgical techniques should be sought for such cases.

Carcinomatous Obstruction of the Colon

MEDICINE is advancing so swiftly at so many points that any slower progress seems disappointing. The mortality from acute obstruction of the colon due to malignant disease is a good example of this slower tempo. In the '30s the operative mortality was about 30%; and since then, despite antibiotics, intestinal antiseptics, and other innovations, it has fallen only to some 18–20%. By contrast, the mortality of operations on uncomplicated carcinoma of the colon has fallen strikingly. The figures of ALLEN et al.[1] indicate a fall from 17.5% to under 2%; and indeed it is reasonably contended that "barring accidents . . . the surgeon may be reasonably confident that his patient will survive such uncomplicated colon resection."[2]

At the Royal Society of Medicine on March 7, Prof. JOHN MORLEY, opening a discussion on large-bowel obstruction due to malignant disease, urged the need for clear instructions to registrars, who are most commonly required to cope with this emergency. Nevertheless the greatest skill may not suffice, for obstruction of this sort is often a late complication, and the patient may arrive with the bowel already perforated; moreover many of these patients have what SAMUEL JOHNSON termed the most incurable of all diseases—old age. Obstruction does not usually come without warning; diarrhœa, with mucus in the stools, and colicky pain drive most patients into seeking advice. Occasionally, however, as Mr RODNEY SMITH pointed out, the doctor may be deceived by the complaint of right-sided abdominal pain, due to cæcal distension or mobility of a distended sigmoid loop.[3] In 90% of cases the obstruction—usually of the "napkin-ring" type—is in the left colon; and involvement of the right colon nearly always indicates an advanced growth. There must be

---

[1] Allen, W. A., Welch, C. E., Donaldson, G. A. Ann. Surg. 1947, 126, 19.

[2] Pemberton, J. de J. Proc. Mayo Clin. 1947, 22, 501.

[3] Lyons, A. S. Ann. Surg. 1948, 127, 198.

THE FLYING-SPOT MICROSCOPE

At a recent meeting of the Society of Experimental Biology, Prof. J. Z. Young, F.R.S., and Mr. F. Roberts[1] demonstrated a new method of producing, by combination of optical and electronic techniques, a magnified image of a microscopic object. The method consists in scanning an object by focusing on it the image of the flying-spot of a cathode ray tube, and allowing the light transmitted to fall on a multiplier photocell, the output of which is used to modulate the luminosity of a televising tube. The luminous spot of the cathode ray tube moves along a system of closely spaced parallel lines to form an even luminous area, known as the scanning rastor. Thus all elements of the object are illuminated during scanning. The cathode ray and the televising tubes are locked together, that is to say, the motion of the flying spot of one tube is synchronised with that of the other. It follows that, if the elements of structure absorb or scatter light, the intensity of the flying spot of the televising tube will be modified as each element is illuminated, and a picture which represents the object will be developed on the screen.

Twenty years ago Synge[2] suggested increasing resolution by passing the object over an illuminated aperture whose dimensions are very small compared with the wave-length of light, and building up a magnified image with photoelectric apparatus as in telephotography. Because of technical difficulties he abandoned this idea but suggested that a spot of light might be projected into the moving object by a microscope-objective. He concluded, however, that no increase of resolution would be gained by this method. In the flying spot microscope a microscope objective is used as a condenser. The rastor of the cathode ray tube is situated in the primary image plane of the lens—i.e., approximately in the position occupied by the eye lens of the ocular when the objective is used in the normal way. The light transmitted by the object may be concentrated on the photocell by a collector lens, but this does not seem to be of importance, for the high sensitivity of the photocell allows illumination of low intensity to be used.

An important feature of the method is the ease with which the contrasts may be increased or decreased according to whether the object is of low or high opacity. These changes are strikingly demonstrated when transparent objects, such as diatoms, are examined. Magnification can be continuously varied by merely increasing or decreasing the area of the scanning rastor. The brightness of the background, which is easily controlled, is not affected by changes in magnification. For teaching and demonstration purposes a cathode ray tube of the projection type is substituted for the televising tube, and a bright image covering an area 3 ft. square can be projected on a lantern screen. The image of the spot of light scanning the object will, in general, be similar to that of a point source and will consist of a diffuse disc of light surrounded by diffraction rings. This distribution is not present in the spot which builds up the image on the viewing screen, and on theoretical grounds it seems that resolution may be increased beyond the limits of ordinary microscopical methods.

As the method is developed, its applications may be extended to include scanning by ultraviolet and infra-red radiations and accurate determination of the absorption of structures in living and stained materials. At the moment interest is chiefly confined to developing a technique for counting and measuring the sizes of cells and other microscopic objects, and the method may prove of unique value for counting blood-cells.

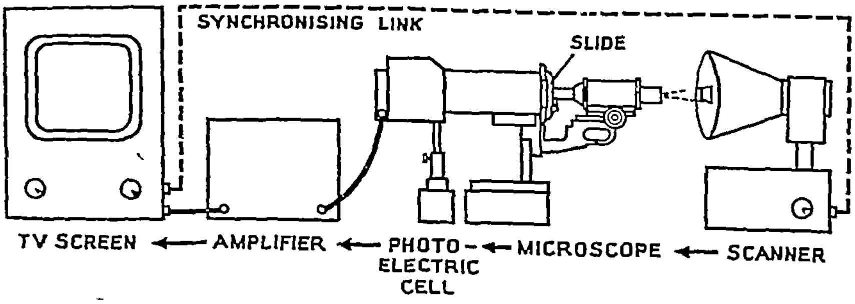
COMPARATIVE ALLERGY

Anaphylaxis as induced in laboratory animals bears little resemblance to allergic disorders as seen in man. There is increasing evidence, however, that domestic animals suffer from a variety of allergic diseases comparable with those of human beings. Dr. W. R. Thrower, speaking at a joint meeting of the National Veterinary Medical Association and the British Association of Allergists in London a few weeks ago, classified the allergic reactions common to man and animals into those in which the symptoms and signs are mainly respiratory, and those in which they are mainly cutaneous. The latter group includes not only eczema, urticaria, and angioneurotic œdema, but also unclassified but still mainly ectodermal responses such as laminitis in horses.

Thrower pointed out that, though allergic disorders are endemic in every human community, they are much commoner among immigrants who become exposed to sensitising agents not previously encountered. This explains, he says, why they are more prevalent in young countries like Australia and the United States than in Great Britain. Among animals the same holds true; and dogs and cattle imported into the United States show a higher incidence of allergic diseases than in their native land. Before diagnosing such diseases in animals one must be careful to exclude extraneous factors such as infection; thus in dogs, identification of the true basic condition is usually difficult, because parasitic mange and secondary coccal infection are often superimposed. Nevertheless, after making allowances for this, American dogs seem to be abnormally allergic. Allergic reactions in dogs do not depend solely on a true antibody reaction because endocrine imbalance may be a contributory factor, a striking example is the acute angioneurotic œdema seen in recently whelped bitches. Horses are especially liable to allergic disorders, of which urticaria and laminitis are the commonest. But acute urticaria may not always be truly allergic, for horses are very sensitive to nettle stings, which can excite a generalised reaction.

The use of the anti-histamine compounds in treating certain superficial allergic conditions in animals shows them to be as effective as they are in similar conditions in man, and it is important to note that in both man and animals it is the allergic reactions of epiblastic structures which can be successfully treated by their use. It was the successful clinical trial of the effect of anti-histamine drugs in laminitis which revealed the allergic nature of this serious cause of lameness.

In man a tendency to allergic responses is often inherited, and comparative studies of the genetic factor in animals are needed. Among cattle there are many specific antigenic reactions which are directly transmissible, but it is doubtful whether the common cutaneous allergies of cattle are passed to the offspring. The most striking example of cutaneous allergy is bloat, which is almost certainly due to sensitisation to the proteins of *Hypoderma bovis*; acute attacks can be induced by careless manual extrusion of the


SYNCHRONISING LINK
SLIDE
TV SCREEN ← AMPLIFIER ← PHOTO-ELECTRIC CELL ← MICROSCOPE ← SCANNER

---

1. Young, J. Z., Roberts, F. *Nature, Lond.* 1951, 167, 231.
2. Synge, E. H. *Phil. Mag.* 1928, 6, 356; *Ibid*, 1931, 11, 65.

wound scar, a fresh end to end anastomosis, and replacement of the bowel within the peritoneal cavity is now a safe undertaking, especially with intestinal antiseptics Spur crushing entails a wait of six weeks to two months before the surrounding tissue is soft enough to turn in snugly and safely In such circumstances **PAUCHET**'s manœuvre of slitting each bowel loop and then fashioning an anastomosis yields a first-class closure [7]

The ultimate prognosis is relatively poor In a small series of cases **NICKELL** and **DOCKERTY** [8] found the chance of five year survival half that for the non-obstructing lesion, and they suggested that the massaging effect of the vigorous peristalsis and the inflammatory œdema would encourage cancer-cell spread There can be no better adornment to the house surgeon's room than a plaque with the words "Never let the sun set or the sun rise on an intestinal obstruction"

Annotations

BREAKDOWN IN STUDENTS

THE examination syllabus, the discovery that a brain well respected at school may after all be second rate, and the concurrent flowering of the sexual instinct, combine to press hardly on undergraduates, and they seldom confide their difficulties to anyone but a friend in like case This state of stress is reflected in the figures given on another page by Dr Parnell for mortality and prolonged illness among Oxford undergraduates, and in the American studies he quotes In his series, mental illness and nervous breakdown accounted for more than half the illness lasting more than a term, and the suicide rate was significantly higher than that of the civilian population of the same age Tuberculosis accounted for nearly another quarter of the total illness, though only one undergraduate died of tuberculosis during the investigation As Dr Parnell points out, the relative importance of mental disorder and tuberculosis among students has not so far been generally recognised, and the fact that two thirds of those who lost a full term's residence because of mental illness and nervous breakdown later returned to continue their university course does not make things much better He notes the need for more detailed study of the mental health of students and of the means for preventing mental illness among them As an interim measure, we should surely admit to these young people that this is a period of special stress If at the start of their course they were clearly warned by their schoolmasters or tutors that they are entering an experience which many find troubling, and if some experienced person—whether doctor, psychiatrist, or college authority—could be mentioned as a recognised adviser to those in difficulties, undergraduates, even if they ignored the proffered help, would not feel that overwhelming shame at failure to reach an intended mark which contributes to many breakdowns

REABLEMENT FOR MENTAL PATIENTS

THE moment of discharge from a mental hospital is inevitably disturbing for the patient Not only must he change a sheltered and encouraging environment for one of competition and indifference, but he must perforce do it without much confidence in his own powers of resistance to strain Moreover, he is going to encounter some conscious and unconscious cruelty from the less imaginative of his associates all of which he foresees, or suspects may come That he needs some help in adjusting himself to such stresses goes without saying, and there are several ways of providing it It comes best and most naturally, perhaps, through a quiet and secure home life, but relationships in the home have often contributed to his breakdown, and what should be a place of safety becomes, or remains, a danger point During the war the National Association for Mental Health gave such people great help through their community care scheme, under which a psychiatric social worker would make personal friends with them, and stand by them with advice, sympathy, and practical help, until they were again able to face their full responsibilities Unfortunately this scheme had to be largely given up under the National Health Service, since the duty for such after care was laid on the local authorities Some of these are making good use of the experience gained from the N A M H scheme, but few have organised any comparable service as yet

Another way of helping the patient is to give him the chance to attend a social club Many mental hospitals nowadays arrange such clubs for their discharged patients, and find them very successful, and the Institute of Social Psychiatry has long run therapeutic social clubs, not only for discharged patients, but for others who are mentally disturbed, neurotic, psychopathic, or delinquent, as well as some who are merely unstable, or abnormally reserved and solitary The parents of maladjusted children, too, may benefit by joining such clubs, and the children enjoy a secondary gain in security A new After Care Rehabilitation Centre, recently set up by the institute, was officially opened by Mr Hilary Marquand, the Minister of Health, on March 14, at Christchurch House, Chancel Street, London, S E 1 Patients attend daily for occupational therapy, group discussions, and cultural activities, all of which help them to express themselves, to get to know each other, and to take a growing amount of responsibility Those who need psychological help can have it from the Social Psychotherapy Centre run by the institute. In his opening address the Minister spoke of the part the institute can take in the reablement of ex Servicemen suffering from neuroses or psychoneuroses, and wished the work well The institute is anxious to forward research in this field, but, as Dr Noel Harris, chairman of the board of governors, pointed out, this needs funds

A RURAL PERIL

IN his Ernestine Henry lecture at the Royal College of Physicians eighteen months ago, Dr Donald Hunter[1] drew attention to the very serious accidents possible through careless use of the toxic substances now employed in agriculture as weedkillers and insecticides —notably the organic phosphorus insecticides In the United States all too much information has already been collected about the signs and symptoms of poisoning among those who have used toxic sprays without taking proper precautions, and among those who have been otherwise exposed to the poisons Since the report of a working party set up by the Ministry of Agriculture with Prof S Zuckerman, M D, F R S, as chairman, the National Farmers' Union has issued warnings to farmers,[2] and the Ministry has conferred with the British Medical Association on the medical side To remind doctors of the risk, the symptoms, and the recommended treatment, of this kind of industrial poisoning, the B M.A last week sent a circular to general practitioners, consultants, and medical officers of health When spraying is to take place, the Ministry of Agriculture will inform the county or county borough M O H, who will pass on the information, through the B M.A divisional secretaries, to all doctors in the area

---

[7] Sanders G B Haffner A Lynn R S *Ibid* 1948 127 243

[8] Nickell, D F, Dockerty M B *Surg Gynec Obstet* 1948 87 519

[1] *Brit. med. J* 1950 i 449 556, see also *Lancet* 1950 i 407

[2] *Lancet* Feb 24 1951 p 478

Special Articles

MORTALITY AND PROLONGED ILLNESS AMONG OXFORD UNDERGRADUATES

R W PARNELL
D M Oxfd, M.R C.P
PHYSICIAN IN CHARGE OF STUDENT HEALTH SERVICE, INSTITUTE OF SOCIAL MEDICINE OXFORD

VERY little has been published in this country on mortality and morbidity among students The present survey is the first to present figures from Oxford University, and has been made possible by the friendly cooperation of the college authorities Twenty six colleges and halls have supplied information about undergraduates' mortality and prolonged illness (i e , illness causing the loss of at least one full term's residence) between Jan 1, 1947, and Dec 31, 1949 Wherever possible the nature of the illness was stated and the end result recorded in the form "returned to college," "went down," or 'still in doubt" The data may be incomplete because time and labour did not suffice for an exhaustive study of college records, and because such records are commonly kept for financial purposes, not for recording sickness Nevertheless, the figures contribute to our knowledge of the relative incidence, and to some extent of the actual prevalence, of prolonged absence on account of sickness

The total population annually at risk during the period under review was 6142 (5048 men and 1094 women)* This figure was arrived at by determining the average number of undergraduates in residence during the four academic years 1946–49 and subtracting the appropriate number for two colleges from which no return was received.

TABLE I—PRINCIPAL CAUSES OF DEATH IN YOUNG MALE ADULTS

Oxford University 1947–49 compared with England and Wales 1947

Causes	England and Wales Ages 15–24			Oxford University		
	No	Annual rate per 100 000 living	% all causes	No in 3 yr	Annual rate per 100,000 living	% all causes
All causes	3986	183 4	—	33	217 9	—
Tuberculosis (respiratory 994) (other forms 209)	1203	55 4	30 2	1	6 6	3 0
Violence (road accident 419) (other violence 520)	939	43 2	23 6	16	105 7	48 5
Heart-disease	251	11 5	6 3	—	—	—
Respiratory (pneumonia 121) (bronchitis 51) (other 48)	220	10 1	5 5	—	—	—
Alimentary (appendicitis 83) (ulcer of stomach or duodenum 23) (other digestive 75)	181	8 3	4 5	2	13 2	6 1
Cancer	156	7 2	3 9	—	—	—
Nephritis	126	5 8	3 2	—	—	—
Suicide	114	5 2	2 9	9	59 4	27 3
Acute poliomyelitis and encephalitis	84	3 9	2 1	2	13 2	6 1

Total male civilian population ages 15–24—2 173 000

MORTALITY

There were 35 deaths (33 men, 2 women) 17 (16 men 1 woman) were accidental—6 on the roads, 4 in mountaineering, and 3 by drowning Suicide accounted for 9 deaths (all men) , poliomyelitis for 2 (men) tuberculosis for 1 (man) , and other causes for 6 (1 woman)

The annual death rate of men undergraduates at Oxford in the period 1947–49 was 218 per 100,000 living This is 119% of that of the age group 15–24 in England and Wales in 1947 (table I) Tuberculosis, which caused 30% of all civilian deaths in this age group in 1947 killed only 1 Oxford undergraduate in 1947–49 and heart-disease, mainly rheumatic, which caused 6 3% of all deaths in this age group did not cause any undergraduate death at Oxford In fact, these two causes of death, which are known to be more common at lower socio-economic levels, were almost absent among undergraduates On the other hand, risks which are more prevalent in the upper social classes figured prominently in this series For example, accidents were responsible for 48% of undergraduate deaths as compared with 24% of all deaths among civilians of the same age in England and Wales The suicide rate among undergraduates (59 per 100,000 living) was 11 times that of the 15–24 civilian age group as a whole (5 3 per 100,000 living) and 17 times that of the same age group in the Armed Forces (3 5 per 100,000 living) Further, whereas suicide caused only 2 9% of all deaths in young male adults in this country (1947), it caused 27% of male undergraduate deaths at Oxford (1947–49) However caution must be observed in interpreting these figures, because the total university suicides numbered only 9 in three years

TABLE II—STANDARDISED MORTALITY RATIOS BY REGISTRAR GENERAL'S SOCIAL CLASSES AT AGES 15–24

Cause of death related to social class	Social class		
	I and II	III	IV and V
A *Uninfluenced*			
All causes	95	92	79
Tuberculosis (other than pulmonary)	87	86	94
Nephritis	96	91	99
B *Higher in IV and V*			
Pulmonary tuberculosis	72	97	101
Pneumonia	69	88	110
Ear and mastoid	—	88	122
Rheumatic fever	—	90	102
Heart disease	75	87	99
Valvular disease	77	83	100
C *Higher in I and II*			
Accidents	131	103	95
Appendicitis	108	105	91
Suicide	174	87	107

Greenwood et al (1941) showed how the suicide rate in England and Wales has risen during this century, and they pointed out that as long ago as 1880 the Registrar General said that suicide was commoner among the educated than the uneducated. The question arises whether suicide is a special hazard of student life, or is merely more common in the social classes to which undergraduates belong This question is easily answered The standardised mortality ratio (S.M R) of suicide in social classes I and II (from which 78% of undergraduates are drawn) was 174 in 1930–32 , 100 is taken as the S M R for all social classes (table II) Among students, however, the suicide rate is far higher even than that of classes I and II

It might be argued on the evidence presented so far that the high suicide rate is a post war phenomenon which is unlikely to continue in peace time It is known from inquest reports that 4 at least of the 9 suicides occurred in ex Servicemen, and the difficulty of their readjustment warble larvæ. Another bovine disease very similar to the condition seen in man is the so called spring catarrh, seen at its maximum during the pollen season, when human beings are suffering from hay fever. Its diagnosis has various pitfalls because a cow may cough for many different reasons, the commonest being the mechanical irritation of dust derived from concentrates in the cow house or grass pollen in the field. Skin sensitivity tests reveal that certain allergic reactions may be due to the common pollens, or often to various moulds found on grasses, and particularly in musty hay. The term food allergy is often used without a real understanding of its meaning, for sometimes it is not the food itself that is at fault but some contaminant, which is often found to be a mould.

---

* These figures are substantially less than the totals recorded in the University Calendar for undergraduates on the books The latter figure is 9718 (men 8437 women 1281) but the number in residence is believed to be more correct for the purpose of the survey

ADMINISTRATIVE FAILURE

As a people who are attempting to follow on a national scale that difficult injunction about loving our neighbours, we have at the moment some cause for self respect. At first sight, the difference between private charity and public responsibility is that one depends on people and the other on regulations, and it is easy to say that regulations are less human and flexible than people, and that you cannot hope to do by rule what good men have always done from kindness. But good men have always been fewer than the occasions on which they were needed: less than a century ago (before the idea of mutual responsibility had taken such a hold on our sense of justice) people were more often left in need than succoured, and the need was often dire. Legislation has so changed things that nowadays we hear not of misfortunes successfully relieved but of the individual case where someone was denied an undoubted necessity. That we are more disturbed by one such case than our forerunners would have been by twenty of the kind proves that we have at least some confidence in regulations: having made them we expect them to work, and we are rightly indignant when the machine breaks down.

Two days before Christmas, an elderly man was found dying outside the hut in which he had been living, on Urmston Meadows, Manchester. The evening before, he had been refused admission to a general hospital (because he was not thought to be ill enough to need a bed) and to a welfare hostel (because he was too ill to be accepted). Between two sets of regulations, it may be said, the poor man was denied a bed to die in—a result which certainly suggests some failure in human flexibility. According to the *Manchester Guardian*,[1] the West Manchester Hospital Management Committee, after an inquiry, exonerated the doctors responsible, but at once made temporary arrangements to set aside beds for those who need care rather than urgent medical treatment, until a "realistic liaison" can be established between the hospital service and the local authority service responsible for looking after such cases. On the other hand, the Minister of Health,[2] answering Mr. Samuel Storey's question on March 15, described the failure as due to an error of judgment in not admitting this man to hospital and not to any lack of liaison between the health and welfare services; he said that such patients will in future be admitted to hospital, and that they will not be sent on to another hospital until it has been ascertained that there is a bed for them. This is surely a moral duty which every hospital in the country should now accept.

The story makes vividly clear the need for hostels, of the type now being set up by the National Association for Old People's Welfare and King Edward's Hospital Fund[3] to work with the hospitals, receiving from them old people who are well enough for discharge but not well enough to go back to their former homes, and sending into them infirm old people who fall sick while they are resident in the hostel. The need for such a two way service has become increasingly clear since the Act did away with both the relieving officer, and the statutory duty to admit which formerly rested on public assistance institutions. Nowadays the busy hospital resident has no hospital to which he can count on sending the unwanted—or unsuitable—patient, and his own judgment of the patient's need, as this case reminds us, can never be infallible. He has, however, three other sources of help to which he can turn: the general practitioner, the medical officer of health, and the voluntary associations. The M.O.H. can at least send to the patient's bedside a district nurse and a home help, the voluntary bodies will provide such things as bedding and blankets. The family doctor may have sent the patient in, and will be ready enough to discuss the home conditions and the possibilities of adapting them to the sick man's needs. All these helpers are at the end of a telephone wire in the day time (though as a rule only the family doctor will be available at night), but it is not certain that they are always used as fully as they might be. Collaboration in the health service is still intermittent, local, and variable. Regulations in the last resort must always be put into effect by people, and there will always be some people who will attend to the letter of a regulation rather than the spirit. For this reason responsible bodies in every part of the country should take thought to ensure that regulations are properly backed by facilities.

WORLD HEALTH DAY

To the peoples of its member countries the United Nations Organisation has proved a disappointment. This is understandable, because they hear most about the proceedings of the General Assembly and the Security Council where amicable agreement on world problems has been rare, and misunderstanding, argument, and the veto depressingly common. It is unfortunate, therefore, that they know so little about those special agencies of UNO which have achieved so much. Of these the World Health Organisation is one of the most successful, for it has used its relatively small resources to good effect, and it particularly needs to be better known because it works chiefly by helping people to help themselves. Before they will do this, they must be told of the health problems of their own and other countries, and of the ways in which they can help to solve these problems. Accordingly, W.H.O. suggests that April 7 of each year should be observed as World Health Day, and asks that on this day all the resources of modern publicity be used to tell the public about the work of their own health services and of W.H.O. For this year's World Health Day, W.H.O. has adopted the theme "Health for your Child and the World's Children," for it recognises that any long term plan for improving world health must have as its basis the mental and physical needs of the child. It is in this sphere that the help of the public is especially needed, and they must be told what has already been done and how much more can be done if they will do it.

Sir WILLIAM DOUGLAS, permanent secretary of the Ministry of Health since 1945, is to retire on April 30. Sir William has remained at his post till the changes due to the creation of a separate Ministry of Local Government and Planning were completed.

Mr. J. M. K. HAWTON, C.B., at present a deputy secretary at the Ministry of Health, will succeed Sir William, and Mr. I. F. ARMER, now an under-secretary, will take Mr. Hawton's place.

ON March 19 Dr. W. RUSSELL BRAIN was re-elected president of the Royal College of Physicians of London.

---

[1] *Manchester Guardian*, Jan. 1.
[2] See p. 717.
[3] *Lancet*, March 17, 1951, p. 625, and March 24, 1951, p. 696.

It affects a student population of about 70 000 at British universities, in addition to the large number at technical and training colleges

SUMMARY

1 Accident caused 17 of 35 undergraduate deaths at Oxford University in the three years 1947–49

2 Suicide accounted for 9 undergraduate deaths (during both term and vacation) A suicide rate calculated from this data gives a significantly higher figure than that for the civilian population of the same age, higher than that for the Registrar-General's social classes I and II, and higher than that in the Armed Forces

3 Tuberculosis caused 1 death only, and rheumatic heart-disease none

4 During the same three years 145 undergraduates lost one full term's residence on account of illness.

5 Mental illness and nervous breakdown accounted for 52 5%, tuberculosis for 23%, and other conditions for 24 5% The relative importance of mental disorder and tuberculosis among students has not received general recognition in the past

6 Two thirds of those who lost a full term's residence because of mental illness and nervous breakdown returned later to continue their university course.

7 In the absence of earlier records there is no evidence of an alteration in mortality rates or in the actual or relative frequency of particular causes of prolonged illness

8 There appears to be ample justification for further and more detailed investigation into the mental health of students and the prevention of mental disorder

I am indebted to various health officers for discussion on this subject and to Dr A. H. T Robb Smith for advice on the method of survey The university kindly supplied figures from which the population at risk was calculated My special thanks are due to colleagues on the staff of the institute, to Mrs C C Standley for checking the analysis of returns to Dr W T Russell and Dr L Sutherland for statistical advice, and to Dr Alice Stewart for various helpful suggestions

REFERENCES

Fry C C Rostow E. G (1942) Mental Health in College New York p 348
Greenwood M. Martin W J Russell W T (1941) *J roy Stat Soc* 104 ii 156
Harvard College Department of Hygiene Report for 1939–40 Cambridge Mass
Michigan University Student Health Tables (1945) Health Service 1913–42. Ann Arbor Michigan.
Parnell R. W (1947) *Lancet* ii 939
Raphael T Power S H Berridge, W L (1937) *Amer J Orthopsychiat* 7 1
Registrar-General's Decennial Supplement 1931

EDUCATION ON ALCOHOLISM

FORBES CHESTON *

IN the U S.A. the National Committee for Education on Alcoholism was founded in October, 1944 For the first five years, as the fifth division of the Yale Plan on Alcohol it existed under the sponsorship of the Laboratory of applied physiology of Yale University, but just over a year ago this connection was severed. The committee now known as the National Committee on Alcoholism, has reached the maturity of independence as a public health organisation

The committee was formed because of general ignorance about alcoholism As Mr Yvelin Gardner, acting executive director of the committee remarked in his report for 1949[1]

> "The mantle of stigma covered the subject. Constructive action on the part of individuals alcoholics or others, was still spotty and isolated largely because of lack of knowledge of where to go or what to do and the shame attendant on everything concerning alcoholism. The therapeutic professions were almost entirely unconcerned with the problem. Governmental activity was limited to punishment in jails and in a few hospitals, to temporary drying out techniques not related to any treatment of the condition"

It was felt that unless people learned at least some of the facts, nothing at all would be done The original aim was to disseminate the findings of the other divisions of the Yale Plan, presenting these in a form understandable by everyone, and now the committee seeks by education to mobilise public opinion for action on the problem The committee's educational work rests on three concepts (1) that alcoholism is a disease and the alcoholic a sick person, (2) that the alcoholic can be helped and is worth helping, and (3) that this is a public-health problem and therefore a public responsibility

When the N C E.A officially announced the opening of its New York offices, everyone of the nine daily newspapers of New York City carried the story Within a few days the news had spread all over the country and mail began to pour in. Mr Dwight Anderson, executive director of the Medical Society of the State of New York wrote

> "Looking back ten years we realise that the idea that the alcoholic was an utterly hopeless person was practically universal, not only among the public but among the medical profession as well Today the public is ready for educational work on a broad scale such as the National Committee is to take It is the beginning of a new public health movement It is the first step towards getting the alcoholic out of gaol and into hospital towards making it possible for the medical man and the psychiatrist the social worker and the lay therapist to pool their skills in modifying the ravages of an illness to which society has been indifferent almost to this very moment'

In September, 1946, just two years after the founding of the committee, Mrs Marty Mann, its executive director, stated that 14 cities in the U S.A had formed representative citizens' committees, affiliated with the national committee, and that these committees had already launched programmes of community action, and she pointed out that this type of coordinated organisation reduced the problem to a more manageable scale Mrs Mann noted that 'our stated primary aim, that of arousing public interest in the problem of alcoholism, seems well on the way to achievement", and she quoted her own final words in the March of Time film *Problem Drinkers* 'The problem of alcoholism can be solved by a plan of community action The National Committee stands ready to help your community to plan such action"

In the years since 1946 the function of the National Committee has changed from one of stimulation to one of guidance The annual report for 1949 showed the great expansion which had taken place The number of affiliated committees had risen to over 50, and clinical and hospital facilities and information centres had been established in many cities. There were now 22 State-sponsored programmes on alcoholism, developed from the work and guidance of the national committee

Industry, too, is beginning to acknowledge that it has a costly problem on its hands. Several major industries have disclosed programmes undertaken on the premise that alcoholics are sick people who can be rehabilitated The Consolidated Edison Company of New York has revealed that it is now pensioning chronic alcoholics where the employee has long been with the company and medical study indicates a compulsive urge to drink Du Pont de Nemours & Company has announced through its medical director that over one hundred valued employees have been restored to the company through the initiation of a programme which recognised and treated alcoholism as an illness In Wisconsin a pro-

---

* Hon secretary Interim Committee on Alcoholism, 8 Lygon Place London S W 1

[1] *Quart. J Stud. Alcohol* 1949 10 501

to academic life was stressed at the inquests. Pre-war figures are not available for British universities, but the University of Michigan (1945) published student death-rates from 1913 to 1942, during which period suicide caused about 15% of all deaths, accident 35%, and illness 50%.† At the University of Michigan, where the average annual entry was 11,614, Raphael et al. (1937) found that suicide or the possibility of suicide was deemed an important element in 313 students who had attended the mental hygiene unit of the university health service during the previous five years. At Harvard, where the entry in 1939–40 was 6400, there were 6 deaths, including 2 by suicide in that year. At Yale, where the annual entry was about 5000, Fry and Rostow (1942) reported 8 deaths from suicide in the ten years following 1924. In fact, the importance of suicide was recognised by university health services in the U.S.A. before the second world war.

PROLONGED ILLNESS

The total number of undergraduates who missed at least one full term's residence through illness was 145 (113 men, 32 women). Tuberculosis and mental illness (which are discussed below) were responsible for 23% and 52.5% respectively. In the remaining 24.5% the causes of absence included epilepsy, jaundice, asthma, peptic ulcer, concussion, accident, appendicitis, war wounds, and tropical diseases.

Tuberculosis.—33 undergraduates (28 men, 5 women) lost a term or more on account of tuberculosis during the three years under review. It may be assumed that this absence was caused by serious illness, and was not due to minimal lesions detected by mass radiography; the latter was performed at only three colleges and their 6 cases each required at least three months' bed rest, or hospital or sanatorium treatment.

Mental illness and nervous breakdown.—Of the 76 absent for not less than a term, 49 (64.5%) returned to college; 16 (21%) went down without a degree not to return; and 11 (14.5%) went down but their future is undecided. 9 (12%) were stated to have been in a mental hospital or to have been diagnosed as schizophrenia. Of these 3 returned to college, and 2 others were said to have been cured, although they did not return.

The returns show that mental illness, including nervous breakdown, was responsible for just over half the illness, serious enough to cause absence for at least a full term.

However, it has already been stated that, owing to certain factors connected with the method of survey, the morbidity figures probably fall short of the truth. As far as the mental cases are concerned, there are further reasons for this belief. The 9 suicides are not included in the total, nor is there any information about the attempted but unsuccessful suicides which are known to have occurred in the university. Several nervous breakdowns were precipitated by pre-examination stress, and, in the case of any breakdown occurring towards the end of term, and in particular the Trinity Term, at least two months were available for mental rest and recovery without loss of a term's residence. Then, there are other forms of serious mental disturbance involving extreme problems of discipline or behaviour, deep anxieties, obsessions, or ideas of persecution which do not entail absence from college. Fry and Rostow (1942), after ten years' experience at Yale, noted that 16 of their 116 serious cases did not require to leave college at all, and 12 others required only a short period of hospital or other care. In fact, it may be estimated that not less than 0.5% and probably nearer 1% of the undergraduate population in residence each year at Oxford suffers some serious form of mental illness or nervous breakdown.

For many years enlightened college authorities and college doctors have been convinced of the importance of mental hygiene. When, however, the question of preventive action is discussed there is a general feeling that "common sense" is an adequate tool for handling the problem, and no special measures are required. Those interested in the mental welfare of students are thought to be prejudiced, and their personal experience unrepresentative. I found from routine health examinations that psychological disturbances, although mostly of a minor character, were unduly common (Parnell 1947), but the significance of the finding was doubtful. It might have been due to the excessive thoroughness of the examination, or possibly even to the over-sympathetic outlook of the examiner. It was the need for objective confirmation of a clinical impression which first prompted this objective survey, which shows that mental disorder is the principal cause of prolonged illness.

In these circumstances it is natural to ask what preventive steps might be taken, although no scheme is likely to prevent all forms of psychosis.

Preventive measures need not and should not pay too much attention to individuals. They should not involve healthy young men in routine psycho-analysis, nor need they, in a popular but ugly phrase, "stir up the mind" unnecessarily. They need not provoke hypochondria or encourage introspection, nor need they sap self-reliance or engender a feeble and dependent state of mind. Serious opposition to the adoption of preventive measures is founded on the alleged ineffectiveness of individual methods. Close tutorial supervision, with particular attention to the early signs of mental staleness and cumulative fatigue, should help. Better individual instruction in the principles of mental hygiene, in particular in the optimum hours of work, is also required, and it would be desirable to have a doctor or psychiatrist well versed in college life readily accessible for consultation. There is evidence that less severe forms of mental or nervous disorder are more common than the severe forms discussed so far, and the preventive measures suggested apply to them with equal force.

In war, inactivity because of uncertainty about the technique of victory is inexcusable. So too, in the fight against mental ill health preventive measures should not wait indefinitely upon the improbable discovery of some new technical device for early detection. On the other hand whatever action is contemplated in the light of present knowledge, it is clear that further and more detailed study of the problem is urgently needed.

DISCUSSION

The question will certainly be asked whether this paper draws attention to a state of affairs long present but hitherto unrecognised, or whether there has been a recent increase in the prevalence of mental disorder. Since no report has been discovered of any previous survey on these lines, precise evidence on this point is lacking. The gravity of the position may not have been recognised because the undergraduates with tuberculosis, mental illness, and the like have been treated by a number of different departments. In any event, it is clearly desirable that the facts should be widely known.

At a recent conference student health officers expressed concern at the absence of precise information on the incidence of mental ill health among students. To remedy this, and to make comparative study possible between universities, some uniform system of recording serious and prolonged illness is clearly desirable. Preliminary work to establish such a system is now advanced, and it is reasonable to hope that before long it will be ready

---

† Only deaths occurring during the nine months per year sessions were recorded. The Oxford figures include accidents which occurred during the vacation.

It affects a student population of about 70,000 at British universities, in addition to the large number at technical and training colleges

SUMMARY

1 Accident caused 17 of 35 undergraduate deaths at Oxford University in the three years 1947–49

2 Suicide accounted for 9 undergraduate deaths (during both term and vacation) A suicide rate calculated from this data gives a significantly higher figure than that for the civilian population of the same age, higher than that for the Registrar General's social classes I and II, and higher than that in the Armed Forces

3 Tuberculosis caused 1 death only, and rheumatic heart-disease none

4. During the same three years 145 undergraduates lost one full term's residence on account of illness

5 Mental illness and nervous breakdown accounted for 52 5%, tuberculosis for 23%, and other conditions for 24 5% The relative importance of mental disorder and tuberculosis among students has not received general recognition in the past

6 Two thirds of those who lost a full term's residence because of mental illness and nervous breakdown returned later to continue their university course.

7 In the absence of earlier records there is no evidence of an alteration in mortality rates or in the actual or relative frequency of particular causes of prolonged illness

8 There appears to be ample justification for further and more detailed investigation into the mental health of students and the prevention of mental disorder

I am indebted to various health officers for discussion on this subject and to Dr A. H. T Robb-Smith for advice on the method of survey The university kindly supplied figures from which the population at risk was calculated My special thanks are due to colleagues on the staff of the institute, to Mrs C C Standley for checking the analysis of returns, to Dr W T Russell and Dr L Sutherland for statistical advice, and to Dr Alice Stewart for various helpful suggestions

REFERENCES

Fry, C C Rostow E. G (1942) Mental Health in College New York p 348
Greenwood M. Martin W J Russell W T (1941) *J roy Stat Soc* 104 ii 156
Harvard College Department of Hygiene Report for 1939–40 Cambridge Mass.
Michigan University Student Health Tables (1945) Health Service 1913–42 Ann Arbor Michigan.
Parnell, R W (1947) *Lancet* ii 939
Raphael T Power S H Berridge W L (1937) *Amer J Orthopsychiat* 7 1
Registrar-General's Decennial Supplement, 1931

EDUCATION ON ALCOHOLISM

FORBES CHESTON *

IN the U S A the National Committee for Education on Alcoholism was founded in October, 1944 For the first five years, as the fifth division of the Yale Plan on Alcohol it existed under the sponsorship of the laboratory of applied physiology of Yale University, but just over a year ago this connection was severed The committee now known as the National Committee on Alcoholism, has reached the maturity of independence as a public health organisation

The committee was formed because of general ignorance about alcoholism As Mr Yvelin Gardner, acting executive director of the committee remarked in his report for 1949 [1]

> "The mantle of stigma covered the subject. Constructive action on the part of individuals alcoholics or others, was still spotty and isolated largely because of lack of knowledge of where to go or what to do, and the shame attendant on everything concerning alcoholism. The therapeutic professions were almost entirely unconcerned with the problem. Governmental activity was limited to punishment in jails and in a few hospitals, to temporary 'drying out' techniques not related to any treatment of the condition '

It was felt that unless people learned at least some of the facts, nothing at all would be done The original aim was to disseminate the findings of the other divisions of the Yale Plan, presenting these in a form understandable by everyone, and now the committee seeks by education to mobilise public opinion for action on the problem The committee's educational work rests on three concepts (1) that alcoholism is a disease and the alcoholic a sick person, (2) that the alcoholic can be helped and is worth helping, and (3) that this is a public health problem and therefore a public responsibility

When the N C E A officially announced the opening of its New York offices, everyone of the nine daily newspapers of New York City carried the story Within a few days the news had spread all over the country and mail began to pour in Mr Dwight Anderson, executive director of the Medical Society of the State of New York wrote

> ' Looking back ten years we realise that the idea that the alcoholic was an utterly hopeless person was practically universal, not only among the public, but among the medical profession as well Today the public is ready for educational work on a broad scale such as the National Committee is to take It is the beginning of a new public health movement It is the first step towards getting the alcoholic out of gaol and into hospital towards making it possible for the medical man and the psychiatrist, the social worker and the lay therapist to pool their skills in modifying the ravages of an illness to which society has been indifferent almost to this very moment '

In September, 1946, just two years after the founding of the committee, Mrs Marty Mann, its executive director, stated that 14 cities in the U S A had formed representative citizens' committees, affiliated with the national committee, and that these committees had already launched programmes of community action, and she pointed out that this type of coordinated organisation reduced the problem to a more manageable scale Mrs Mann noted that ' our stated primary aim, that of arousing public interest in the problem of alcoholism, seems well on the way to achievement '' , and she quoted her own final words in the March of Time film *Problem Drinkers* "The problem of alcoholism can be solved by a plan of community action The National Committee stands ready to help your community to plan such action ''

In the years since 1946 the function of the National Committee has changed from one of stimulation to one of guidance The annual report for 1949 showed the great expansion which had taken place The number of affiliated committees had risen to over 50, and clinical and hospital facilities and information centres had been established in many cities. There were now 22 State-sponsored programmes on alcoholism, developed from the work and guidance of the national committee.

Industry too, is beginning to acknowledge that it has a costly problem on its hands Several major industries have disclosed programmes undertaken on the premise that alcoholics are sick people who can be rehabilitated The Consolidated Edison Company of New York has revealed that it is now pensioning chronic alcoholics where the employee has long been with the company and medical study indicates a compulsive urge to drink Du Pont de Nemours & Company has announced through its medical director that over one hundred valued employees have been restored to the company through the initiation of a programme which recognised and treated alcoholism as an illness In Wisconsin a pro to academic life was stressed at the inquests Pre war figures are not available for British universities, but the University of Michigan (1945) published student death-rates from 1913 to 1942, during which period suicide caused about 15% of all deaths, accident 35%, and illness 50% † At the University of Michigan, where the average annual entry was 11,614, Raphael et al (1937) found that suicide or the possibility of suicide was deemed an important element in 313 students who had attended the mental hygiene unit of the university health service during the previous five years At Harvard, where the entry in 1939–40 was 6400, there were 6 deaths, including 2 by suicide in that year At Yale, where the annual entry was about 5000, Fry and Rostow (1942) reported 8 deaths from suicide in the ten years following 1924 In fact, the importance of suicide was recognised by university health services in the U S.A before the second world war

---

* Hon secretary Interim Committee on Alcoholism 8 Lygon Place London S W 1

[1] *Quart. J Stud. Alcohol* 1949 10 501

PROLONGED ILLNESS

The total number of undergraduates who missed at least one full term's residence through illness was 145 (113 men, 32 women) Tuberculosis and mental illness (which are discussed below) were responsible for 23% and 52 5% respectively In the remaining 24 5% the causes of absence incl ded epilepsy, jaundice, asthma, peptic ulcer, concussion, accident, appendicitis, war wounds, and tropical diseases

Tuberculosis —33 undergraduates (28 men, 5 women) lost a term or more on account of tuberculosis during the three years under review It may be assumed that this absence was caused by serious illness, and was not due to minimal lesions detected by mass radiography , the latter was performed at only three colleges and their 6 cases each required at least three months' bed rest, or hospital or sanatorium treatment

Mental illness and nervous breakdown —Of the 76 absent for not less than a term, 49 (64 5%) returned to college , 16 (21%) went down without a degree not to return , and 11 (14 5%) went down but their future is undecided 9 (12%) were stated to have been in a mental hospital or to have been diagnosed as schizophrenia Of these 3 returned to college, and 2 others were said to have been cured, although they did not return

The returns show that mental illness, including nervous breakdown, was responsible for just over half the illness, serious enough to cause absence for at least a full term

However, it has already been stated that, owing to certain factors connected with the method of survey, the morbidity figures probably fall short of the truth As far as the mental cases are concerned, there are further reasons for this belief The 9 suicides are not included in the total, nor is there any information about the attempted but unsuccessful suicides which are known to have occurred in the university Several nervous breakdowns were precipitated by pre examination stress, and, in the case of any breakdown occurring towards the end of term, and in particular the Trinity Term, at least two months were available for mental rest and recovery without loss of a term's residence Then, there are other forms of serious mental disturbance involving extreme problems of discipline or behaviour, deep anxieties, obsessions, or ideas of persecution which do not entail absence from college Fry and Rostow (1942), after ten years' experience at Yale, noted that 16 of their 116 serious cases did not require to leave college at all, and 12 others required only a short period of hospital or other care In fact, it may be estimated that not less than 0 5% and probably nearer 1% of the undergraduate population in residence each year at Oxford suffers some serious form of mental illness or nervous breakdown

For many years enlightened college authorities and college doctors have been convinced of the importance of mental hygiene When, however, the question of preventive action is discussed there is a general feeling that "common sense" is an adequate tool for handling the problem, and no special measures are required. Those interested in the mental welfare of students are thought to be prejudiced, and their personal experience unrepresentative I found from routine health examinations that psychological disturbances, although mostly of a minor character, were unduly common (Parnell 1947), but the significance of the finding, was doubtful. It might have been due to the excessive thoroughness of the examination, or possibly even to the over sympathetic outlook of the examiner It was the need for objective confirmation of a clinical impression which first prompted this objective survey, which shows that mental disorder is the principal cause of prolonged illness

In these circumstances it is natural to ask what preventive steps might be taken, although no scheme is likely to prevent all forms of psychosis

Preventive measures need not and should not pay too much attention to individuals They should not involve healthy young men in routine psycho analysis, nor need they, in a popular but ugly phrase, "stir up the mind" unnecessarily They need not provoke hypochondria or encourage introspection, nor need they sap self reliance or engender a feeble and dependent state of mind Serious opposition to the adoption of preventive measures is founded on the alleged ineffectiveness of individual methods Close tutorial supervision, with particular attention to the early signs of mental staleness and cumulative fatigue, should help Better individual instruction in the principles of mental hygiene, in particular in the optimum hours of work, is also required, and it would be desirable to have a doctor or psychiatrist well versed in college life readily accessible for consultation There is evidence that less severe forms of mental or nervous disorder are more common than the severe forms discussed so far, and the preventive measures suggested apply to them with equal force

In war, inactivity because of uncertainty about the technique of victory is inexcusable So too, in the fight against mental ill health preventive measures should not wait indefinitely upon the improbable discovery of some new technical device for early detection On the other hand whatever action is contemplated in the light of present knowledge, it is clear that further and more detailed study of the problem is urgently needed

DISCUSSION

The question will certainly be asked whether this paper draws attention to a state of affairs long present but hitherto unrecognised, or whether there has been a recent increase in the prevalence of mental disorder Since no report has been discovered of any previous survey on these lines, precise evidence on this point is lacking The gravity of the position may not have been recognised because the undergraduates with tuberculosis, mental illness, and the like have been treated by a number of different departments In any event, it is clearly desirable that the facts should be widely known

At a recent conference student health officers expressed concern at the absence of precise information on the incidence of mental ill health among students To remedy this, and to make comparative study possible between universities, some uniform system of recording serious and prolonged illness is clearly desirable Preliminary work to establish such a system is now advanced, and it is reasonable to hope that before long it will be ready

---

† Only deaths occurring during the nine months per-year sessions were recorded The Oxford figures include accidents which occurred during the vacation

General practitioners not in the dispensary service did not come under the scheme as first proposed, except in so far as they might be absorbed into it when new appointments were being made. Compensation for loss of practice was not mentioned; but, after protests, the minister intimated that he was prepared to allow general practitioners to enter the scheme if a sufficient number applied to do so.

Not unnaturally these proposals, changing almost the entire basis of medical practice in Ireland, have been closely scrutinised by the Irish Medical Association and by the profession generally. The response to the scheme cannot be regarded as enthusiastic. In the first place it is regarded as a long step, without any prior consultation, towards a completely salaried profession. With a ringside view of the British experiment—possibly more attractive—few practitioners in Ireland desire to copy it.

Secondly, on the basis of British figures, the I.M.A. has estimated that the scheme would cost not less than £12 million annually. This figure may not seem exorbitant, and may even appear fantastically cheap to English eyes, until it is realised that the Irish budget is of the order of £83 million.

The third ground of criticism bears on the implied charge that the profession has failed in its duty of effectively lowering the infant mortality rate. In a brochure just issued to the public the rate is given as 53 per 1000—the 1949 figure. The 1947 figure was 68, and that for 1950 was 45. The I.M.A. claims that further substantial reductions can only come from a wider approach through better housing, nutrition, and hygiene. Even though the maternal mortality rate has been reduced to 1·9 per 1000 births, far more maternity hospital beds are also needed.

All are agreed, however, that some form of assistance is required to meet the cost of modern medicine. The I.M.A., acting on the principle that "preventive, consultant and ancillary services should be provided for all immediately—free for the poor, assisted for the middle income groups and paid for by the rich," has proposed a grant-in-aid scheme. This has been rejected by the minister on the ground that it involves a means test, to which he is adamantly opposed. He says that he is willing to meet the association providing the means test is not in question. In an effort to end the deadlock the association has offered to discuss health services generally, without prior conditions, through a joint committee presided over by a neutral chairman.

Medical opposition to the scheme is hardening. Both the private practitioners' and the dispensary medical officers' groups of the I.M.A. have declared against it. The minister has probably the power to compel the latter group to operate the scheme—but compulsion has never been a very satisfactory weapon in Ireland! Differences have so far dominated the picture, and the fact that both parties agree that a scheme of some kind is necessary has been overlooked. If a way out of the impasse is to be found concessions will have to be made by both sides.

Public Health

POLIOMYELITIS IN SEMI-CLOSED COMMUNITIES

A. H. GALE
D.M. Oxfd, D.P.H.
LECTURER IN EPIDEMIOLOGY, UNIVERSITY OF BRISTOL; LATELY A SENIOR MEDICAL OFFICER, MINISTRY OF HEALTH

A COMPARATIVE study has been made of the epidemiology of poliomyelitis in camps, residential schools, and other semi-closed communities. In addition to published accounts of such outbreaks unpublished accounts in the records of the Ministry of Health have been used, and school doctors have very willingly helped both by furnishing accounts of hitherto undescribed incidents and by supplementing the information which already existed in published papers or in the records of the Ministry.

The last similar survey in this country was published by Smith (1939), and all the outbreaks described by him have been included with many others. Usually only those outbreaks in which more than one paralytic case occurred have been included, but exceptions have been made where detailed descriptions of the sequence of events were available and these seemed to be of special interest. Names of schools have been omitted throughout because of the danger of causing embarrassment to the school authorities, but the name of the county in which the school was situated is given.

One of the difficulties has been that the reports vary a great deal in their method of presentation, in the amount of detail given, and in the nomenclature of the various types of case. So far as possible, the different accounts have been reduced to a common nomenclature. "Epidemic" means a fairly widespread prevalence in a group of communities or in the country as a whole, and "outbreak" the experience of a single community. For convenience of description and of diagrammatic representation the outbreaks have been grouped as follow:

(1) Four outbreaks in camps for boys.

(2) Three outbreaks in children's homes.

(3) The epidemic in Broadstairs, Kent, in 1926 (Ministry of Health 1926, Aycock 1927, Watts 1927).

(4) Sixteen outbreaks in residential schools and one in an American University reported in 1917–45. The Broadstairs schools are excluded from this group, but another school which experienced an outbreak in 1926 is included.

(5) Thirteen outbreaks in residential schools in England and Wales in 1947–49. These are discussed separately from those of group 4 because the very high prevalence in the country as a whole in 1947 and 1949 was a new experience.

(6) A miscellaneous group of outbreaks which did not fall into any of the other groups but occurred in semi-closed communities. These did not lend themselves to diagrammatic representation.

Figs. 1–5 show the time relations of the onsets of cases in groups 1–5. The same symbols have been used throughout, but fig. 1 shows the history of the illness in each case, whereas figs. 2–5 show only the time relations of the onsets of cases. It is only in the outbreaks in the U.S.A. that the distribution of virus has been investigated in detail.

CAMPS (FIG. 1)

(1) *Detroit* (Brown et al. 1945).—There were 2 paralytic cases among a group of 10 boys, aged 13–17, in one cabin; 4 healthy boys in the same cabin had virus in their stools. Stools from 10 boys in the next cabin were all negative. Messing arrangements were common to the whole camp.

(2) *Massachusetts* (Rubenstein et al. 1948).—There were 5 cases (4 bulbar, with 1 death) among 31 boys, aged 13–17, in one group out of three. The groups slept in small tents, 2 boys to a tent. Stools from 7 boys in other groups were negative for virus. Messing arrangements were common to all groups, but each group had a separate table.

(3) *Sussex* (Conybeare 1946).—In a large camp of some 1200 scouts there were 6 paralytic cases in a group of 131 boys, aged 13–18. 5 of the cases were in a small subgroup of 30 boys. There was 1 associated case in a sister of a boy who had been quite well at camp. There was a good deal of minor illness among the boys in camp. The camp lasted from July 30 to Aug. 10, and for the last week the weather was so bad that the boys had to stay in their tents a good deal during the day.

(4) *West Riding of Yorkshire* (unpublished).—There were 2 paralytic cases and 1 non-paralytic among 18 boys and 1

gramme embracing more than a dozen large companies working in conjunction with the State programme on alcoholism is being conducted with the cooperation of the national committee

Perhaps the most important statement in the 1949 report comes under the heading "legislation" The report says

> "The intensive campaign on alcoholism during the past few years has resulted in a definite trend toward State legislation with respect to the treatment and cure of the alcoholic Approximately three fourths of the State legislatures considered some type of legislation on alcoholism during the 1949 sessions Committees, commissions, groups, governmental bodies, and individuals from most of these States turned to the National Committee on Alcoholism for education and guidance"

In December, 1950, a W H O expert subcommittee on alcoholism as a public health problem met in Geneva After defining alcoholism, the subcommittee recommended that its prevention and treatment should become a regular function of public health administrations, and that it should be treated on medical and scientific lines, as opposed to the approach of lay reform Treatment facilities and advisory, educational, and other services should be provided The subcommittee suggested that efforts be made to uncover early cases of alcoholism, where treatment was most likely to succeed Outpatient clinics were necessary, and were best situated in well equipped general hospitals If adequate networks of such clinics were to be developed, the need for specialised residential institutions for alcoholics would progressively diminish The subcommittee indicated the extreme variation in social drinking customs in different countries, and pointed out that the per caput level of alcoholic consumption in a country was no certain evidence of the incidence of alcoholism in that country It urged the development of national statistics on this matter in every country Figures were given for the incidence of chronic alcoholism in certain countries, the number of chronic alcoholics in England and Wales was said to be 86,000 †

In a broadsheet *Facts on Alcoholism*, published by the National Committee on Alcoholism, the following statements occur

> At least 12 000 alcoholics die each year in the States from chronic alcoholism
>
> Five out of six alcoholics are men between the ages of 30 and 55—the most productive years
>
> Every industry, every business, every profession, every community suffers from this problem
>
> Present methods of dealing with the problem of alcoholism are in very many cases expensive, sometimes barbaric, and often do not rehabilitate or prevent
>
> A majority of alcoholics can be rehabilitated

These statements apply to America, but the problem exists in this country and cannot be ignored It may be a smaller problem, but, apart from numerical differences, all these statements undoubtedly apply here In America the National Committee on Alcoholism has provided communities and the professions, industries, and businesses involved with the medical, scientific, and practical knowledge needed to rehabilitate the alcoholic and to prevent alcoholism Can this country afford to ignore the problem of this disease, which is costing us thousands of man hours in industry and thousands of pounds in money, and which has a very high rate of mortality ?

---

† According to Dr E M Jellinek secretary of the expert subcommittee an approximation of the number of chronic alcoholics for a country can be roughly determined compiled from various sources Mrs Mann (personal communication) remarks The figures Dr Jellinek has released refer only to alcoholics in the most advanced stage To get the number of chronic excessive drinkers, or alcoholics he multiplies that figure by 5 '

RESEARCH AND TEACHING IN NEW ZEALAND

FROM OUR NEW ZEALAND CORRESPONDENT

THE following members have been appointed to the newly incorporated Medical Research Council of New Zealand

Ex officio Dr John Cairney, director general of health (chairman), Sir Charles Hercus, dean of the medical faculty, Otago University, and Mr F R Callaghan, secretary of the Council of Scientific and Industrial Research

Appointed Sir James Elliott (on recommendation of the board of health), Dr P P Lynch (British Medical Association), Dr L Bastings (Royal Society of New Zealand), Dr R S Aitken, Dr F Walsh (academic board of the senate of the University of New Zealand), Prof F H Smirk (New Zealand committee of the Royal Australasian College of Physicians), and Mr Douglas Robb (New Zealand committee of the Royal Australasian College of Surgeons)

The council's first meeting is to be held in May

Postgraduate course in obstetrics at Auckland—The first major educational effort of the new foundation for postgraduate studies under Auckland University College was a fortnight's postgraduate course in obstetrics and gynæcology, held between March 5 and 16 Pending an appointment to the chair of obstetrics, the course was organised by Sir Bernard Dawson, who has lately retired from the chair at Otago University Sir William Gilliatt's visit to inaugurate the New Zealand regional council of the Royal College of Obstetricians and Gynæcologists coincided with the course, and he participated in lectures and discussions

FREE MEDICAL CARE OF MOTHER AND CHILD

FROM OUR DUBLIN CORRESPONDENT

MUCH discussion among the profession in Ireland has been engendered by the proposals of the minister for health, Dr N C Browne, for a comprehensive Mother and Child Welfare Service based on part III of the Health Act, 1947.

Popularly known as the Mother and Child Scheme, this is to provide free medical and nursing care for all mothers "before, during, and after childbirth," and for all children up to the age of 16 years Mothers are to receive free family practitioner, specialist, consultant, and hospital treatment, domiciliary visits from midwives, and also dental and ophthalmological treatment All children under the age of 16 years are to be eligible for free medical care for all illnesses, free specialist, consultant, surgical, and hospital treatment, visits from public health nurses, and dental and eye treatment While nobody is to be compelled to use the service, it will be completely free for those who do there will be no means test, and in the words of the department of health "there will be no doctor's bills in respect of maternity or the health of children up to the age of 16" Not only is the scheme to be free, but those availing themselves of it will not have to pay contributions of any kind, whether by means of insurance or otherwise Part III of the Health Act, while giving the minister power to make regulations as to the manner in which the service is to be set up and carried on, does not in fact enact that it must be free

The working of the service is to be based in the first place on the dispensary doctor—or district medical officer—and the dispensary districts will be modified, new doctors being appointed where necessary By such means there would be, except in some remote areas, a choice of from two to six or more doctors It is stated that the doctor patient relationship will be preserved, but, as the employer will be the local authority, this statement seems rather ingenuous.

was seventeen days There were some abortive cases in all three wards

BROADSTAIRS EPIDEMIC IN 1926 (FIG 3)

Although many schools were affected in this epidemic all were affected at about the same time, and it must be regarded as a single event The institutions affected were as follow

School A, for 73 boys (all boarders), had 12 cases (1 case in a member of the staff)

School B for 21 boys (all boarders), had 5 cases

School C for 24 boys (3 boarders and 21 day boys), had 4 cases (3 in day boys)

School D, for 28 boys (all boarders), had 2 cases

School E for 43 boys (25 boarders, and 18 day boys), had 2 cases in boarders

School F for 74 girls (all boarders), had 2 cases in girls and 2 in members of the staff

School G for 53 girls (all boarders), had 3 cases

School H, for boys and girls (boarders and day pupils), had 6 cases

School I for boys and girls (boarders and day pupils), had 3 cases

Convalescent home X had 1 case in a boy patient

Convalescent home Y had 5 cases, of which the first 2 were in children (patients) and the rest in female members of the staff

An elementary school had 4 cases

Schools A–I were largely for boys and girls up to the age of about 13, but some of the schools had older girls

This epidemic was described by the Ministry of Health (1926) and Aycock (1927) Aycock believed that the infection was milk borne but MacNalty, who investigated the outbreak on behalf of the Ministry of Health, never accepted this view Fig 3 suggests that there were two waves, the first one affecting schools A–I, and the second the convalescent homes and the elementary school There is, however, some overlapping, and it is difficult to be sure on this point Aycock maintained that the whole outbreak could be explained on the hypothesis of a simultaneous infection dating from Oct 10, and that there was a good deal of confusion about dates of onset in the earlier cases In America this outbreak is often cited as definitely milk borne, but this explanation seems doubtful. There was an extraordinarily high attack rate, and the epidemic is of particular interest in that, with one exception (see fig 4), it seems to be the only occasion on which multiple paralytic cases have been reported in boarding-schools for girls (schools F and G were for girls only) This may be due to the fact that outbreaks in schools are comparatively rare and that the number of boarding schools for boys is much greater than that for girls A possible explanation might be, however, that girls at boarding schools are generally sent to bed for rather less serious complaints than are boys and thus have less opportunity of infecting others.

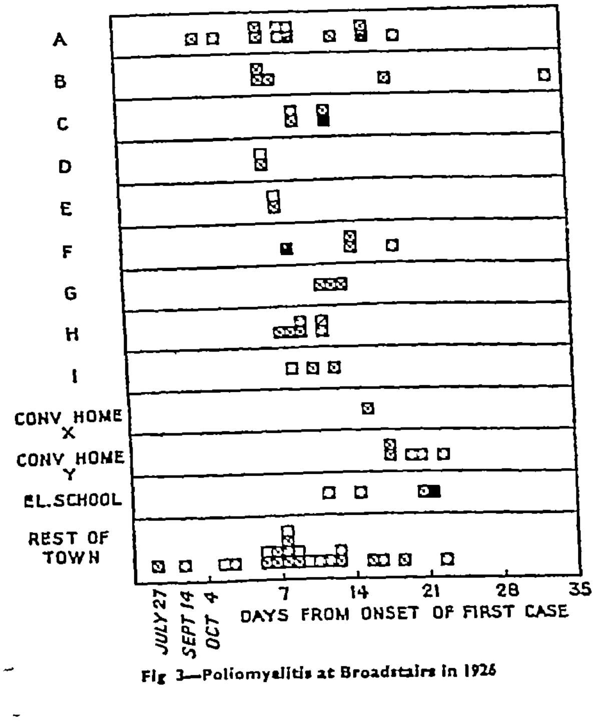


Fig 3—Poliomyelitis at Broadstairs in 1926

RESIDENTIAL SCHOOLS 1917–45 (FIG 4)

The schools concerned were as follows

(1) *Gloucestershire* (Local Government Board 1918) —This school for boys, aged 13–18 had 400 boarders in six houses and 200 day boys There were 3 paralytic cases (1 fatal) in 1917, 2 were in one house and 1 in another

(2) *Berkshire* (Smith 1939) —This school had 350 boys boarded in eight houses The outbreak of 7 cases occurred in the middle of an influenza epidemic in 1918 and seems to have been explosive The cases were in different houses This is the same school as no 16

(3) *Rutland* (Ministry of Health 1926) —This school for 500 boys, aged 13–18, boarded in thirteen houses had 3 cases in different houses in 1926, 1 of them occurred in the holidays

(4) *Kent* (Brown 1931) —This mixed school for boys and girls, aged 6–13 had 56 boarders, 11 teachers, and 8 domestic staff In 1929 there were 2 paralytic cases among the children (1 fatal), 2 cases with nasal voice but no other signs of paralysis and 1 non paralytic case in a member of the staff. 1 child developed nystagmus and nasal voice sixteen days after the dispersal of the school All the paralytic cases had cranial nerves alone affected

(5) *Mid western College U S A* (Rosenow 1932) —479 male and 448 female students lived in six dormitories on the campus and had a common dining room There were 8 cases in 1930 Dates of onset are not given. Rosenow considered that a streptococcus was responsible

(6) *Dorset* (unpublished) —This school of 370 boys aged 13–18 had a small catarrhal wave at the beginning of the Michælmas term in 1932 The 2 cases were in different houses and forms Six boarding houses and one day boys' house shared a common dining room. This school is the same as no 28 (fig 5)

(7) *West Riding of Yorkshire* (unpublished) —This school of 88 male boarders aged 10–18 had 7 cases in 1933 There had not been any illness at all up to June 10 The boys lived in two houses both of which were affected. The boys used a common dining room

(8) *Herefordshire* (unpublished) —This school of 91 boys (49 boarders and 42 day boys), aged 9–19 had 2 cases in 1933 There were two dormitories in one building with common dining arrangements Both dormitories had a case

(9) *Boston, Mass* (Aycock 1942) —This American school of 190 boys aged 13–18, had 18 cases in 1936 No details are given of dormitories or dining rooms

(10) *Devon* (unpublished) —This school for a few boys, aged 8–13, had 3 cases in 1937 The first outside case was in the brother of a boy taken ill at school on Sept 25 The fatal outside case (onset Oct 14) was in the sister of a boy who went home from school on Sept 25 for two days and again on Oct 7 He had had a slight bilious attack at school on Sept 22

(11) *Essex* (Barber 1938) —This school of 400 boys aged 13–18 boarded in four houses in the main school and two outside, had 4 cases in 1938 All the cases were in the same house and 2 of them in the same dormitory

(12) *Essex* (Gammie 1939) —This school of 284 boys, aged 9–18, had 214 boarders in four houses and a preparatory department, and 70 day boys In 1938 there were 4 cases It is not stated definitely whether all the cases were in one house, but it seems that at least 2 in boys and 1 in a maid were

(13) *Berkshire* (Lambert 1939) —This boys' school of 670 boarders, aged 13–18, had 3 cases in 1938 The main building

young scoutmaster living in five tents One of the paralytic cases was fatal

These four outbreaks are particularly interesting because the limits of the period in which infection probably took place are better defined than they are in most outbreaks In the Detroit and Massachusetts outbreaks virus studies were done One of the cases in the Detroit outbreak is often cited because virus was found in the stools nineteen days before the onset of paralysis In both outbreaks there was evidence that at an early stage virus was widely disseminated within the affected group but had not spread outside that group

Fig 1 illustrates the difficulty of working out the chronology of infection from the dates of onset of cases This point has been made by Horstmann and Paul (1947) The case associated with the Sussex camp was in the sister of a boy who attended the camp but had no illness either at the camp or afterwards The minor illnesses which affected at least 15 boys while they were at the camp were not definitely diagnosed They might have been illnesses of infection, but that in case 1 was probably an illness of onset Possibly some of the boys in this outbreak were infected after they got home from the camp, but this does not seem very likely

In the West Riding outbreak the weather was good and the only incident of note during the camp was that on Aug 27 one boy (case 2) had a headache which lasted about half an hour It is uncertain which was the source case The sequence of events in this outbreak was very different from that in the Sussex outbreak In Sussex the onsets of paralysis were scattered over about a month after the end of the camp, whereas in Yorkshire the scoutmaster was dead, one boy had a quadriplegia, and another signs of meningeal irritation, all within twelve days of the end of the camp

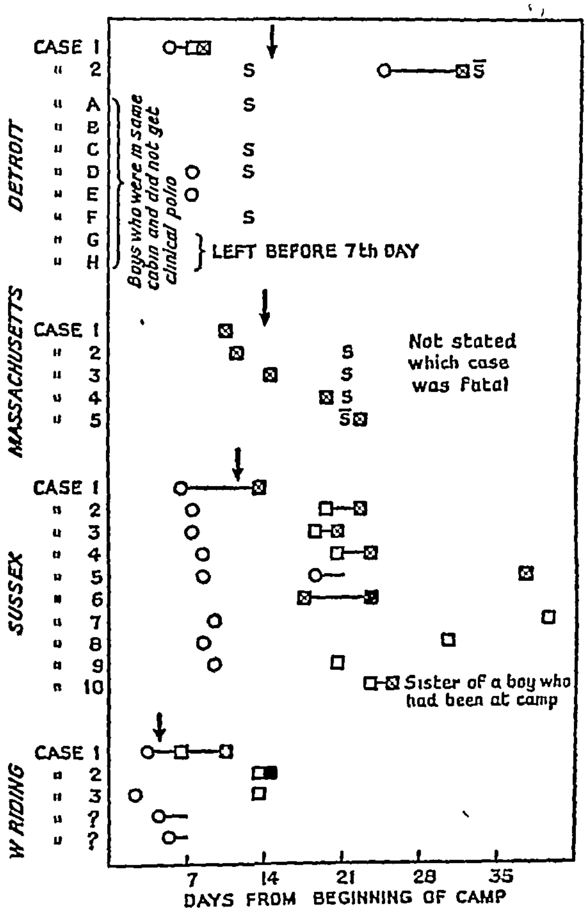


Fig 1—Poliomyelitis in camps.

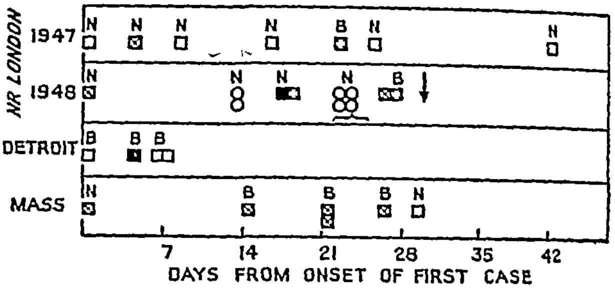


Fig 2—Poliomyelitis in children's homes.

Daley (1948) reported that, when the epidemic of 1947 was at its height in London, 1 case occurred in a party of 240 secondary school children who went into camp at the end of July, and 3 cases occurred in the party which followed on Aug 9 It seemed clear that all these children were already infected when they arrived at the camp, and that no spread took place in the camp Everyone was on the alert for poliomyelitis at the time, and all the patients were promptly isolated These two incidents are not shown in Fig 1

CHILDREN'S HOMES (FIG 2)

(1) *Near London* (Daley 1948)—This home contained 125 children under the age of 5 years, and a staff consisting mostly of adolescent girls In July, 1947, there were 1 paralytic and 5 non paralytic cases among the staff, and only 1 case in a baby (aged 14 months) There was a good deal of minor illness among the staff and later some cases of infectious hepatitis occurred among them but not among the children

(2) *Near London* (unpublished)—This home contained 34 children under the age of 5 years, 63 young adult girl trainees, and 15 resident and 3 non resident older staff In July, 1948 there were 3 paralytic cases in young adult girls 1 fatal case in a member of the staff aged 31, and 1 paralytic case in a baby aged 8 months

(3) *Detroit* (Kramer et al 1939)—This home contained 10 children under the age of 5 years, 14 children aged 5–16, and a staff of 17 There were 1 fatal and 3 non paralytic cases among the children in August, 1939 Stools from 5 unaffected children and 1 member of the staff were positive for virus on Aug 11, and 2 were still positive nineteen days later

(4) *Massachusetts* (Silverman 1941)—This home was in two sections an orphanage of 117 children under the age of 6 years, and a hospital section with 17 children of all ages in it The preschool and hospital sections (49 children and 23 staff) had 5 cases in March, 1939 The adults of the two main sections had contact with each other, but the children were kept separate The first case was a paralytic one in a nursemaid in the orphanage 4 infants, of whom 3 were in the hospital had paralytic attacks, and 1 adult, who worked in the laundry, had a non paralytic attack. This adult was in the habit of visiting her baby in the orphanage Virus studies were done, but the results obtained by different workers were contradictory

The first and second outbreaks near London were regarded as unusual at the time of their occurrence in that all the cases except two, one in each, occurred among the staff—mostly young women aged 18–30

Another outbreak (Bloomberg and Barenberg 1924), not shown in fig 2, occurred in a home for 300 infants aged from 6 months to 2 years There were 10 paralytic cases—5 in one ward, 4 in a second, and 1 in a third 6 cases occurred within a day or two of one another, and the longest interval between cases in the same ward

KEY TO SYMBOLS IN FIGURES

○ MINOR ILLNESS
□ MENINGEAL SIGNS
⊠ PARALYSIS
☒ PARALYSIS DOUBTFUL
■ DEATH
S VIRUS POSITIVE STOOL
S̄ VIRUS POSITIVE STOOL AND THROAT
↓ DISPERSAL
— PERIOD OF ILLNESS (PRODROMAL)
N NURSE
B BABY

boys), had 3 cases in 1947 affecting two masters and one boy The mother of a day boy also developed paralytic poliomyelitis on July 12 Her two children had slight attacks of vomiting on July 14 Four day boys had minor illnesses between July 13 and July 20, but on the whole there was little minor illness in the school.

(22) *Warwickshire* (unpublished)—This school of 600 boys aged 13–18 (550 boarders and 50 day boys), had 4 cases in 1947 This was a public school with ten separate boarding houses All the cases were in one house and nearly all in one dormitory 2 cases occurred in the summer holidays There were 8 cases of minor illness in the same house between July 2 and July 24

(23) *Berkshire* (unpublished)—This school of 99 boys aged 8–13 (all boarders) had 4 cases in 1947 1 case occurred on the last day of term and 1 paralytic and 2 non paralytic in the holidays The boy who had developed the disease first had been in the sanatorium with bronchitis and asthma for a week before the onset of poliomyelitis

(24) *Cornwall* (unpublished)—This school of 360 boys aged 12–18 (215 boarders and 145 day boys) had 2 fatal cases in 1948 They were in separate houses which had a common dining room.

(25) *West Riding* (unpublished)—This school of 400 boys, aged 13–18 (all boarders living in seven houses), had 4 cases in 1948 3 cases were in one house and 1 in another but the last was in the same class as one of the earlier ones There was unusual prevalence of minor illness at the time

(26) *Middlesex* (unpublished)—This school of 520 boys aged 13–18 living in eleven houses had 3 cases in three different houses in 1948 There was an epidemic of sore throats in the school at the time

(27) *Buckinghamshire* (unpublished)—This school of 183 boys aged 8–13 (60 boarders and 123 day boys all in one building) had 3 cases in 1948 An associated case occurred in a dental attendant employed by the dentist who looked after the school Several boys and masters visited the dentist when virus was presumably widespread among them. There were other cases in the neighbourhood at the time

(28) *Dorset* (unpublished)—This school of 400 boys, aged 13–18 (350 boarders and 50 day boys in six houses plus a day boys house with a common dining room) had 7 cases in 1949 There were 3 cases in one house and several cases of minor illness This is the same school as no 6

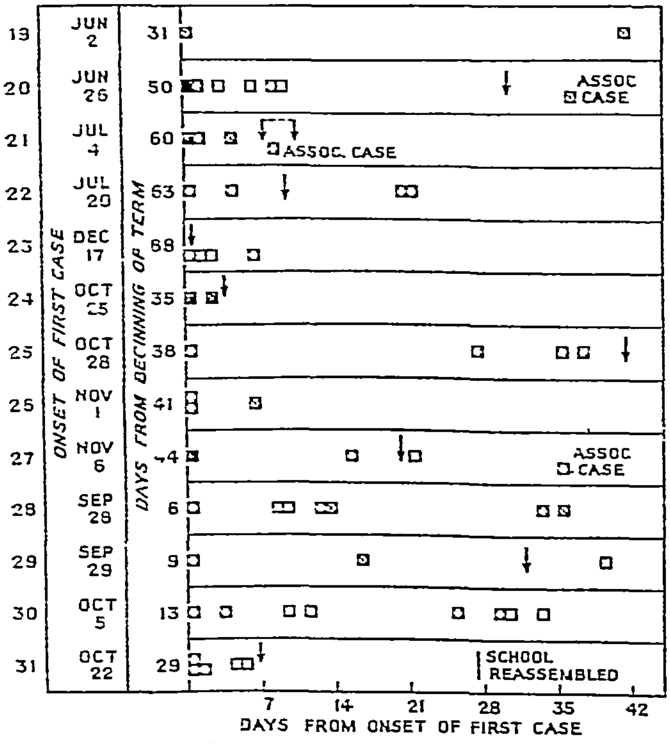


Fig 5—Poliomyelitis in schools in 1947–49

(29) *Hampshire* (unpublished)—This school of 49 boys aged 6–13 (42 boarders and 7 day boys), had 3 cases in 1949 One boy developed a non paralytic attack at home in the subsequent holidays There were 19 cases of minor illness (headache, vomiting &c) between Oct 7 and Oct. 27

(30) *Huntingdon* (unpublished)—This school of 81 boys, aged 7–13, and living in two houses but with a common dining-room, had 8 cases spread between both houses in 1949 There were a few cases of minor illness

(31) *Lancashire* (unpublished)—This school of 400 boys aged 7–18 (mostly boarders in eight houses with a common dining room and two separate ones), had 5 cases in 1949 Cases occurred in the main block and in the separate junior school The school was disbanded for three weeks and then reassembled No further cases occurred after reassembly

These twelve outbreaks (nos 19–30) have been grouped together because the incidence of poliomyelitis was so much higher in the country as a whole than it had ever been that importation of infection into a school was an almost continuous risk.

Minor illnesses have been omitted from fig 5 because in some outbreaks so many were reported that the diagrams would have become confusing

As in the outbreaks in schools in 1917–45, the epidemiological pattern varied greatly, from that exemplified in school 24, with 2 fatal cases in three days and no more, to that exemplified in school 28, in which the onset of the first case was right at the beginning of term and further cases occurred throughout the term It is again difficult to find any definite association between the type of school and the duration of the outbreak Schools 19, 22, 25, 26, 28, and 31 were large public schools run on the house system, schools 24 and 30 were of intermediate type with two boarding-houses, and schools 20, 21, 23, 27 and 29 were preparatory schools in which all the boys lived in one building In school 22 all the cases occurred in one house, but in school 26 the cases were all in different houses, though all occurred within a week of one another In school 19 there were 2 cases, with nearly six weeks between, in different houses and apparently unassociated

Associated Cases—In school 20 the associated case (onset Aug 1) was in the small brother, aged 3½ years, of a boy who had returned home from school on July 26 In school 21 the associated case was in the mother of a day boy In school 27 the associated case was in a dental nurse employed by the dentist who attended the masters and boys Her illness began on Dec 13 Masters or boys had visited the dentist on Nov 25 Dec 2, and Dec 9

Time of Year—Nine of the outbreaks occurred in the autumn and four (all in 1947) in the summer term It is perhaps worthy of note that in 1947, in the country as a whole, incidence began to rise earlier than usual and, although the peak of incidence was much higher in 1947 than in 1949 and very much higher than in 1948, the peak was sharper than it was in 1948 and 1949

SINGLE PARALYTIC CASES IN SCHOOLS

We know less about the occurrence of single paralytic cases than about the occurrence of multiple cases because very naturally, everyone heaves a sigh of relief when only one paralytic case occurs and does not consider the incident worth reporting This is a pity since negative evidence might be just as interesting from the epidemiological point of view as positive evidence

The Medical Officers of Schools Association (Smith 1939) obtained incomplete information from fifty one schools for 1912–32 No cases were reported from ten girls' public schools or from eleven preparatory schools Of thirty boys public schools eleven had no cases and with about 450 boys was divided into ten dormitories with a common dining hall The other 220 boys lived in four outside boarding houses Cases occurred in boys from nine out of ten dormitories in the main building, 15 (some abortive) occurred in the holidays, and one boy infected a brother (also a member of the school) after dispersal

(14) *Durham* (unpublished)—This school of 300 boys, aged 11–18 (200 boarders and 100 day boys), had 6 cases in 1944 Cases 1–4 and 6 were in boarders, and case 5 in a day boy The boarders lived in one building with one dining room

(15) *Oxfordshire* (unpublished)—This school of 360 boys had 3 cases in 1944 All the cases were in different houses, and the last was in a boy in the preparatory house, members of which have contact with the boys in the main school in the dining room only

(16) *Berkshire* (unpublished)—This boys' school of 300 boarders had 8 cases in 1945 There were two groups of buildings (1) The college (divided into three houses) and two outside boarding houses, with a common dining room for 200 boys, and (2) two houses in one building with a common dining room for 100 boys Cases occurred in both groups, but only 1 in the second group of buildings, and there is evidence that the college and one of the associated houses were affected first There was an outside case in a baby not closely connected with the school This is the only school outbreak which I have been able to find occurring so early as March The school is the same as school no 2

(17) *Hampshire* (Ministry of Health 1945)—This school of 132 boys (43 boarders and 89 day boys) had 6 cases in 1945 There were 5 cases with paralysis 1 was in a boarder, 2 in day boys 1 in the infant sister of a day boy, and 1 (fatal) in an adult living in the same house as three day boys, none of whom was ill

(18) *Devon*—A girls' boarding school had 2 cases in 1937

It has been impossible to check the details of the outbreaks shown in fig 4, and the number of cases of minor illness and the exact dates of onset were often doubtful If only paralytic cases are considered, fourteen of the outbreaks were over in a fortnight so far as the school itself was concerned The outbreaks in schools 4, 14 and 15 lasted longer There seems to be no definite association between the length of an outbreak and any particular type of school The outbreak in school 4 was unusual in that, in the cases with paralysis, only cranial nerves were affected (Brown 1931)

Associated cases have been shown only when the association with a member of the school was a close one In school 10 the first case was in a boy taken ill on the day before he should have returned to school His brother (the second case shown) fell ill five days later at school The fatal case was in the sister of a boy who was at the school and returned home seven days before the onset of his sister's illness In school 17 the 2 associated paralytic cases occurred in the infant sister of a day boy and in an adult (a fatal case) who lived in the same house as three of the day boys, none of whom was ill It is impossible to be sure that the apparent source of infection of the associated cases was the true one, but it is noteworthy that in all instances the infection was apparently conveyed by a healthy carrier

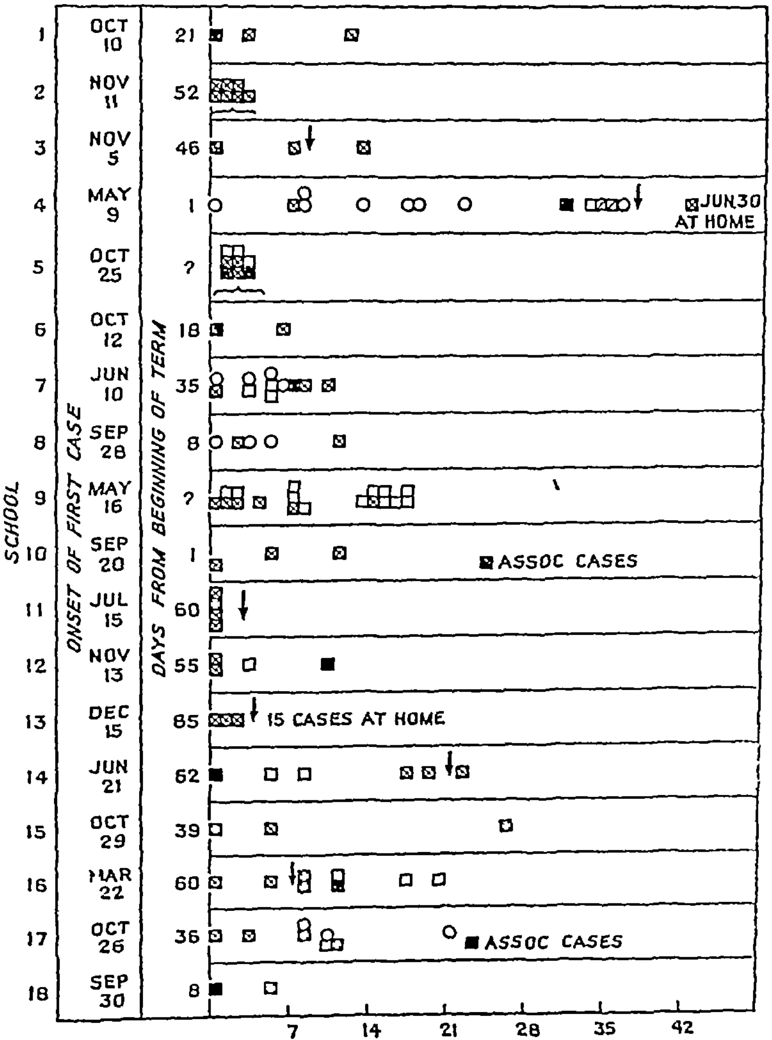


Fig 4—Poliomyelitis in schools in 1917–45

Building Arrangements—Ten of the outbreaks occurred in schools run on the house system or modifications of it In school 15 all the boys affected were in one house, and two were in one dormitory In schools 7, 13, and 16 the cases occured only in a group of houses with a common dining room In school 15 the last case occurred in the preparatory department, the members of which met boys of the senior school only in the dining hall In the remaining outbreaks cases occured in different houses There is no very convincing evidence that an outbreak tends at first to be confined to one house or group of houses, but there is a suggestion that it does

Time of Year—Twelve of the eighteen outbreaks were in the autumn term five in the summer term, and one in the Easter term There does not seem to be any stage of the term at which an outbreak is particularly liable to begin

RESIDENTIAL SCHOOLS 1947–49 (FIG 5)

(19) *Dorset* (unpublished)—This school of 506 boys aged 13–18 (502 boarders and 4 day boys), in 1947, had 2 cases in separate houses with no apparent connection between them There was no remarkable incidence of minor illnesses in the school

(20) *Dorset* (unpublished)—This school of 67 boys, aged 8–13 (all boarders), had 6 cases in 1947 All the boys lived in one house Between June 15 and June 23 many boys had complained of minor illnesses—sore throats and headaches—and some had vomited The date of onset of the first case was June 26 and the boy died on July 4 in coma without developing definite paralysis Many boys went home at the beginning of July, but some remained until the end of term on July 20 On Aug 1, the younger brother aged 3½ years, of one of the boys who had returned from the school developed paralytic poliomyelitis The schoolboy had had no illness either at school or after his return home

(21) *Hertfordshire* (unpublished)—This school of 97 boys aged 8–13 (54 boarders and 43 day

communities in this country Meanwhile the accumulation of purely clinical accounts should go on. If these accounts are detailed and presented in a uniform way, the task of comparing them is made very much easier

Nothing has been said here about the best procedure to adopt in face of an outbreak in a semi closed community, partly because the great variety of form which outbreaks assume makes it impossible to lay down hard and fast rules, and partly because a conference assembled by the Medical Officers of Schools Association (1946) has already issued sound general advice The only recent work which may perhaps be regarded as reinforcing that advice is that of Russell (1947) and Horstmann (1950) on the evil effects of exercise in the early stages of poliomyelitis

SUMMARY

Summaries have been given of four outbreaks of poliomyelitis in school camps, of four in children's homes, of the epidemic in Broadstairs of 1926, and of thirty one outbreaks in boarding-schools reported in 1917–49 An attempt has been made to present these in a uniform way so that comparisons can be made between them

My thanks are due to many past and present members of the medical staff of the Ministry of Health whose reports I have consulted, to fellow members of the Medical Officers of Schools Association, and to Medical Officers of Health who have supplied me with much information hitherto unpublished.

REFERENCES

Aycock W L (1927) *Amer J Hyg* 7 791
— (1942) *Amer J med Sci.* 204 455
Barber G O (1935) *Brit. med. J.* ii 1137
Bloomberg M. W Barenberg L. H (1924) *Arch. Pediat* 41 339
Brown G C Francis T jun. Pearson H. E (1945) *J Amer med Ass* 129 121
Brown W G S (1931) *Lancet* ii 1237
Conybeare E. T (1946) *Mon Bull. Min Hlth* 5 15
Curnen E. C Shaw E W Melnick, J L. (1949) *J Amer med. Ass* 141 894.
Daley A (1948) *Proc. R. Soc. Med* 41 52
Dalldorf G., Sickles G M. (1948) *Science* 108 61
Gammie R. P (1939) *Proc. R Soc. Med.* 32 430
Horstmann D M. (1950) *J Amer med. Ass.* 142, 236.
— Paul J R (1947) *Ibid* 135 11
Kramer S D, Gilliam A. G Molner J G (1939) *Publ. Hlth Rep. Wash.* 54, 1914
Lambert, J (1939) *Proc. R. Soc. Med.* 32 430
Local Government Board (1918) *Rep loc Govt Bd publ Hlth* n.s. no 120
Medical Officers of Schools Association (1946) see *Lancet* i 972
Medical Research Council (1935) *Spec. Rep Ser med. Res Coun. Lond* no 227
Ministry of Health (1926) *Rep med. Offr Minist. Hlth* p 88.
— (1945) *Ibid*, p 23
Rosenow E. C (1932) *J infect Dis* 50 377
Rubenstein, A D Milnor J P von Magnus H., Melnick, J L. (1948) *New Engl. J Med.* 238 218
Russell W R. (1947) *Brit. med. J* ii 1023
Ryle J C (1948) *Lancet* i 945
Silverman A C (1941) *Amer J publ Hlth*, 31 593
Smith R. E. (1939) *Guy's Hosp Rep.* 89 139
Speijer N (1946) *Ned. Tijdschr Geneesk* 90 130
Van der Wey A P (1945) De Poliomyelitis Epidemie te Amsterdam in 1943 M.D thesis. Amsterdam
Watts A. M. (1927) see *Brit med J* i 113.

Measles

After a slight decline during the previous week notifications of measles in England and Wales increased sharply during the week ended March 17, when 31,837 cases were reported The position in London and the home counties, recently most heavily infected, was almost unchanged Increases of some size took place in Lancaster, the West Riding of Yorkshire, Southampton, Warwick, and Derby Of the county boroughs Plymouth, with 610 cases, had the highest rate of incidence, and notifications in Birmingham rose to 885, compared with 590 the week before

Whooping-cough

In England and Wales the number of whooping-cough notifications has fallen for two weeks running In the week ended March 17 the total was 5516—121 fewer than in the previous week. The most noteworthy decreases were in Kent and Stafford. Liverpool and Birmingham, with 136 and 105 cases, were again the county boroughs with most cases

Influenza

During the week ended March 17 deaths from influenza in the 126 great towns of England and Wales totalled 88, compared with 130 in the preceding week. This was the lowest total since the week ended Dec. 16, just before the epidemic began Of the 88 deaths, all but 12 were of patients over 55 years of age. The epidemic can now be regarded as ended.

Poliomyelitis

During the week ended March 17 notifications of poliomyelitis in England and Wales were as follows paralytic 18 (9), non-paralytic 0 (4), total 18 (13) Figures for the previous week are in parentheses

Medicine and the Law

Agenised Flour

A YEAR ago Sir Wilson Jameson's committee reported [1] that there was no evidence of harm to human beings from agenised flour, but it recommended that the 'Agene' process should be replaced by treatment with chlorine dioxide This recommendation was accepted by the Ministries of Food and Health and by the milling industry, but the industry has been unable so far to complete this substitution, and the testimony at a recent inquest suggests that the public may have continuing misgivings about our bread supply

The dead bodies of a husband and wife and their infant child were discovered in their home in Hull. The husband's body was hanging by a rope from the ceiling of the bathroom, the wife had been asphyxiated by a cord round her neck, and the child had died from drowning Dr Philip Science, police-surgeon, told the coroner that there were no signs of poisoning The jury found that the husband had murdered his wife and child and had then committed suicide.

Dr J J Coghlan said that the deceased husband had complained to him of palpitation, pain over the heart, inability to sleep, and a feeling that he was losing his mental grip Dr Coghlan associated these symptoms with the consumption of agenised flour The treatment of wheat or other cereals with nitrogen trichloride, he said, produced a poison which had not yet received a name, flour so treated had been banned in every country in the world except this. The death-rate from heart disease had risen by 40,000 per year since the flour was introduced "practically every person who comes to me is suffering from agenised poisoning", the bulk of the people in the country were feeling the effects of agenised flour, and 250,000 had already lost their lives from this cause since 1940 On the other hand, Dr H E Magee, senior medical officer (nutrition) at the Ministry of Health, emphasised to the coroner and jury that there was no evidence that agenised flour had any harmful effect on man Toxic effects were produced on dogs and ferrets, but not on rats or guineapigs or on man He explained that the object of treating flour with nitrogen trichloride was to give effects similar to those produced by simply storing the flour for some time, it resulted in a whiter and more palatable loaf.

The coroner, in summing up, placed the conflicting evidence before the jury, indicating his own opinion that the weight of evidence was against chronic poisoning by agenised flour He told the jurors that, if they agreed with that opinion, they could add a rider accordingly They seem to have refrained from pronouncing upon an issue which a coroner's jury is not ideally equipped to decide nineteen had 32 cases between them 16 being single cases, and 16 associated with others The association attempted another survey in 1947 and 1948, but again the information collected was incomplete In 1947 single paralytic cases occurred in at least seven boys' schools and five girls' schools in term time One of these incidents was described in detail by Ryle (1948), who considered that there was a widespread epidemic of indefinite illness and non-paralytic poliomyelitis affecting two houses There can be little doubt that in boarding schools the single paralytic case is very much more common than are multiple cases, but on the present information it is impossible to say how much more common

---

[1] See *Lancet* 1950 i 227 *Ibid* p. 219

MISCELLANEOUS OUTBREAKS

(1) *In a training ship* for 229 boys aged 13–16 the first case had onset on Jan 19, 1948, and the second on Feb 3 The boys had returned from Christmas leave on Jan 6, and there had been a very extensive outbreak (at least 35 cases) of pharyngitis among them before Jan 19 This went on, and subsequently *Strep hæmolyticus* type 18 was isolated from many cases The community was an unusually closed one, because the boys went ashore only in parties on Sundays They slept in hammocks on very extensive decks Some of the staff lived ashore

(2) *In a concentration camp* in Holland in August–December, 1943 (Speijer 1946), there were 58 cases, 31 being paralytic with recovery and 3 fatal in a total population of about 9000 1 single case occurred in July, 1 in August, 4 in September, 12 in October, 37 in November, and 3 in December There had been an epidemic in Amsterdam in July–October, 1943 (Van der Wey 1945) The curve of incidence resembled that of the Broadstairs outbreak, except that it was spread over a much longer period

(3) *In a troopship* returning from the East in 1947 with 4000 troops 2 cases occurred in soldiers with dates of onset Sept 5 and Sept 14, and a third in an officer with date of onset Sept 16 The voyage lasted from Sept 1 to Sept 29, and there was a good deal of minor illness on the voyage, with a peak of incidence at the time of onset of the first paralytic case So far as is known, there were no secondary cases in the communities to which the passengers dispersed on arrival in this country

(4) *In an orthopædic hospital* the first case, with date of onset July 9, 1949, was transferred from a hospital for infectious diseases to the orthopædic hospital on Aug 31, twenty two days after onset Case 2 (date of onset July 19) was transferred on Aug 18 (thirty days after onset) Case 3 was in a child, aged 5 years, who had been in the orthopædic hospital for many months with a tuberculous hip The date of onset was Aug 30, twenty eight days after the admission of case 1 and twelve days after the admission of case 2 Case 4 was in another child in the ward, and the date of onset was Sept 16, forty five days after the admission of case 1 and twenty nine days after the admission of case 2 Both case 3 and case 4 played particularly with case 2 This is the incident to which reference was made earlier in the discussion of length of infectivity (see also fig 5, no 19) There was a high incidence of poliomyelitis in the neighbouring city at the time, and possibly the virus was introduced into the ward by some person other than case 1 or case 2 In view of the usual teaching about the short period of infectivity and the rarity of cross infections, however, this incident is disquieting and seems to justify a close lookout for, and the accurate recording of, similar incidents in other hospitals

DISCUSSION

The outbreaks described here have varied greatly in duration, seasonal incidence, and severity, and it is difficult to trace any clear relationships between these features and the type of community involved The following tentative generalisations are perhaps justified

Camp outbreaks seem to have a high attack rate of paralytic cases, and the virus seems to be confined, at first, to a fairly restricted group, though it is quickly and widely disseminated within that group

In the outbreaks in children's homes an unexpected feature has been the relatively high attack rate in the staff In view of the fact that attack rates in the general population are considerably higher in children than in adults it is surprising to find outbreaks like those in the two homes near London (fig 2) It is not clear whether this has something to do with susceptibility or whether the conditions for the spread of infection were particularly favourable in one section of the community

In schools there seems to be no way of prophesying what is likely to happen when a paralytic case occurs Short sharp outbreaks and long drawn out ones have occurred both in small homogeneous communities of the preparatory school type and in more complex communities of the public-school type There is perhaps a little evidence that in the public school one house tends to be affected first, and that, as in the camp outbreaks, the virus may at first be confined to a fairly narrow circle, though widely distributed within that circle The difficulty is that, if none of the early cases is paralytic, dissemination of the virus may be a silent process, and the first sign of an outbreak may be the occurrence of paralytic cases in different houses In the accounts of outbreaks there are many instances of a boy having a mild indefinite illness, returning to school for perhaps a week, and then developing paralysis This is the well known "dromedary" type of onset, and it is likely that in the stage of remission the patient may disseminate virus widely It has been noted that the occurrence of multiple paralytic cases seems to be very uncommon in schools for girls, and it is possible that this relative immunity may be associated with the fact that girls are usually kept in bed in isolation for more trivial illnesses than are boys (Medical Research Council 1938) The problem is, however, full of difficulties, because the occasions when indefinite minor illnesses are really a harbinger of poliomyelitis must be very rare compared with the occasions when they are not There seems to be no satisfactory solution until some practicable way of detecting non paralytic cases is discovered

Outbreaks are undoubtedly most common in the autumn term, less common in the summer term, and very uncommon in the Lent term, but there seems to be no particular stage of term at which an outbreak is likely to occur It is, however, difficult to be sure of this, because the true beginning of an outbreak may be, and probably usually is, a silent process

Instances have been found of apparent prolongation of the period of infectivity of the disease beyond that usually regarded as the danger period These have been few and necessarily uncertain, but it seems desirable that in future a careful record should be made of such occurrences It is worthy of note that in all the outbreaks studied there has not been a single instance of a definite paralytic case in a kitchen worker

It must be admitted that the accurate study of outbreaks of poliomyelitis is difficult and somewhat discouraging Even when elaborate facilities for examination of specimens for virus are available, it is necessary to select certain cases for examination and to make deductions which may or may not be true about what is happening in the community as a whole The discovery of the viruses of the Coxsackie group (Dalldorf and Sickles 1948, Curnen et al 1949), which are easier to work with than the virus of poliomyelitis, offers hope that in future it may be possible to get more help from the laboratory in the epidemiological investigation of some outbreaks of a similar type of disease in semi closed

Letters to the Editor

INFECTION OF "CLEAN" SURGICAL WOUNDS

SIR,—The excellent article (March 17) by the late Mr Girdlestone and his colleagues states that "no good purpose is served by pasting fabric on the skin with mastic before making an incision the mastic is one more material to sterilise and keep sterile" Admittedly, the convenient practice of making an incision through stockinet pasted on with 'Mastisol' has many defects The stockinet is not waterproof, it is in fact freely porous, and if it becomes wet by perspiration or blood it should form a continuous medium for the passage of organisms from the skin to its surface Furthermore, the skin edges are exposed when the incision is made and they remain exposed during the operation But the practice has something to recommend it and, faute de mieux, it may I suggest, be accepted

In the first place, the mastisol is not one more material to sterilise, but is in fact antiseptic and when it has set it forms a barrier between the skin and the surface of the stockinet If the stockinet remains dry, as in moderately short operations under tourniquet, the stockinet and mastisol form a barrier and lessen the chances of contact of hands, needles, ligatures, and sutures with skin, even though, because the skin edges are exposed, the barrier is only partial One should remain mindful of this defect

Skin towels are certainly no better as they are not waterproof and the method of fixing them damages the skin edges and may make holes in the towels themselves Instead of stockinet I have used oil silk, sterile waterproof strapping without the adhesive, and 'Nylon' film in an effort to find a waterproof cover that could be used as stockinet is used but these materials do not adhere to and fit, the contours of the operation area as well as the stockinet and they are more likely to come unstuck during operation

With regard to the general draping of the operation field, as distinct from the immediate vicinity of the wound, it is surprising how varied is the insistence among different surgeons on waterproof draping Yet the practice of using towels without sterile mackintoshes under them over an area which becomes damp with blood and skin exudation cannot be justified as effective for if the towel becomes damp there is a continuous medium between the skin and the surface of the towel.

Reference is made in the article to the storage of nylon in 1-60 phenol Though nylon is unharmed by any of the usual sterilising agents phenol is an exception, after a day in 1-60 phenol nylon breaks easily

Scunthorpe Lincolnshire **DAVID F THOMAS**

SIR,—The article by the late Mr Girdlestone and his colleagues recalled to my mind that I had been associated with a series of "clean" surgical cases which became infected

This occurred during the earlier part of last year Since I was concerned with all the cases either as surgeon or assistant I felt sure that I was to blame The wounds all became infected with a penicillin resistant strain of *Staphylococcus aureus* I had my throat swabbed and cultured, with negative results but my hands persistently grew a similar strain My wife at this time was having a recurrence of an old osteomyelitis, and cultures of the discharge grew a similar resistant staphylococcus I was becoming increasingly depressed by the prospects of having to give up surgery when one of my chiefs told me of a method of ridding oneself of this plague

The method is that after the usual 'scrubbing up" the hands are dried and the tips of the fingers dipped into a 1% solution of iodine in 70% spirit and the gloves put on Unless one is doing a series of short cases this treatment does not stain the fingers It is, however, rather hard on skin, and after a fortnight of this I found that the skin was beginning to desquamate The swabs taken from my hands no longer grew any *Staph aureus* and no more wounds have gone septic I therefore stopped the treatment, and since then have had no cause to return to it I was most grateful to the surgeon who suggested the course to me, and feel that his advice may prove useful to others

Norfolk and Norwich Hospital **N K CONNOLLY**

SIR—Does a surgical mask really retain all infective particles? A little work in a coal cellar has seemed to me to throw doubt on this

Wearing a surgical mask I riddled some slack in my coal cellar By the time the work was finished there was a haze of coal dust, and on emerging from the cellar I found that the mask round the area covering my nostrils was much smudged and on taking off the mask that my nostrils, my moustache in front of the nostrils, my nasal passages, and the mucus from the back of my pharynx were black with coal dust

If coal dust particles are not held back, can one expect the very much smaller microbic particles to be retained?

Eastbourne **T HUNTER**

MUNCHAUSEN'S SYNDROME

SIR,—Between two admissions to the Queen Elizabeth Hospital, 26 hospitals (including Dr Short's) seem to have lodged the resourceful guest described by Dr Short (March 17) Both admissions here were on account of blood in the urine, the second was after his return from France in August, 1950 Our travel stained file on this patient is at the moment with us

Queen Elizabeth Hospital
Birmingham **G H ARMITAGE**

SIR,—I was interested to read of Dr Short's patient, This man was admitted to Chester City Hospital in September 1950, having collapsed at Crewe Station

He again complained of renal colic type of pain and hæmaturia He developed bleeding from the ears and nose while in the ward He had acute stomatitis which he was reluctant to have treated and he would not allow anyone to catheterise him He discharged himself and was intending to go to Glasgow If he reached his destination he has apparently not attended the Western Infirmary again.

Another patient is a man, aged about 35, claiming to be an ex Commando

He presents as an acute abdominal emergency—usually a leaking perforated ulcer He claims to have been operated on in Carlisle and Inverness I first saw him at Liverpool Royal Infirmary in February 1950 where he was admitted After several days observation it was decided to excise a persistent sinus from a lower midline wound The patient was transferred to a convalescent home shortly after operation and readmitted to Liverpool Royal Infirmary about a week later as he was thought to have renal colic After two days treatment on fluids only the patient was discharged About the beginning of April, 1950 the patient was admitted to this hospital with a diagnosis of leaking perforation I was then a house physician here, and saw the patient being admitted He must have recognised me as he discharged himself an hour or two later before I had the opportunity to confront him

Royal Infirmary Chester **ROSEMARY J BOLAM**

SIR—The patient described by Dr Short was admitted to this hospital on Feb 19, 1951

He had been found collapsed in the street with bleeding from the ears On apparently recovering consciousness he complained of severe griping pain in the lower abdomen and gave a history of hæmaturia for two days In the course of the next few days he refused investigation and treatment, and he told a story of having had purpura

In England Now

A Running Commentary by Peripatetic Correspondents

MARCH SURGERY

When bicycles stand by the wall
And Mr Shepherd shows his nail
(Ingrowing toe-) and Mrs Small
Wants pills because she's feeling pale,
When cheek to cheek and jowl by jowl
The patients sit in rows and growl
" Me next, not you "—a merry note,
While Mr Jones describes his throat

When all around the rain doth pour
And coughing drowns the frequent plaint,
When gas is cut and what is more
The electric light is dim and faint,
With piles thrombosed and feeling foul
Small wonder that they sit and growl
" Me next not you "—a merry note
While Mr Jones describes his throat

* * *

In the war years we got used to things coming through the roof, they were part of the game Some were even more or less welcome—the rattle of our own flak on the rooftops, for instance—but some went too far, as when in Normandy some benevolent Teutons holidaying on the outskirts of Ranville persisted in knocking holes in the roof of my R A P Still, as I say, we got used to these things, so that by the time we took part in the airborne landings around Hamminkeln, on the far bank of the Rhine, we were fully prepared for the pannier of blankets which came through the tiled roof of the farmhouse in which the dressing station had been established The R A F supply drop was right on the target area, and the blankets were badly needed

After five years of so called peace one no longer expects things to come through the roof I was therefore unprepared for the incident of the other day I was down in a provincial cathedral town examining new entrants to the railway service All was going quietly I remember hearing footsteps overhead, which surprised me, for I had always understood that my room was on the top floor, but I did not stop to wonder what room actually was up there Anyway, footsteps they certainly were, and for a time there was a fair amount of coming and going overhead Suddenly there was a loud explosive noise followed by a tearing sound, whereupon the room was filled with thick clouds of dust and large pieces of plaster were strewn all over the place When the air cleared a little all that could be seen was one large black booted foot protruding through a hole in the ceiling It was an extraordinary sight, unique in the annals of our department We are used to looking at feet, but not with the boots on, and, like the house of Saxone, we examine *both* feet

For once in my life I managed to say the appropriate thing on the spur of the moment " That," I declared in a cool level voice, " is what the obstetricians call a foot presentation " But alas, my lay audience comprehended it not, and my words fell on heedless ears Apart from my brilliant but futile effort nobody said a word, the suddenness of the event stilled every tongue and above our heads silence reigned Strangely enough, there was not even a muffled voice, and more strangely still not even a muffled curse, to be heard—only the sound of falling plaster as the great booted foot waggled to and fro in an attempt to extricate itself from our ceiling Finally, scattering a parting shower of plaster and laths for good measure it disappeared into the heights of the roof, leaving a gaping ugly hole in the ceiling, an obvious exit wound with ragged everted edges

As we swept the plaster aside I noticed that the largest pieces were grouped in neat clusters round the chair from which I had risen a few seconds before the Black Foot appeared A few minutes later a startled sweep appeared and tendered his apologies While clearing soot from a chimney overhead he had missed the plank laid across the joists and had trodden heavily on the plaster My chief clerk remarked ' I've often had money on a horse, but that's the nearest I've been to getting anything from a sweep " But the highest mark went to Albert, our porter handyman, who came to tidy up the mess " And to think," said Albert, " that I recommended him "

* * *

I had a rewarding experience a week or two ago One of the men in my St John first aid class shook me vigorously by the hand and thanked me deeply for saving his wife's life I suppose I looked puzzled, for his wife was not a patient of mine, so he explained " You did it by proxy, doctor," he said, " and I was the proxy Last Saturday morning, when I was at home, she was suddenly struck down with acute pain " He described her signs and symptoms with an astonishing amount of clinical detail, and went on " I phoned our doctor but he was out on his rounds I remembered what you told us and decided she probably had either an internal hæmorrhage or an acute abdomen So I got on to the hospital, not saying who I was, and told them to get the theatre ready at once for an acute abdomen I rang off before they could ask too many questions, so I hoped they would think I was a real doctor Then my neighbour got out his car and we rushed the wife along They operated straight away and the house surgeon told me afterwards that she had a ruptured ectopic and bringing her in quickly undoubtedly saved her life "

One does not often get such dramatic evidence of the value of first aid lectures in peace-time During the war their importance was more obvious It seems a little giving up an evening every week to this job in general practice—you must expect to be called away in the middle of a lecture now and then—but the classes are so keen that you soon find yourself looking forward to the lectures

The main thing is to tell plenty of clinical stories be dramatic, and wring all you can out of your cases Don't just go over the book with the class—they can read the St John textbook for themselves, and it is very clearly written In the practical classes I always tell the victims who are being bandaged or splinted to imagine they are in Hollywood and put on a really convincing act as an injured person When they are having a fracture of the forearm put up, for example, they must not stick out their arm to make it easy to bandage If they can groan a bit and look alarmingly ill, so much the better Every first aid class loves a good drama

* * *

" NO CONSULTING HOURS
' IF YOU HAVE FLU TAKE 2 ASPIRINS AND GO TO BED

So read the notice posted on the plate over the usual " 9–10, 6–7, except Thursdays " Is this a pointer to the future by a man ahead of his time ? If, as many contend, there is no real need to see your patients at all, and they can be treated just as well by rule of thumb, why should the G P go traipsing round the houses—upstairs, downstairs, and in the patient s chamber ?

Slot-machine medicine may be just round the corner The *Mechanical G P* will have to be more complicated than those that used to sell you a bar of chocolate, milk or cream, or stamp out your name on a zinc strip—remember ? I visualise a row of buttons, like a cash-register, with a symptom or sign printed over each When you press *Headache,"* *Tired in the Morning,"* " *Too many Cocktails,"* and ' *Whites of the Eyes Yellow* ' there'll be a whirring noise and—Bob's your uncle !—out will come Form E C 10 bearing your (signed) prescription, a certificate for sickness benefit, a card of instructions on diet and general behaviour and a slip in triplicate stating your weight, height and diagnosis and your fortune—one for the Executive Council, one for the M O H, and a third for you as a souvenir

There will be an ingenious protective device for the Saturday night joker who tries to wreck the Auto doctor ' by pressing *Frequency of Micturition* and *Can't Pass my Water "* at the same time I mustn't reveal the details of this, but no joker will need a second lesson Every doctor starting in practice will receive a new machine with screws for fixing it to the front gate, in lieu of basic salary

But perhaps it won't be like this at all and consultations will be " By Television Only " Who knows

* * *

Aphorism of the Week

Children's orthopædics is becoming a staple industry

Letters to the Editor

INFECTION OF "CLEAN" SURGICAL WOUNDS

SIR,—The excellent article (March 17) by the late Mr Girdlestone and his colleagues states that "no good purpose is served by pasting fabric on the skin with mastic before making an incision   the mastic is one more material to sterilise and keep sterile" Admittedly, the convenient practice of making an incision through stockinet pasted on with 'Mastisol' has many defects The stockinet is not waterproof, it is in fact freely porous and if it becomes wet by perspiration or blood it should form a continuous medium for the passage of organisms from the skin to its surface Furthermore, the skin edges are exposed when the incision is made and they remain exposed during the operation But the practice has something to recommend it and faute de mieux it may, I suggest, be accepted

In the first place, the mastisol is not one more material to sterilise, but is in fact antiseptic and when it has set it forms a barrier between the skin and the surface of the stockinet If the stockinet remains dry as in moderately short operations under tourniquet the stockinet and mastisol form a barrier and lessen the chances of contact of hands needles, ligatures and sutures with skin, even though, because the skin edges are exposed, the barrier is only partial One should remain mindful of this defect

Skin towels are certainly no better as they are not waterproof and the method of fixing them damages the skin edges and may make holes in the towels themselves Instead of stockinet I have used oil silk sterile water proof strapping without the adhesive and 'Nylon' film in an effort to find a waterproof cover that could be used as stockinet is used but these materials do not adhere to and fit, the contours of the operation area as well as the stockinet and they are more likely to come unstuck during operation

With regard to the general draping of the operation field as distinct from the immediate vicinity of the wound it is surprising how varied is the insistence among different surgeons on waterproof draping Yet the practice of using towels without sterile mackintoshes under them over an area which becomes damp with blood and skin exudation cannot be justified as effective, for if the towel becomes damp there is a continuous medium between the skin and the surface of the towel.

Reference is made in the article to the storage of nylon in 1–60 phenol Though nylon is unharmed by any of the usual sterilising agents phenol is an exception, after a day in 1–60 phenol nylon breaks easily

Scunthorpe Lincolnshire DAVID F THOMAS

SIR,—The article by the late Mr Girdlestone and his colleagues recalled to my mind that I had been associated with a series of "clean" surgical cases which became infected

This occurred during the earlier part of last year Since I was concerned with all the cases either as surgeon or assistant I felt sure that I was to blame The wounds all became infected with a penicillin resistant strain of *Staphylococcus aureus* I had my throat swabbed and cultured with negative results but my hands persistently grew a similar strain My wife at this time was having a recurrence of an old osteomyelitis, and cultures of the discharge grew a similar resistant staphylococcus I was becoming increasingly depressed by the prospects of having to give up surgery when one of my chiefs told me of a method of ridding oneself of this plague

The method is that after the usual "scrubbing up" the hands are dried and the tips of the fingers dipped into a 1% solution of iodine in 70% spirit and the gloves put on Unless one is doing a series of short cases this treatment does not stain the fingers It is, however, rather hard on skin, and after a fortnight of this I found that the skin was beginning to desquamate The swabs taken from my hands no longer grew any *Staph aureus* and no more wounds have gone septic I therefore stopped the treatment and since then have had no cause to return to it I was most grateful to the surgeon who suggested the course to me and feel that his advice may prove useful to others

Norfolk and Norwich Hospital N K CONNOLLY

SIR,—Does a surgical mask really retain all infective particles ? A little work in a coal cellar has seemed to me to throw doubt on this

Wearing a surgical mask I riddled some slack in my coal cellar By the time the work was finished there was a haze of coal dust, and on emerging from the cellar I found that the mask round the area covering my nostrils was much smudged and on taking off the mask that my nostrils, my moustache in front of the nostrils, my nasal passages, and the mucus from the back of my pharynx were black with coal dust

If coal dust particles are not held back, can one expect the very much smaller microbic particles to be retained ?

Eastbourne T HUNTER

MUNCHAUSEN'S SYNDROME

SIR,—Between two admissions to the Queen Elizabeth Hospital, 26 hospitals (including Dr Short's) seem to have lodged the resourceful guest described by Dr Short (March 17) Both admissions here were on account of blood in the urine, the second was after his return from France in August, 1950 Our travel stained file on this patient is at the moment with us

Queen Elizabeth Hospital
Birmingham G H ARMITAGE.

SIR,—I was interested to read of Dr Short's patient, This man was admitted to Chester City Hospital in September 1950, having collapsed at Crewe Station

He again complained of renal colic type of pain, and hæmaturia. He developed bleeding from the ears and nose while in the ward. He had acute stomatitis which he was reluctant to have treated and he would not allow anyone to catheterise him He discharged himself and was intending to go to Glasgow If he reached his destination he has apparently not attended the Western Infirmary again

Another patient is a man aged about 35, claiming to be an ex Commando

He presents as an acute abdominal emergency—usually a leaking perforated ulcer He claims to have been operated on in Carlisle and Inverness I first saw him at Liverpool Royal Infirmary in February 1950 where he was admitted After several days observation it was decided to excise a persistent sinus from a lower midline wound The patient was transferred to a convalescent home shortly after operation, and readmitted to Liverpool Royal Infirmary about a week later as he was thought to have renal colic After two days treatment on fluids only the patient was discharged About the beginning of April 1950 the patient was admitted to this hospital with a diagnosis of leaking perforation I was then a house physician here, and saw the patient being admitted He must have recognised me as he discharged himself an hour or two later before I had the opportunity to confront him

Royal Infirmary Chester ROSEMARY J BOLAM

SIR,—The patient described by Dr Short was admitted to this hospital on Feb 19 1951

He had been found collapsed in the street with bleeding from the ears On apparently recovering consciousness he complained of severe griping pain in the lower abdomen and gave a history of hæmaturia for two days In the course of the next few days he refused investigation and treatment and he told a story of having had purpura

Telegrams to hospitals in Ireland which he mentioned revealed that at one of them, in 1947, he had been admitted under similar circumstances and discharged as a mental defective with self inflicted wounds They had apparently discovered that he added blood from his ears to the urine after it was passed He discharged himself, refusing to have treatment or to be cystoscoped

I warned other hospitals in the district, and I found that just before he came to Ramsgate he had been discharged from another hospital in Kent

General Hospital, Ramsgate P J COOK

SIR,—The patient described by Dr Short has undoubtedly been our guest recently

He was admitted on March 1, 1951, apparently bleeding from both ears, the nose, and the urinary tract, and he was complaining of pain resembling renal colic He told us, among other things, that he had been in hospital in Paris and at Maidstone After a few hours we suspected that he was malingering, but it was difficult to explain away a considerable amount of blood in the urine His locker and clothing were searched, but only a safety pin was found It seemed fairly certain that he transferred blood from his nose into the urine bottle while lying curled up in bed under the clothes with screens around him This he persisted in doing from time to time, and he would not allow the screens to be removed He gave evidence of some medical knowledge and incidentally helped to make his own bed very efficiently ! A suggested cystoscopy led to his demand for discharge The police were informed and took a statement, and then, signing a certificate to say that he was going out on his own responsibility, he left the hospital four days after admission

Lister Hospital
Hitchin, Hertfordshire A GREVILLE YOUNG

SIR,—I should like to report on one more case of Munchausen's syndrome I have now known the patient personally for nearly seven years The fact that he has a tuberculous chest lesion has enabled us to keep to some extent a record of his odyssey through the various hospitals I am, however, convinced that this record is far from complete

All who have dealt with him will no doubt remember him if we call him Robinson Crusoe He is single, 38 years old His occupation is given as capstan operator, kitchen help in a holiday camp, painter and decorator, or more often as lorry driver, but he never works

He was first referred to our chest clinic in 1940, after a presumably quiescent tuberculous lesion at the left apex had been found at Brompton Hospital He then gave a history of having collapsed in the street with chest pain on three occasions in 1935, and of having been admitted to local hospitals for short periods He attended the clinic very erratically

In March, 1947, he attended the Middlesex Hospital as an outpatient, complaining of symptoms suggestive of colitis He was admitted no cause for his complaints was found, and he landed eventually in the psychiatric department The psychiatrist gave the opinion that the patient was a pathological liar and a psychopath on whom any form of psychological treatment was wasted He was discharged in May, 1947

In August, 1947, he collapsed in the street with "stomach pain," and was admitted to Ashford Hospital He was discharged from there after three weeks but was advised to attend again at the chest clinic His left apical lesion had broken down The radiograph showed a cavity, and his sputum was positive He was most uncoöperative regarding treatment, but eventually we persuaded him to have a left phrenic crush as an outpatient in January 1948

In October, 1948, he presented himself at St George's Hospital with bloodstained underwear, giving a history of hæmaturia after having been kicked in the stomach and perineum in a street fight From this time he has kept to this kind of history with minor variations

In January, 1949, he was again admitted to Ashford Hospital with a history of hæmaturia after injury to the abdomen and lumbar region He was soon discharged and referred to the chest clinic His chest lesion had apparently become quiescent Tomograms showed no evidence of cavitation, and repeated sputum investigations were negative

In May, 1950, he was brought by car to Hill End Hospital, St Albans, complaining of hæmaturia after injury to the left lumbar region sustained whilst cranking a lorry

In June, 1950, he obtained admission to the Central Middlesex Hospital stating that he had brought up a mouthful of blood and passed blood with his urine after being hit by the door of a lorry

His latest exploit brought him into the Prince of Wales Hospital, Tottenham in January, 1951, again with a history of hæmaturia and hæmoptysis after a lorry accident He described himself as a lorry driver, and stated that he had received chest injuries during the war and had been a prisoner of war He first gave an address in Glasgow In view of his chest lesion, arrangements were made to have him transferred to the chest unit of a large general hospital in our clinic area He was most anxious not to be sent there, giving as the reason that we had 'killed all his family there " However he was persuaded to let himself be transferred, but asked to be discharged during my first ward round after his admission

I have no doubt that he will sooner or later reappear in other hospitals

Chest Clinic
Hounslow, Middlesex. R HELLER

INCOME-TAX ALLOWANCES

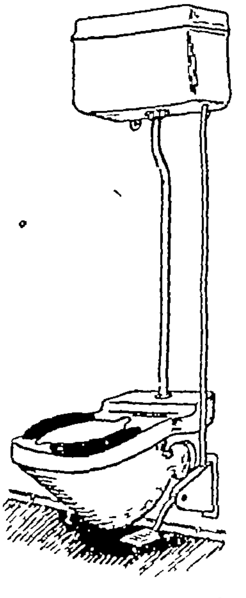
SIR,—Income tax allowances for subscriptions to journals and societies, and the purchase of textbooks, are awarded somewhat paradoxically General practitioners and part time specialists obtain this relief, in addition to numerous other benefits, from the Inland Revenue Full time employees of the N H S, mainly house officers and registrars, earning smaller salaries receive none of these allowances The Revenue authorities demand proof that the contracts of this group contain a clause requiring these subscriptions as a condition of employment This clause is not included in the usual contracts, and reasoning with the Inland Revenue is useless since they are allowed no scope for remedying such quirks

London, W 1 E M M BESTERMAN

PERSONAL HYGIENE AND SPREAD OF DISEASE

SIR,—I would like to endorse the views expressed by Dr Bourne (Jan 27) in relation to the spread of disease via closet impedimenta, and the lack of personal hygiene.

Foot operated lavatories have been in use in hospitals for many years and are a standard fitting of many sanitary fitting manufacturers Dr Bourne's adaptation of a hand pull closet to a foot-operated pattern is, however, open to criticism because wooden pedals, hinged to the floor, are used Firstly, wood, being an absorbent material, is liable to retain bacteria and will even permit organisms to grow and multiply, secondly, lavatory floors should be kept free from all obstruction, to facilitate efficient cleaning To this end I would recommend to all food factories the "Corbel type" pan, fitted with inserted pads instead of a seat, and foot operated cisterns fixed with a "Corbel hinge" into the wall



The greatest menace in most food factories is the lack of supervision of workers' personal hygiene, and the unnecessary handling of products I would recommend that all food-handlers should wear white coats Pegs should be provided for the reception of these coats near a wash-hand basin with hot and cold taps outside the w c, and no operator should be permitted to enter the lavatory without first removing his white coat The hands should be thoroughly washed and the nails scrubbed before touching the white coat again There is a grave danger that the soilings of carriers may be collected on white coats in fair concentration and taken into the factory, and therefore these coats should be treated with great care and not allowed outside the precincts of the factory building I have seen workers from food factories using their white coats as part of their normal dress, wearing them at home, shopping in them, and at break-time sitting on the ground or playing football in them

I think Dr Bourne has performed a most useful service in reminding us of the foot-operated lavatory flush

W A BULLOUGH

The Counties Public Health Laboratories
66 Victoria Street London S W 1

SIR,—Dr Bourne's admirable article (Jan 27) is a reminder of many unpleasant conditions He observes that the high seated European water closet is unsuitable for small children, and that in the primary schools the lavatories are apt to become very rapidly "a hygienist's nightmare" Without detracting in any way from the truth of what he says I would suggest that he consider seriously the merits of the Oriental (squatting) latrine It is easy for the newcomer to the tropics to condemn this utensil as insanitary, but it has no seat which can be fouled and it favours a more natural position for defæcation than the European type The small child could cope with it more readily, providing it avoided falling in, but the need for some degree of acrobatic skill is discouraging to the corpulent and the ancient

Similarly an unbiased comparison of the methods of anal cleansing deserves attention. The irritation of hæmorrhoids with dry sheets of paper admittedly defends the fingers to some extent, but the Oriental method of washing with plain water offers progressive dilution —perhaps to a point of bacteriological insignificance A method encountered occasionally in English country districts, where wads of cabbage leaves are suspended on a nail on the door of the earth closet, is cheap and soothing but presents some difficulty when cabbages are out of season

One mild criticism of the modifications to the water-closet suggested by Dr Bourne the two pedals on the floor offer great possibilities to small children and fractures of the lavatory pan might very well result from fibrillation of the seat I remember a practitioner returning from Germany in 1920 armed with a combined toilet roll holder and musical box After its installation his two small sons were evicted from the lavatory with some difficulty, leaving behind them a sea of paper The foot pedals could be almost as attractive

Abadan S Iran

I S STEWART
Pathologist,
Anglo Iranian Oil Company Ltd

THEORY OF CEREBRAL LOCALISATION

SIR,—How splendidly Dr Jefferson allies himself to other neurological giants, such as Hughlings Jackson and Sherrington, in your issue of March 17! His work on the pyramidal tract of the ferret (an animal conspicuously successful as an absolute localiser) well suits him to do so

How unhappily therefore does he use as his own ideas to belabour us, some of the points Mr McKissock and I specially made in our paper of March 3 For example, we stated (para 3) that Jackson did not believe in absolute localisation We have no disrespect for techniques obviously for are not clinical examination, hemispherectomy, and thinking techniques to be learnt? Also, we particularly cited Dr Walshe's arguments that the function of organs is positive, and not preventive.

A critic never appears at his best when he implies, despite his own complete silence on a subject, that he has known all about it for years If it is true, he should be ashamed at having kept so many of us deliberately in the dark If it is false, the least serious among us has no difficulty in detecting the peevish and unbecoming deception

The National Hospital,
Queen Square London W C 1

WILLIAM GOODDY

UNFAIR QUESTIONS

SIR,—If I may make so bold as to disagree with Sir John Conybeare, I do so only from my advantage of having sat the Finals much more recently than he

Sir John says (March 17) that he regards some questions asked in examinations as unfair I agree, but I think the example he selected—the surgical complications of typhoid—singularly inappropriate The majority of young doctors nowadays are required to join the Forces after qualifying, and they may be posted to countries where typhoid and other diseases seldom seen in this country are common I was posted to the Middle East, and it was not long before I was very sorry that I had not received more training in the prevention, diagnosis, and treatment of typhoid, malaria and dysentery and less in the identification of pathological curiosities, which is such a popular pursuit at teaching hospitals

If Sir John really thinks some questions are unfair or unusual, he should have been present at my Final examination

In my medicine oral I was asked to identify from a classical 100-year old collection of paintings a case of advanced generalised ichthyosis My clinical case was one of Boeck's sarcoid of lung, which I managed to diagnose correctly, to the astonishment of my examiners by virtue of having sneaked a preview of the radiologist's report which had been left by the patient's bed by mistake I have never seen a case of either of these conditions since qualifying but I have been concerned with many outbreaks of typhoid fever

In my surgery oral I was handed a number of instruments to identify Among these was something that looked very much like the starting handle of a car At my wits end to think of what the thing could be used for in clinical surgery, I blurted out "It's a car's starting handle" in order to gain some time "Quite right" said my tormentor without the slightest display of emotion, "an instrument, with which every doctor must be familiar" Among other instruments which I was asked to identify at this extraordinary session was a dinner fork. On seeing my look of amazement when handed this commonplace tool the examiner gave me a lengthy account of an operation he had once performed in Darkest Africa and in which a dinner fork had been an invaluable aid

After this nerve shattering interview I was ushered into the ward for the clinical oral After examining a patient suffering from some unheard-of condition, I saw the venerable and aged examiner approach His first question without any preamble was "Who was Sun Yat Sen?" My mouth dropped agape in utter bewilderment at this astonishing question in a frantic effort to correlate it with the case I had just seen I glanced furtively at the patient to see whether I had perhaps missed the fact that he was a Chinaman. But he was not I could only turn to the examiner, who was patiently awaiting an answer, and say "He was Chinese, Sir" This reply appeared to satisfy him, but I was completely demoralised for the rest of the interview.

My final ordeal in this nightmare of preposterous questions was when I was handed a jam jar containing a piece of something obviously grossly distorted by disease The specimen was so small however, that it could have been anything from a parathyroid gland to a piece of a big toe Taking a shot in the dark I said it was a testicular tumour I was wrong It was, *in fact* a breast biopsy

I am sure that my experiences are not unique, and that many other doctors must have similar tales to tell. But I have learned my lesson when the time comes for me to sit my membership I shall make sure that I have given close and detailed study to the highlights of modern Chinese history This, at least, should ensure a pass

London N 4 ADAIR GIRBY

P S —In fairness to the examiner concerned I should perhaps explain how Sun Yat Sen came into the picture at all Apparently somebody who invented some surgical instrument or other, the name of which I have long since forgotten, had befriended the good doctor when he qualified as the first graduate of medicine at the University of Hong Kong in 1891 The examination cannot be said to have been a total loss as I did at least learn this much

SIR,—Sir John Conybeare (March 17) takes exception to the question recently set in a paper for a higher qualification "Discuss the diagnosis *in a young woman* presenting herself with the complaint of double vision"

Russell Brain[1] states that, in this country, in disseminated sclerosis, females outnumber males by about 3 2 As disseminated sclerosis often presents with diplopia, the examiner may have had this in mind when the question was set

Royal Victoria Infirmary
Newcastle upon Tyne

J B HOLROYD
Medical Registrar

BREAST-FEEDING IN BRISTOL

SIR,—The survey by Dr Ross and Mr Herdan (March 17) is to be welcomed, but, while I agree that breast feeding is to be preferred for the majority of babies, I am not sure that this can be deduced from the histiogram depicting weight distribution at six months of age

We are not told the birth weight distribution in the two groups, which is surely an important factor in determining subsequent weight Any group of artificially fed babies must be weighted with babies of both low and high birth weight since these are more difficult to sustain at the breast The former are handicapped by some degree of weakness in suckling, and the latter more commonly need temporary or continued complementary feeds, the additional work involved being for many mothers a deterrent to breast feeding It seems reasonable to expect a greater variation in both birth and subsequent weights in the artificially fed group, and it would be extremely interesting to know if this is indeed the case

Stretford, Manchester J N DOBSON

MATERNITY AND THE ADMINISTRATOR

SIR,—Perhaps it is not realised what repercussions the policy of the London Local Medical Committee may have if their resolution is fully implemented

According to Dr Frank Gray,[2] secretary of this committee, its aim is to force a return to more domiciliary midwifery Many are agreed that given the right conditions there is much to be said in support of home delivery What are these conditions? They include sufficient housing accommodation, freedom from undue economic anxiety, and adequate domestic help From the purely obstetric angle what women in labour, in addition to a skilled midwife, should have immediately available are the full resources of a modern obstetric service, which should include a flying squad equipped to deal with the emergencies of labour An efficient service of this nature can only spring from a base hospital where problems affecting childbirth are constantly being examined

Dr Frank Gray says that "a considerable number of people would still be alive today if only beds could have been found for them in hospitals" It would be interesting to know the age of and the illness which killed these patients Few occupy a position of greater value to the community than the expectant mother, particularly if she already has a young family Merely to deny her a hospital bed whilst really satisfactory home conditions do not exist in many places, is to take away with both hands

There is still an appalling wastage of infant lives, which amounts to about 53,000 a year in England and Wales This figure includes stillbirths (21,000), neonatal (17,000), and infant deaths (15,000) Will these be reduced by the present trend of administrative policy? Medical and lay administrators, in view of the power now vested in them, need to consider deeply the consequences for the community as a whole of any policy they initiate

Obstetric Hospital University College
Hospital London W C 1

W C W NIXON

PILONIDAL SINUS IN A BARBER

SIR,—It seems worth while to record a fifth case of pilonidal sinus in a barber's hand Attention was drawn to this condition by Patey and Scarff,[1] who cited three examples, a further case was also recorded by Ewing

A married man, aged 40, who had been a barber for 25 years, attended the outpatient clinic at the Cardiff Royal Infirmary in August, 1950 He was seen by Mr A C Lysaght who has kindly given me permission to publish the case

The patient complained of a swelling of his right hand which had been present for 18 months About 6 years previously he had first begun to notice that hair clippings became fixed in the skin of the web between the index and middle fingers of his right hand These hairs would have to be removed by pulling them from a small punctum which had formed in this position 18 months before he was seen, he had become aware of a swelling "about the size of a pea" deep to the punctum This used to vary in size, but at that time he was not aware of any discharge from the punctum 5 months previously he had had acute inflammation of the area surrounding the swelling, this had yielded to conservative treatment For the past 3–4 months the swelling had steadily increased, and for 3 weeks before his admission to hospital in September, 1950, there had been a constant discharge of watery fluid from the punctum The patient had tuberculosis of the left hip at the age of 3 years, and as a result he walked with a limp He was otherwise healthy

In the web between the 2nd and 3rd fingers of his right hand there was a dimpled opening exactly like that of the ordinary postanal pilonidal sinus Deep to this was a discrete, spherical, mobile swelling, about 1 cm in diameter, which was not tender A little glairy discharge from the punctum was noted The opening would admit the blunt end of a straight cutting needle, and this passed easily for 5–6 mm, the end of the needle then appeared to be lying in the centre of the swelling

The sinus and the attached "cyst" were excised intact, and the wound sutured Healing did not take place by first intention but was complete in about 3 weeks The wound has remained firmly healed during the 5 months since then On cutting the swelling with a scalpel after removal, it was found to be solid with a central channel leading from the sinus opening There were dozens of hair clippings a few millimetres in length scattered throughout the solid material, and many lying loose in the central channel Microscopically, the lesion was an inflammatory granuloma Sectioned hairs were present in every field Unfortunately, the block was cut in such a way that the lining of the sinus was not identified with certainty It was clear to the naked eye that the mouth of the sinus was lined with epithelium, but how far this extended is uncertain

This appears to be the fifth recorded case of a hair bearing sinus in a barber's hand It differs from the four previously reported only in that the sinus was in the web between the 2nd and 3rd fingers Three of the previous cases were between the 3rd and 4th fingers, and the fourth was between the 4th and 5th fingers

There is no reason to doubt that in this case the lesion was caused by trauma to the skin by hairs, followed by penetration of the subcutaneous tissue by hairs In my view, these cases provide valuable evidence in support of a plausible alternative hypothesis to the unsatisfactory explanation of postanal pilonidal sinus as a congenital disorder

---

[1] Brain W R Diseases of the Nervous System London, 1947 p 503

[2] See *Lancet* March 10 1951 p 595

[1] Patey D H Scarff R W *Lancet* 1946 ii 181 *Ibid* 1948 ii 13

[2] Ewing M R *Ibid* 1947 i 427

D H JENKINS
Senior Surgical Registrar
Royal Infirmary Cardiff

WILL WE NEVER LEARN?

SIR,—I am grateful to Sir Heneage Ogilvie for emphasising, in his letter of March 3, the deductions to be drawn from my report (Jan 27) on the treatment of wounds in the Korean campaign As he says, the report was based upon the work of other surgeons It was not my intention to criticise their work I had no first hand experience of the difficulties they had to overcome At that time, U N Forces were penned into a small area around Pusan, and the degree of organisation was much less than it is now

It did seem important, however, to draw attention to mistakes in treatment which were being made War surgery is not a big branch of the surgical tree at the moment, but this may not always be the case I hoped that other surgeons might be taught to avoid making the same kind of mistakes

I was fully aware that there was nothing new in what I wrote As Mr Shepherd pointed out (March 17), the monograph by Professor Trueta on the treatment of war wounds gives the basic rules for this branch of surgery The disheartening thing is that these rules were discovered, or rather rediscovered, during the 1939–45 war, and it seems that the discovery may have to be made again It is also clear that antibiotic therapy can only be a valuable ancillary

With regard to Sir Heneage's mention of a "young naval surgeon," and of the secondary suture and skin grafting which I did on patients who were under my care for only 42 hours, I must point out (*a*) that he has made an assumption which is not as accurate as I should like, (*b*) that the wounds so treated had been properly managed in the first place, and that the patients concerned were in a base hospital within an hour of leaving this ship, so that, for all practical purposes, they were under continuous surgical supervision, and (*c*) that with a number of years of experience of the treatment of war wounds and the like, I feel I ought to be able to recognise by now a wound which may safely be closed

H M. Hospital Ship *Maine* R M LATTA

PERARTERIAL BLOOD-TRANSFUSION

SIR,—Mr Delorme's report (Feb 3) on his carefully controlled and convincing experiments with arterial perfusion of the liver of exsanguinated dogs, raises again a related question of practical importance It is now over ten years since Brigadier General S Seely first reported from the Walter Reed Hospital, Washington (where he is now chief of the surgical service), on the value of perarterial blood transfusion for patients in extremis from exsanguination

I have recently had the opportunity of hearing Brigadier General Seely discuss his experience of this method He reserves it for patients who are truly in extremis—that is, in the state of so called irreversible shock, when continued intravenous blood transfusion no longer produces a response or recordable blood pressure on the arterial side Some such patients, if then given a retrograde perarterial transfusion through any readily available peripheral artery such as the radial, show response and return of their blood pressure to readable levels They can by this means be rendered fit enough for surgical treatment to control a source of internal hæmorrhage Brigadier General Seely was quite clear that perarterial transfusions are best reserved for such cases of advanced or neglected internal hæmorrhage which have failed to respond to intravenous transfusion

The success of the method appears to depend upon Pascal's law, which states in effect that an increase in pressure in any part of a closed fluid system is transmitted unchanged to all parts of the fluid The arterial system is not a closed system, but is nearly enough so to act for a time as such If a bottle of blood is suspended 6 ft above the patient and connected to the arterial system by the radial artery, then the pressure at the point of the cannula is the equivalent of 120 mm Hg This pressure may be transmitted to all other parts of the arterial system, at least for a time The rate at which blood flows out of the transfusion bottle into the arterial system is an indication of the rate at which it is being lost at the site of the hæmorrhage Brigadier-General Seely believes that this fact may help in determining the relative priority for operation of two or more injured patients admitted in extremis The patient whose blood runs from the bottle most quickly into his artery is the one who is bleeding most rapidly and is most in need of surgery

Clearly the method is not without danger, especially to the viability of the hand It should be reserved for patients who have failed to respond to intravenous blood, when there are reasonable grounds to believe that a source of hæmorrhage controllable by surgery is the cause of their condition

Experience of this method at the Walter Reed Hospital is said to encourage the view that it may be possible to revise upward some of our conceptions of irreversibility, for a limited group of casualties Arterial transfusion certainly deserves a careful investigation here

London W 1 PATRICK CLARKSON

Parliament

QUESTION TIME

Admission to Hospital Refused

Mr SAMUEL STOREY asked the Minister of Health if he would now make his promised statement upon the circumstances preceding the death of Charles Walter, who was found dying outside a lonely hut in Urmston Meadows, to which he had been returned after being refused admission to Park Hospital, Davyhulme, because he was not sufficiently ill, and to a welfare hostel at Ancoats, because he was too ill to be admitted there —Mr H A MARQUAND replied Full inquiry has established that the failure in this case was due to an error of judgment in not admitting this man to hospital, and not to any lack of liaison between the health and welfare services I am satisfied that the regional hospital board concerned has taken the steps necessary to prevent any repetition of the occurrence

Mr STOREY Is the Minister aware that diagnosis in this case was made in the open air and in the ambulance? Will he see that such a thing does not happen again?—Mr MARQUAND I am glad to say that arrangements have been made to set aside special beds for this type of patient, and that instructions have been given that when they are to be admitted to hospital or sent to another hospital, accommodation must be certain to be there before the patient is sent away

Distribution of Doctors

In answer to questions Mr MARQUAND gave the following figures for the population and number of doctors resident in different areas

	Population	*Doctors*
Bath	77 040	40
Blackpool	149 000	65
Southend-on Sea	151 400	60
Salford	177,700	66
Oldham	119 500	43
Leicester	287 200	120
Eastbourne	58 040	38
Hastings	65 670	44
Sunderland	178,100	58
Southport	85 490	47
Leeds	509 400	238
Bournemouth	139 600	82
Brighton	157 000	65
Reading	115 470	64
Stoke-on Trent	275,700	94

Tuberculosis Benefits

Brigadier J G SMYTH asked the Minister of National Insurance what was the position of a general practitioner under the new Tuberculosis Benefits Scheme of March 1, 1951 —Dr EDITH SUMMERSKILL replied The new regulations, like the Industrial Injuries Act under which they are made, only apply to persons in insurable employment As general practitioners as such are not so employed the regulations will not apply to them

Supplies of Aureomycin

Sir THOMAS MOORE asked the Minister whether he was aware that there was a great shortage of 'Aureomycin' in this country to meet the requirements of the medical profession, and what steps he was taking to make good the deficiency —Mr MARQUAND replied A recent temporary shortage has now been overcome Deliveries of aureomycin in capsule form from the British factory are adequate to meet present needs

Dental Students

Sir HUGH LUCAS TOOTH asked the Minister what was the *annual intake of dental schools in the years 1946, 1947,* 1948, 1949, and 1950 respectively —Mr MARQUAND replied 641, 654, 662, 611, and 606 respectively Sir HUGH LUCAS TOOTH How long does the Minister think it will be before there is an adequate number of dentists in this country ?—Mr MARQUAND The recent decrease is explained by the fact that during the war there was a lowered intake and therefore in the first few years after the war it was possible to increase the entry It is now necessary to get a balance and the numbers have been slightly reduced I agree that the total intake is not satisfactory in the country as a whole

Cost of Supplementary Services

Sir HUGH LUCAS TOOTH asked the Minister of Health how the various fees included in the total amount of £43,048,000 which was payable to dentists during the financial year 1949–50 were divided between fees for extractions, provision of new dentures, dental examinations, and dental conservative treatment, respectively —Mr ARTHUR BLENKINSOP replied Full information in this detail is not available But, on the basis of a sample, it is estimated that the total cost may be divided as follows examinations 5%, extractions 6%, dentures 61%, conservative work 28%

Sir HUGH LUCAS TOOTH asked the Minister whether he would give details showing how the £22,725,000 payable during the financial year 1949–50 for the testing of sight and the supply of optical appliances was divided as between fees for sight testing, fees for dispensing optical appliances, and the cost of supplying optical appliances, respectively —Mr BLENKINSOP replied Fees for testing of sight accounted for £4,719,847 out of the total of £21,733,620 paid in the financial year 1949–50 Separate figures are not available for dispensing fees and cost of supplying appliances, the estimated apportionment is £8,800,000 and £8,200,000 respectively

Mortality Statistics

Replying to a question Mr MARQUAND stated that the average age at death in Great Britain in the years 1939 and 1945 was 59 and 60 respectively The provisional figure for 1949 was 64

X-ray Examination of Miners

In reply to a question Mr P J NOEL BAKER, Minister of Fuel and Power, stated that the National Joint Pneumoconiosis Committee *recently decided that an experimental* scheme for the periodic X ray examination of miners was required before any general plan could be drawn up The personnel, equipment and organisation of the experimental scheme were now under consideration In the meantime all miners who had been diagnosed as having pneumoconiosis, including many thousands who continued their work at the mines, were re-examined from time to time, 50,000 other miners had been examined by miniature radiography under the National Health Service

Dr CHARLES HILL Will the Minister consult the Minister of Health with a view to diverting some of the mass radiography facilities to this even more important work than that upon which it is normally engaged ? Mr NOEL BAKER The Ministry of Health are represented on the committee which deals with this matter There is some division of opinion among the experts on whether mass miniature radiography *does detect pneumoconiosis* in its early stages

Obituary

JOHN ALEXANDER NIXON

C M G , B A , M D Camb , F R C P

Dr J A Nixon, who died in Bristol on March 17 at the age of 76, was emeritus professor of medicine in the *University of Bristol* and consulting physician to the Bristol Royal Hospital and to Southmead Hospital

He was born in Edinburgh, the son of Robert Nixon, a freight broker of Bombay, and his mother was the daughter of a surgeon-major in the Madras Army He was educated at Hurstpierpoint, Caius College, Cambridge, and St Bartholomew's Hospital, where he formed a lifelong friendship with the late G E Gask His literary tastes developed early, and he was editor of the hospital journal, as well as president of the Abernethian Society He qualified in 1900, and after holding resident posts in London he went to Bristol in 1902 as senior resident officer at the Bristol Royal Infirmary Four years later he was elected to the staff as assistant physician, in 1908 he became full physician, and later professor of medicine in the University of Bristol He acted as dermatologist as well as physician at the Infirmary In 1911 he was elected F R C P

During the 1914–18 war with the rank of colonel he served in France, alongside his friend Gask, as medical consultant to the Fourth Army He was twice mentioned in despatches, and he was appointed C M G in 1919

Between the two wars he filled numerous and varied offices He was regional adviser to the Ministry of Health, a member of the Industrial Health Board, county director of the Bristol branch of the British Red Cross, and inspector of examinations for the General Medical Council, and he took an active interest in Brentry Institute, Stoke Park Colony, and Southmead Hospital. In its jubilee year he was president of the Bristol Medico-chirurgical Society, and it was characteristic of his wide interests that he chose as the subject of his presidential address the Debt of Medicine to the Fine Arts Members of a Hellenic cruise in 1939 will also remember his address on Greek athletics As Abernethian president he had proved himself a ready speaker, and ease in debate was the natural prelude to ease in journalism, and from 1926 to 1947 he was editor of the *Bristol Medico chirurgical Journal*

The port of Bristol stimulated his interest in naval medicine and the medical aspects of sea voyages His writings on these topics ranged from a spirited defence of Dr Dover against the charge of piracy to his more formal war-time FitzPatrick lectures to the Royal College of Physicians on Health and Sickness in the Merchant Navy He was early interested in nutritional disorders—he was one of the first workers in this country to use insulin—and with his wife he wrote a *Textbook of Nutrition* in 1938 In the thirties when the shortage of domestic workers in hospital was already beginning to be felt Nixon met the situation with sympathy and imagination Bristol ward maids were among the first in the country to become hospital orderlies, and a neat uniform and a badge further increased their self respect and prestige

When war broke out in 1939, although he was nearly 70 Nixon travelled up and down the country lecturing on civil defence and anti gas measures He was also regional adviser in medicine to the Emergency Medical Service

But medicine occupied only a part of his life He loved music—he had held a choral exhibition at Cambridge—and he was lately chairman of the Bristol Light Opera Company A zealous freemason he was past-master of St Vincent Lodge, and he held provincial grand lodge rank A friend after reading an obituary notice in a Bristol paper writes " It gives no inkling of the man himself, his bonhomie, and the good companion that he was. One never had a dull moment talking to John. It mentions his versatility but not his charm and his music and his pleasure in all things good and beautiful, which combined to make him the good friend he was to all of us. He was no self seeker nor trouble-maker, and it is true, and not mere platitude, to say that he leaves a gracious memory behind him."

He married Dr Doreen Walker in 1924, and he leaves her with a son and daughter. A memorial service was held in Bristol Cathedral on March 21.

GEORGE HASWELL WILSON

M.D. Birm., M.B. Glasg.

Prof. Haswell Wilson, who died on Feb. 28, had held the chair of pathology in the University of Birmingham for over 25 years.

The son of a Scots doctor, he qualified in 1906 at Glasgow University, where he was Coates memorial scholar, John Reid prizeman, and Carnegie research fellow. He represented his university at three sports, captained its rugby XV, and in 1908 represented Great Britain in the high jump at the Olympic Games. Throughout his life he retained a keen interest in the athletic side of university life, and he was for many years a vice-president of the Birmingham University Athletic Club, and one of the judges—a post of which he was secretly proud—at its annual sports.

After qualification he went into general practice for a short time, but his appointment to a lectureship in pathology at the University of Glasgow under Sir Robert Muir, introduced him to the scientific and academic career for which his interests and talents peculiarly fitted him. During the 1914–18 war he was medical superintendent of the Western Infirmary, Glasgow. He was appointed to the chair at Birmingham in 1922, and he held it till he retired in 1949. He was also pathologist to the United Birmingham Hospitals.

As a morbid histologist he was in the front rank of his profession; and his wide knowledge and experience of both theory and practice, and the strong sense of duty and responsibility that he brought to his work, made his verdicts in the post-mortem room and the laboratory of great value to his clinical colleagues, his staff and his students. Possessed of a remarkable manual dexterity, his post-mortem technique was beautiful to watch in its accuracy, rapidity, and tidiness, and he took a justifiable pride in its performance. Such was the innate gentleness of his nature, however, that, while he never shrank from any professional duty in the post-mortem room, he always paid, and exacted from his colleagues, a due reverence for the dead. Some of the pathological investigations that he undertook for the coroner of the City of Birmingham were brilliant in their clear and simple solution of problems that appeared to be intricate and obscure, and it is much to be regretted that his disablement prevented him from preparing some of them for publication in his retirement. But though he published little in his own name, many of the publications by the members of his staff were the direct result of his encouragement. He was always willing and eager to help any member of his staff, not only in their academic and professional work, but also with their personal difficulties and private troubles and his advice was always valuable and his judgment sound.

In his professional work, however, he was happiest when he was teaching his students, or when he had gathered two or three members of his staff around him to expound some difficult matter in histological or microscopical technique, of which he was a master. His lectures, to the preparation of which he gave much time and care, and which he kept up to date by constant revision, were lucid in presentation and masterly in exposition. They were generally illustrated with some of the superb lantern slides that he made himself from the excellent photomicrographs he took on the apparatus that he built, 28 years ago, from scrap material that he found in the department. His manual skill as a worker in wood and metal was outstanding, and the optical bench which he also built out of scrap materials is in constant use in the department today, and is still enabling workers to produce photomicrographs the equal of any produced by the other medical schools of this country. He had a remarkably efficient workshop splendidly equipped, in his own house, where he spent many happy hours of his leisure, devising and making things for the department or for members of his staff. I have a miniature optical bench, designed to take photomicrographs at magnifications of from 2 to 40 diameters, which he made for me—again out of scrap materials—and which will stand comparison with the product of any of the firms who manufacture microscopical equipment.

I could write much more about his love for children and his joy in the company of his own grandchildren; of his gentleness towards the sick in mind and body; of his love of nature and his wide and intimate knowledge of natural history; of his proficiency in fly-fishing; of his sure eye for a picture and his mastery of photographic technique; of his kindly and infectious humour; but it must suffice to say that he was the fortunate possessor of many talents, a connoisseur of several arts, and an able exponent of more than one science. Above all, he was a man of high principles, who was fearless in the discharge of what he considered to be his duty, but who respected the beliefs and honest opinions of others—a man who never attempted to dictate, and who scorned to evade. To me, who knew him so well, and who owe him so much, he has left an indelible memory of the gracious and kindly figure of one who, in success and in sorrow, in health and in the illness that marred the last three years of his life, fought always till, as Bunyan's character said: 'My sword did cleave to my hand; and when they were joined together, as if a sword grew out of my arm, and when the blood ran through my fingers, then I fought with most courage.'

J. F. D. S.

DAVID WHYTE

M.B. N.Z., F.R.C.S., F.R.A.C.S.

Mr David Whyte, who died in Wellington on Dec. 29 at the age of 61, was the son of the Rev. Alexander Whyte, a pioneer of Presbyterian Church Schools in New Zealand. He graduated at Otago University in 1912, and after serving as a resident in Dunedin Hospital he came to England where he joined the R.A.M.C. in 1914, serving in France and on the North-west Frontier of India.

After demobilisation he took the F.R.C.S. in 1922, and held an appointment as house-surgeon at the Royal Cancer Hospital in London before he returned to New Zealand, to settle in practice as a surgeon in Wellington. For 25 years he was a member of the staff of the Wellington Hospital, becoming a senior surgeon in 1940. He also gave freely of his time to postgraduate teaching at the hospital, and to the cancer work of the Royal Australasian College of Surgeons, and for some years he was assistant editor of the *New Zealand Medical Journal*.

A colleague writes: "David Whyte was industrious and devoted to his practice and the welfare of his patients. Well up in surgical literature, he showed courage and insight in developing new fields, particularly in abdominal and œsophageal surgery. His charm of manner endeared him to patients, nurses, and colleagues, and everywhere he inspired great confidence."

RICHARD IRVINE POSTON

T.D., M.D. Belf.

Colonel Richard Poston, who died in Manchester on March 16 at the age of 54, was born in Belfast, and was a graduate of Queen's University; but all his professional life was spent in the Oldham district where he settled, at Failsworth, shortly after he qualified in 1922. From 1927 till 1938 he acted as surgeon to the Oldham Royal Infirmary and the Boundary Park Municipal Hospital.

During the first world war he served as a captain in the Royal Garrison Artillery, and he was wounded in Belgium in 1917. After qualifying he joined the Territorial Army and became battalion medical officer to the 9th Manchester Regiment, later transferring to the 125th Field Ambulance which in the second world war he commanded and took to France. After the evacuation at Dunkirk he took over the command of the 1st Casualty Clearing Station, and in 1942 he formed the 97th General Hospital which he took to North Africa. At the end of the North African campaign Colonel Poston commanded the 69th General Hospital in Italy He was invalided from the Army in October, 1944, because of a fractured leg On his retirement from active military service he became honorary colonel of the 7th (Western) General Hospital and of the 12th (Western) C C S.

For 27 years Poston played an active part in the affairs of the Order of St John of Jerusalem, of which he was an officer, and he served as a member of the the council for the County Palatine of Lancaster At the time of his death he was assistant commissioner (no 4 area), St John Ambulance Brigade, Manchester He was also a member of the Oldham and District hospital management committee and president of the local branch of the British Legion

His widow, Dr Margaret Poston, is an anæsthetist, and his son is a medical student at St Andrews University

Diary of the Week

APRIL 1 TO 7

Monday, 2nd

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture-demonstration

Tuesday, 3rd

Royal College of Surgeons, Lincoln's Inn Fields W C 2
5 P M Mr R P Jepson Raynaud s Phenomenon (Hunterian lecture)
Institute of Ophthalmology, Judd Street W C 1
5 30 P M. Mr T K Lyle Diagnosis and Treatment of Ocular Palsies in Cases of Exophthalmic Ophthalmoplegia.

Wednesday, 4th

Royal College of Surgeons
3 45 P M Mr P H Mitchiner Tubercle of Bone (Erasmus Wilson demonstration)
Royal Institute of Public Health and Hygiene 28 Portland Place W 1
3 30 P M Dr C H Andrewes, F R S The Common Cold
Yorkshire Society of Anæsthetists
8 P.M (General Infirmary, Leeds) Dr. John Gillies American Journey
University of Glasgow
8 P M. (Department of Ophthalmology) Dr T A S Boyd Ascorbic Acid and Corneal Lesions

Thursday, 5th

Society for Endocrinology
5 30 P M (1 Wimpole Street W 1) Prof J S L Browne (Montreal) Studies in A C T H and Cortisone in Disease
Institute of Ophthalmology
5 30 P M Mr E Wolff Pathology of Fat

Friday, 6th

Royal College of Surgeons
5 P M Mr F J F Barrington Diagnosis of Stone in the Urinary Tract
Institute of Ophthalmology
5 30 P.M Dr S Behrman Ophthalmological Aspects of Disseminated Sclerosis and Allied Diseases
Biochemical Society
2 P M (Department of Physiology, University of Bristol, Bristol 8) Scientific papers

Births, Marriages, and Deaths

BIRTHS

Clark —On March 21 at Bromley Kent the wife of Dr David H Clark—a daughter

Dunn —On March 19 the wife of Dr D M Dunn M B E —a son

Halle —On Feb 20 in Sheffield Dr Frances Halle (née Saunders) wife of Dr Hugh Halle—a son

Harris —On March 21 in London the wife of Dr Nigel H Harris —a son

Macdonald —On March 12 in London, the wife of Dr G G Macdonald—a son

Playfair.—On March 21, at Cambridge, the wife of Dr A S Playfair—a daughter

MARRIAGES

Brown—Waterfall —On March 17 in London, Alastair Kingsley Brown M.B E M B to Joan Margaret Waterfall M B

DEATHS

Bowring —On March 15, Walter Andrew Bowring F R C.S aged 89

Cromie —On March 15 at Surbiton, Surrey Mortimer John Cromie M R C.S lieut -colonel R A.M C retd aged 70

Dalgliesh —On March 11 William Dalgliesh M.B Aberd , aged 70

Gibson —On March 20 at Aldershot John Hutchinson Gibson, M R C.S aged 92

Hirst —On March 18 at Bristol Geoffrey Greatrix Hirst M.R C.S lieut -colonel I.M S retd aged 72

Jack.—On March 14, at Aberdeen William James Jack M.B Aberd , aged 54

Nixon —On March 17 John Alexander Nixon C M G M.D Camb , F R C P

Poston —On March 16 Richard Irvine Poston T D M D Belf of Failsworth Manchester husband of Margaret M Poston, M.B

Notes and News

HEALTH SERVICE ESTIMATES

The estimates of the cost of the National Health Service in 1951–52, published this week,[1] show a gross increase of £4,108,400 on the cost in 1950–51 for England, Wales, and Scotland the gross cost is put at £469,127,700, compared with £465,019,300 in 1950–51 Appropriations in aid during the coming financial year are estimated at £71,044,700, compared with £72,079,390 in the present year In England and Wales, the gross cost is expected to increase by £4,022,400 to £417,284,700 The cost of hospital, specialist, and ancillary services in England and Wales is expected to rise by £13,497,900 to £251,479,900 The principal reductions are in the general dental services, whose cost is expected to fall by £5,775,000 to £35,790,000 , and in the supplementary ophthalmic services, whose cost is put at £17,560,000, compared with £25,665,000 in 1950–51 The estimate for general medical services—£42,900,000—is £166,000 higher than in the present year

COST OF ANTIBIOTICS

The expense involved when a new antibiotic is released for use in general practice is illustrated by the figures for chloramphenicol (' Chloromycetin ') In the seven weeks from its release on Dec 9, 1950, to Jan 31, 1951, the chloramphenicol dispensed by retail pharmacists for National Health Service patients amounted to £300,000 , and dispensing, containers, &c , added a further £50,000, making a total of £350,000 The influenza epidemic was causing a big increase in prescriptions at this time, so the period cannot be considered a fair sample Nevertheless, for that period, the chloramphenicol prescribed in fact raised the average cost of all N H S prescriptions by about 2*d* The antibiotic is packed in vials of 12 capsules at a net cost of 50*s* a vial The average amount ordered on a prescription probably lies between two and three vials, so the average net cost per prescription is from £5 to £7 10*s* or, with the pharmacist's dispensing and other charges included, from nearly £6 to £8 15*s*

THE NEW STUDENT

We are so often told that we live in an age of hustle, where there is little time for old world courtesy, that it is a relief to find new customs being started with the kindly intention of putting people at their ease For instance, new patients today are often offered a helpful leaflet introducing them to their hospital Now Birmingham, in a booklet entitled *Introduction to a University*, has tried to give sixth forms some general ideas of what university education means and of the careers which are open to graduates Later sections describe undergraduate life at Birmingham, and give the qualifications required for admission and details of prospects in the different professions Competition for entry to the medical school is noted as exceptionally keen The annual intake of medical students is 100, and 25 of the places are reserved for women

The University of Edinburgh has adopted a different method of introduction, and last year for the first time held a conference for " freshers " during the weekend before the opening of the autumn term The conference, which was organised by the Students' Representative Council, included lectures on the history and administration of the university, conducted tours to the different departments, a concert, and a dance

A LIST OF SERIAL PUBLICATIONS

A *British Union Catalogue of Periodicals* has been proposed and is being compiled, but may take some time to complete Meanwhile the Harveian librarian of the Royal College of Physicians has thought it useful to prepare a list of the serial publications in the college library, and this is now available The term " periodical " has been interpreted literally, and the list contains such things as yearbooks as well as journals Since the college library specialises in the history of medicine, a relatively large proportion of the periodicals listed bear on this subject Belonging as they do to a reference library the periodicals are not available for loan except to other libraries, and for use by readers in the reference department , but 'Photostat copies of articles can be made

---

[1] Civil Estimates for the year ending March 31 1952 Class V Local government and Planning Housing Labour and National Insurance H M Stationery Office Pp 174 1*s*

PROVISION FOR ILLNESS

Many people still prefer to have private medical and nursing attention during serious illness, and it was for such people that the British United Provident Association—a non profit making organisation—was formed in 1947 By paying an annual subscription, which varies according to the benefits desired, members are assured of a grant towards medical and nursing expenses incurred by themselves or their dependents

Under the presidency of Lord Nuffield the association (61, Bartholomew Close London, E C 1) has become a financially sound and useful organisation, and in their annual report for the year ended last June the board of governors announce an increase in the number of new members

---

University of London

The following have been recognised as teachers in the faculty of medicine

Simon Behrman medicine J D M Cardell, R C Davenport C L Gimblett A G Leigh P McG Moffat, A Seymour Philps, F T Ridley, and Eugene Wolff ophthalmology all at the Institute of Ophthalmology, Chapple Gill-Carey, G H. Howells otorhinolaryngology Institute of Laryngology and Otology C P Blacker mental diseases, Institute of Psychiatry William Gunn medicine Royal Free J. N Hunt physiology Guy's R W Raven surgery J H. Wilkinson, pathology Westminster W W Sargant mental diseases St Thomas's R. W Wilson pathology St Mary's, O L C Sibley anæsthetics Royal Dental

University of Dublin

At a recent examination for the diploma in gynæcology and *obstetrics the following were sucessful*

F A Akerele L R Ashley, Wadie Amin Guindi Bishai, Russell Brown D C J Carter A J R Clarke Madanmohan Debnath J P M Droulers, W H D Fairbank Sami Wassef Ghali, Shaukat Haroon, Salah el Din Hussein Issa, Soosainathan Lourdenadin, P C McAuliffe M B Millerick G E Peters Aron Press Albert Schutz Anish Ranjan Sen Somasundrum Thuraíretnam

Dr J H. Burn, F.R.S, professor of pharmacology in the University of Oxford, has been appointed John Mallet Purser lecturer for 1951 It is hoped that he will deliver the lecture in Trinity College, Dublin, on Wednesday, May 9 He is to speak on the Importance of Noradrenaline

University of Leeds

Dr M J Parsonage, who is assistant physician to the United Leeds Hospitals, has been appointed clinical lecturer in the department of neurology

The council of the university have recommended the institution of a part time course leading to the award of the diploma in public health.

Royal College of Physicians of Ireland

On March 16, the following, having passed the final examination of the Conjoint Board in Ireland, were admitted licentiates in medicine and midwifery

D B Barnett P B Carvill W F Clifford J L Davidson Emanuel Fischer J C Grogan P D McCarthy E S McDaniel Philip McGovern Dympna MacNamara Margaret M J O Dea Ignatius Ryan Dennis White

Royal Army Medical Corps Funds

The annual general meeting will be held at 11, Chandos Street, London, W 1, on Monday, April 9, at 5 P.M, when the following resolution will be considered

> That the administration of the Auxiliary Royal Army Medical Corps Funds be handed over to the Royal Army Medical Corps Fund to be administered in accordance with the Trust Deed of 1916 and objects of the 1939 Fund representation of the interests concerned being secured on the appropriate central committee.

National Coal Board

Dr John Rogan has been appointed chief medical officer in succession to Dr E H Capel, who has resigned

Dr Rogan who is 37 was born in Glasgow He graduated in medicine at Edinburgh University in 1935 and after holding junior hospital appointments was appointed tutor in clinical medicine at Edinburgh Royal Infirmary in 1937 In 1939 he took his M D During the war Dr Rogan served in the R.A.M.C, with the rank of lieut.-colonel as medical specialist to the Malaya Command and as officer in charge of the medical division of general hospitals in the Far East Later he was responsible for clinical research on malaria in the India Command After demobilisation he became senior medical officer with the Austin Motor Company then lecturer in industrial medicine at Glasgow University At present he is head of the environmental medicine section at the headquarters of the Medical Research Council. He became F.R.C.P.E. in 1947

Institute of Psychiatry

Dr Erik Essen-Möller, professor of psychiatry in the University of Lund, will deliver two lectures at the Maudsley Hospital, Denmark Hill, London, S.E 5, at 2 P.M on Friday, April 6, and at 3 P.M on Monday, April 9 He will speak on Recent Swedish Studies in Mental Health

On Thursday, May 31 at 3 P.M, at the Maudsley Hospital, Denmark Hill, London, S.E 5, Dr Jacques Le Beau is to lecture on Neurosurgical Difficulties in Performing Limited Prefrontal Operations

Birmingham and Midland Obstetrical and Gynæcological Society

The following office bearers have been elected president Prof J Chassar Moir, vice presidents, Mr H J Malkin and Mr S W Maslen-Jones, treasurer, Mr Samuel Davidson, secretary, Prof H C McLaren, members of council, Mr H. R Duval, Mr William Hawksworth, Mr L M Park, and Mr A. Wentworth Taylor

Army Dental Service

Colonel John Wren, B.D S late Royal Army Dental Corps, has been appointed director of the Army Dental Service in succession to the late Major General H J. Higgins

British Association

This year the annual meeting of the association will be held in Edinburgh from Aug 8 to 15 under the presidency of the Duke of Edinburgh

Congress of Catholic Doctors

The fifth International Congress of Catholic Doctors will be held in Paris from July 6 to 9 The offices of the congress are at 120, rue du Cherche-Midi, Paris, VI

Medical Art Society

On Monday, April 2, at 6 15 P.M, the society will hold their annual general meeting and dinner at Kettner's Restaurant, London, W 1 There will also be a private view of the annual exhibition at Walker's Galleries, New Bond Street, W 1 The exhibition will be open to the public from April 2 to 14

Transfer of a Hampshire Hospital

Queen Alexandra Hospital, Cosham, is to be transferred on April 1 from the Ministry of Pensions to the Ministry of Health, and will be incorporated in the Portsmouth Hospital Management Committee group This group already includes fifteen hospitals, and the committee also manages the Portsmouth and Isle of Wight Area Pathological Service No beds are closed because of lack of nursing staff

Higher Pay for Hospital Workers

The National Arbitration Tribunal have awarded increases in pay (8s a week for men and 6s a week for women) to domestic workers in hospitals and allied institutions and local authority residential establishments Porters, ward maids, orderlies, cleaners, and laundry and kitchen staff will all receive the increase About 120,000 whole time and 33 300 part time employees under the National Health Service, and 20,000 whole time and 5000 part time employees of local authorities, will be affected.

Salaries of Local-authority Dentists

The Dental Whitley Council (Local Authorities) have agreed on salaries and conditions of service for whole time dental officers employed by local authorities in Great Britain. These new scales, which are to operate from Oct 1, 1950, are as follows

Dental Officers—£500 per annum rising by annual increments of £50 to a maximum of £1250 per annum the employing authority having discretion to allow one increment for each year of experience in practice up to a maximum of five years

Chief Dental Officer—This range of salaries is governed by the population of the area served

Population not exceeding	*Salary Scales* (£)
100 000	1250 rising by one increment of 50 to a maximum of 1300
150 000	1250–50–1350
250 000	1250–50–1400
400 000	1250–50–1450
600 000	1250–50–1500
Over 600 000	At discretion

Ministry of Health

Sir Selwyn Selwyn Clarke has been appointed a principal medical officer of the Ministry He has lately retired from the governorship of the Seychelles, and during the late war he was director of medical services at Hong Kong

Position of the Doctor in Time of War

A meeting of members of the medical and legal professions is to be held to discuss this subject on Wednesday, April 25, at the Centre Universitaire Méditerranéen, Nice Further information may be had from the Institut d'Études Juridiques, Avenue Saint-Laurent, Nice, France

Faculty of Anæsthetists

Mr A D Marston has been re elected dean and Dr Frankis Evans vice dean of the faculty Mr Marston, Dr Ronald Woolmer, and Dr E W Rowbotham have been re elected to represent the fellows, and Dr S A Mason has been elected to represent the members, on the board of the faculty

Vellore Christian Medical College

A concert in aid of the Vellore college and hospital in South India is to be given in the Albert Hall at 7 30 P M , on Monday, April, 16, by the London Philharmonic Orchestra, conducted by Sir Adrian Boult, with Miss Eileen Joyce as the pianist Tickets can be obtained from the "Friends of Vellore," Annandale, North End Road, London, N W 11

Calling the Doctor

London local medical committee has expressed its concern at the increasing number of requests for visits received needlessly late in the day, thus preventing doctors from arranging their work to the best advantage Reporting to London Executive Council on March 22, the medical benefit committee observed that a patient who wishes his doctor to visit him is expected, if at all possible, to notify the practitioner before 10 A M The committee suggests that this requirement, which is already stated on all medical cards, should be widely publicised

Western Union Public-health Committee

At a meeting in Marseilles on March 20–22 the Brussels Treaty Public health Committee continued its study of the protection of the civil population's health in time of war and drew up a programme of work for the coming months The committee reviewed the programme of exchanges of medical and paramedical personnel of the five countries, which in 1950 enabled some forty doctors to travel in Western Union countries in order to study the general administrative structure of public health services Other subjects discussed included the standardisation of methods of control of food stuffs and proprietary medicines Finally, the committee took note of the entry into operation within the five Western Union countries of a uniform system of health control for sea traffic These measures complete the committee's work in this sphere since a similar organisation for the control of air traffic has already been established (see *Lancet*, 1950, i, 131)

Diets for Invalids

A new edition has been published of the Ministry of Food's memorandum for doctors setting out the arrangements for granting special rations and priority allowances of food The revised memorandum, which is known as Med 2 (1950), replaces Med 2 (Revised 1948) Doctors can obtain copies from their local food offices Newly qualified doctors will be sent copies as their names are added to the Medical Register

The Minister of Food announces that, on the recommendation of the Food Rationing (Special Diets) Advisory Committee of the Medical Research Council, patients suffering from nephritis with gross œdema and albuminuria or from hypoproteinæmia are to be allowed six extra meat rations a week instead of four Patients under 5 years will now be allowed the same amount of meat as adult patients No increases have been recommended in the extra allowances of meat granted to patients suffering from diabetes mellitus hepatitis (acute infective or chronic), or steatorrhœa Patients with hypertension who are being treated with the Kempner rice diet may now be allowed three extra rations of sugar a week on cancellation of their bacon, cheese, and fat rations

National Marriage Guidance Council

The council have chosen Education for Marriage and Family Life as the theme of their fifth annual conference, which is to be held at Harrogate Hydro from May 17 to 21 Further particulars may be had from the secretary of the council, 78, Duke Street, London, W 1

Wessex Rahere Club

The spring dinner of this club will be held at the Royal Clarence Hotel, Exeter, at 7 30 P M , on Saturday, April 21 Prof L P Garrod will be guest of honour Membership of the club is open to old Barts men resident in the west country The secretary is Mr A Daunt Bateman, 3, The Circus, Bath

Manx Hospital Extensions

The foundation stone of a new nurses' home at Noble's Hospital, Douglas, Isle of Man, was laid by Air Vice Marshal Sir Geoffrey Bromet, the lieutenant-governor of the island, on March 15 The home is to cost £157,000, and will have accommodation for 138 sisters and nurses

Plans were also on view at the hospital of a new children's wing, which will take 50 children in small wards of not more than four beds each The Cubbon wing, provided by members of the Cubbon family at a cost of £41,000, is expected to be ready in July or August It will provide 30 beds for convalescents The hospital has a waiting list of 300, of which 50 are children

---

Prof John McMichael and Prof C Lovatt Evans, F R S , are visiting Madrid and Barcelona, under the auspices of the British Council, to advise on medical education in Spain

Appointments

Brown, M M M B Camb , F R C S asst thoracic surgeon, Godalming Milford, and Liphook group of sanatoria

Gilmour S J G , M.D Belf , D P.M. second consultant psychiatrist Tyrone and Fermanagh Hospital Armagh

Henderson Stanley, M B Lpool F R C S E., M R C.O G consultant obstetrician and gynæcologist Macclesfield area

Leahy, M R , M B N U I , D P M consultant psychiatrist St. James s Hospital, Leeds

Lewis Delfun M R.C S D.P M psychiatrist and deputy medical superintendent Barnsley Hall, Bromsgrove, Worcs

Reid, Frank, M D Leeds, D M R D consultant radiologist Harrogate and Ripon hospital groups

Rogers A C M R C S , D M R D consultant radiologist, Hull A and B and East Riding hospital groups

Sharkey James M B Lond M R.C.P consultant physician Burton on Trent group of hospitals

Simons E L M B Camb consultant in pathology Goole Howden Selby, Pontefract, and Castleford hospital groups

Stanley, R J , M B. Lond , D P H psychiatrist and deputy medical superintendent, Birmingham (mental D) group

Sweetnam W P M D Manc , M R C P , D P H , D C H consultant pædiatrician Huddersfield and Halifax hospital groups

Teunon G J M M B Aberd asst radiologist, Blackburn area, Lancs

Hospital for Sick Children, Great Ormond St , London

Asst Medical Registrars (Registrar Grade)

Cox P J N B M Oxfd M R C P , D C H

Garrow, D H , B M Oxfd M R C P

Luder, Joseph M D Lond M R.C.P D C H

Welch R G M D Lond M R C.P

Surgical Registrars (Senior Registrar Grade)

Rose I F M B.E M.A B.M. Oxfd F R.C S

Rowntree, T W , M.B Camb , F R C S

Appointed Factory Doctor:

Craig David M R.C.S Egham District Surrey

Colonial Service

Christianson Edward M D Edin M O North Borneo

Foster H C M A , M.D Toronto D T M & H senior M O Tanganyika

Harland R D M R C.S M O Kenya

Hutchison A F M B Durh M O Tanganyika

Laxton G K , M B Leeds M O Kenya

Merson G P M B Aberd senior M O Tanganyika

O Hare H I L.R C P I M O Tanganyika

Reid J D M.B. Edin D P H , D T M & H D C P senior pathologist Sierra Leone

Rosenwald C D M B Lpool D.P H M O Kenya

Stevenson A J M., M R.C.S M O Nigeria

Trepiak Zygmunt Med Dip Warsaw district M.O (temporary) Windward Islands

FADS AND FANCIES
THIRTY YEARS OF TUBERCULOSIS*

CHARLES CAMERON
M.A, M.D Glasg, F.R C.P.E, F R.F.P S, D.P H
PROFESSOR OF TUBERCULOSIS IN THE UNIVERSITY OF EDINBURGH

IT is salutary to look back in Medicine Its path is strewn with discarded theories and treatments which held the field for short and credulous periods, and when some are thrown up again by the whirligig of time, a knowledge of the part which they have played in the evolution of our ideas is always helpful It is often chastening When orthodox medicine fails, unorthodox methods appear, and that is easy enough to understand. What we often do not recognise is the frequency with which ill founded theories become accepted by the orthodox, and how ideas of slender foundation may dominate for a time a whole branch of medicine The fact that ideas or treatments have been discarded does not mean that they were ill founded or completely without results. They may have been followed by better ideas or treatments Sometimes they are unjustly displaced, and in the process much that was good becomes forgotten Today I wish to look back on thirty years of tuberculosis and on the changes which have taken place in that time

REST

In these remote days little of a specific nature could be done for the disease—I speak now of pulmonary tuberculosis—and indirect methods of treatment were exploited until they became a ritual. The days of unlimited exercise were passing The era of rest had dawned, and rest in these days meant what the word implied Today the jargon of "strict bed" has as much meaning as the slang of its expression Then absolute rest meant rest on the back without a pillow, and a vegetative existence which was prolonged until all clinical evidence pointed to a slowing down of the disease process, with healing and repair We know that this rest did not close huge cavities, but many a patient survived for years with cavities rendered quiescent, and many a very ill patient reached a stage of stabilisation of his disease There were theories at the time just as there are theories today, but the theories of today rest on better foundations and are worthy of careful thought by those who have not given any consideration to them The needle and the operation play a necesssary part in our work, but they would play a still better part if the lessons of the era of true rest were better known and better understood

The dynamics of the low-pressure pulmonary circulation demand true horizontal rest in the healing of pulmonary disease Such rest is difficult to secure in these days with their nursing difficulties, but patients should at least be told that the position to adopt in bed is the horizontal, not the vertical which is so commonly adopted and approved. Is it too much to ask that the bed rest should be used by prescription, and is it too much to suggest that the virtues of the tipped up beds, with patients all lying in one plane, are to be found in that very rest and modification of the pulmonary circulation which I have described?

Is it too much to suggest that clinical methods still have a part to play in tuberculosis, that there are right and wrong ways of taking temperatures and that in consequence there are informative and uninformative temperature charts that the X ray film is extremely difficult to interpret, that much imaginative pathology often goes to its reading, and that it is merely an accessory, albeit important, method which Science has placed at our disposal? Is it, in fact, too much to suggest that we should be first and foremost physicians, and not traders on the work of technicians?

DIET

Thirty years ago the stuffing habit had passed A war had led to food shortages, and necessity had modified ideas previously current The knowledge of nutrition was growing, and elaborate dieting tended to take a secondary place in treatment Grumbling about food was perhaps even commoner in sanatoria than it is today Now we talk little of diet, and I wonder if we don't think even less about it The dietitian holds the field and saves us a lot of thinking on the foundations of life

We have been taught to be grateful for our mercies, and there is a tendency to forget the qualitative aspects of food We agreed long ago that excess of *fat* was difficult to digest and unnecessary for the consumptive After that we probably stopped thinking altogether, for it has recently been asked quite seriously if fat is necessary at all It is a fair assumption that, when Nature has made provision for dealing with fat, fat is necessary for maintenance of efficiency and health Apart from calorie and vitamin loss, lack of fat leads in fact to great loss of physical efficiency Twenty-four years ago, in the *Lancet* of Jan 8 1927, there appeared an article by W D Vaile, practitioner medical officer to the Church Army Sanatorium for Boys near Aldershot, which led to a great deal of subsequent controversy Under the heading of "Pulmonary Tuberculosis a Simple Preventive" Vaile propounded the view, founded on careful observation of families infected with tuberculosis, that those members who ate fat escaped overt disease while those who would not eat fat developed it The findings did not hold in every case—nothing ever does—but they did in the majority, and I wonder if we are not today missing something simple I am not thinking of the curative value, or otherwise, of excess of fat in sanatorium dietaries but of the preventive value of a proper supply of fat in the everyday diet Fat has not been abundant during the war and subsequent years, and more and more young people seem to be taught to reject the fats of meat as unfit for consumption

How many of you are familiar with the *Gerson diet* or its Sauerbruch-Herrmannsdorfer modification? How many of us pause to reflect that the constitution of a diet may not only affect general nutrition and health but may have a profound effect on local tissue reactions? We know the effects of certain diets on water retention, and we are familiar clinically with the fat flabby child fed on excess of carbohydrate, prone to eczema, rhinorrhœa, and hypertrophy of adenoid tissue Some of us know that certain of the allergic phenomena of tuberculous infection and disease—for example severe phlyctenular conjunctivitis—can be modified by eliminating, as far as possible, starch from the diet and replacing it by protein and fresh vegetables and fruit, and it was on a similar basis that Gerson introduced his diet He did so originally for the treatment of migraine and he found that it had a favourable effect on associated tuberculous conditions

Gerson was a country doctor As such his views were bound sooner or later to be suspect, and when he staked his claims over too wide a field the inevitable happened His first publication appeared in 1924, and his diet, which was salt-free, poor in carbohydrate and protein, and rich in fat, and contained a large allowance of raw vegetables and fruit, and was supplemented by cod liver oil, was claimed to have a curative value in a large number of diseases Sauerbruch and Herrmannsdorfer later modified the diet and Gerson was submerged by these two more scientific personalities They however made for the modified diet more rational and modest claims which were based on careful experimental work,

principally on the healing of wounds and of tuberculous tissues The application of the diet to tuberculosis showed it to have a profound effect on the healing of lupus and scrofuloderma, and a less defined effect on other forms of the disease, and there was little doubt that the course of some tuberculous lesions could be modified favourably by its use

---

* An address delivered to the Tuberculosis Society of Scotland on Jan. 26

The fires of controversy over the Gerson diet have long been extinguished More specific methods have come along, but with the death of the Gerson diet there died in tuberculosis an idea, to which I shall refer later, that in our attack on disease the basic structure and function of the cell must never be forgotten We are the product of what we consume, and diet can alter tissue reactions to disease The frontal is not the only method of approach or attack

TUBERCULIN

There were two phases in the history of tuberculin The first started in 1890 when Koch distributed his original tuberculin to a group of clinical workers of whom Robert Philip was one It was employed by these men in the large doses which were believed at the time to be correct, and innumerable disasters led to its speedy abandonment In the words of the report of the Tuberculin Treatment Subcommittee of the Brompton Hospital published in 1905, it was found to promote the formation of cavities, to lead to extension of the disease, to exhaust the patient, and to cause loss of strength and weight In all too many it caused death Some people at that time saw the potentialities of tuberculin if used in proper doses, but they were few in number and their advice fell on the deaf ears of a profession which was startled by a catastrophe

In Germany a revival came in 1901 with the publication of clinical work based on a system of modified increasing dosage, and before 1910 the use of tuberculin in treatment was widespread In England it was the researches of Almroth Wright into the mechanism of immunisation by bacteria and their products, and his specific recommendation in 1903 of tuberculin in the treatment of localised tuberculous lesions, which led to its reintroduction

When I took up tuberculosis work some thirty two years ago, tuberculin was quite widely used, but the variety of forms employed and the varying beliefs in the virtues of the different types compelled one to view it critically This aspect of the value of tuberculin is often enough portrayed What is not portrayed is that it was the troublesome reactions which tuberculin caused which led to the constant search for more highly purified and supposedly safer products None of these in time was shown to have any advantage over Koch's original Old Tuberculin, which ultimately became the standard form and was employed both in diagnosis and treatment

There were theories about the use of tuberculin, and the workers of that period knew as much about it as we do today The term "tuberculin sensitiveness" was used in a correct sense long before von Pirquet coined the word "allergy" It is often forgotten that Koch stated emphatically that tuberculin does not kill the bacilli present in the tissues, but that the tissue alone which encloses the bacilli is affected by the action of the remedy In it, he said, there occurred well marked circulatory disturbances and great metabolic changes, resulting often in necrosis and the casting of a slough which in superficial lesions may as we know lead to cure This is of course the well known focal allergic reaction, and its comparative safety in superficial glandular and skin lesions, and its danger in lung and ocular lesions, is readily appreciated It was not a treatment which could be standardised and left to routine administration Each patient presented his own problems with his own sensitivity, and it was the trouble to which tuberculin treatment gave rise and its potential dangers, not its lack of efficacy, which led to its ultimate abandonment

Until quite recently tuberculin was practically discredited as a therapeutic agent, and those who condemned it were very often those who had never used it and had hardly read a line about it Rich dismisses it as a desensitising agent which removes allergy from the path of immunity, and he dismisses the possibility of the focal reaction exercising a healing influence One might have left the question of tuberculin treatment at that had the revolutions of time not brought it round again Last August Honor Smith and R L Vollum from Sir Hugh Cairns' Oxford Surgical Unit published their work on the treatment of tuberculous meningitis with intrathecal injections of streptomycin and the purified protein derivative (P P D) form of tuberculin I do not propose to do any more than refer to this interesting work The virtue of tuberculin causes no surprise to those who have employed it and have given critical thought to its use, but it disturbs me to learn that many are now using this combined form of treatment who know nothing of tuberculin itself In their discussion of the action of intrathecally administered tuberculin Smith and Vollum give full consideration to Rich's desensitising theory but state that at the same time there is some indication that the acute inflammatory reaction provoked by the tuberculin is in itself beneficial —perhaps because it activates a fibrinolytic process and brings streptomycin or the natural humoral and chemical defence mechanisms into closer contact with the site of infection

If we are on the threshold of another tuberculin era I hope fervently that none will enter who have not read Koch's work and the excellent works on tuberculin which appeared in the first decade of the century

DIAPLYTE TUBERCULIN

There have been fancies in tuberculin, and one of the most recent—itself witness to the problems raised by its use—was the diaplyte tuberculin of Prof Georges Dreyer of Oxford In 1923 Dreyer published in the *British Medical Journal* under the heading "A Specific Treatment of Tuberculosis" an abstract of a report on new principles in bacterial immunity and their application in respiratory infections including tuberculosis He pointed out that vaccines had succeeded chiefly in diseases caused by non acid fast and gram negative organisms Postulating that the waxy and fatty substances present in such bacteria protected the specific bacterial proteins and prevented their liberation from the body of the bacterium, thus checking or stopping the production of an adequate stimulus for the immunity reaction of the infected host, Dreyer concluded that if these substances could be removed without damaging the proteins of the bacteria the latter might become suitable for immunising purposes To this end he devised the following procedure after preliminary treatment with formalin the organisms were extracted with acetone and the residuum was suspended in saline and used as a vaccine In the case of the tubercle bacillus this was his diaplyte vaccine or tuberculin

Dreyer's name carried great authority and the vaccine was tried in London hospitals by several competent physicians It is interesting that it was introduced as a vaccine and recommended for treatment After the publication of a series of cases treated by L S T Burrell of the Brompton Hospital, the Medical Research Council carried out an investigation which had obviously not been planned by statisticians Most of the publications on the use of the vaccine were uncritical, and the investigations of the Medical Research Council merely elicited a number of conflicting results

Diaplyte tuberculin is probably the last chapter in the story of tuberculin as a therapeutic agent It is a story with confused issues, and tuberculin finally became discredited partly because of careless work and partly

by the prejudice which it aroused It was a substance which was not without danger and its potentialities for good were soon forgotten

TUBERCLE VACCINES

Almroth Wright's work ushered in the vaccine era, and the vaccine of those days was looked upon as something which might stimulate an immune response during the course of the disease It was inevitable that hopes of success in tuberculosis should arise, and when orthodox methods failed unorthodox methods entered the field The danger of the living virulent organism was always well known, but any attempts to affect the viability of the living organism by heat or chemical methods interfered with its antigenic properties There arose then the idea of using a type of bacillus from another species, and one of the best known vaccines of this type was the bovo vaccine of von Behring, which consisted of human tubercle bacilli and was used intravenously for the immunisation of cattle The reverse process—the use of living bovine organisms in humans—was naturally impossible, but the idea remained

Friedmann's turtle vaccine was a perfectly reputable preparation It was made from a tubercle bacillus isolated by Friedmann in 1903 from the lungs of a tuberculous sea turtle It was said to be antigenic for man and free from danger, and it was administered as a prophylactic much as B C G is used now It was used also as a therapeutic agent in early lung tuberculosis and tuberculosis of bones and joints One full session of the annual meeting of the Tuberculosis Association held in June, 1929, was devoted to a discussion of the vaccine, the principal speaker being Dr Franz Nagelschmidt, of Berlin, who put forward a strong case for its use but failed to convince his audience Calmette had already expressed doubts as to whether the organism was in fact a tubercle bacillus of reptilian origin, and (I speak from memory) I believe that the final verdict was that it was *not* a tubercle bacillus at all. B C G took the field and very little was heard of the turtle vaccine after this meeting, but in its lifetime it led to a great volume of experimental and investigational work

From 1925 to 1932 the long *Spahlinger* controversy raged, and during these years it was very difficult to disentangle facts from hypotheses and prejudice from belief

Henri Spahlinger was a Swiss who abandoned the study of Medicine, founded the Bacterio-Therapeutic Institute at Carouge, near Geneva, and devoted much time to the bacteriology of tuberculosis. He prepared an elaborate treatment of tuberculosis, the details of which varied from time to time—a fact which made it very difficult to follow such particulars as Spahlinger made public

The treatment was first used in this country by Dr Henry Latham on a number of his private patients during the winter of 1913–14, but little more was heard of it here until 1921 In 1922, as a result of press clamour, the British Red Cross, on M Spahlinger's statement that he had come to the end of his financial resources, voted £30,000 to be offered to him for the right to distribute his preparations in this country Spahlinger replied that he could not possibly produce the large number of doses required, and this was probably true After pressure in Parliament, the Ministry of Health offered to appoint an impartial committee of recognised medical authorities to observe the treatment in a series of cases of tuberculosis, leaving the selection of the cases to a physician to be nominated by Spahlinger himself This offer was declined In the same year (1922) in response to the persistent requests of the *Lancet*, Spahlinger published in that journal an account of his products and his methods of using them

This article is difficult to follow, but it seemed that he employed at least three so-called partial sera prepared from horses inoculated with different "toxins" of the tubercle bacillus which were produced in media "under varying types of physicochemical stimulation applied at definite intervals." Three partial sera were obtained in this way and were combined to form his antituberculosis serum A somewhat elaborate technique for the dosage and intervals of dosage was given In addition to this purely passive method, active immunisation was carried out in cases of chronic pulmonary tuberculosis and in non-pulmonary forms of the disease, and here he claimed to have isolated various antigenic fractions of the organism which he injected separately The whole process was suspiciously elaborate, and he stated further that the different bacterial fractions were injected separately so as to secure a series of immunities against all the deleterious products of bacterial disintegration This calls to mind Much's partial antigens which had no success and were soon abandoned

Spahlinger gained strong and influential adherents in this country In 1926 the science committee of the British Medical Association issued a statement and gave their blessing to an appeal which was being launched for funds to enable him to proceed with his work, but at the same time they pointed out the fallacies of many of his theories and expressed scepticism about his antisera In 1927 the central committee of the Fédération des Médecins Suisses sent a letter to the president of the British Medical Association stating that Spahlinger's methods had been tried by only a few individual Swiss doctors and that the contents and methods of preparation of his sera and vaccines were unknown to the Swiss profession The letter stated that the Geneva Medical Society had no more extensive or accurate information at its disposal This did not end the controversy which dragged on through certain immunising experiments in cattle until finally its impetus seemed to slacken and public interest disappeared

The impression left by this long-drawn-out affair was of a man trained in scientific methods but without any knowledge of medicine working on purely theoretical lines and creating furore and controversy in this country alone The rest of the world—with the exception of New South Wales, which sent a doctor to investigate the work—seemed to have little interest in the controversy and less in Spahlinger himself

It is very unlikely that we shall ever hear any more of diaplyte tuberculin, of turtle vaccines, or of Spahlinger's methods, but although all were fancies all were based on the idea, which dominated the vaccine era, of stimulating by specific methods the natural defence reactions of the body

TREATMENT BY LIGHT

I wonder how many of you were interested in the development of treatment by artificial light and I wonder how many of you have read Rollier's fascinating book on heliotherapy—this is its title—and know that it was the visit of Axel Reyn of the Finsen Institute to the annual meeting of the British Medical Association in 1923 which started a great wave of enthusiasm for the ultraviolet light treatment of tuberculous conditions In this country summers are short and sunshine is uncertain The easy applicability of the artificial product made an instant appeal, and the demand for lamps at first outstripped the supply Manufacturers, however, were not slow in their development of lamps to meet all purposes, and very soon few institutions were without their light rooms

The wave of enthusiasm has now, I think, largely spent itself. The administration of light treatment has passed to the physiotherapist and faith in its virtue seems to be half hearted. Yet those of us who worked in these days when we had to be physician, surgeon, and technician learned much of what this form of radiant energy could achieve and of its effects upon health and disease It was something which influenced the reactions of the body and its power of resistance, and its passing can only be regretted

This was no fad It was something of great value, and if it is disappearing from our armoury the fault lies with us and not with it

METHODS OF COLLAPSE AND OTHER SURGICAL MEASURES

Thirty years ago the average tuberculosis physician had barely heard of artificial pneumothorax, although

principally on the healing of wounds and of tuberculous tissues The application of the diet to tuberculosis showed it to have a profound effect on the healing of lupus and scrofuloderma, and a less defined effect on other forms of the disease, and there was little doubt that the course of some tuberculous lesions could be modified favourably by its use

The fires of controversy over the Gerson diet have long been extinguished More specific methods have come along, but with the death of the Gerson diet there died in tuberculosis an idea, to which I shall refer later, that in our attack on disease the basic structure and function of the cell must never be forgotten We are the product of what we consume, and diet can alter tissue reactions to disease The frontal is not the only method of approach or attack

TUBERCULIN

There were two phases in the history of tuberculin The first started in 1890 when Koch distributed his original tuberculin to a group of clinical workers of whom Robert Philip was one It was employed by these men in the large doses which were believed at the time to be correct, and innumerable disasters led to its speedy abandonment In the words of the report of the Tuberculin Treatment Subcommittee of the Brompton Hospital published in 1905, it was found to promote the formation of cavities, to lead to extension of the disease, to exhaust the patient, and to cause loss of strength and weight In all too many it caused death Some people at that time saw the potentialities of tuberculin if used in proper doses, but they were few in number and their advice fell on the deaf ears of a profession which was startled by a catastrophe

In Germany a revival came in 1901 with the publication of clinical work based on a system of modified increasing dosage, and before 1910 the use of tuberculin in treatment was widespread In England it was the researches of Almroth Wright into the mechanism of immunisation by bacteria and their products, and his specific recommendation in 1903 of tuberculin in the treatment of localised tuberculous lesions, which led to its reintroduction

When I took up tuberculosis work some thirty two years ago, tuberculin was quite widely used, but the variety of forms employed and the varying beliefs in the virtues of the different types compelled one to view it critically This aspect of the value of tuberculin is often enough portrayed What is not portrayed is that it was the troublesome reactions which tuberculin caused which led to the constant search for more highly purified and supposedly safer products None of these in time was shown to have any advantage over Koch's original Old Tuberculin, which ultimately became the standard form and was employed both in diagnosis and treatment

There were theories about the use of tuberculin, and the workers of that period knew as much about it as we do today The term "tuberculin sensitiveness" was used in a correct sense long before von Pirquet coined the word "allergy" It is often forgotten that Koch stated emphatically that tuberculin does not kill the bacilli present in the tissues, but that the tissue alone which encloses the bacilli is affected by the action of the remedy In it, he said, there occurred well marked circulatory disturbances and great metabolic changes, resulting often in necrosis and the casting of a slough which in superficial lesions may as we know lead to cure This is of course the well known focal allergic reaction, and its comparative safety in superficial glandular and skin lesions, and its danger in lung and ocular lesions, is readily appreciated It was not a treatment which could be standardised and left to routine administration Each patient presented his own problems with his own sensitivity, and it was the trouble to which tuberculin treatment gave rise and its potential dangers, not its lack of efficacy, which led to its ultimate abandonment

Until quite recently tuberculin was practically discredited as a therapeutic agent, and those who condemned it were very often those who had never used it and had hardly read a line about it Rich dismisses it as a desensitising agent which removes allergy from the path of immunity, and he dismisses the possibility of the focal reaction exercising a healing influence One might have left the question of tuberculin treatment at that had the revolutions of time not brought it round again Last August Honor Smith and R L Vollum from Sir Hugh Cairns' Oxford Surgical Unit published their work on the treatment of tuberculous meningitis with intrathecal injections of streptomycin and the purified protein derivative (P P D) form of tuberculin I do not propose to do any more than refer to this interesting work The virtue of tuberculin causes no surprise to those who have employed it and have given critical thought to its use, but it disturbs me to learn that many are now using this combined form of treatment who know nothing of tuberculin itself In their discussion of the action of intrathecally administered tuberculin Smith and Vollum give full consideration to Rich's desensitising theory but state that at the same time there is some indication that the acute inflammatory reaction provoked by the tuberculin is in itself beneficial —perhaps because it activates a fibrinolytic process and brings streptomycin or the natural humoral and chemical defence mechanisms into closer contact with the site of infection

If we are on the threshold of another tuberculin era I hope fervently that none will enter who have not read Koch's work and the excellent works on tuberculin which appeared in the first decade of the century

DIAPLYTE TUBERCULIN

There have been fancies in tuberculin, and one of the most recent—itself witness to the problems raised by its use—was the diaplyte tuberculin of Prof. Georges Dreyer of Oxford In 1923 Dreyer published in the *British Medical Journal* under the heading "A Specific Treatment of Tuberculosis" an abstract of a report on new principles in bacterial immunity and their application in respiratory infections including tuberculosis He pointed out that vaccines had succeeded chiefly in diseases caused by non acid fast and gram negative organisms Postulating that the waxy and fatty substances present in such bacteria protected the specific bacterial proteins and prevented their liberation from the body of the bacterium, thus checking or stopping the production of an adequate stimulus for the immunity reaction of the infected host, Dreyer concluded that if these substances could be removed without damaging the proteins of the bacteria the latter might become suitable for immunising purposes To this end he devised the following procedure after preliminary treatment with formalin the organisms were extracted with acetone and the residuum was suspended in saline and used as a vaccine In the case of the tubercle bacillus this was his diaplyte vaccine or tuberculin

Dreyer's name carried great authority and the vaccine was tried in London hospitals by several competent physicians It is interesting that it was introduced as a vaccine and recommended for treatment After the publication of a series of cases treated by L S T Burrell of the Brompton Hospital, the Medical Research Council carried out an investigation which had obviously not been planned by statisticians Most of the publications on the use of the vaccine were uncritical, and the investigations of the Medical Research Council merely elicited a number of conflicting results

Diaplyte tuberculin is probably the last chapter in the story of tuberculin as a therapeutic agent It is a story with confused issues, and tuberculin finally became discredited partly because of careless work and partly

by the prejudice which it aroused It was a substance which was not without danger and its potentialities for good were soon forgotten

TUBERCLE VACCINES

Almroth Wright's work ushered in the vaccine era, and the vaccine of those days was looked upon as something which might stimulate an immune response during the course of the disease It was inevitable that hopes of success in tuberculosis should arise, and when orthodox methods failed unorthodox methods entered the field The danger of the living virulent organism was always well known, but any attempts to affect the viability of the living organism by heat or chemical methods interfered with its antigenic properties There arose then the idea of using a type of bacillus from another species, and one of the best known vaccines of this type was the bovo-vaccine of von Behring, which consisted of human tubercle bacilli and was used intravenously for the immunisation of cattle The reverse process—the use of living bovine organisms in humans—was naturally impossible, but the idea remained

Friedmann's turtle vaccine was a perfectly reputable preparation It was made from a tubercle bacillus isolated by Friedmann in 1903 from the lungs of a tuberculous sea turtle It was said to be antigenic for man and free from danger, and it was administered as a prophylactic much as B C G is used now It was used also as a therapeutic agent in early lung tuberculosis and tuberculosis of bones and joints One full session of the annual meeting of the Tuberculosis Association held in June, 1929, was devoted to a discussion of the vaccine, the principal speaker being Dr Franz Nagelschmidt, of Berlin, who put forward a strong case for its use but failed to convince his audience Calmette had already expressed doubts as to whether the organism was in fact a tubercle bacillus of reptilian origin, and (I speak from memory) I believe that the final verdict was that it was not a tubercle bacillus at all. B C G took the field and very little was heard of the turtle vaccine after this meeting, but in its lifetime it led to a great volume of experimental and investigational work

From 1925 to 1932 the long *Spahlinger* controversy raged, and during these years it was very difficult to disentangle facts from hypotheses and prejudice from belief

Henri Spahlinger was a Swiss who abandoned the study of Medicine, founded the Bacterio-Therapeutic Institute at Carouge, near Geneva, and devoted much time to the bacteriology of tuberculosis He prepared an elaborate treatment of tuberculosis, the details of which varied from time to time—a fact which made it very difficult to follow such particulars as Spahlinger made public

The treatment was first used in this country by Dr Henry Latham on a number of his private patients during the winter of 1913–14, but little more was heard of it here until 1921 In 1922, as a result of press clamour, the British Red Cross, on M Spahlinger's statement that he had come to the end of his financial resources, voted £30,000 to be offered to him for the right to distribute his preparations in this country Spahlinger replied that he could not possibly produce the large number of doses required, and this was probably true After pressure in Parliament, the Ministry of Health offered to appoint an impartial committee of recognised medical authorities to observe the treatment in a series of cases of tuberculosis, leaving the selection of the cases to a physician to be nominated by Spahlinger himself This offer was declined In the same year (1922) in response to the persistent requests of the *Lancet*, Spahlinger published in that journal an account of his products and his methods of using them

This article is difficult to follow, but it seemed that he employed at least three so called partial sera prepared from horses inoculated with different "toxins" of the tubercle bacillus which were produced in media "under varying types of physicochemical stimulation applied at definite intervals." Three partial sera were obtained in this way and were combined to form his antituberculosis serum A somewhat elaborate technique for the dosage and intervals of dosage was given In addition to this purely passive method active immunisation was carried out in cases of chronic pulmonary tuberculosis and in non-pulmonary forms of the disease, and here he claimed to have isolated various antigenic fractions of the organism which he injected separately The whole process was suspiciously elaborate, and he stated further that the different bacterial fractions were injected separately so as to secure a series of immunities against all the deleterious products of bacterial disintegration This calls to mind Much's partial antigens which had no success and were soon abandoned

Spahlinger gained strong and influential adherents in this country In 1926 the science committee of the British Medical Association issued a statement and gave their blessing to an appeal which was being launched for funds to enable him to proceed with his work, but at the same time they pointed out the fallacies of many of his theories and expressed scepticism about his antisera In 1927 the central committee of the Fédération des Médeçins Suisses sent a letter to the president of the British Medical Association stating that Spahlinger's methods had been tried by only a few individual Swiss doctors and that the contents and methods of preparation of his sera and vaccines were unknown to the Swiss profession The letter stated that the Geneva Medical Society had no more extensive or accurate information at its disposal This did not end the controversy which dragged on through certain immunising experiments in cattle until finally its impetus seemed to slacken and public interest disappeared

The impression left by this long-drawn out affair was of a man trained in scientific methods but without any knowledge of medicine working on purely theoretical lines and creating furore and controversy in this country alone The rest of the world—with the exception of New South Wales, which sent a doctor to investigate the work—seemed to have little interest in the controversy and less in Spahlinger himself

It is very unlikely that we shall ever hear any more of diaplyte tuberculin, of turtle vaccines, or of Spahlinger's methods, but although all were fancies all were based on the idea, which dominated the vaccine era, of stimulating by specific methods the natural defence reactions of the body

TREATMENT BY LIGHT

I wonder how many of you were interested in the development of treatment by artificial light and I wonder how many of you have read Rollier's fascinating book on heliotherapy—this is its title—and know that it was the visit of Axel Reyn of the Finsen Institute to the annual meeting of the British Medical Association in 1923 which started a great wave of enthusiasm for the ultraviolet light treatment of tuberculous conditions In this country summers are short and sunshine is uncertain The easy applicability of the artificial product made an instant appeal, and the demand for lamps at first outstripped the supply Manufacturers, however, were not slow in their development of lamps to meet all purposes, and very soon few institutions were without their light rooms

The wave of enthusiasm has now, I think, largely spent itself The administration of light treatment has passed to the physiotherapist and faith in its virtue seems to be half hearted Yet those of us who worked in these days when we had to be physician, surgeon, and technician learned much of what this form of radiant energy could achieve and of its effects upon health and disease It was something which influenced the reactions of the body and its power of resistance, and its passing can only be regretted

This was no fad It was something of great value, and if it is disappearing from our armoury the fault lies with us and not with it

METHODS OF COLLAPSE AND OTHER SURGICAL MEASURES

Thirty years ago the average tuberculosis physician had barely heard of artificial pneumothorax, although

principally on the healing of wounds and of tuberculous tissues The application of the diet to tuberculosis showed it to have a profound effect on the healing of lupus and scrofuloderma, and a less defined effect on other forms of the disease, and there was little doubt that the course of some tuberculous lesions could be modified favourably by its use

The fires of controversy over the Gerson diet have long been extinguished More specific methods have come along, but with the death of the Gerson diet there died in tuberculosis an idea, to which I shall refer later, that in our attack on disease the basic structure and function of the cell must never be forgotten We are the product of what we consume, and diet can alter tissue reactions to disease The frontal is not the only method of approach or attack

TUBERCULIN

There were two phases in the history of tuberculin The first started in 1890 when Koch distributed his original tuberculin to a group of clinical workers of whom Robert Philip was one It was employed by these men in the large doses which were believed at the time to be correct, and innumerable disasters led to its speedy abandonment In the words of the report of the Tuberculin Treatment Subcommittee of the Brompton Hospital published in 1905, it was found to promote the formation of cavities, to lead to extension of the disease, to exhaust the patient, and to cause loss of strength and weight In all too many it caused death Some people at that time saw the potentialities of tuberculin if used in proper doses, but they were few in number and their advice fell on the deaf ears of a profession which was startled by a catastrophe

In Germany a revival came in 1901 with the publication of clinical work based on a system of modified increasing dosage, and before 1910 the use of tuberculin in treatment was widespread In England it was the researches of Almroth Wright into the mechanism of immunisation by bacteria and their products, and his specific recommendation in 1903 of tuberculin in the treatment of localised tuberculous lesions, which led to its reintroduction

When I took up tuberculosis work some thirty two years ago, tuberculin was quite widely used, but the variety of forms employed and the varying beliefs in the virtues of the different types compelled one to view it critically This aspect of the value of tuberculin is often enough portrayed What is not portrayed is that it was the troublesome reactions which tuberculin caused which led to the constant search for more highly purified and supposedly safer products None of these in time was shown to have any advantage over Koch's original Old Tuberculin, which ultimately became the standard form and was employed both in diagnosis and treatment

There were theories about the use of tuberculin, and the workers of that period knew as much about it as we do today The term "tuberculin sensitiveness" was used in a correct sense long before von Pirquet coined the word "allergy" It is often forgotten that Koch stated emphatically that tuberculin does not kill the bacilli present in the tissues, but that the tissue alone which encloses the bacilli is affected by the action of the remedy In it, he said, there occurred well marked circulatory disturbances and great metabolic changes, resulting often in necrosis and the casting of a slough which in superficial lesions may as we know lead to cure This is of course the well known focal allergic reaction, and its comparative safety in superficial glandular and skin lesions, and its danger in lung and ocular lesions, is readily appreciated It was not a treatment which could be standardised and left to routine administration Each patient presented his own problems with his own sensitivity, and it was the trouble to which tuberculin treatment gave rise and its potential dangers, not its lack of efficacy, which led to its ultimate abandonment

Until quite recently tuberculin was practically discredited as a therapeutic agent, and those who condemned it were very often those who had never used it and had hardly read a line about it Rich dismisses it as a desensitising agent which removes allergy from the path of immunity, and he dismisses the possibility of the focal reaction exercising a healing influence One might have left the question of tuberculin treatment at that had the revolutions of time not brought it round again Last August Honor Smith and R L Vollum from Sir Hugh Cairns' Oxford Surgical Unit published their work on the treatment of tuberculous meningitis with intrathecal injections of streptomycin and the purified protein derivative (P P D) form of tuberculin I do not propose to do any more than refer to this interesting work The virtue of tuberculin causes no surprise to those who have employed it and have given critical thought to its use, but it disturbs me to learn that many are now using this combined form of treatment who know nothing of tuberculin itself In their discussion of the action of intrathecally administered tuberculin Smith and Vollum give full consideration to Rich's desensitising theory but state that at the same time there is some indication that the acute inflammatory reaction provoked by the tuberculin is in itself beneficial —perhaps because it activates a fibrinolytic process and brings streptomycin or the natural humoral and chemical defence mechanisms into closer contact with the site of infection

If we are on the threshold of another tuberculin era I hope fervently that none will enter who have not read Koch's work and the excellent works on tuberculin which appeared in the first decade of the century

DIAPLYTE TUBERCULIN

There have been fancies in tuberculin, and one of the most recent—itself witness to the problems raised by its use—was the diaplyte tuberculin of Prof Georges Dreyer of Oxford In 1923 Dreyer published in the *British Medical Journal* under the heading "A Specific Treatment of Tuberculosis" an abstract of a report on new principles in bacterial immunity and their application in respiratory infections including tuberculosis He pointed out that vaccines had succeeded chiefly in diseases caused by non acid fast and gram negative organisms Postulating that the waxy and fatty substances present in such bacteria protected the specific bacterial proteins and prevented their liberation from the body of the bacterium, thus checking or stopping the production of an adequate stimulus for the immunity reaction of the infected host, Dreyer concluded that if these substances could be removed without damaging the proteins of the bacteria the latter might become suitable for immunising purposes To this end he devised the following procedure after preliminary treatment with formalin the organisms were extracted with acetone and the residuum was suspended in saline and used as a vaccine In the case of the tubercle bacillus this was his diaplyte vaccine or tuberculin

Dreyer's name carried great authority and the vaccine was tried in London hospitals by several competent physicians It is interesting that it was introduced as a vaccine and recommended for treatment After the publication of a series of cases treated by L S T Burrell of the Brompton Hospital, the Medical Research Council carried out an investigation which had obviously not been planned by statisticians Most of the publications on the use of the vaccine were uncritical, and the investigations of the Medical Research Council merely elicited a number of conflicting results

Diaplyte tuberculin is probably the last chapter in the story of tuberculin as a therapeutic agent It is a story with confused issues, and tuberculin finally became discredited partly because of careless work and partly

the nature of suspicious lesions noted at necropsy, the rest were submitted simply because the occupational history or the clinical and radiological signs during life had raised the question of exposure to dust In the London area I often made the post mortem examination myself, but specimens were received from all parts of the country, generally accompanied by a summary of the necropsy findings

Most of the deceased persons had been in the same occupations for the greater part of their lives Skilled workers predominated, the majority being men Women were only met with to any great extent in the pottery and asbestos industries The dusts responsible were free silica, various silicates, clays, emery, iron, and various kinds of carbon (coal, graphite, soot, lamp black, and carbon black) Most of the workers were exposed to risks arising from mixed dust All the workers in the asbestos group had worked in the industry before the special regulations for the control of this dust came into force in 1932

METHOD

In the selection of tissue for section, portions from apparently healthy looking areas of lung were included whenever possible These often displayed the best early uncomplicated pneumoconiotic lesions, and were of particular value where malignant disease or tuberculosis complicated the picture The examination of hilum glands was also found to be important The standard paraffin embedding and staining techniques were employed as a routine, supplemented where necessary by frozen sections

TABLE I—PNEUMOCONIOSIS (ALL FORMS)

Group	*Occupation*	Silicosis	Other forms *of* pneumoconiosis	No *pneumo*coniosis	Total
1	Pottery workers	327	13	54	394
2	Coalminers	213	80	9	302
3	Asbestos workers	—	121	11	132
4	Stonemasons and quarriers	88	2	13	103
5	Iron and steel foundry workers metal grinders, and sandblasters of metal castings	75	3	24	102
6	Miscellaneous occupations and occupations not stated	93	21	58	172
	Total	796	240	169	1205

In statistical analysis of the cases the ages at death have been classified in three groups 15–44, 45–64, and 65 or more. Information as to the duration of exposure to dust was often incomplete Moreover, so many factors had to be taken into account in each case history—e g, illness and periods of unemployment and military service—that a comprehensive statistical investigation on this point seemed to be impracticable. Furthermore, the record of the population at risk was not available for such a varied group of workers over a period of twenty years, hence it was impossible to calculate the death rates Again, the occupational records of industrial pulmonary disease have increased greatly in complexity during this period, as more and more cases have come under review. The first detailed classification of occupations was made by Middleton (1936) The latest figures are given by the Chief Inspector of Factories (1949), who assigns the deaths from silicosis alone to no fewer than twenty four occupations It therefore seemed best in the present investigation to limit the classification to five large groups—(1) pottery workers, (2) coalminers (underground workers only), (3) asbestos workers, (4) stonemasons and quarriers, and (5) iron and steel foundrymen, metal grinders, and sandblasters of iron castings—and to assemble the remainder in a 6th group, miscellaneous occupations and occupations not stated

TABLE II—MEAN AGES AT DEATH

Occupation		Silicosis		Other forms of pneumoconiosis	
		No of patients whose ages were stated	Mean age (yr)	No of patients whose ages were stated	Mean age (yr)
Pottery workers		304*	53·2	12†	43·9
Coalminers		186	56·2	67	52·8
Asbestos workers	Males	—	—	41	38·5
	Females	—	—	61	33·5
	Total	—	—	102	35·5
Stonemasons and quarriers		78	54·9	2	60·5
Iron and steel workers metal grinders and sandblasters		61	51·4	3	62·7
Miscellaneous occupations and occupations not stated		49	54·3	15	61·4
Total		678	54·3	201	43·1

* Including 24 females † Including 1 female.

ANALYSIS OF CASES

Of 1247 cases examined, 42 were deleted by reason of inadequate data, leaving 1205 for analysis Of these, 169 were negative for pneumoconiosis and 1036 positive. In the negative group, 111 persons had been engaged in industries with a recognised pneumoconiosis risk, whilst the remaining 58 had been exposed to various kinds of dust not known to carry this risk. The positives have been subdivided into examples of (1) silicosis with or without other forms of pneumoconiosis, and (2) other forms of pneumoconiosis The details of this classification are given in table I

Causes of Death

In the negative group the causes of death were chronic pulmonary tuberculosis 93 (55%), bronchiectasis 18 (10·7%), non industrial pulmonary fibrosis 15 (8·9%), primary malignant disease of the lung 14 (8·3%), pneumonia 5 (3%), miscellaneous respiratory diseases 6 (3·6%), and non respiratory diseases 18 (10·7%)

In the positive group 796 had silicosis and 240 other forms of pneumoconiosis Of the latter, 50·4% had asbestosis and 40·8% the dust reticulation type of lesion (of which 81·6% were coalminers) In the silicosis subgroup 21% had minimal lesions which had not been detected by naked eye

Ages at Death

The mean ages at death are given in table II.

Sex

The only pneumoconiosis group in which the number of females was sufficiently large for statistical analysis was that of asbestosis Here there were 52 males and 69 females The mean age at death for the males was 38·5 and for the females 33·5 In the males the highest percentage of deaths occurred in the 45–64 age group, as in other occupations, but in the females it was in the 15–44 group

Pneumoconiosis Accompanied by Tuberculosis

Table III shows that 43% of the 1036 cases of pneumoconiosis had active tuberculosis of the lungs also (58·6% of the cases of silicosis and 32% of the other forms of pneumoconiosis)

The highest incidence (64·1%) occurred in group 5 (iron and steel foundry workers, metal grinders, and sandblasters) and was due to the inclusion of 46 sandblasters with an incidence of 69·6% In spite of the fact that group 3 (asbestos workers) included a considerable number of young females (68·1% of the deaths in females occurred

Forlanini had published his first case in 1894 and in 1906 had reported the results of fourteen years' use My first pneumothorax was induced in 1924, and even then I had not even seen anyone else give a refill That was probably not long after the beginning of the era of surgical treatment in this country, and phrenic evulsion, adhesion cutting, and thoracoplasty had followed pneumothorax Indications for their use were often vague, and the thoracoplasty of the day was a serious operation We practised some of these treatments on indications which would not be accepted today, and the temporary popularity which phrenic evulsion enjoyed was a true surgical fancy Though the surgery of the lung and chest has evolved, and our indications are now more defined and precise, I often think that fads have not altogether passed

Pneumothorax fell under a cloud because of its mis application by uncritical, and even unskilled, people, and a few years ago it became fashionable to condemn it Pneumoperitoneum began to take its place because it seemed to lead to fewer complications, and much of the application of this undoubtedly valuable method of treatment was, and perhaps still is, of the nature of a fad We are now, I think, viewing things again in a truer perspective, but the enthusiasm for the tension theory of cavities and for ablation of lung tissue has its dangers, and fads still lie before us We must be progressive, but we must hold fast to our judgment

DRUGS

During these thirty years many drugs have flitted across the scene I remember well—it was the era of antiseptics and I acted under orders—when I used to inject iodoform and chinosol daily into the veins of consumptives, when I gave intramuscular injections of saccharose for reasons which I never quite understood, when 20 grains of potassium iodide was given in half a pint of water after breakfast followed four hours later by an ounce of aqua chlori in half a pint of fresh lemonade, repeated twice at two hourly intervals The chlorine was said to liberate iodine in the blood and the nascent iodine acted on the tuberculous foci It was a nice equation and it appeared in books There were others

What rubbish it must seem to those born into the era of sulphonamides and antibiotics, and how credulous must that generation seem to you! Yet are *you* bringing judgment to bear on the drugs which you use? Has it ever seemed to you that you are using the patient as a species of Aunt Sally at which you shy your streptomycin and P A S? Have the patients' tissues not a part to play? Are you not so obsessed with methods of frontal attack that you are forgetting the potentialities of the resistance movement? Is there, in fact, not also the important factor of host resistance, and, if there is, how much of what has been jettisoned in the past might profitably be reclaimed?

The past has lessons which we might well recall I am not pleading for the wholesale return of tuberculin or vaccines or of obsolete methods of treatment, but I do plead for a reconsideration of certain principles which we are tending to forget The old physicians who elaborated the true sanatorium régime were not fools, and methods which cured without treatment by collapse—which was in its infancy thirty years ago—and without modern drugs will reinforce powerfully our methods of today Why does calciferol cure lupus? It is probable that calcium plays only an intermediate part and that the vitamin per se has no direct action on the lesion It is more likely that the drug exercises an effect on cell metabolism and vascular endothelial permeability similar to what a discredited diet produced We do not know why some develop tuberculosis and others do not, and we hardly know on what immunity in tuberculosis is based, but the reversal of the body changes which go with a breakdown of immunity demands more than mechanical methods of treatment, and a reorientation of our views is overdue

THE DEATH RATE

These years have undoubtedly brought advances and we are wont to point with pride to a falling tuberculosis death rate as a product of our efforts I am the last to cast doubt on the efficacy of what we do, but it is difficult to correlate our efforts with the statistics of the past 80 years Tuberculosis in Scotland has been decreasing steadily since 1870, and apart from wars and pestilences nothing seems to have disturbed its course, although the rate of fall has been more uniform since 1918 when the tuberculosis provisions of the National Health Insurance Act became operative Now—when the number of deaths had risen and when by all utterances, semi official, municipal, and otherwise, things, under the schism of the National Health Service Act, were going from bad to worse, when everything, including beds, was failing us—the mortality has started suddenly to drop What has caused this sudden reversal? Tuberculosis is both an endemic and an epidemic, and if a secondary wave of the epidemic is now subsiding by natural causes let us accept the fact and be grateful for it Surely it were fancy to say that we have brought about this fall, but it is no fancy to say that we can help, for the tuberculosis epidemic has, like all epidemics, an infective side, and it is extremely susceptible to factors of national and local well being which we can perhaps in some way hope to influence Who can wield the greater influence here, the chest physician, or the sanitarian? Perhaps we are at this moment witnessing the establishment of the greatest fancy of all

There is much in the epidemiology of tuberculosis which we do not understand, and the disease has clinical aspects which we cannot explain Its treatment is no more static now than it was thirty years ago, and it is just as true today as it was then that everything that is new is not necessarily true or good There is still room for clinical observation and pathological study, and the better the judgment we bring to bear on these the more likely we shall be to advance our understanding of the many obscure problems which tuberculosis still presents.

PNEUMOCONIOSIS

A HISTOLOGICAL SURVEY OF NECROPSY MATERIAL IN 1205 CASES

S Roodhouse Gloyne*
M D Leeds, D P H
CONSULTING PATHOLOGIST, LONDON CHEST HOSPITAL AND KING EDWARD VII SANATORIUM, MIDHURST
From the Institute of Social Medicine, Oxford

The meaning of the term pneumoconiosis is being enlarged year by year, and at the present time it is used to include pulmonary disease, both acute and chronic, attributable to many different kinds of dust In Statutory Instrument (1948) no 1371 the word is defined as "fibrosis of the lungs due to silica dust, asbestos dust or other dust, and includes the condition of the lungs known as dust reticulation but does not include byssinosis" In this paper the term is confined to this use

MATERIAL

The material reviewed here comprises a consecutive series of 1247 lungs, or portions thereof, received during the years 1920–49 for microscopical examination for the presence of pulmonary disease attributable to the inhalation of dust Most of the specimens were sent either to confirm the naked eye diagnosis or to determine the nature of suspicious lesions noted at necropsy, the rest were submitted simply because the occupational history or the clinical and radiological signs during life had raised the question of exposure to dust. In the London area I often made the post mortem examination myself, but specimens were received from all parts of the country, generally accompanied by a summary of the necropsy findings.

---

* Dr Gloyne was working with a grant from the Medical Research Council He died on Sept 25 1950

Most of the deceased persons had been in the same occupations for the greater part of their lives. Skilled workers predominated, the majority being men. Women were only met with to any great extent in the pottery and asbestos industries. The dusts responsible were free silica, various silicates, clays, emery, iron, and various kinds of carbon (coal, graphite, soot, lamp black, and carbon black). Most of the workers were exposed to risks arising from mixed dust. All the workers in the asbestos group had worked in the industry before the special regulations for the control of this dust came into force in 1932.

METHOD

In the selection of tissue for section, portions from apparently healthy-looking areas of lung were included whenever possible. These often displayed the best early uncomplicated pneumoconiotic lesions, and were of particular value where malignant disease or tuberculosis complicated the picture. The examination of hilum glands was also found to be important. The standard paraffin embedding and staining techniques were employed as a routine, supplemented where necessary by frozen sections.

TABLE I—PNEUMOCONIOSIS (ALL FORMS)

Group	Occupation	Silicosis	Other forms of pneumoconiosis	No pneumoconiosis	Total
1	Pottery workers	327	13	54	394
2	Coalminers	213	80	9	302
3	Asbestos workers	—	121	11	132
4	Stonemasons and quarriers	88	2	13	103
5	Iron and steel foundry workers metal grinders and sandblasters of metal castings	75	3	24	102
6	Miscellaneous occupations, and occupations not stated	93	21	58	172
	Total	796	240	169	1205

In statistical analysis of the cases the ages at death have been classified in three groups: 15–44, 45–64, and 65 or more. Information as to the duration of exposure to dust was often incomplete. Moreover, so many factors had to be taken into account in each case-history—e.g., illness and periods of unemployment and military service—that a comprehensive statistical investigation on this point seemed to be impracticable. Furthermore, the record of the population at risk was not available for such a varied group of workers over a period of twenty years, hence it was impossible to calculate the death rates. Again, the occupational records of industrial pulmonary disease have increased greatly in complexity during this period, as more and more cases have come under review. The first detailed classification of occupations was made by Middleton (1936). The latest figures are given by the Chief Inspector of Factories (1949), who assigns the deaths from silicosis alone to no fewer than twenty four occupations. It therefore seemed best in the present investigation to limit the classification to five large groups—(1) pottery workers, (2) coalminers (underground workers only), (3) asbestos workers, (4) stonemasons and quarriers, and (5) iron and steel foundrymen, metal grinders, and sandblasters of iron castings—and to assemble the remainder in a 6th group, miscellaneous occupations and occupations not stated.

TABLE II—MEAN AGES AT DEATH

Occupation		Silicosis		Other forms of pneumoconiosis	
		No of patients whose ages were stated	Mean age (yr.)	No of patients whose ages were stated	Mean age (yr.)
Pottery workers		304*	53·2	12†	43·9
Coalminers		186	56·2	67	52·8
Asbestos workers	Males	—	—	41	38·5
	Females	—	—	61	33·5
	Total	—	—	102	35·5
Stonemasons and quarriers		78	54·9	2	60·5
Iron and steel workers metal grinders and sandblasters		61	51·4	3	62·7
Miscellaneous occupations and occupations not stated		49	54·3	15	61·4
Total		678	54·3	201	43·1

* Including 24 females. † Including 1 female.

ANALYSIS OF CASES

Of 1247 cases examined, 42 were deleted by reason of inadequate data, leaving 1205 for analysis. Of these, 169 were negative for pneumoconiosis and 1036 positive. In the negative group, 111 persons had been engaged in industries with a recognised pneumoconiosis risk, whilst the remaining 58 had been exposed to various kinds of dust not known to carry this risk. The positives have been subdivided into examples of (1) silicosis with or without other forms of pneumoconiosis, and (2) other forms of pneumoconiosis. The details of this classification are given in table I.

Causes of Death

In the negative group the causes of death were chronic pulmonary tuberculosis 93 (55%), bronchiectasis 18 (10·7%), non industrial pulmonary fibrosis 15 (8·9%), primary malignant disease of the lung 14 (8·3%), pneumonia 5 (3%), miscellaneous respiratory diseases 6 (3·6%), and non respiratory diseases 18 (10·7%).

In the positive group 796 had silicosis and 240 other forms of pneumoconiosis. Of the latter, 50·4% had asbestosis and 40·8% the dust reticulation type of lesion (of which 81·6% were coalminers). In the silicosis subgroup 21% had minimal lesions which had not been detected by naked eye.

Ages at Death

The mean ages at death are given in table II.

Sex

The only pneumoconiosis group in which the number of females was sufficiently large for statistical analysis was that of asbestosis. Here there were 52 males and 69 females. The mean age at death for the males was 38·5 and for the females 33·5. In the males the highest percentage of deaths occurred in the 45–64 age group, as in other occupations, but in the females it was in the 15–44 group.

Pneumoconiosis Accompanied by Tuberculosis

Table III shows that 43% of the 1036 cases of pneumoconiosis had active tuberculosis of the lungs also (58·6% of the cases of silicosis and 32% of the other forms of pneumoconiosis).

The highest incidence (64·1%) occurred in group 5 (iron and steel foundry workers, metal grinders, and sandblasters) and was due to the inclusion of 46 sandblasters with an incidence of 69·6%. In spite of the fact that group 3 (asbestos workers) included a considerable number of young females (68·1% of the deaths in females occurred

Forlanini had published his first case in 1894 and in 1906 had reported the results of fourteen years' use My first pneumothorax was induced in 1924, and even then I had not even seen anyone else give a refill That was probably not long after the beginning of the era of surgical treatment in this country, and phrenic evulsion, adhesion cutting, and thoracoplasty had followed pneumothorax Indications for their use were often vague, and the thoracoplasty of the day was a serious operation We practised some of these treatments on indications which would not be accepted today, and the temporary popularity which phrenic evulsion enjoyed was a true surgical fancy Though the surgery of the lung and chest has evolved, and our indications are now more defined and precise, I often think that fads have not altogether passed

Pneumothorax fell under a cloud because of its misapplication by uncritical, and even unskilled, people, and a few years ago it became fashionable to condemn it Pneumoperitoneum began to take its place because it seemed to lead to fewer complications, and much of the application of this undoubtedly valuable method of treatment was, and perhaps still is, of the nature of a fad We are now, I think, viewing things again in a truer perspective, but the enthusiasm for the tension theory of cavities and for ablation of lung tissue has its dangers, and fads still lie before us We must be progressive, but we must hold fast to our judgment

DRUGS

During these thirty years many drugs have flitted across the scene I remember well—it was the era of antiseptics and I acted under orders—when I used to inject iodoform and chinosol daily into the veins of consumptives, when I gave intramuscular injections of saccharose for reasons which I never quite understood, when 20 grains of potassium iodide was given in half a pint of water after breakfast followed four hours later by an ounce of aqua chlori in half a pint of fresh lemonade, repeated twice at two hourly intervals The chlorine was said to liberate iodine in the blood and the nascent iodine acted on the tuberculous foci It was a nice equation and it appeared in books There were others

What rubbish it must seem to those born into the era of sulphonamides and antibiotics, and how credulous must that generation seem to you! Yet are *you* bringing judgment to bear on the drugs which you use? Has it ever seemed to you that you are using the patient as a species of Aunt Sally at which you shy your streptomycin and P A S? Have the patients' tissues not a part to play? Are you not so obsessed with methods of frontal attack that you are forgetting the potentialities of the resistance movement? Is there, in fact, not also the important factor of host resistance, and, if there is, how much of what has been jettisoned in the past might profitably be reclaimed?

The past has lessons which we might well recall I am not pleading for the wholesale return of tuberculin or vaccines or of obsolete methods of treatment, but I do plead for a reconsideration of certain principles which we are tending to forget The old physicians who elaborated the true sanatorium régime were not fools, and methods which cured without treatment by collapse—which was in its infancy thirty years ago—and without modern drugs will reinforce powerfully our methods of today Why does calciferol cure lupus? It is probable that calcium plays only an intermediate part and that the vitamin per se has no direct action on the lesion It is more likely that the drug exercises an effect on cell metabolism and vascular endothelial permeability similar to what a discredited diet produced We do not know why some develop tuberculosis and others do not, and we hardly know on what immunity in tuberculosis is based, but the reversal of the body changes which go with a breakdown of immunity demands more than mechanical methods of treatment, and a reorientation of our views is overdue

THE DEATH RATE

These years have undoubtedly brought advances and we are wont to point with pride to a falling tuberculosis death rate as a product of our efforts I am the last to cast doubt on the efficacy of what we do, but it is difficult to correlate our efforts with the statistics of the past 80 years Tuberculosis in Scotland has been decreasing steadily since 1870, and apart from wars and pestilences nothing seems to have disturbed its course, although the rate of fall has been more uniform since 1918 when the tuberculosis provisions of the National Health Insurance Act became operative Now—when the number of deaths had risen and when by all utterances, semi official, municipal, and otherwise, things, under the schism of the National Health Service Act, were going from bad to worse, when everything, including beds, was failing us—the mortality has started suddenly to drop What has caused this sudden reversal? Tuberculosis is both an endemic and an epidemic, and if a secondary wave of the epidemic is now subsiding by natural causes let us accept the fact and be grateful for it Surely it were fancy to say that we have brought about this fall, but it is no fancy to say that we can help, for the tuberculosis epidemic has, like all epidemics, an infective side, and it is extremely susceptible to factors of national and local well being which we can perhaps in some way hope to influence Who can wield the greater influence here, the chest physician, or the sanitarian? Perhaps we are at this moment witnessing the establishment of the greatest fancy of all

There is much in the epidemiology of tuberculosis which we do not understand, and the disease has clinical aspects which we cannot explain Its treatment is no more static now than it was thirty years ago, and it is just as true today as it was then that everything that is new is not necessarily true or good There is still room for clinical observation and pathological study, and the better the judgment we bring to bear on these the more likely we shall be to advance our understanding of the many obscure problems which tuberculosis still presents.

PNEUMOCONIOSIS

A HISTOLOGICAL SURVEY OF NECROPSY MATERIAL IN 1205 CASES

S ROODHOUSE GLOYNE *
M D Leeds, D P H
CONSULTING PATHOLOGIST, LONDON CHEST HOSPITAL AND KING EDWARD VII SANATORIUM, MIDHURST
From the Institute of Social Medicine, Oxford

THE meaning of the term pneumoconiosis is being enlarged year by year, and at the present time it is used to include pulmonary disease, both acute and chronic, attributable to many different kinds of dust In Statutory Instrument (1948) no 1371 the word is defined as " fibrosis of the lungs due to silica dust, asbestos dust or other dust, and includes the condition of the lungs known as dust reticulation but does not include byssinosis " In this paper the term is confined to this use

MATERIAL

The material reviewed here comprises a consecutive series of 1247 lungs, or portions thereof, received during the years 1929–49 for microscopical examination for the presence of pulmonary disease attributable to the inhalation of dust Most of the specimens were sent either to confirm the naked eye diagnosis or to determine the nature of suspicious lesions noted at necropsy, the rest were submitted simply because the occupational history or the clinical and radiological signs during life had raised the question of exposure to dust. In the London area I often made the post-mortem examination myself, but specimens were received from all parts of the country, generally accompanied by a summary of the necropsy findings.

---

* Dr Gloyne was working with a grant from the Medical Research Council He died on Sept 25 1950

Most of the deceased persons had been in the same occupations for the greater part of their lives. Skilled workers predominated, the majority being men. Women were only met with to any great extent in the pottery and asbestos industries. The dusts responsible were free silica, various silicates, clays, emery, iron, and various kinds of carbon (coal, graphite, soot, lamp black, and carbon black). Most of the workers were exposed to risks arising from mixed dust. All the workers in the asbestos group had worked in the industry before the special regulations for the control of this dust came into force in 1932.

METHOD

In the selection of tissue for section, portions from apparently healthy-looking areas of lung were included whenever possible. *These often displayed the best early* uncomplicated pneumoconiotic lesions, and were of particular value where malignant disease or tuberculosis complicated the picture. The examination of hilum glands was also found to be important. The standard paraffin embedding and staining techniques were employed as a routine, supplemented where necessary by frozen sections.

TABLE I—PNEUMOCONIOSIS (ALL FORMS)

Group	Occupation	Silicosis	Other forms of pneumo-coniosis	No pneumo-coniosis	Total
1	Pottery workers	327	13	54	394
2	Coalminers	213	80	9	302
3	Asbestos workers	—	121	11	132
4	Stonemasons and quarriers	88	2	13	103
5	Iron and steel foundry workers, metal grinders, and sandblasters of metal castings	75	3	24	102
6	Miscellaneous occupations and occupations not stated	93	21	58	172
	Total	796	240	169	1205

In statistical analysis of the cases the ages at death have been classified in three groups: 15–44, 45–64, and 65 or more. Information as to the duration of exposure to dust was often incomplete. Moreover, so many factors had to be taken into account in each case-history—e.g., illness and periods of unemployment and military service—that a comprehensive statistical investigation on this point seemed to be impracticable. Furthermore, the record of the population at risk was not available for such a varied group of workers over a period of twenty years, hence it was impossible to calculate the death-rates. Again, the occupational records of industrial pulmonary disease have increased greatly in complexity during this period, as more and more cases have come under review. The first detailed classification of occupations was made by Middleton (1936). The latest figures are given by the Chief Inspector of Factories (1949), who assigns the deaths from silicosis alone to no fewer than twenty-four occupations. It therefore seemed best in the present investigation to limit the classification to five large groups—(1) pottery workers, (2) coalminers (underground workers only), (3) asbestos workers, (4) stonemasons and quarriers, and (5) iron and steel foundrymen, metal grinders, and sandblasters of iron castings—and to assemble the remainder in a 6th group, miscellaneous occupations and occupations not stated.

TABLE II—MEAN AGES AT DEATH

Occupation	Silicosis: No of patients whose ages were stated	Silicosis: Mean age (yr.)	Other forms of pneumo-coniosis: No of patients whose ages were stated	Other forms of pneumo-coniosis: Mean age (yr.)
Pottery workers	304*	53·2	12†	43·9
Coalminers	186	56·2	67	52·8
Asbestos workers Males	—	—	41	38·5
Females	—	—	61	33·5
Total	—	—	102	35·5
Stonemasons and quarriers	78	54·9	2	60·5
Iron and steel workers metal grinders and sandblasters	61	51·4	3	62·7
Miscellaneous occupations and occupations not stated	49	54·3	15	61·4
Total	678	54·3	201	43·1

* Including 24 females. † Including 1 female.

ANALYSIS OF CASES

Of 1247 cases examined, 42 were deleted by reason of inadequate data, leaving 1205 for analysis. Of these, 169 were negative for pneumoconiosis and 1036 positive. In the negative group, 111 persons had been engaged in industries with a *recognised pneumoconiosis risk*, whilst the remaining 58 had been exposed to various kinds of dust not known to carry this risk. The positives have been subdivided into examples of (1) silicosis with or without other forms of pneumoconiosis, and (2) other forms of pneumoconiosis. The details of this classification are given in table I.

Causes of Death

In the negative group the causes of death were chronic pulmonary tuberculosis 93 (55%), bronchiectasis 18 (10·7%), non-industrial pulmonary fibrosis 15 (8·9%), primary malignant disease of the lung 14 (8·3%), pneumonia 5 (3%), miscellaneous respiratory diseases 6 (3·6%), and non-respiratory diseases 18 (10·7%).

In the positive group 796 had silicosis and 240 other forms of pneumoconiosis. Of the latter, 50·4% had asbestosis and 40·8% the dust reticulation type of lesion (of which 81·6% were coalminers). In the silicosis subgroup 21% had minimal lesions which had not been detected by naked eye.

Ages at Death

The mean ages at death are given in table II.

Sex

The only pneumoconiosis group in which the number of females was sufficiently large for statistical analysis was that of asbestosis. Here there were 52 males and 69 females. The mean age at death for the males was 38·5 and for the females 33·5. In the males the highest percentage of deaths occurred in the 45–64 age group, as in other occupations, but in the females it was in the 15–44 group.

Pneumoconiosis Accompanied by Tuberculosis

Table III shows that 43% of the 1036 cases of pneumoconiosis had active tuberculosis of the lungs also (58·6% of the cases of silicosis and 32% of the other forms of pneumoconiosis).

The highest incidence (64·1%) occurred in group 5 (iron and steel foundry workers, metal grinders, and sandblasters) and was due to the inclusion of 46 sandblasters with an incidence of 69·6%. In spite of the fact that group 3 (asbestos workers) included a considerable number of young females (68·1% of the deaths in females occurred

TABLE III—PNEUMOCONIOSIS (ALL FORMS) ASSOCIATED WITH TUBERCULOSIS

Group	Occupation	No of cases of pneumoconiosis	No of cases with tuberculosis
1	Pottery workers	340	146 (42 94%)
2	Coalminers	293	100 (34 13%)
3	Asbestos workers	121	43 (35 54%)
4	Stonemasons and quarriers	90	18 (53 33%)
5	Iron and steel workers metal grinders and sandblasters of metal castings	78	50 (64 10%)
6	Miscellaneous occupations and occupations not stated	114	58 (50 88%)
	Total	1036	445 (42 95%)

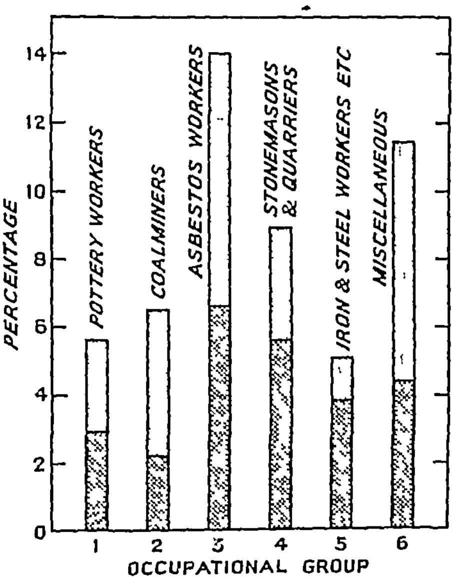
in the 15–44 age group), the incidence of tuberculosis for the whole of the asbestosis series was only 35 5% In 13 5% of the 445 cases of active pulmonary tuberculosis in all forms of pneumoconiosis, the tuberculous lesions were only detected on microscopy

Pneumoconiosis Accompanied by Malignant Disease

The incidence of malignant disease in the 1036 cases of pneumoconiosis is shown in the accompanying figure

Primary Neoplasm of the Lung—There were 80 cases of primary neoplasm of the lung distributed as follows 55 in the silicosis group (i e, 6 9%), 17 in the asbestosis group (i e, 14 1%), and 8 in the other forms of pneumoconiosis (i e, 6 7%) In the asbestosis group the rates for male and female workers were 19 6% and 9 7% respectively

The growths included 26 columnar cell, 52 squamous cell, and 2 oat cell In 6 cases (7 5%) the lesion was first discovered on microscopy



Malignant neoplasms associated with pneumoconiosis stippled columns, primary of lung cross-hatched columns other malignant growths at all sites other than lung

Neoplasm of other Sites—There were 37 cases with neoplasms at other sites, of which 30 were in the digestive tract and 7 elsewhere (14 were associated with secondary deposits in the lung) All were carcinomata except 1 hypernephroma and 1 tumour of the skull The asbestosis cases accounted for 8, of which 2 were in females

Pneumoconiosis Accompanied by Malignant Disease and Tuberculosis

Of the 80 cancers of the lung 15 (18 7%) had active pulmonary tuberculosis also, and of the 37 growths at other sites 8 (21 6%) had this combination of diseases

DISCUSSION

When the term pneumoconiosis is limited to fibrosis of the lung due to the inhalation of mineral dust, silicosis is the commonest form of the disease In the present series of necropsies it accounted for 798 cases (77%) Its characteristic whorled nodule of reticulin and collagenous fibres was best seen in the lungs of stonemasons and quarriers, where admixture of the silica with carbon dusts was less common than in other groups, but it was present in all cases in which silicosis was diagnosed. It was found in both discrete and conglomerate forms in the usual peribronchial, perivascular, subpleural, and interlobular sites, where the small lymphoid follicles, which are inconspicuous in the normal lung, arrest the silica particles, and it was the essential component of the massive fibrotic nodules which are so characteristic a feature of the radiograph With age, the fibres of this whorled nodule become more hyaline and less permeable to aniline dyes, but the nodule remains a diagnostic feature of the silicotic lung to the end

Many attempts have been made to grade cases of silicosis for compensation purposes on the basis of the size, number, and distribution of these nodules, but all these classifications are apt to be arbitrary and to break down in practice There is, however, good reason for reserving the term minimal silicosis for those lungs in which characteristic nodules are diagnosed only on histological examination Accompanying this nodule formation there was also an increase in the collagenous fibres which normally, as described by Snow Miller, surround the walls of the terminal portions of the bronchial airway and the accompanying branches of the pulmonary artery The geodetic arrangement of these fibres only becomes obvious in serial sections This type of irregular non nodular fibrosis lesion is most pronounced in mixed dust pneumoconiosis, and in the present state of our knowledge the part played in its formation by the different dusts is obscure

The term "infective silicosis" is also not infrequently used It is a vague phrase employed in different senses by different writers Some confine it to certain types of tuberculo silicosis, others enlarge it to include infections with other organisms which produce the intermittent pneumonias of silicosis The lesion has two main histological characteristics—namely, an excessive amount of non nodular fibrosis and a zone of cellular proliferation round the silicotic nodule The latter has been well depicted by Simson et al (1930) in the South African cases

Several writers have now described the histological lesion of asbestosis, with its characteristic asbestosis bodies and its reticular fibrosis of the primary lobule of the lung, where the long asbestosis fibre is held up athwart the terminal portion of the respiratory bronchiole, and the saccular dust Roughly whorled nodules may be encountered occasionally in cases of asbestosis where there has been no known exposure to silica—they were present in 7 cases in the present series—but asbestosis is usually a primary lobule rather than a peribronchial nodule fibrosis In long standing cases both the asbestos fibres and the asbestosis bodies were smaller and less often seen than in the lungs of workers more recently exposed to asbestos, suggesting that in course of time the asbestos fibres are slowly dissolved

Dust reticulation, the type of mixed dust pneumoconiosis described by Belt and Ferris (1942) in coal miners, has now been found also in the lungs of potters, foundrymen (McLaughlin et al 1950), and other workers In introducing this term as a more detailed and precise portraiture of the original word anthracosis, Belt and Ferris laid stress on the reticulin element in the fibrosis, its characteristic distribution, and its ultimate development into a "reticulin nodulation" It is a tissue response to a mixed dust of which silica and coal are the chief ingredients, and shows that the place of coal may be taken by other forms of carbon—e g, graphite (Gloyne et al. 1949). Heppleston (1947) has described the basic early lesion as seen in the coalminer.

Some of the other forms of pneumoconiosis in the present series have already been described elsewhere. One was a reticular fibrosis resembling that of asbestosis, in which the lesion was produced by montmorillonite in a fuller's earth worker (Campbell and Gloyne 1942). Graphite has already been referred to. With the extremely varied nature of industry in this country these unusual forms of pneumoconiosis will presumably increase in number, but they are hardly likely to displace silicosis as the most serious risk among diseases due to mineral dust.

One of the chief difficulties encountered in the histological examination of the pneumoconiotic lung is the prevalence of mixed dusts in our factories. The production of fibrosis of the lung by the inhalation of a pure dust belongs to the domain of the experimental pathologist. It is doubtful how far such a condition exists in industry. King et al. (1950) have done much to separate the components of these mixed dusts.

The picture of pneumoconiosis described here therefore is that of a chronic tissue reaction to a mixed dust, the particles of which vary in size, solubility, and toxicity. In the lung the drift of the particles is towards the hilum by way of the superficial and deep lymphatic drainage trunks which are the channels of communication between the terminal portions of the airway and the root glands. The passage of these particles from airway to hilum is marked by a complicated protective tissue response at strategic points en route, and the relative importance of these defence posts varies, to some extent at least, with the size and nature of the component dusts. In the case of the long needle-like asbestos fibre, for example, the terminal portion of the respiratory bronchiole is the crucial site; with the minute silica particle it is the peribronchial and perivascular lymph node.

In several types of pneumoconiosis the dust particles become coated with the plasma protein of the capillary exudate to form elongated segmented bodies of a golden yellow colour with a central core of dust particle. They do not stain with the ordinary aniline dyes, but the potassium ferrocyanide test for iron turns them blue. They were first described by Cooke and Stuart McDonald in 1927 in the lungs of an asbestos worker under the noncommittal term "curious bodies." Since then they have been found in the lungs of coalminers, graphite workers, and talc workers. They are probably of no particular diagnostic significance except in the case of asbestosis, where they are sufficiently characteristic to form an essential part of the histological picture. It would seem that the ætiology of all these bodies is now sufficiently understood to merit the abandonment of the vague term "curious bodies" in favour of a generic phrase—"pneumoconiosis bodies."

Until recently it was believed that the protective tissue reaction of the whole respiratory tract was such that the lung itself was called on to deal with probably not more than 25% of the inhaled dust particles, the rest being excreted by the upper respiratory tract and the extrapulmonary bronchi. The particles which reached the lung tissue were considered to be generally of the size of bacteria—i.e., less than 10 μ. With the development of the new techniques of X-ray diffraction analysis and the electron microscope, however, study of an ultramicroscopic particle in the pneumoconiotic lesion is opening up, and a "lower limit of detectability" (King et al. 1950) is now recognised. The use of prophylactic dusts, such as aluminium, will also affect the histological picture in the near future.

In view of the interference with the pulmonary circulation, the hæmo-respiratory exchange, and the lymphatic drainage system it is not surprising that there should be a group of diseases so commonly associated with pneumoconiosis as to be an essential part of its pathology—e.g., chronic bronchitis and emphysema, various types of cardiac failure, and the terminal bronchopneumonias. Pathologically these are, for the most part, naked-eye diagnoses which do not come within the scope of this paper. Two others, however, are based on histological investigation—namely, tuberculosis and malignant disease. Tuberculosis has long been recognised as ætiologically important in pneumoconiosis, but it is only within recent years that a high incidence of primary pulmonary carcinoma has been suspected.

For pneumoconiosis of all forms, the incidence of 42.95% of tuberculosis in the present series may be compared with the figures for silicosis found by other investigators. Thus in a series of necropsies on sandstone workers, Meiklejohn (1949) found that 44.3% of those with silicosis had tuberculosis also whilst in pottery workers the percentage was 40. Merewether (1936) found that of 38 sandblasters who had died of silicosis 28 (73.7%) also had tuberculosis. The figure for this occupation in the present series is 69.6%. Sandblasting has now been abolished in this country in favour of the less harmful operation of shot blasting, for which mortality figures are not yet available.

No satisfactory control group has been found with which to compare the incidence (7.7%) of primary lung cancer in the 1036 cases of pneumoconiosis. In the 169 cases which proved not to be pneumoconiosis the incidence was 8.3%. In both groups, selection may have been exercised in picking out cases in which the radiographs and clinical histories had been unusual for an uncomplicated pneumoconiosis. Bradford Hill and Lewis Faning (1948), investigating the mortality in an arsenic factory, noted a proportional and significant excess of deaths attributed to cancer of all sites (and especially of the lung and skin) in the arsenic workers (29%), compared with the mortality of three other occupational groups living in the same area (13%).

The necropsy records for 1928–39 at the London Chest Hospital, where selection is obviously at work in picking out these cases for special observation and treatment, show the high incidence of 151 primary lung cancers (21.3%) in 706 necropsies, whereas at the other end of the scale the Registrar General (1950) reports for 1948 2.4% (3.9% of males and 0.9% of females) of the deaths from all causes in the general population over the age of 15 as being due to primary malignant disease of the lung (all forms). This last figure is an increase on those of previous years. Although comparable sets of statistics appear to be lacking, the evidence on all sides seems to point to an increase of deaths from primary cancer of the lung in the general population. It seems reasonable to suppose that workers with a dust hazard have their share in this increase. Whether they have a risk over and above this as a result of their occupation cannot yet be clearly shown, but the mortality of the asbestos workers is disturbing. In the present series 14% of the patients with asbestosis also had primary cancer of the lung. This is all the more striking because so many of them (41.2%) were females. This proportion of female deaths is greater than that in the general population, where the incidence of primary cancer of the lung is 4.4 males to 1 female.

The association of active pulmonary tuberculosis with cancer of the lung has been noted by several observers, both in general and in chest hospitals. Simpson (1929) found active tuberculosis in 4.2% of the necropsies on cases of primary pulmonary carcinoma at the London Hospital, Maxwell (1930) in 5.4% at the Royal Chest Hospital and St. Bartholomew's, Davidson (1930) in

TABLE III—PNEUMOCONIOSIS (ALL FORMS) ASSOCIATED WITH TUBERCULOSIS

Group	Occupation	No of cases of pneumo coniosis	No of cases with tuberculosis
1	Pottery workers	340	146 (*42 94%*)
2	Coalminers	293	100 (*34 13%*)
3	Asbestos workers	121	43 (*35 54%*)
4	Stonemasons and quarriers	90	48 (*53 33%*)
5	Iron and steel workers metal grinders and sandblasters of metal castings	78	50 (*64 10%*)
6	Miscellaneous occupations and occupations not stated	114	58 (*50 88%*)
	Total	1036	445 (*42 95%*)

in the 15–44 age group), the incidence of tuberculosis for the whole of the asbestosis series was only 35 5% In 13 5% of the 445 cases of active pulmonary tuberculosis in all forms of pneumoconiosis, the tuberculous lesions were only detected on microscopy

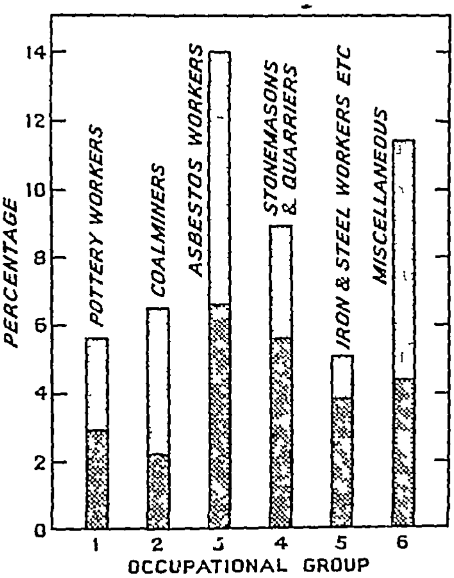
Pneumoconiosis Accompanied by Malignant Disease

The incidence of malignant disease in the 1036 cases of pneumoconiosis is shown in the accompanying figure

Primary Neoplasm of the Lung —There were 80 cases of primary neoplasm of the lung distributed as follows 55 in the silicosis group (i e , 6 9%), 17 in the asbestosis group (i e , 14 1%), and 8 in the other forms of pneumoconiosis (i e , 6 7%) In the asbestosis group the rates for male and female workers were 19 6% and 9 7% respectively

The growths included 26 columnar cell, 52 squamous cell, and 2 oat cell In 6 cases (7 5%) the lesion was first discovered on microscopy

Neoplasm of other Sites —There were 37 cases with neoplasms at other sites, of which 30 were in the digestive tract and 7 elsewhere (14 were associated with secondary deposits in the lung) All were carcinomata except 1 hypernephroma and 1 tumour of the skull The asbestosis cases accounted for 8, of which 2 were in females



Malignant neoplasms associated with pneumoconiosis: stippled columns primary of lung cross-hatched columns other malignant growths at all sites other than lung

Pneumoconiosis Accompanied by Malignant Disease and Tuberculosis

Of the 80 cancers of the lung 15 (18 7%) had active pulmonary tuberculosis also, and of the 37 growths at other sites 8 (21 6%) had this combination of diseases

DISCUSSION

When the term pneumoconiosis is limited to fibrosis of the lung due to the inhalation of mineral dust, silicosis is the commonest form of the disease In the present series of necropsies it accounted for 796 cases (77%). Its characteristic whorled nodule of reticulin and collagenous fibres was best seen in the lungs of stonemasons and quarriers, where admixture of the silica with carbon dusts was less common than in other groups, but it was present in all cases in which silicosis was diagnosed. It was found in both discrete and conglomerate forms in the usual peribronchial, perivascular, subpleural, and interlobular sites, where the small lymphoid follicles, which are inconspicuous in the normal lung, arrest the silica particles, and it was the essential component of the massive fibrotic nodules which are so characteristic a feature of the radiograph With age, the fibres of this whorled nodule became more hyaline and less permeable to aniline dyes, but the nodule remains a diagnostic feature of the silicotic lung to the end

Many attempts have been made to grade cases of silicosis for compensation purposes on the basis of the size, number, and distribution of these nodules, but all these classifications are apt to be arbitrary and to break down in practice There is, however, good reason for reserving the term minimal silicosis for those lungs in which characteristic nodules are diagnosed only on histological examination Accompanying this nodule formation there was also an increase in the collagenous fibres which normally, as described by Snow Miller, surround the walls of the terminal portions of the bronchial airway and the accompanying branches of the pulmonary artery The geodetic arrangement of these fibres only becomes obvious in serial sections This type of irregular non nodular fibrosis lesion is most pronounced in mixed dust pneumoconiosis, and in the present state of our knowledge the part played in its formation by the different dusts is obscure

The term " infective silicosis " is also not infrequently used It is a vague phrase employed in different senses by different writers Some confine it to certain types of tuberculo silicosis , others enlarge it to include infections with other organisms which produce the intermittent pneumonias of silicosis The lesion has two main histological characteristics—namely, an excessive amount of non nodular fibrosis and a zone of cellular proliferation round the silicotic nodule The latter has been well depicted by Simson et al (1930) in the South African cases

Several writers have now described the histological lesion of asbestosis, with its characteristic asbestosis bodies and its reticular fibrosis of the primary lobule of the lung, where the long asbestosis fibre is held up athwart the terminal portion of the respiratory bronchiole, and the saccular dust Roughly whorled nodules may be encountered occasionally in cases of asbestosis where there has been no known exposure to silica—they were present in 7 cases in the present series—but asbestosis is usually a primary lobule rather than a peribronchial nodule fibrosis In long standing cases both the asbestos fibres and the asbestosis bodies were smaller and less often seen than in the lungs of workers more recently exposed to asbestos, suggesting that in course of time the asbestos fibres are slowly dissolved

Dust reticulation, the type of mixed dust pneumoconiosis described by Belt and Ferris (1942) in coal miners, has now been found also in the lungs of potters, foundrymen (McLaughlin et al 1950), and other workers In introducing this term as a more detailed and precise portraiture of the original word anthracosis, Belt and Ferris laid stress on the reticulin element in the fibrosis, its characteristic distribution, and its ultimate development into a " reticulin nodulation " It is a tissue response to a mixed dust of which silica and coal are the chief ingredients, and shows that the place of coal may be taken by other forms of carbon—e g , graphite (Gloyne et al. 1949) Heppleston (1947) has described the basic early lesion as seen in the coalminer

Some of the other forms of pneumoconiosis in the present series have already been described elsewhere One was a reticular fibrosis resembling that of asbestosis, in which the lesion was produced by montmorillonite in a fuller's earth worker (Campbell and Gloyne 1942) Graphite has already been referred to With the extremely varied nature of industry in this country these unusual forms of pneumoconiosis will presumably increase in number, but they are hardly likely to displace silicosis as the most serious risk among diseases due to mineral dust

One of the chief difficulties encountered in the histological examination of the pneumoconiotic lung is the prevalence of mixed dusts in our factories The production of fibrosis of the lung by the inhalation of a pure dust belongs to the domain of the experimental pathologist It is doubtful how far such a condition exists in industry King et al. (1950) have done much to separate the components of these mixed dusts

The picture of pneumoconiosis described here therefore is that of a chronic tissue reaction to a mixed dust, the particles of which vary in size, solubility, and toxicity In the lung the drift of the particles is towards the hilum by way of the superficial and deep lymphatic drainage trunks which are the channels of communication between the terminal portions of the airway and the root glands The passage of these particles from airway to hilum is marked by a complicated protective tissue response at strategic points en route, and the relative importance of these defence posts varies, to some extent at least, with the size and nature of the component dusts In the case of the long needle-like asbestos fibre, for example, the terminal portion of the respiratory bronchiole is the crucial site, with the minute silica particle it is the peribronchial and perivascular lymph node

In several types of pneumoconiosis the dust particles become coated with the plasma-protein of the capillary exudate to form elongated segmented bodies of a golden yellow colour with a central core of dust particle. They do not stain with the ordinary aniline dyes, but the potassium ferrocyanide test for iron turns them blue They were first described by Cooke and Stuart McDonald in 1927 in the lungs of an asbestos worker under the non-committal term "curious bodies" Since then they have been found in the lungs of coalminers, graphite workers, and talc workers They are probably of no particular diagnostic significance except in the case of asbestosis, where they are sufficiently characteristic to form an essential part of the histological picture It would seem that the ætiology of all these bodies is now sufficiently understood to merit the abandonment of the vague term "curious bodies" in favour of a generic phrase—"pneumoconiosis bodies"

Until recently it was believed that the protective tissue reaction of the whole respiratory tract was such that the lung itself was called on to deal with probably not more than 25% of the inhaled dust particles, the rest being excreted by the upper respiratory tract and the extra-pulmonary bronchi. The particles which reached the lung tissue were considered to be generally of the size of bacteria—i.e, less than 10 μ. With the development of the new techniques of X-ray diffraction analysis and the electron microscope, however, study of an ultramicroscopic particle in the pneumoconiotic lesion is opening up, and a "lower limit of detectability" (King et al. 1950) is now recognised The use of prophylactic dusts, such as aluminium, will also affect the histological picture in the near future

In view of the interference with the pulmonary circulation, the hæmo-respiratory exchange, and the lymphatic drainage system it is not surprising that there should be a group of diseases so commonly associated with pneumoconiosis as to be an essential part of its pathology—e g, chronic bronchitis and emphysema, various types of cardiac failure, and the terminal bronchopneumonias. Pathologically these are, for the most part, naked eye diagnoses which do not come within the scope of this paper Two others, however, are based on histological investigation—namely, tuberculosis and malignant disease Tuberculosis has long been recognised as ætiologically important in pneumoconiosis, but it is only within recent years that a high incidence of primary pulmonary carcinoma has been suspected.

For pneumoconiosis of all forms, the incidence of 42 95% of tuberculosis in the present series may be compared with the figures for silicosis found by other investigators Thus in a series of necropsies on sandstone workers, Meiklejohn (1949) found that 44 3% of those with silicosis had tuberculosis also whilst in pottery workers the percentage was 40 Merewether (1936) found that of 38 sandblasters who had died of silicosis 28 (73 7%) also had tuberculosis The figure for this occupation in the present series is 69 6% Sandblasting has now been abolished in this country in favour of the less harmful operation of shot blasting, for which mortality figures are not yet available

No satisfactory control group has been found with which to compare the incidence (7 7%) of primary lung cancer in the 1036 cases of pneumoconiosis In the 169 cases which proved not to be pneumoconiosis the incidence was 8 3% In both groups, selection may have been exercised in picking out cases in which the radiographs and clinical histories had been unusual for an uncomplicated pneumoconiosis Bradford Hill and Lewis Faning (1948), investigating the mortality in an arsenic factory, noted a proportional and significant excess of deaths attributed to cancer of all sites (and especially of the lung and skin) in the arsenic workers (29%), compared with the mortality of three other occupational groups living in the same area (13%)

The necropsy records for 1928–39 at the London Chest Hospital, where selection is obviously at work in picking out these cases for special observation and treatment, show the high incidence of 151 primary lung cancers (21 3%) in 706 necropsies, whereas at the other end of the scale the Registrar General (1950) reports for 1948 2 4% (3 9% of males and 0 9% of females) of the deaths from all causes in the general population over the age of 15 as being due to primary malignant disease of the lung (all forms) This last figure is an increase on those of previous years Although comparable sets of statistics appear to be lacking, the evidence on all sides seems to point to an increase of deaths from primary cancer of the lung in the general population It seems reasonable to suppose that workers with a dust hazard have their share in this increase. Whether they have a risk over and above this as a result of their occupation cannot yet be clearly shown, but the mortality of the asbestos workers is disturbing In the present series 14% of the patients with asbestosis also had primary cancer of the lung This is all the more striking because so many of them (41 2%) were females This proportion of female deaths is greater than that in the general population, where the incidence of primary cancer of the lung is 4 4 males to 1 female

The association of active pulmonary tuberculosis with cancer of the lung has been noted by several observers, both in general and in chest hospitals. Simpson (1929) found active tuberculosis in 4 2% of the necropsies on cases of primary pulmonary carcinoma at the London Hospital, Maxwell (1930) in 5 4% at the Royal Chest Hospital and St Bartholomew's, Davidson (1930) in

6 5% at Brompton, and Gloyne in 6 4% at the London Chest Hospital, making an incidence of 5 5% of 648 necropsies in all the records In the present investigation, where pneumoconiosis is added, the incidence is still greater, there were 15 cases (18 7%) of tuberculosis in 80 cases of pneumoconiosis accompanied by primary carcinoma of the lung In view of the prevalence of tuberculosis in the population of this country it is not surprising that 5% of lung cancers at necropsy should reveal active tuberculosis, but it is not clear why this percentage should rise to four times that proportion when pneumoconiosis is present also At necropsy a lung which has three separate diseases in it is a much damaged organ, and it is not always possible to determine whether the tuberculosis is an exacerbation of an old lesion or a terminal infection In either case the obstruction to the lymphatic absorption produced by the pneumoconiosis and neoplasm together must be very considerable, and may well be a determining factor

The fact that in the pneumoconiosis series 21% of the cases of silicosis, 13 5% of those with tuberculosis, and *7 5% of those with carcinomata of the lungs were only* diagnosed on microscopical examination emphasises the rule (if such emphasis is needed) that a histological examination should never be omitted

Finally this record shows that the majority of the deaths took place in the age group 45–64—i e, in the prime of life, when experience in these skilled occupations counted most

SUMMARY

This paper summarises the findings in a consecutive series of 1247 lungs or portions thereof, examined microscopically for the presence of pneumoconiosis

Of these, 42 were deleted because of inadequate data Of the remainder, pneumoconiosis was not found in 169 but was present in 1036 (silicosis 796, other forms of pneumoconiosis 240) Of the positives, 43% had tuberculosis also, and 7 7% had primary cancer of the lung The histological features of the cases are discussed

Cordial acknowledgments are due for much help generously given by Dr E R A. Merewether and the medical staff of the Factory Department, Ministry of Labour, Dr C L Sutherland and his colleagues, of the Pneumoconiosis Medical Panel, Ministry of National Insurance, Dr K F W Hinson and the staff of the pathological department of the London Chest Hospital, Dr W T Russell and the staff of the statistical department of the Institute of Social Medicine, Oxford, Dr H Wyers, Dr E L Middleton, Dr A Meiklejohn, and the many pathologists who sent specimens

REFERENCES

Belt, T H, Ferris, A A (1942) *Spec Rep Ser med Res Coun, Lond* no 243 p 203
Campbell A H Gloyne S R (1942) *J Path Bact* 54 75
Chief Inspector of Factories (1949) Annual report for the year 1948 H M Stationery Office
Cooke W E (1927) *Brit med J* ii 1024
Davidson M. (1930) Cancer of the Lung and Other Intrathoracic Tumours Bristol
Gloyne S R, Marshall G Hoyle C (1949) *Thorax*, 4 31
Heppleston A G (1947) *J Path Bact* 59, 453
Hill A B, Lewis Faning E (1948) *Brit J industr Med* 5, 1
King E J, Wynn, A H A., Nagelschmidt G, Cochrane, L A (1950) *Min Fuel Power Res Rep* no 10
McDonald S (1927) *Brit med J* ii, 1025
McLaughlin, A I G et al (1950) Industrial Lung Diseases of Iron and Steel Foundry Workers H.M Stationery Office
Maxwell J (1930) *J Path Bact* 33, 233
Meiklejohn, A (1949) *Brit J industr Med* 6 230, 241
Merewether E R A (1936) *Tubercle* 17 385
Middleton E L (1936) *Lancet* ii 1, 59
Registrar General (1950) Statistical Review of England and Wales for the year 1948 H.M. Stationery Office
Simpson, S L (1929) *Quart J Med* 22, 413
Simson, F W Strachen, A S Irvine L G (1930) *Proc Transv Mine med. Offrs Ass* suppl

BLEEDING PEPTIC ULCER

D A FERGUSON
M D Lond, M R C.P
SENIOR REGISTRAR, WHITTINGTON HOSPITAL, LONDON

A L WYMAN
M.D Lond, M R C.P
PHYSICIAN FULHAM HOSPITAL, LONDON,
LATE ASSISTANT PHYSICIAN, WHITTINGTON HOSPITAL

> "An artery had suddenly burst, and as Attila lay in a supine posture, he was suffocated by a torrent of blood, which instead of finding a passage through the nostril regurgitated into the lungs and stomach"—GIBBON's *Decline and Fall of the Roman Empire*, Chap xxxv

SINCE the adoption of early feeding and liberal transfusion in the routine treatment of bleeding peptic ulcer, it is generally assumed that the mortality from this illness has fallen to very low levels The results in expert hands seem to support this conclusion Avery Jones (1947), for example, had a fatality rate of 7 8% in his series Nevertheless, realisation is now more widespread that outside the special clinics such good results are less common (Lewin and Truelove 1949)

TABLE I—THE LESIONS AND MORTALITY

Lesions	Males			Females			Males and females		
	Total	Died	Mortality (%)	Total	Died	Mortality (%)	Total	Died	Mortality (%)
Chronic gastric ulcer	36	15	41 7	13	3	23	49	18	36 7
Chronic duodenal ulcer	37	5	13 5	11	—	—	48	5	10 4
Anastomotic ulcer	4	—	—	1	—	—	5	—	—
'Acute syndrome"	12	2	16 6	16	2	12 5	28	4	14 3
Not proven	12	1	8 3	11	—	—	23	1	4 3
Cirrhosis of liver	1	—	—	1	—	—	2	—	—
Gastric polyposis	—	—	—	1	—	—	1	—	—
Carcinoma of stomach	1	—	—	—	—	—	1	—	—

We report here our experience from January, 1947, to October, 1949, at a general hospital, formerly a separate municipal hospital, which has recently been reorganised as one wing of a larger unit under a regional board The patients were admitted into both medical and surgical wards, and were treated by a number of different physicians and surgeons, including ourselves

To assess accurately the incidence and mortality of bleeding peptic ulcer we scrutinised the notes of every admission during this period, whatever the official diagnosis Sometimes patients discharged as cases of gastric ulcer had been originally admitted with a hæmatemesis "Anæmia" might cloak a slowly progressing melæna Study of all the necropsy reports soon showed us that some bleeding ulcers had not been detected in life Patients with undetected bleeding ulcers have a high death rate and would rarely gain admission to special gastro enterological units Consequently the fatality rate in such units would err on the low side

TABLE II—AGE INCIDENCE AND MORTALITY

Age (yr)	Males			Females			Males and females		
	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)
10–19	—	—	—	1	—	—	1	—	—
20–29	4	—	—	1	—	—	5	—	—
30–39	8	—	—	7	—	—	15	—	—
40–49	24	2	8 3	6	1	16 6	30	3	10 0
50–59	27	6	22 2	6	—	—	33	6	18 2
60–69	25	7	28 0	21	—	—	46	7	15 2
70–79	14	8	55 5	8	2	25·0	22	10	45 4
80 +	1	—	—	4	2	50 0	5	2	40 0
Total	103	23	22 3	54	5	9 2	157	28	17 8

TABLE III—PREVIOUS HÆMATEMESIS OR MELÆNA

No of previous hæmorrhages	Males			Females			Males and females		
	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)
0	76	18	24	45	5	11 1	121	23	19
1	20	4	20	5	—	—	25	4	16
2	4	1	25	3	—	—	7	1	14
3	2	—	—	—	—	—	2	—	—
4	1	—	—	—	—	—	1	—	—
5	—	—	—	1	—	—	1	—	—

The remaining uncertainties were misdiagnosed patients who died without necropsy and the misdiagnosed who recovered despite lack of appropriate treatment

THE PRESENT SERIES

The patients were for the most part drawn from the surrounding neighbourhood and were artisans, labourers, factory workers, small shopkeepers, housewives, and old age pensioners Most belonged to the poorer classes

There were 157 admissions (103 males, 54 females) and 5 patients were admitted twice Although our object was to find out the mortality of hæmorrhage from peptic ulcer, it will be seen from table I that our series includes 1 ulcer which showed evidence of malignancy on histological examination, 1 patient with polyposis of the stomach, and 2 patients who probably had cirrhosis of the liver The rest of the patients fell into the categories of chronic gastric ulcer, chronic duodenal ulcer, anastomotic ulcer, "acute syndrome," or "not proven" (Peptic ulcers with occult blood on routine examinations were not included) Those labelled clearly gastric, duodenal, or anastomotic ulcer were patients in whom an ulcer was demonstrated radiologically, by gastroscopy, at operation or at necropsy The term "acute syndrome" covers those in whom an acute ulcer was seen, usually at necropsy, and those who gave a history suggesting an ulcer of less than four weeks' duration, although no lesion could be demonstrated "Not proven" was a term applied to patients who gave a history of longer than four weeks but in whom no ulcer was found The limit of four weeks is arbitrary, and perhaps it would be more scientific to lump most of the last two classes into the one of "not proven", nevertheless, it seems useful to try to assess the incidence and prognosis of bleeding in cases where acute ulceration is probable Since we were primarily concerned with the outlook in simple peptic ulcer, we have not included patients with obvious carcinoma of the stomach, although we have formed the impression that severe hæmorrhage rarely occurs in this disease

TABLE IV—LENGTH OF ULCER HISTORY AND MORTALITY

Duration	Patients under 50			Patients over 50		
	No	Died	Fatality rate (%)	No	Died	Fatality rate (%)
Less than 1 year	12	—	—	22	4	18·4
1–5 years	7	—	—	13	3	23 1
6–10 years	12	1	8 3	14	4	28 6
Over 10 years	13	1	7 7	31	6	19 4
No history	5	1	20	19	6	31 5
Years	2	—	—	7	2	28 5

Table I shows that 49 patients had chronic gastric ulcer, 48 chronic duodenal ulcer, 5 anastomotic ulcer, and 28 "acute syndrome," and 23 were "not proven"

To give as clear a picture as possible no death has been omitted There were 28 deaths in our total of 157 admissions for gastroduodenal bleeding, a mortality of 17 8% (table II) Even with the strictest criteria it would be permissible to exclude a man, aged 73, who had a very small hæmatemesis on admission but died of a perforation three months later There was also a man, aged 78, admitted for a perforated gastric ulcer, who bled terminally five days after operation As Avery Jones (1947) says "the additional hazard of the prior perforation renders comparison with other groups unreal" This still leaves 26 deaths in 156 admissions, a corrected fatality-rate of 16 6%

FACTORS IN MORTALITY

Age

We agree with other recent workers on the importance of age in determining the issue Of 51 patients under the age of 50, as can be seen from table II, only 3 died (5 9%) Or if 60 is taken as the threshold of old age, 9 died out of 84 (10 7%) Of the 106 patients over 50 years of age 25 died, a fatality rate of 23 6% In patients over the age of 50, mortality from hæmatemesis or melæna was nearly four times heavier than in patients under that age It is obvious that, in comparing different series, the age distribution must be known We had 73 patients over 60 years old (46 5%), compared with 33% in Avery Jones's (1947) series and 42% in Tanner's (1950) series

TABLE V—DISTRIBUTION OF CHRONIC GASTRIC AND DUODENAL ULCER IN PATIENTS UNDER AND OVER THE AGE OF 50

Age group	Males		Females	
	With gastric ulcer	With duodenal ulcer	With gastric ulcer	With duodenal ulcer
Under 50	8	12	3	2
Over 50	28	25	10	9

Sex

Table II shows a big difference in the incidence and mortality in the two sexes. There were nearly twice as many men as women, and whereas 23 of the men died (22 3%) *only* 5 women died (9 2%) This, too, agrees with the findings of other observers There was 1 death in a woman under the age of 50, 2 in women in the 70s, and 2 in women over the age of 80

Previous Ulcer History and Bleeding

A history of past ulcer bleeding in a patient with hæmatemesis and melæna does not make the prognosis worse As shown in table III, there is little difference in the fatality rate between those who have had no previous bleeding and those who have had one or two such episodes Some few patients with a history of three, four, or five past hæmorrhages have survived

The length of the ulcer history furnishes no guide in estimating the outlook for the patient with hæmorrhage (table IV) In our series those patients with no history of previous dyspepsia carried the highest fatality rate In the other categories age seemed to be a more important factor than the duration of the symptoms of peptic ulceration

Type of Lesion

The next inquiry concerned the type of lesion Table I reveals that the numbers of patients with gastric ulcer

TABLE VI—LOWEST AMOUNT OF HÆMOGLOBIN % (HALDANE) RECORDED

Lowest Hb recorded (Haldane)	No of patients	No of deaths
10–19	1	—
20–29	7	2
30–39	32	8
40–49	21	3
50–59	28	2
60–69	17	—
70–79	11	—
80–89	10	1
90–99	11	1
100 +	10	2
Not recorded	9	9

6 5% at Brompton, and Gloyne in 6 4% at the London Chest Hospital, making an incidence of 5 5% of 648 necropsies in all the records In the present investigation, where pneumoconiosis is added, the incidence is still greater, there were 15 cases (18 7%) of tuberculosis in 80 cases of pneumoconiosis accompanied by primary carcinoma of the lung In view of the prevalence of tuberculosis in the population of this country it is not surprising that 5% of lung cancers at necropsy should reveal active tuberculosis, but it is not clear why this percentage should rise to four times that proportion when pneumoconiosis is present also At necropsy a lung which has three separate diseases in it is a much damaged organ, and it is not always possible to determine whether the tuberculosis is an exacerbation of an old lesion or a terminal infection In either case the obstruction to the lymphatic absorption produced by the pneumoconiosis and neoplasm together must be very considerable, and may well be a determining factor

The fact that in the pneumoconiosis series 21% of the cases of silicosis, 13 5% of those with tuberculosis, and 7 5% of those with carcinomata of the lungs were only diagnosed on microscopical examination emphasises the rule (if such emphasis is needed) that a histological *examination should never be omitted*

Finally this record shows that the majority of the deaths took place in the age-group 45–64—i e, in the prime of life, when experience in these skilled occupations counted most

SUMMARY

This paper summarises the findings in a consecutive series of 1247 lungs or portions thereof, examined microscopically for the presence of pneumoconiosis

Of these, 42 were deleted because of inadequate data Of the remainder, pneumoconiosis was not found in 169 but was present in 1036 (silicosis 796, other forms of pneumoconiosis 240) Of the positives, 43% had *tuberculosis also, and* 7 7% *had primary cancer of* the lung The histological features of the cases are discussed

Cordial acknowledgments are due for much help generously given by Dr E R A Merewether and the medical staff of the Factory Department, Ministry of Labour, Dr C L Sutherland and his colleagues, of the Pneumoconiosis Medical Panel, Ministry of National Insurance, Dr K F W Hinson and the staff of the pathological department of the London Chest Hospital, Dr W T Russell and the staff of the statistical department of the Institute of Social Medicine, Oxford, Dr H Wyers, Dr E L Middleton, Dr A. Meiklejohn, and the many pathologists who sent specimens

REFERENCES

Belt T H Ferris, A A (1942) *Spec Rep Ser med Res Coun., Lond* no 243, p 203
Campbell A H, Gloyne S R (1942) *J Path Bact* 54 75
Chief Inspector of Factories (1949) Annual report for the year 1948 H M Stationery Office
Cooke W E (1927) *Brit med J* ii 1024
Davidson M (1930) Cancer of the Lung and Other Intrathoracic Tumours. Bristol
Gloyne S R Marshall, G Hoyle C (1949) *Thorax*, 4, 31
Heppleston, A G (1947) *J Path Bact* 59 453
Hill A B, Lewis Faning E (1948) *Brit J industr Med* 5, 1
King E J, Wynn, A H A Nagelschmidt, G, Cochrane L A (1950) *Min Fuel Power Res Rep* no 10
McDonald S (1927) *Brit med J* ii 1026
McLaughlin A I. G et al (1950) Industrial Lung Diseases of Iron and Steel Foundry Workers H.M. Stationery Office
Maxwell, J (1930) *J Path Bact* 33 233
Meiklejohn, A (1949) *Brit J industr Med* 6 230, 241
Merewether E R A (1936) *Tubercle*, 17 385
Middleton E L (1936) *Lancet* ii 1, 59
Registrar General (1950) Statistical Review of England and Wales for the year 1948 H M. Stationery Office
Simpson S L (1929) *Quart J Med* 22 413
Simson, F W Strachen A S Irvine, L G (1930) *Proc Transv Mine med. Offrs' Ass* suppl

---

BLEEDING PEPTIC ULCER

D A FERGUSON
M D Lond, M R C.P
SENIOR REGISTRAR, WHITTINGTON HOSPITAL, LONDON

A L WYMAN
M.D Lond, M R C.P
PHYSICIAN, FULHAM HOSPITAL, LONDON,
LATE ASSISTANT PHYSICIAN, WHITTINGTON HOSPITAL

> "An artery had suddenly burst, and as Attila lay in a supine posture, he was suffocated by a torrent of blood, which instead of finding a passage through the nostril regurgitated into the lungs and stomach"—GIBBON'S *Decline and Fall of the Roman Empire*, Chap xxxv

SINCE the adoption of early feeding and liberal transfusion in the routine treatment of bleeding peptic ulcer, it is generally *assumed that the mortality from this* illness has fallen to very low levels. The results in expert hands seem to support this conclusion Avery Jones (1947), for example, had a fatality rate of 7 8% in his series Nevertheless, realisation is now more widespread that outside the special clinics such good *results are less common (Lewin and Truelove 1949)*

TABLE I—THE LESIONS AND MORTALITY

Lesions	Males			Females			Males and females		
	Total	Died	Mortality (%)	Total	Died	Mortality (%)	Total	Died	Mortality (%)
Chronic gastric ulcer	36	15	41 7	13	3	23	49	18	36 7
Chronic duodenal ulcer	37	5	13 5	11	—	—	48	5	10·4
Anastomotic ulcer	4	—	—	1	—	—	5	—	—
Acute syndrome"	12	2	16 6	16	2	12 5	28	4	14 3
Not proven	12	1	8 3	11	—	—	23	1	4 3
Cirrhosis of liver	1	—	—	1	—	—	2	—	—
Gastric polyposis	—	—	—	1	—	—	1	—	—
Carcinoma of stomach	1	—	—	—	—	—	1	—	—

We report here our experience from January, 1947, to October, 1949, at a general hospital, formerly a separate municipal hospital, which has recently been reorganised as one wing of a larger unit under a regional board The patients were admitted into both medical and surgical wards, and were treated by a number of different physicians and surgeons, including ourselves

To assess accurately the incidence and mortality of bleeding peptic ulcer we scrutinised the notes of every admission during this period, whatever the official diagnosis Sometimes patients discharged as cases of gastric ulcer had been originally admitted with a hæmatemesis "Anæmia" might cloak a slowly progressing melæna Study of all the necropsy reports soon showed us that some bleeding ulcers had not been detected in life Patients with undetected bleeding ulcers have a high death rate and would rarely gain admission to special gastro enterological units Consequently the fatality rate in such units would err on the low side.

TABLE II—AGE INCIDENCE AND MORTALITY

Age (yr)	Males			Females			Males and females		
	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)	Total	Died	Fatality rate (%)
10–19	—	—	—	1	—	—	1	—	—
20–29	4	—	—	1	—	—	5	—	—
30–39	8	—	—	7	—	—	15	—	—
40–49	24	2	8 3	6	1	16 6	30	3	10·0
50–59	27	6	22 2	6	—	—	33	6	18 2
60–69	25	7	28 0	21	—	—	46	7	15 2
70–79	14	8	55 5	8	2	25·0	22	10	45 4
80 +	1	—	—	4	2	50 0	5	2	40 0
Total	103	23	22 3	54	5	9 2	157	38	17 8

TABLE IX—PATIENTS WITH SEVERE INTERCURRENT DISEASE

No	Age	Type of ulcer	Intercurrent disease	Result
A Females				
1	73	Acute	Cardiac infarction	D
2	87	N p	Hypertensive cardiac disease	R
3	75	G U	Mitral incompetence	D
4	69	N p.	Cerebral thrombosis	R
5	85	Acute	Bronchitis cardiac failure	D
6	75	N p	Hypertensive failure	R
B Males				
1	69	G U	Chronic bronchitis myocardial impairment	D
2	46	G U	*Pulmonary tuberculosis (quiescent)*	R
3	53	Acute	Hypertensive cardiac disease	D
4	61	G U	Bronchopneumonia	D
5	58	D U	Pulmonary tuberculosis	D
6	56	G U	Cardiac failure	D
7	59	G U	Hemiplegia alcoholism	R
8	59	G U	Hemiplegia alcoholism	D
9	58	D U	Coronary disease	R
10	53	D U	Congestive failure	R
11	68	N p	Acute retention prostatectomy	R
12	84	N p	Hypertension cerebral thrombosis	R
13	71	N p	Aortic regurgitation	R
14	66	D U	Coronary disease	R
15	59	G U	Carcinoma pancreas	D
16	70	N p	Bronchitis cardiac failure	D
17	64	G U	Pulmonary tuberculosis	D
18	70	D U	*Bronchopneumonia*	D
19	67	G U	Carcinoma bronchus	D
20	65	G U	Severe bronchitis (? tuberculosis)	R
21	75	G U	Hemiplegia	D
22	68	N p	Hypertensive cardiac disease	R
23	74	N p	Hypertensive cardiac disease	R

N p = not proven
G U = chronic gastric ulcer
D U = chronic duodenal ulcer
R = recovered
D = died

formed, but death ensued from general peritonitis A third patient who underwent emergency gastrectomy died on the table, at necropsy it was found that a purulent bronchitis filled the air passages with pus Another patient died of peritonitis following a "cold" gastrectomy undertaken four weeks after hæmatemesis. In the sixth patient gastric bleeding occurred a few days after operation for perforation

In 2 patients the bleeding seems to have played only a minor part in determining the outcome One feeble old man perforated three months after a small hæmatemesis, and a second died of chronic bronchitis and heart-failure nine weeks after his melæna An old lady recovered from her hæmatemesis sufficiently to become ambulant, but four weeks later she died suddenly of cardiac infarction

TABLE X—DISTRIBUTION OF LESIONS IN PATIENTS WITH SEVERE INTERCURRENT DISEASE

Type of lesion	Males		Females	
	No died	No recovered	No died	No recovered
Acute syndrome	1	0	2	0
Chronic gastric ulcer	8	3	1	0
Chronic duodenal ulcer	2	3	—	—
Not proven	1	5	0	3
Total	12	11	3	3

6 patients had no adequate treatment because their true condition was undiagnosed in life This point is discussed below

In 4 men the bleeding was so rapid and massive that they were moribund before treatment could even be initiated 1 died three minutes after admission, one two hours after Another was admitted for investigation and had an overwhelming terminal hæmorrhage, at necropsy there was a 2 pint clot in the stomach—an artery in the pancreas had eroded In the fourth case death took place twelve hours after admission, an acute ulcer had eroded the splenic artery, and the stomach contained a 2½ pint clot

Severe complicating disease was a prominent feature of other fatal cases 2 patients, for example, had fibrocaseous tuberculosis with cavitation, and another had an advanced carcinoma of the pancreas

1 man, a debilitated alcoholic, recovered from an initial hæmorrhage Gastrectomy was to be done when he should be well enough, but a fatal hæmorrhage took place before the ideal state could be reached

2 men might have been saved by timely operation a man of 64 who died from paralytic ileus after eight days' continual hæmorrhage, and a man of 52 who perforated forty eight hours after admission The 3 remaining fatalities were in a man of 70 who had a localised perforation of his duodenal ulcer, bronchopneumonia, and cirrhosis of the liver, a man of 67, with two chronic gastric ulcers, who had a severe terminal hæmorrhage (he had also a small carcinoma of the lung), and a man of 55 with a complicating bronchopneumonia The 2 last were possibly amenable to surgery at an earlier stage

SEVERE INTERCURRENT DISEASE

As might be expected from the high proportion of old people in this series, intercurrent disease was common Excluding hypertension and atheromatous changes unless there were cardiac and cerebral involvement, complicating diseases were prominent in 29 patients (table IX) There were 6 women, of whom 3 died, and 23 men, of whom 12 died All but 1 of these patients were over the age of 50 The distribution according to the type of peptic ulcer is shown in table X, it will be seen that there were 12 patients with chronic gastric ulcer, and 9 of them died

TABLE XI—FATALITY RATES IN PATIENTS UNDER AND OVER THE AGE OF 50

Age group	Males			Females			Total		
	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)
Under 50	36	2	5 6	15	1	6 7	51	3	5 9
Over 50	67	21	31 3	39	4	10 3	106	25	23 6

Our next consideration was the part played by severe intercurrent disease in causing the great difference in mortality between those under and those over the age of 50 In table XI the fatality rate in males under the age of 50 is 5 6%, whereas over that age it is 31 3%, this difference is significant If patients without severe intercurrent disease are analysed (table XII), we see that the fatality rate in men under the age of 50 was 5 7%, and in men over that age 20% It is doubtful whether this is statistically significant Too much emphasis should not be laid on these figures, which are comparatively small, but it is at any rate suggestive that the increasing mortality with age in bleeding peptic ulcer may be associated with the increasing frequency of severe complicating disease

TABLE XII—FATALITY-RATE IN PATIENTS WITHOUT SEVERE INTERCURRENT DISEASE UNDER AND OVER THE AGE OF 50

Age group	Males			Females			Total		
	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)
Under 50	35	2	5 7	15	1	6 7	50	3	6 0
Over 50	45	9	20 0	33	1	3-0	78	10	12 8

TABLE VII—TRANSFUSIONS

No of bottles	Males	Females	Total
1	4	3	7
2	7	9	16
3	6	6	12
4	13	2	15
5	5	—	5
6	8	1	9
7	3	—	3
8	3	—	3
9	—	1	1
15	1	—	1
23	1	—	1

73 of the patients were transfused 306 bottles were used averaging about 4 bottles per patient transfused 1 bottle = 540 ml of blood

and duodenal ulcer were almost equal In men under the age of 50 there were more instances of chronic duodenal ulcer than of chronic gastric ulcer, but the difference is not significant (table v) Nevertheless the deaths from bleeding gastric ulcer were about three and a half times as numerous as those from duodenal ulcer This difference applied to women as well as men Of interest too is the high death rate in the "acute syndrome"—4 out of 28 patients (14 3%) Ulceration was demonstrated in 105 patients (67%) or about two thirds of our series

BLOOD LOST AND AMOUNT TRANSFUSED

To assess the value of treatment, some idea is necessary of the severity of the bleeding Many patients with slight loss of blood would recover, whatever the treatment It is not always easy to judge the clinical condition from a perusal of the notes As rough guides we tabulated the lowest amount of hæmoglobin recorded and the volume of blood transfused These guides may be misleading Sometimes a large terminal hæmorrhage occurred in a patient who had previously bled only slightly and whose lowest recorded amount of hæmoglobin was 90% (Haldane) On the other hand, some patients bled slowly and steadily for several weeks and readjusted themselves to a hæmoglobin level surprisingly low

The amount of blood transfused (table vii) in a particular instance depended to some extent on the predilection and training of the doctor as well as on the amount of blood lost The tendency was to transfuse early rather than late In the more recent admissions the object was to make the patient fit enough to stand a possible recurrence of hæmorrhage or an emergency operation Of the 73 patients transfused, few received more than six bottles (each bottle contained 540 ml of blood)

At least one patient died so quickly that no blood could be given in time In another case twenty three bottles were given for a succession of severe hæmorrhages In Rh negative patients a difficulty was to obtain sufficient compatible blood, and this caused us to prefer early operation to prolonged transfusion in these cases

The amount of hæmoglobin was recorded in 148 patients As is well known, in those who have recently bled the hæmoglobin may remain high before hæmodilution takes place In those who have bled repeatedly the level of hæmoglobin may be high because of hæmoconcentration Table vi shows that the hæmoglobin was less than 40% (Haldane) in 40 patients (27%), it was over 80% in 31 (20 9%) There were 10 deaths in the former group In another 9 fatal cases no record of the hæmoglobin could be found Most of these cases had not been diagnosed in life and were traced through the necropsy records This increases the difficulty of correlating the degree of anæmia with the fatality rate

THE DEATHS

Much thought has been given to the 28 fatalities to discover where treatment may have erred We have summarised the findings in every patient who died (table viii) There were 18 deaths from chronic gastric ulcer, 5 from chronic duodenal ulcer, 4 from acute ulcer, and 1 from a clinical but not proved duodenal ulcer Of these patients 6 had had an operation In 1 the ulcer was undersewn, but the man bled again ten days later In 2 others emergency gastrectomy was per

TABLE VIII—SUMMARY OF FATAL CASES

No	Age	Sex	Clinical notes
1	73	F	Acute syndrome Died of cardiac infarction a month after admission
2	69	M	G U Hæmatemesis Treated conservatively Improved Second hæmatemesis 6 weeks later Ulcer undersewn within 24 hours. Died of further bleeding 10 days after Chronic bronchitis
3	60	M	G U Partial gastrectomy 5 days after admission Died 3 days later of general peritonitis
4	64	M	D U Transfusions only Died after 8 days—paralytic ileus
5	52	M	G U Perforated on second day Died after 8 days
6	53	M	Overwhelming hæmorrhage 12 hours after admission. Necropsy acute ulcer with erosion of splenic artery, hypertension, cardiac involvement
7	73	M	D U Small hæmatemesis Died after perforation 3 months later
8	61	M	G U and acute ulcer Severe hæmorrhage 4 days after admission Emergency gastrectomy 5 days later but died on the table
9	41	F	G U with hour glass stomach Bled while in hospital for investigation Emergency gastrectomy Died of peritonitis
10	58	M	D U Transfused but relapsed Necropsy bronchopneumonia, active tuberculosis with cavitation
11	56	M	G U Undiagnosed Untreated Cardiac failure
12	75	M	G U Admitted for investigation Overwhelming terminal hæmorrhage Necropsy eroded artery in pancreas 2 pint clot in stomach.
13	87	F	G U Thought to be carcinoma Not seriously treated
14	59	M	G U Terminal hæmorrhage in known carcinoma of pancreas
15	75	F	G U Known mitral regurgitation and hypertension Bleeding unrecognised in life Necropsy large gastric ulcer calcification of mitral valve
16	75	M	Admitted with hemiplegia. Moribund Died three minutes after admission Necropsy gastric ulcer
17	70	M	Clinical D U but not confirmed Melæna Died of chronic bronchitis and heart failure 9 weeks later
18	78	M	D U Unrecognised Treated as anæmia
19	44	M	G U Recovered with medical treatment "Cold" gastrectomy 4 weeks later Died of peritonitis
20	55	M	G U Transfusion only Terminal bronchopneumonia
21	43	M	Acute ulcer Desperately ill Died 2 hours after admission
22	78	M	G U Hæmorrhage after perforation
23	64	M	G U Probably inadequately transfused but had also advanced caseous tuberculosis with cavitation
24	71	M	G U Unrecognised Treated as hæmoptysis
25	70	M	D U Probably inadequately transfused Necropsy localised perforation bronchopneumonia, and cirrhosis of liver
26	67	M	Two G Us Severe terminal hæmatemesis Small carcinoma of lung
27	60	M	G U Medical treatment only Debilitated alcoholic thought unfit for surgery Severe terminal hæmorrhage
28	85	F	Treated as anæmia Necropsy acute gastric ulcer, bronchopneumonia cardiac hypertrophy

G U = chronic gastric ulcer
D U = chronic duodenal ulcer

TABLE IX—PATIENTS WITH SEVERE INTERCURRENT DISEASE

No	Age	Type of ulcer	Intercurrent disease	Result
A Females				
1	73	Acute	Cardiac infarction	D
2	87	N p	Hypertensive cardiac disease	R
3	75	G U	Mitral incompetence	D
4	69	N p	Cerebral thrombosis	R
5	85	Acute	Bronchitis cardiac failure	D
6	75	N p	Hypertensive failure	R
B Males				
1	69	G U	Chronic bronchitis myocardial impairment	D
2	48	G U	Pulmonary tuberculosis (quiescent)	R
3	53	Acute	Hypertensive cardiac disease	D
4	61	G U	Bronchopneumonia	D
5	58	D U	Pulmonary tuberculosis	D
6	56	G U	Cardiac failure	D
7	59	G U	Hemiplegia alcoholism	R
8	59	G U	Hemiplegia alcoholism	D
9	55	D U	Coronary disease	R
10	53	D U	Congestive failure	R
11	63	N p	Acute retention prostatectomy	R
12	84	N p	Hypertension cerebral thrombosis	R
13	71	N p	Aortic regurgitation	R
14	66	D U	Coronary disease	R
15	59	G U	Carcinoma pancreas	D
16	70	N p	Bronchitis cardiac failure	D
17	64	G U	Pulmonary tuberculosis	D
18	70	D U	Bronchopneumonia	D
19	67	G U	Carcinoma bronchus	D
20	65	G U	Severe bronchitis (? tuberculosis)	R
21	75	G U	Hemiplegia	D
22	65	N p	Hypertensive cardiac disease	R
23	74	N p	Hypertensive cardiac disease	R

N p = not proven
G U = chronic gastric ulcer
D U = chronic duodenal ulcer
R = recovered
D = died.

formed, but death ensued from general peritonitis A third patient who underwent emergency gastrectomy died on the table, at necropsy it was found that a purulent bronchitis filled the air passages with pus Another patient died of peritonitis following a "cold" gastrectomy undertaken four weeks after hæmatemesis. In the sixth patient gastric bleeding occurred a few days after operation for perforation

In 2 patients the bleeding seems to have played only a minor part in determining the outcome One feeble old man perforated three months after a small hæmatemesis, and a second died of chronic bronchitis and heart-failure nine weeks after his melæna An old lady recovered from her hæmatemesis sufficiently to become ambulant, but four weeks later she died suddenly of cardiac infarction.

TABLE X—DISTRIBUTION OF LESIONS IN PATIENTS WITH SEVERE INTERCURRENT DISEASE

Type of lesion	Males		Females	
	No died	No recovered	No died	No recovered
Acute syndrome	1	0	2	0
Chronic gastric ulcer	8	3	1	0
Chronic duodenal ulcer	2	3	—	—
Not proven	1	5	0	3
Total	12	11	3	3

6 patients had no adequate treatment because their true condition was undiagnosed in life This point is discussed below

In 4 men the bleeding was so rapid and massive that they were moribund before treatment could even be initiated 1 died three minutes after admission, one two hours after Another was admitted for investigation and had an overwhelming terminal hæmorrhage, at necropsy there was a 2 pint clot in the stomach—an artery in the pancreas had eroded In the fourth case death took place twelve hours after admission, an acute ulcer had eroded the splenic artery, and the stomach contained a 2½-pint clot

Severe complicating disease was a prominent feature of other fatal cases 2 patients, for example, had fibrocaseous tuberculosis with cavitation, and another had an advanced carcinoma of the pancreas

1 man, a debilitated alcoholic, recovered from an initial hæmorrhage Gastrectomy was to be done when he should be well enough, but a fatal hæmorrhage took place before the ideal state could be reached

2 men might have been saved by timely operation a man of 64 who died from paralytic ileus after eight days' continual hæmorrhage, and a man of 52 who perforated forty eight hours after admission The 3 remaining fatalities were in a man of 70 who had a localised perforation of his duodenal ulcer, bronchopneumonia, and cirrhosis of the liver, a man of 67, with two chronic gastric ulcers, who had a severe terminal hæmorrhage (he had also a small carcinoma of the lung), and a man of 55 with a complicating bronchopneumonia The 2 last were possibly amenable to surgery at an earlier stage

SEVERE INTERCURRENT DISEASE

As might be expected from the high proportion of old people in this series, intercurrent disease was common Excluding hypertension and atheromatous changes unless there were cardiac and cerebral involvement, complicating diseases were prominent in 29 patients (table IX) There were 6 women, of whom 3 died, and 23 men, of whom 12 died All but 1 of these patients were over the age of 50. The distribution according to the type of peptic ulcer is shown in table X, it will be seen that there were 12 patients with chronic gastric ulcer, and 9 of them died.

TABLE XI—FATALITY-RATES IN PATIENTS UNDER AND OVER THE AGE OF 50

Age group	Males			Females			Total		
	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)
Under 50	36	2	5·6	15	1	6·7	51	3	5·9
Over 50	67	21	31·3	39	4	10·3	106	25	23·6

Our next consideration was the part played by severe intercurrent disease in causing the great difference in mortality between those under and those over the age of 50 In table XI the fatality-rate in males under the age of 50 is 5·6%, whereas over that age it is 31·3%, this difference is significant If patients without severe intercurrent disease are analysed (table XII), we see that the fatality rate in men under the age of 50 was 5·7%, and in men over that age 20% It is doubtful whether this is statistically significant Too much emphasis should not be laid on these figures, which are comparatively small, but it is at any rate suggestive that the increasing mortality with age in bleeding peptic ulcer may be associated with the increasing frequency of severe complicating disease

TABLE XII—FATALITY-RATE IN PATIENTS WITHOUT SEVERE INTERCURRENT DISEASE UNDER AND OVER THE AGE OF 50

Age-group	Males			Females			Total		
	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)	No of patients	Died	Fatality rate (%)
Under 50	35	2	5·7	15	1	6·7	50	3	6·0
Over 50	45	9	20·0	33	1	3·0	78	10	12·8

DIAGNOSIS

Mention has already been made of 6 patients in whom the diagnosis was made only at necropsy Except for a man of 55, they were all well stricken in years (71, 78, 85, and 87) In another 5 patients the diagnosis was missed at first It must be remembered that bleeding peptic ulcer is not always dramatic, and that in the old, the sick, the anæmic, and the demented memory is vague and history obscure Care and great patience are required to enable one to reach the diagnosis before the pathologist does For example

A man of 56 was referred to medical outpatients as a case of cardiac dyspnœa It was found that six days previously he had had a brisk hæmorrhage from an acute ulcer and his hæmoglobin was 50% (Haldane)

A man of 56 was admitted as a case of bronchopneumonia His hæmoglobin was 22% (Haldane) and he had pulmonary œdema

A man of 78 was admitted with hæmoglobin 22% (Haldane) and normal stools He was thought to have pernicious anæmia, until a fatal hæmorrhage gave the answer

Such experience has caused us to view with suspicion any anæmia of recent onset, even though there is no clear gastric history In these circumstances a rectal examination may reveal melæna

SURGERY

Of the 31 patients treated surgically, 5 died, a mortality of 16% 20 of these were "cold" gastrectomies, with 1 death (5% mortality), and the remaining 11 had emergency operations leading to 4 deaths (36%) 21 of those operated on had gastric ulcer, 8 duodenal ulcer, 1 anastomotic ulcer, and 1 gastric polyposis All 5 deaths took place in those with gastric ulcer The *patient with hæmorrhage after perforation is not included*

Among the 15 patients under the age of 50 there were 5 emergency operations with 1 death, and 10 "cold" operations with no deaths Among the 16 over the age of 50 there were 6 emergency operations with 3 deaths and 10 "cold" operations with none The numbers are small but emergency operation in patients over the age of 50 seems to be hazardous It must, however, be admitted that these patients were operated on at various times after the hæmorrhage had begun and were usually gravely ill

Gastrectomy done in selected cases after bleeding has ceased is safe even in the elderly

DISCUSSION

The burning question in the treatment of bleeding ulcer *at present is the rôle of surgery* Excellent results have been achieved by those with a medical bias, such as Avery Jones, and equally good results by those with a surgical bias, such as Tanner In our study we have sought guiding generalisations and like other observers we have found that the prognosis is worse in the elderly, in men, and in those with gastric ulcer A history of previous bleeding, or of symptoms over a long period, affects the outcome but little Before treatment, diagnosis is necessary, and it was disquieting to find that in 6 cases no diagnosis had been made in life In others the diagnosis was late Elderly people with chronic peptic ulceration who have been bleeding for a long time are often cachectic to a degree that suggests advanced malignant disease It would be a grave error to withhold energetic treatment on the mistaken supposition that the prognosis is hopeless

We have tried to find a reason for the higher *fatality-rates* in the older patients One possibility would be an increasing proportion of the more lethal chronic gastric ulcer in older people, but in our series the difference in distribution of chronic gastric and duodenal ulcer below and above the age of 50 is not significant A second possibility is that severe intercurrent disease is more likely to be present in the elderly This seems to us a very important factor and is too often overlooked

The treatment of the present patients was usually medical in the first instance, but if this appeared to be failing, surgery was undertaken at the earliest possible moment This was the practice both of physicians and surgeons, although it is likely that the surgeons would the sooner recognise the failure of medical methods With early and close cooperation of physician and surgeon the charge that patients are left too late for surgery can be avoided Confronted with a bleeding patient the doctor must decide whether medical measures alone will stop the hæmorrhage or whether surgery must be invoked without delay As Lewison (1950) succinctly puts it, the problem is "to differentiate by as precise a means as possible which cases cannot be controlled short of surgery" Statistics and laboratory tests here are little help The exceptions are too many From the study of the patients who died we are not convinced that immediate routine surgery would save more lives than would careful selection In our 28 fatal cases we think it possible that 3 or 4 patients would have had a better chance if treated surgically We doubt whether much more could have been done for the others This would still leave a mortality of about 14–15% In the end all rests on the experience and judgment of the clinician and on the surgical facilities to hand

SUMMARY

157 consecutive admissions for gastroduodenal bleeding are reviewed There were 28 deaths, a fatality rate of 17 8%

The prognosis was worse in men, in those over the age of 50, and in those with chronic gastric ulcers Severe complicating disease and failure of correct diagnosis affect the prognosis adversely in the elderly

There is no rigid formula enabling one to detect the cases that will respond only to surgery Surgical treatment should be based on careful selection of patients *and close cooperation of physician and surgeon*

We wish to thank our colleagues for their very helpful criticism, in particular Dr F Binks, Mr W Davey, Dr A. L Jacobs, and the late Mr I I Price

REFERENCES

Jones F A (1947) *Brit med J* ii 441, 477
Lewin D C Truelove, S (1949) *Ibid* i 383
Lewison E F (1950) *Surg Gynec Obstet* 90 suppl 1
Tanner N C (1950) *Proc R Soc Med* 43 147

STILBŒSTROL SULPHATE, ŒSTRONE, AND EQUILIN

FURTHER OBSERVATIONS ON THE POTENCY AND CLINICAL ASSESSMENT OF ŒSTROGENS

P M F Bishop
D M Oxfd
ENDOCRINOLOGIST TO GUY'S HOSPITAL AND CHELSEA HOSPITAL FOR WOMEN, AND DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY, POSTGRADUATE MEDICAL SCHOOL OF LONDON

N A Richards
M B Adelaide, M R C O G
CHIEF ASSISTANT, CHELSEA HOSPITAL FOR WOMEN

With statistical assistance from

W L M Perry
M D St And
MEMBER OF STAFF, MEDICAL RESEARCH COUNCIL

In previous studies the potencies of the synthetic œstrogens stilbœstrol, dienœstrol, hexœstrol, and bis dehydrodoisynolic acid (Bishop et al 1948) and of the compounds ethinyl œstradiol and equine conjugated œstrogen (Bishop et al 1950) were compared by observing their action in the production of uterine bleeding in women with amenorrhœa

"Equine conjugated œstrogen" denotes the extract f œstrogenic substances from the urine of pregnant ares The extract is prepared by collecting urine rom pregnant mares kept in stables during the winter The urine is immediately cooled to low temperatures by tanding the collecting barrels out of doors The resulting extract is a mixture of conjugated œstrogens, containng among other compounds œstrone sulphate. Equine conjugated œstrogen proved to be almost half as potent is stilbœstrol and therefore probably considerably more potent than œstrone

Accordingly it seemed desirable to study the potencies of the sulphates of the stilbene group of synthetic œstrogens, so as to determine whether these salts were also more potent than their corresponding œstrogens It soon became clear that they were not going to prove to be so, and consequently further studies of dienœstrol sulphate and hexœstrol sulphate were abandoned Work on stilbœstrol sulphate was nevertheless continued and the results are recorded here

At the same time we were provided with supplies of pure œstrone and pure equilin by Dr H F Hailman, of the Upjohn Company, Kalamazoo, U S.A , and were therefore able to compare the potency of these two natural œstrogens with that of stilbœstrol

METHOD

The method of clinical assessment was the same as in the previous study, and the following description is quoted from Bishop et al. (1948)

> The œstrogen was given by mouth in daily doses for a fortnight to induce 'withdrawal bleeding' within fourteen days of the last dose, the usual interval being from two to four days The first course consisted of a 'sighting dose (usually 2 mg daily in the case of stilbœstrol) Depending on whether the response was positive or negative, the daily dose of the second course (the first bracketing' dose) was either lowered or raised—usually halved or doubled The daily dose of the third course (the second bracketing dose) was similarly adjusted according to the response of the first bracketing dose In this way a therapeutic unit was obtained being the mean of the daily doses of two courses one of which consisted of the highest and the other of the lowest, daily dose to fail or succeed, respectively to produce a withdrawal bleeding
>
> 'The patients selected had primary amenorrhœa or secondary amenorrhœa of at least some months' standing
>
> In general an attempt was made first to determine the therapeutic unit of stilbœstrol, and subsequently the therapeutic unit of one or more of the other œstrogens, on the same patient"

RESULTS

Of the 29 patients studied, 26 had secondary amenorrhœa and 3 primary amenorrhœa, 236 courses of œstrogen were given , 29 therapeutic units of stilbœstrol, 15 of stilbœstrol sulphate, 14 of œstrone, and 17 of equilin were obtained.

The statistical analysis was made in the same way as that previously used by Dr C W Emmens (Bishop et al. 1948) The logarithm of the ratio of the effective doses of two of the œstrogens on an individual patient was taken as the statistical unit The potencies and limits of error thus reached are shown in table I the comparisons being made with the therapeutic unit of stilbœstrol expressed as unity.

TABLE I

Substance	No of comparisons	Potency	Fiducial limits of error (P = 0·05)
Stilbœstrol sulphate	15	0 44235	0 27305–0 71145 (62 2–160 82 %)
Œstrone	14	0 04665	0·027632–0·078832 (59 2–168 9 %)
Equilin	17	0 32557	0 19546–0 42154 (63 6–145 7 %)

As in the previous trials (Bishop et al. 1950) the logarithms of the actual effective doses were subjected to analysis of variance (table II)

TABLE II

Œstrogens compared	Degree of freedom	Sum of squares	Mean ratio	F	P
Stilbœstrol v. stilbœstrol sulphate					
Between substances	1	1 00703	1 00703	10 341	< 0 01
Within substances	28	2 72653	0 09738		
Total	29	3 73356			
Stilbœstrol v œstrone					
Between substances	1	12 39882	12 39882	66 00	< 0 001
Within substances	26	4 88439	0 18786		
Total	27	17 28321			
Stilbœstrol v equilin					
Between substances	1	1·64939	1·64939	14 5719	< 0 001
Within substances	34	3 84857	0 11319		
Total	35	5 49796			

Potency ratios	*Potency*	*Fiducial limits of error* (P = 0·05)
Stilbœstrol sulphate v stilbœstrol	0 4301	0 2941–0 6259 (68 4–146 %)
Stilbœstrol v œstrone	0 04665	0·0270–0·0808 (57 8–173 %)
Stilbœstrol v equilin	0 37340	0 2572–0 5421 (68 9–145 %)

It will be seen that, as in the previous trial (Bishop et al. 1948), the potency worked out on this basis very closely resembles that calculated by the original method (table I)

TOXICITY

No toxic effects were encountered within the range of doses of stilbœstrol sulphate, œstrone, or equilin used in these trials.

DISCUSSION

Choice of End-point

In the previous report (Bishop et al 1948) reasons were given for our choice of œstrogen withdrawal bleeding in cases of amenorrhœa as the most suitable endpoint for a clinical assessment of œstrogenic potency These reasons may be briefly recapitulated here

Other possible end points are relief of menopausal symptoms conversion of an atrophic to an œstrous type of vaginal smear and suppression of lactation

Relief of Menopausal Symptoms—These symptoms are entirely subjective and difficult to assess quantitatively Even if the daily hot-flush count were accepted as a semiquantitative end point, considerable alterations in the count would have to occur to be significant, and after each course of œstrogen which gave a positive result the hot-flush count would have to be allowed to return to its pre-treatment baseline At least two œstrogens would have to be tested on each patient The assessment might therefore take many months during which the œstrogenic status of the patient might be constantly changing Finally the patient would be disinclined to endure the series of relapses which the return to the base line after each course of effective œstrogen therapy would entail

Changes in Vaginal Smear—We have seldom found menopausal women with a sufficiently labile smear to change from the atrophic to the œstrous condition and vice versa quickly enough to allow assessment of at least two œstrogens by this method

Suppression of Lactation—Only one course of œstrogen is given to succeed or fail to suppress lactation in any one patient on one occasion. It is therefore impossible to compare two œstrogens in the same patient

There are variables in the present method which might have been expected to vitiate the results seriously—

TABLE III—RELATIVE POTENCY (COMPARED WITH STILBŒSTROL) OF ŒSTROGENS ADMINISTERED ORALLY IN RATS AND THE HUMAN SPECIES

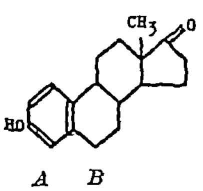
Œstrogen	Rat	Man
Stilbœstrol	100	100
Dienœstrol	68	26
Hexœstrol	10	5
Bis dehydrodoisynolic acid	500	21
Ethinyl œstradiol	18	2567
Equine conjugated œstrogen	5	49
Stilbœstrol sulphate (Broom 1951)	50	44
Œstrone	2	5

e g, the possibility of occasional spontaneous periods being mistaken for withdrawal bleedings, and the level of response in any one patient varying during the investigation That such variables did not in fact seriously affect the results seems clear from the statistical analysis

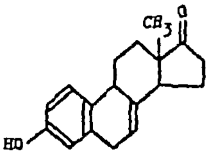
Comparison of Clinical Assessment and Animal Assay

Harmer and Broom (1948, 1950) and Broom (1951) have made large scale experiments to assess, by means of the changes in the vaginal smears, the activity of certain œstrogens given by mouth to ovariectomised adult rats Their results, set side by side with ours, show considerable, and in some instances fundamental, differences (table III) For instance, the two results agree in showing that stilbœstrol is more potent than dienœstrol, hexœstrol, equine conjugated œstrogen, stilbœstrol sulphate, and œstrone, ethinyl œstradiol is twenty-five times as potent as stilbœstrol in man, and only one fifth as potent in the rat, and bis dehydrodoisynolic acid is five times as potent in the rat and only a fifth as potent in man Among the œstrogens compared here it is interesting to note that stilbœstrol sulphate bears almost exactly the same ratio to stilbœstrol in man as it does in the rat, whereas œstrone is only a fiftieth as potent in the rat, though it is a twentieth as potent in man

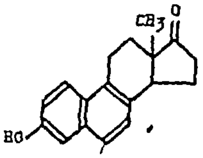
It was somewhat of a surprise to find equilin to be such an active œstrogen It was known that the activity of natural œstrogens is lowered when ring B of the steroid nucleus is aromatic as in equilenin Miescher 1948) The presence of a double bond at C7 in ring B, as in equilin, is said to have no effect on the œstrogenic activity (Miescher 1948), but the activity, as estimated by the vaginal smear, is stated to be only a quarter that of œstrone, and by the immature mouse uterine weight method only about a tenth (Pearlman 1948) Broom has not yet determined the oral potency of equilin by his method In view of the high activity of equilin as compared with œstrone found in the present study, it would be interesting to know whether the introduction of an ethinyl side chain at C17 would increase the oral potency of equilin as it does that of œstradiol The potency of ethinyl equilin is now being compared by us with that of stilbœstrol.



Œstrone



Equilin



Equilenin

SUMMARY

A method is described for comparing the potency of œstrogens in man It consists in giving the œstrogen daily by mouth in fourteen day courses to amenorrhœic women and recording whether œstrogen-withdrawal bleeding takes place

The results obtained indicate that stilbœstrol sulphate is half as potent as stilbœstrol, œstrone one twentieth as potent, and equilin one third as potent

"Toxicity" manifested as nausea was not encountered with these three œstrogens in the range of doses administered

Reasons are given for choosing this end point and for the failure to devise any other suitable method of assessment at different levels of œstrogenic response, such as relief of menopausal symptoms, the production of an œstrous vaginal smear, or the suppression of lactation

We wish to thank Sir Jack Drummond, F.R.S., for facilities to enable us to carry out this work, and Dr H F Hailman for generous supplies of œstrone and equilin The stilbœstrol sulphate, dienœstrol sulphate, and hexœstrol sulphate were supplied by Boots Pure Drug Co Ltd and the œstrone and equilin by the Upjohn Corporation, of Kalamazoo, Michigan, U S A

REFERENCES

Bishop, P M F Kennedy, G C Wynn Williams G (1948) *Lancet* ii 764
— Richards N A, Neal Smith, D J (1950) *Ibid*, i 848
Broom W A (1951) Ciba Foundation Conference on Administration and Dosage of Steroid Hormone and Related Compounds London (in the press)
Harmer, G L M, Broom W A (1948) *Lancet*, ii 766
— — (1950) *Ibid* i 850
Miescher K (1948) Recent Progress in Hormone Research New York vol iii p 52
Pearlman, W H. (1948) The Hormones New York vol i p 367

THE SERUM-PROTEIN LEVELS OF SAMOANS, FIJIANS, AND INDIANS IN FIJI

LUCY WILLS
M A Camb, M B Lond

MURIEL E BELL
M.D N Z, F.N.Z.I.C.

From the Department of Nutrition Research Otago Medical School, Dunedin, New Zealand

DURING nutritional surveys in Fiji and Samoa the serum protein was estimated in 823 persons (Fijian and Indian) in Fiji, and 249 persons (all Samoans) in Samoa As the results show a marked deviation from the average findings reported for Europeans and for Indians in India, they are recorded in this note

MATERIAL AND METHODS

Those examined were as far as possible representative of the three races and of all age groups. The surveys were done in 1950, in January and February, which are wet months, it was therefore impossible to get into the remote inland districts in Fiji Groups of people were, however, examined in the principal towns and in the villages of the coastal zones in the islands of Viti Levu (Fiji) and of Upolu (Samoa), and in a large group of inland villages on the transisland road in Viti Levu A group of European hospital sisters and N Z R A F personnel who had been some time in Fiji were examined also

The total serum protein was determined by the copper sulphate specific gravity method of Phillips, Van Slyke et al (1945), with the use of Hoch and Marrack's (1945) formula, $P = 364\ (Gs - 1.0060)$ for calculating the percentage of protein The majority of the determinations were done on capillary blood The reliability of the method was checked by duplicate estimations on capillary and venous blood, the results showed close agreement The estimations were done as soon as possible after the blood had been taken, but a delay of 3–4 hours did not affect the values The results in the different groups are strictly comparable. Some samples of serum were flown to Dr Hans Hoch in America, who most kindly determined the total content of protein by estimating the specific gravity by direct weighing and also made electrophoretic analysis

TABLE I—MEAN SERUM-PROTEIN VALUES FOR DIFFERENT RACES IN FIJI AND SAMOA AT DIFFERENT AGES

Racial groups	Under 2 yr			2–5 yr			6–14 yr			15–30 yr			Over 30 yr		
	No	Serum protein		No	Serum protein		No	Serum protein		No	Serum protein		No	Serum protein	
		g /100 ml	SD		g /100 ml	SD		g /100 ml	SD		g /100 ml	SD		g /100 ml	SD
Samoan	24	7 25 ±0 18	0 90	34	7 96 ±0 09	0 54	102	8 25 ±0 05	0 47	42	8 45 ±0 07	0 44	15	8 29 ±0 18	0 70
Fijian	29	7 12 ±0 09	0 47	45	7 36 ±0 07	0 50	159	7 85 ±0 03	0 34	110	7 85 ±0 03	0 35	22	7 65 ±0 08	0 39
Indian	28	6 83 ±0 10	0 51	21	7 01 ±0 13	0 61	119	7 59 ±0 03	0 34	106	7 80 ±0 03	0 35	19	7·64 ±0 05	0 22
Europeans in Fiji										19	7 30 ±0 06	0 28			
Europeans in Samoa										1	7 10				

RESULTS

The results have been classified by race, age, and condition and the figures are shown in tables I and II There was no significant difference between the values obtained for men and women so these have been grouped together under their appropriate age group If the findings in pregnant women are excluded the figures show that by the age of 6–14 years the mean serum protein values for all the coloured races were significantly raised above the levels usual in Europeans and above those found in the present survey in people of European race living in Fiji In Samoan children the rise had already appeared by the age of 2–5 years, when the mean value was 7 96 ± 0 09 g per 100 ml compared with an expected figure of about 7 0 g per 100 ml All three races showed the same tendency, but in all age groups the mean values in Samoans were significantly higher than in the other two races, individual figures as high as 9 0 g per 100 ml and over being not uncommon in all age groups over 2 years In all three racial groups there was a slight fall in the protein level after the age of 30 years

The results obtained by electrophoresis by Dr Hoch for a sample of serum from a healthy young Fijian male are shown in table III The total protein value of 7 9 g per 100 ml agrees with our finding for this case The combined value for albumin and α globulin is within normal limits, though the percentage is low on account of the high γ globulin value which is about twice the normal figure The amount of β globulin is slightly reduced, both absolutely and relatively

The values obtained during pregnancy were considerably lower than the mean figure for other adults, the fall in all three race groups being by approximately 1 0 g per 100 ml by the third trimester, a fall of a similar order to that found by Hoch and Marrack (1948) and Macarthur (1948) and other workers, in European women during pregnancy

DISCUSSION

The raised total serum protein values found in apparently healthy individuals among Fijians, Indians in Fiji, and Samoans are in strong contrast with the levels reported for the European race, including members of it living in Fiji, and for Indians living in India The usually accepted mean level for normal adult Europeans, Indians, and Chinese of both sexes is about 7 0 g per 100 ml (Marrack and Hoch 1949, Havens and Williams 1948, Seibert et al. 1947, Hynes and Lehmann 1946, Walters et al 1947, Yi et al. 1948), though Datta and Chakravarty (1947) found a mean value of 7 5 g per 100 ml for healthy adult Indians of both sexes In our own small series from Fiji the figure for Europeans was 7 3 ± 0 06 g per 100 ml, a value significantly lower than those found in the other races after the age of 5–9 years

Similar high serum protein values have been reported in other races In West Africa Stephen (1948) made an extensive study of different groups of Africans, using the copper sulphate specific gravity method to determine the protein levels He found a progressive fall in the protein values from one of 7 8 g per 100 ml in a Service group with 6 weeks' service, through one of 7 4 g for a group with from 6–8 months' service, to a figure of 7 2 g for men with 2 or more years' service, much spent in India on European scale rations Adult male villagers had a mean value of 7 5 g per 100 ml In contrast with these findings the mean value for a group of 50 European soldiers stationed at Accra for from 3 to 18 months was only 6 9 g per 100 ml It should be noted that all these values would be about 0 4 g higher if Hoch and Marrack's formula had been used to calculate them instead of Phillips and Van Slyke's, the values would then agree very closely with the ones we obtained for the three coloured races and for Europeans in Fiji In two villages in Gambia Barakat and Smith (1949) found in the adult population a mean serum protein level of 7 7 g per 100 ml, there was clinical evidence in both villages of deficiencies in total calories and in the vitamin B complex Mohun (1946) reported a similar but smaller increase in the mean protein value in a small group of young African Servicemen Similarly, Milam (1946) found that negroes in North Carolina had a higher mean serum protein value than whites in the same district and that the increase was due to a raised globulin value, associated in this case, however, with a decreased

TABLE III—DISTRIBUTION OF PROTEIN FRACTIONS IN THE BLOOD SERUM OF A HEALTHY YOUNG MALE FIJIAN, COMPARED WITH THE NORMAL VALUES
(Dr Hans Hoch's Figures)

Protein fraction	Amount (g /100 ml)		Fraction of total protein %	
	Fijian	Normal	Fijian	Normal
Albumin and globulin	4 2	4 5	53 0	61·6
α_2 globulin	0 75	0 75	9 5	10·4
β-globulin	0 65	1 00	8 5	13 8
γ-globulin	2 3	1 05	29 0	14 2
Total proteins	7 9	7 3	100 0	

TABLE II—MEAN SERUM PROTEIN VALUES IN PREGNANT WOMEN OF DIFFERENT RACES IN FIJI AND SAMOA AT DIFFERENT STAGES OF PREGNANCY

Racial groups	At 1–40 wks			At 1–16 wks			At 17–28 wks			At 29–40 wks		
	No	Serum protein		No	Serum protein		No	Serum protein		No	Serum protein	
		g /100 ml	SD		g /100 ml	SD		g /100 ml	SD		g /100 ml	SD
Samoans	32	7 46 ±0 10	0 53	9	7 72 ±0 18	0 53	16	7 46 ±0 08	0 31	7	7 13 ±0 31	0 83
Fijians	58	7 05 ±0 06	0 43	9	7 29 ±0 18	0 53	18	7 03 ±0 41	0 41	31	7 01 ±0 07	0 39
Indians	88	6 97 ±0 04	0 36	11	7 16 ±0 15	0 51	40	7 01 ±0 04	0 29	37	6 88 ±0 06	0 39

albumin value But high serum protein values are not a racial characteristic of the African Quinton and Barnes (1942) in Johannesburg, using the biuret method, found an average figure of 7 3 g per 100 ml in a group of 68 healthy Bantu males having a diet relatively good if somewhat high in carbohydrate Youmans et al (1943) using the micro Kjeldahl and biuret methods found in an ill fed population in middle Tennessee that both whites and Africans had a mean serum-protein value under 7 3 g per 100 ml, which was often associated with reduced albumin and raised globulin values

Snell (1950) examined 935 Japanese, who were so called "healthy" people though a large proportion of them suffered from hookworm, ascaris, and other worm infestations, and the incidence of tuberculosis also was probably high The diet was largely rice with fish as the source of animal protein The serum protein values determined by the copper sulphate method were significantly raised above the European standard in all age groups and in both sexes, and reached a mean level of 7 7 g per 100 ml in adult women

The pathological or physiological condition underlying the high values for serum protein in the different racial groups in Fiji and Samoa is at present unknown It should be noted, however, that the individual often appeared to be in fine physical condition, witness the athletic prowess of the Fijians, and yet the sera of these magnificent specimens showed the same high protein values Injury or infection and liver disease may cause an increase in the globulin fraction of the serum protein (Marrack and Hoch 1949) which in certain conditions such as kala azar may result in total values as high as 12 0 g per 100 ml serum It is thought that, in kala-azar as in malaria and some other infections, liver injury plays a part as well as the immune reaction In these conditions it is the γ globulin fraction that is so markedly increased It is known also that serum globulins increase in conditions associated with lipæmia and high serum values for cholesterol

In the different series quoted above, the common factors seem to have been relative poverty, a high incidence of infection and infestation with intestinal parasites, and a high carbohydrate diet, often, but not always deficient in animal protein and fat It should be noted, however, that such deficient diets may be associated in the same peoples with hypoproteinæmia (Youmans et al 1943, Trowell and Muwazi 1945, Altmann 1948, Walt and Wills 1950) In our present series, infestation with intestinal worms, including hookworm and ascaris, was common, though clinical signs and anæmia were rarely seen Children up to the age of 7 or 9 years also suffered severely from sores, particularly of the arms and legs, which were variously ascribed to impetigo, infected scabies, and scratched mosquito bites As the rise in serum protein values did not occur in the Fijian and Indian children until a later age than in the Samoans, intestinal parasites and the common infections of the skin can be excluded as major factors in the production increase of the increased serum protein Similarly such tropical diseases as malaria, kala azar, and filarial infections can be excluded, since the first two do not occur in Fiji and the third is extremely uncommon at the present day The prevalence of yaws, however, is a major problem in Samoa, where the disease is often acquired in the first two years of life and is very severe In Fiji, though we saw only a few cases, mostly in school children, the majority of the population is said to have had yaws, but to have had sufficient treatment to suppress the symptoms and make the individual no longer infectious though not enough to reverse the almost universally positive Kahn reaction The high sedimentation rate reported for many seemingly healthy Fijians and Samoans is apparently related to the presence of a positive Kahn reaction If infection with yaws is related to a high serum protein level and if infection generally occurs earlier in the Samoans than in the Fijians, the disparity in the age at which the serum protein level rises in the two races would be explained The Indians in Fiji are said not to suffer from yaws and there was no obvious clue to the possible cause of the somewhat high values in the older age groups The possible significance of diet is difficult to assess since it varied widely in amount and between the different racial groups studied Further work should be directed to a study of the diet in the different racial groups and to an investigation of the relation between the high serum protein values and the occurrence of a positive Kahn reaction and of yaws in all its stages A study should also be made of the other infections such as those due to the salmonella group of organisms which also cause a rise in the serum γ globulin due to antibody formation

SUMMARY

The serum protein was estimated by the copper sulphate method in 823 Fijians and Indians in Fiji and 249 Samoans in Samoa

The people examined were as far as possible a cross section of the three races, of all age groups, and, with few exceptions, apparently healthy

There was no significant difference between the values obtained for the two sexes and these were grouped together

The mean serum protein levels of all three races and all age groups after 6–14 years were significantly higher than the levels usual in Europeans, including Europeans living in Fiji and Samoa

The rise appeared by the age of 2–5 years in Samoan children

The values for Samoans were significantly higher than for the other two races in all age groups over 2 years.

Electrophoretic analysis of serum from a healthy young Fijian male showed a γ globulin value about twice the normal figure

The significance of these findings and their possible relationship to infection with yaws is discussed

We wish to thank the many assistant medical practitioners, schoolmasters and schoolmistresses, health sisters, and nurses of many races who, by their willing coöperation made this work possible We are deeply indebted to Mr Pery Johnston, superintendent of the laboratory of the Colonial Memorial Hospital, Suva, for technical help given most ungrudgingly, and to Dr J M Cruikshank, inspector general, South Pacific Health Service, Suva, Fiji, and to Dr J C. Lopdell, director of public health, Apia, Samoa Our thanks are due to the British Colonial Development Fund, the N.Z Department of Health, and the N.Z Department of Island Territories for providing the funds that enabled us to carry out the investigation

REFERENCES

Altmann A (1948) *Clin Proc* 7 32
Barakat M R Smith D A (1949) *Lancet* ii, 12
Datta, N C, Chakravarty, R K (1947) *Indian J med Res* 35, 281
Havens W P, Williams, T L (1948) *J clin Invest* 27 340
Hoch H, Marrack J R (1945) *Brit med. J* ii 161
— — (1948) *J Obstet, Gynæc* 55, 1
Hynes M, Lehmann H (1946) *J Physiol* 104 305
Macarthur T L (1948) *Amer J Obstet Gynec* 55, 382
Marrack, J R Hoch, H (1949) *J clin Path.* 2, 161
Milam, D F (1946) *J Lab clin Med* 31, 285
Mohun A F (1946) *Ann trop Med.* 40 29
Phillips R A Van Slyke, D D Dole, V P Emerson, K, Hamilton P B, Archibald R M (1945) Copper Sulphate Method for Measuring Specific Gravity New York
Quinton M. H, Barnes, H D (1942) *S Afr J med Sci* 7, 42
Seibert, F B Seibert M V Atno, A J, Campbell H W (1947) *J clin Invest* 26 90
Snell, F M (1950) *Blood* 5, 89
Stephen, J D (1948) *Trans R Soc trop Med Hyg* 41 829
Trowell H C, Muwazi E M K (1945) *Ibid* 39 229
Walt H Wills L, Nightingale, R. P (1950) *S Afr Med. J* 24, 920
Walters, J H Rossiter R J Lehmann H (1947) *Lancet* i, 205
Yi, C L Chao H Chow, Y C Lin Y M. (1948) *Chinese med J* 66 477
Youmans J B Patton, E W Sutton W R Kern R. Steinkamp R (1943) *Amer J publ Hlth* 33 955

RECOVERY OF HUMAN RED BLOOD-CELLS AFTER FREEZING

H. A. SLOVITER*
M.D., Ph.D. Pennsylvania
From the National Institute for Medical Research, Mill Hill, London

IT was recently discovered by Smith (1950) that the hæmolysis which normally occurs after freezing and thawing of whole blood can be prevented by the prior addition of a diluent containing glycerol. She found that if the final concentration of glycerol in the diluted blood was between 10% and 20% rapid freezing in a bath at −79°C, followed by rapid thawing at 40°C, left nearly all the red blood-cells intact. Red blood cells of both the human and the rabbit were used in these experiments. Other reports (Florio et al. 1943, Luyet 1949, Strumia 1949, Griffits et al. 1949, Walter and Gibson 1949) of the survival of red blood cells after freezing and thawing describe methods which involve either very small quantities of blood or very special conditions.

Red blood cells which contain glycerol (whether previously frozen or not) hæmolyse rapidly when placed in plasma or other isotonic media not containing glycerol. This occurs because the glycerol has increased the osmotic tension of the contents of the cell. The hypertonic cell draws in water rapidly, swells, and ruptures. It was evident, therefore, that to make further use of the cells which have been frozen and thawed in the presence of glycerol it would be necessary to recover the cells by some method other than rapid washing. The slow removal of glycerol from red blood cells has been successfully accomplished by dialysis against saline solutions containing progressively decreasing concentrations of glycerol. Red blood-cells which have thus been freed of glycerol can then be separated by centrifuging, washed and suspended in plasma.

PROCEDURE

The complete procedure for small quantities of blood is as follows:

1. Equal volumes of whole blood and glycerol diluent (30 g. glycerol and 0·85 g. NaCl per 100 ml. of solution) are well mixed in an ordinary test-tube and allowed to stand at 5°C for one to two hours.

2. The test-tube is immersed in a −79°C bath (solid CO_2, alcohol).

3. After remaining in the −79°C bath for several hours the mixture is thawed rapidly by immersing the test-tube in a 37°C water bath only until the contents have liquefied.

4. The thawed mixture is dialysed at 5°C successively against 6%, 4%, 2%, and 0% glycerol in 0·85% NaCl solution for three hours or more at each concentration. Dialysis is conveniently performed in a bag made by tying off the ends of a section of cellulose sausage casing.

5. The cells are separated by centrifuging and washed three times with cold 0·85% NaCl solution. The cells are then suspended in plasma.

TABLE I—EXPERIMENTAL CONDITIONS

Treatment	Packed cell volume (%)	Cell-count (million per c.mm.)	Hæmolysis
Equilibrated not frozen	20·0	1·77	None
Equilibrated frozen rapidly thawed rapidly	20·0 21·0 21·0	1·64 1·78 1·77	Very slight
Equilibrated frozen rapidly, thawed slowly	19·5	1·63	Slight
Equilibrated, frozen slowly thawed slowly	15·0	1·23	Moderate
Not equilibrated frozen rapidly thawed slowly	14·5	1·12	Heavy

EXPERIMENTAL CONDITIONS

The experimental factors which are of some importance in this procedure are (1) the concentration of glycerol, (2) the equilibration of the cells with glycerol prior to freezing, (3) the rate of freezing, and (4) the rate of thawing. Data from experiments evaluating the last three of these factors are shown in table I.

The exact concentration of glycerol is not critical. A final concentration of glycerol between 10% and 20% will prevent hæmolysis. Accordingly, the diluent used contained 30% glycerol, this on mixing with an equal volume of blood yields a final glycerol concentration of 15%.

If the blood and the glycerol solution are mixed immediately before freezing, considerable hæmolysis results. In the procedure adopted the blood was equilibrated with the glycerol at 5°C for an hour or longer prior to freezing.

TABLE II—RECOVERY OF HUMAN RED BLOOD-CELLS

Sample	Packed cell volume (%)	Cell-count (million per c.mm.)	Cells recovered (%)
Original blood A	41	3·4	—
A 1	35	2·8	82
A 2	36	3·2	94
A 3	35	3·2	94
A 4	34	3·1	91
Original blood B	44	3·8	—
B 1	35	3·0	79
B 2	38	3·4	90
B 3	36	3·2	84
B 4	35	3·1	82

When an ordinary 6 × ½ in. test-tube containing 10 ml. of blood-glycerol solution mixture is immersed in a −79°C bath, the central portion of the mixture reaches −70°C in approximately two minutes. If the mixture is gradually brought to −70°C over the course of about thirty minutes, appreciable hæmolysis results.

The rate of thawing of the frozen cells is of less importance than the rate of freezing. If the frozen mixture is allowed to thaw in air at room-temperature a little hæmolysis results. Minimal hæmolysis results when the mixture is thawed rapidly.

RESULTS

Quantitative experiments have been performed to measure the recoveries of human red blood cells carried through the complete procedure. The freezing was carried out in ordinary 6 × ½ in. test tubes. Starting with accurately measured 5 ml. portions of blood the recovered cells were suspended in plasma to a total volume of 5 ml. Recoveries were calculated from cell counts of the original blood and of the suspension of recovered cells. Experiments were done with portions drawn from two different bottles of human blood. The results obtained are shown in table II.

The recovered red blood cells are normal in appearance and have the same resistance to hypotonic solutions as the original cells. The plasma suspensions of recovered cells and the original blood show approximately the same rate of deterioration in storage at 5°C.

Problems arising from the present work which are now being investigated include the effect of long time storage at −79°C on the survival of the red blood-cells, the in vivo survival of the recovered red blood cells, the freezing of larger quantities of blood, and the mechanism whereby glycerol prevents hæmolysis.

SUMMARY

Human blood has been rapidly frozen and rapidly thawed in the presence of glycerol, as previously described by Smith (1950).

---

* Damon Runyon senior clinical research fellow 1950–51.

sodium ions in solution can be exchanged for those on the resin A series of experiments have been done to test quantitatively the exchange properties of such modified resins In the first place the resin was partially presaturated by treating it with amounts of potassium and calcium below its exchange capacity (1 m eq of each to 1 g of resin), whereas in later experiments it was completely saturated (6 m eq to 1 g of resin), the subsequent behaviour of the modified resins towards sodium chloride solution being observed in each case

The first experiments showed that the treatment with sodium of a partially saturated resin merely replaces the hydrogen remaining in the resin by sodium, and causes no appreciable replacement of the cation bound during the preliminary treatment It seems, therefore, that nothing is to be gained by such partial presaturation

In the second group of experiments the resin was (1) saturated with calcium and then studied as an exchange material (*a*) for sodium, and (*b*) for potassium, calcium, and sodium ions in solution in the relative proportions present in an average meal (with added sodium chloride), (2) the resin was saturated with potassium before being treated with (*a*) sodium and (*b*) potassium, calcium, and sodium as before The results were as follows

(*1a*) In first stage, 1 g of resin exchanged 2 55 m eq Ca (100% saturation)
In second stage when 1 g of calcium saturated resin was treated with 6 0 m eq of sodium chloride, the Na uptake was 1 30 m eq and the Ca release 1 30 m eq—i e, 51% replacement

(*2a*) In first stage, 1 g of resin exchanged 2 30 m eq of potassium (92% saturation)
In second stage, when 1 g of potassium saturated resin was treated with 6 0 m eq of sodium chloride, the Na uptake was 1 35 m eq and the K release 1 30 m eq—i e, 57% replacement, with a small additional hydrogen exchange as a result of incomplete presaturation

(*1b*) First stage as in *1a*
In second stage, when 1 g of calcium saturated resin was treated with solution containing 6 0 m eq of Na, 1 5 m eq of K, and 0 5 m eq of Ca, the final solution showed a Na uptake of 0 6 m eq, a K uptake of 0 4 m eq, and a Ca release of 1 0 m eq—i e, 39% replacement

(*2b*) First stage as in *2a*
In second stage, when 1 g of potassium saturated resin was treated with solution containing 6 0 m eq of Na, 1 5 m eq of K, and 0 5 m eq of Ca, the final solution showed a Na uptake of 1 0 m eq, a K release of 1 2 m eq, and a Ca uptake of 0 4 m eq—i e, 52% replacement, with an additional hydrogen exchange for calcium sufficient for full saturation of the resin

It is evident from these few in vitro experiments that neither calcium nor potassium resins would be quantitatively efficient substitutes for the original hydrogen exchange resin The effects of the relative affinities for the resin of the three elements studied are clearly demonstrated It is unfortunate, from the clinical point of view, that the resin's affinity for sodium is so much weaker than for the other metals It follows that acidosis and deficiencies of potassium and calcium could not be efficiently prevented by preliminary saturation of the resin with these metals

Effect of Magnesium Trisilicate on Cation Exchange

The idea occurred to me that the problem of acidosis might be solved by adding magnesium trisilicate to the exchange system Parallel experiments with and without added magnesium trisilicate were therefore performed and the efficiency of the trisilicate as an acid adsorbent was determined by alkalimetric titration of the exchange solution The results were as follow

Experiment 1—1g of resin alone, and with 0 2 g of magnesium trisilicate, was equilibrated with a solution containing 6 0 m eq of sodium chloride With the resin alone, the Na uptake was 2 25 m eq and the H release 2 24 m eq With the resin + 0 2 g of trisilicate, the Na uptake was 1 54 m.eq and the H release 1 35 m eq

Experiment 2—1 g of resin alone, and with 0 5 g of magnesium trisilicate, was equilibrated with a solution containing 3 0 m eq of potassium chloride With the resin alone the K uptake was 1 88 m eq and the H release 1 88 m eq With the resin + 0 5 g of trisilicate, the K uptake was 1 14 m eq and the H release nil

These experiments show that the trisilicate leads to a serious loss of efficiency of cation exchange The reason has not been investigated It may be that a small amount of magnesium is liberated from the trisilicate and competes with sodium or potassium for the resin, or perhaps that, owing to its small particle size and bulkiness, the trisilicate hinders cation exchange mechanically under the conditions of the experiments

CATION EXCHANGE UNDER GASTRO INTESTINAL CONDITIONS

The behaviour of the resin has been studied under experimental conditions similar as regards mineral composition to those of the stomach and small intestine.

The mineral content of a simple everyday diet was determined from the analytical data of McCance and Widdowson (1946) and the daily food bulk was assumed to be 2 5 litres The food meets with a gastric secretion assumed to amount to 500 ml per day and containing an average of 135 m eq of H ion and 40 m eq of Na ion per litre at the peak of digestion The next stage is contact with intestinal secretions of about 3 litres per day, though there are considerable variations in the electrolyte patterns of the several intestinal secretions, the base is essentially sodium at a concentration of 175 m eq per litre These two stages have been imitated in the two phases of the in vitro experiments

Setting out the data in a numerical form, we have

Diet contains Na 160 m eq, K 50 m eq, Ca 20 m eq Total cation=230 m eq per day (allowing for additional salt in cooking, &c) Theoretical resin requirement=90 g Food bulk=2500 ml per day

Gastric secretion 500 ml per day at peak of digestion, composed of 135 m eq of H ion and 40 m eq of Na ion per litre

Intestinal secretions 3000 ml per day, containing 175 m eq of Na ion per litre

For experimental purposes it was found convenient to take a hundredth part of each of these amounts

Phase 1 (*Gastric*)
Representing food 25 ml of solution containing 1 60 m eq of Na, 0 50 m eq of K, and 0 20 m eq of Ca
Representing gastric secretion 5 ml of solution containing 0 70 m eq of H ion as HCl and 0 20 m eq of Na.
The two solutions, with 0 9 g of resin added, were put in the mechanical mixer for 3 hours
At the end of phase 1 the total cation exchange, calculated from a duplicate experiment, was 1 48 m eq (uptake of Na 0 93, K 0 35, and Ca 0 20 m eq)

Phase 2 (*Intestinal*)
Representing intestinal secretions 30 ml of 0 9% (*w/v*) NaCl, equivalent to 4 61 m eq of Na
This was added to the tube containing the end products of phase 1, and mixed for an hour
At the end of phase 2 the total cation exchange was 1 56 m eq (uptake of Na 1 13, K 0 23, and Ca 0 20 m eq)

These results show that at the end of the final stage the resin has exchanged 1 74 m eq of cation per gramme (i e, 70% of its theoretical saturation) The over all efficiency of the process, calculated on the original amount of cation in the "food," was 76%, in these experimental conditions, the resin removed 70% of the sodium, 46% of the potassium, and all the calcium As might have been expected there was an additional exchange on the resin for sodium, accompanied by a release of potassium An experiment of this kind of course cannot determine the effects of intestinal absorption of cation, but the absorption of potassium by the gut should improve the over all uptake of sodium

DISCUSSION

The clinical applications of cation exchange resins have presented some interesting problems to both physician and biochemist These resins are highly efficient under certain conditions—e g , where weak solutions of inorganic salts slowly percolate through beds of the resin The present experiments show that zeo karb 225 cannot efficiently remove cations from solutions if it is presented with a relatively large mass of the salt, except perhaps in the case of salts of metals with exceptionally high exchange potentials The apparently unfavourable exchange properties of the resin studied here, from the clinical point of view, arising from its unduly high affinity for calcium and potassium compared with sodium, are likely to be counterbalanced to some extent by the preponderance of sodium in the alimentary tract

Judging by these in vitro experiments, preliminary saturation of the resin with calcium and potassium will not prevent the possible production of calcium and potassium deficiencies, or of acidosis, when the resin is being used to abstract sodium from the diet after ingestion, because of the quantitatively poor power of sodium to replace these other metallic ions The deficiencies may, on the other hand, be corrected by giving supplementary doses of the metals concerned at suitable times of the day, when they will be absorbed by the gut before they can be acted on by the resin The experiment simulating gastro intestinal conditions suggests that satisfactory results may be attained by giving the resin in somewhat larger doses than are theoretically necessary, or by restricting the patient's sodium intake

The treatment of patients with cation exchange resins will have to be carefully controlled. In particular, the state of the renal function should be determined at the outset, and periodical determinations of the plasma-alkali reserve, serum calcium and serum potassium, and of the urinary sodium will provide the data needed for assessing the efficiency of the resin

SUMMARY

The cation exchange resin, ' Zeo Karb 225,' has been examined quantitatively with regard to its exchange efficiency towards sodium, potassium, and calcium ions under various conditions

The resin shows a very high relative affinity for calcium, a lower one for potassium, and a much lower one for sodium

Presaturation of the resin with calcium and potassium gave products whose exchange efficiency for sodium was poor

Magnesium trisilicate is capable of eliminating acid produced during cation exchange, but it was found to cause a well marked loss of efficiency of the resin

An in vitro experiment simulating the mineral conditions in the alimentary tract was devised in order to study the effect on cation exchange of the great preponderance of sodium ions

I wish to acknowledge the critical interest and pertinent suggestions of my colleague Dr J S McKinnell during these investigations.

REFERENCES

Irwin L Berger E Y Rosenberg, B Jackenthal R (1949) *J clin. Invest* 28 1403
Kuhn S S Emerson K (1950) *Ibid* 29 827
Kraus H (1950) *Ibid* p 829
McCance R A Widdowson E M (1946) Chemical Composition of Foods *Spec Rep Ser med Res Coun Lond* no 235
Morton F (1945) *Analyst* 70 247
Stanford R V Wheatley A H M. (1925) *Biochem J* 19 710
Treadwell F P Hall W T (1935) Analytical Chemistry London

CONGENITAL INDIFFERENCE TO PAIN

H G FARQUHAR
B.M. Oxfd, M R C P , D C H
VISITING PÆDIATRICIAN

T SUTTON
M B N U I
FORMERLY HOUSE SURGEON

PROVIDENCE FREE HOSPITAL, ST HELENS, LANCS

CONGENITAL indifference to pain has been described by Schilder and Stengel (1931), who saw ten cases and related the symptoms to a lesion of the left supramarginal gyrus Hemphill and Stengel (1940) reported a further case, which followed cerebral trauma and exhibited an indifference to painful stimuli as well as to abnormally strong visual and auditory stimuli and pure word-deafness There was a fracture of the squamous part of the left temporal bone as well as of the left petrous bone Ford and Wilkins (1938) described three cases, two of which showed mild mental retardation, the third patient being apparently of normal intelligence Critchley (1934) recorded one case of his own and cited three others Rubins and Friedman (1948) had four cases all with lesions in or around the supramarginal gyrus and showing various degrees of aphasia Arbuse et al (1949) reported a case with many similarities to the one we are about to describe, and summarised the literature Recently Leys (1950) has also reported a case

A girl, aged 7 years, was brought to hospital because she walked badly, did not talk clearly or play with other children, and had had a cough for five years She was the third of four children, the rest of the family being healthy Her birth had been at full term after a normal pregnancy, and there was no history of birth injury Developmental progress had been slow, and she had only just begun to sit up at the age of 1 year when she had ' meningitis,' but an accurate report of this illness could not be obtained She had first spoken at the age of 2, and walked at the age of 2½ She had had measles, two attacks of pneumonia and a facial laceration, extending from the angle of the mouth almost to the ear, which had been sutured apparently without causing any pain The mother complained that corporal punishment was useless because the child was apparently insensitive to pain.

Examination revealed abnormalities in both the nervous and the respiratory systems Save for a few words the patient would not talk to adults, though she would talk to children of about half her own age , her speech was then heard to be indistinct She had a coarse tremor of the head and hands, and her gait was slightly unsteady Her pupils were small and oval, and responded very sluggishly to light after she had been in the dark for half an hour , but they responded well to accommodation The other cranial nerves appeared to be normal, as were the superficial and deep reflexes Sensation of light touch, position, and hot and cold was accurate but there seemed to be no reaction whatever to pain. A pin thrust deeply into the child's back while her attention was diverted produced no reaction even when her attention was drawn to what was going to be done she evinced no sign of fear or apprehension. Pinching the tendo achillis with the utmost force was received with the same equanimity as were both venepuncture and lumbar puncture

Signs of a left basal bronchiectasis were confirmed by bronchography No other abnormality was found The blood Wassermann reaction was negative both before and after a provocative dose of arsenic The cerebrospinal fluid was normal to all routine tests, including the Wassermann and gold curve A blood count was normal as was radiography of the skull The child s intelligence quotient was estimated to be 72

It may be suggested that in the above case the condition is not congenital but due to the illness at the age of 1 year Though this cannot be denied, the history of retarded development before this illness suggests a previous abnormality of the brain An association between indifference to pain and slight mental retardation is evident in many cases previously described, but in the present case that the abnormal reaction to pain is not part of the general mental retardation seems clear sodium ions in solution can be exchanged for those on the resin. A series of experiments have been done to test quantitatively the exchange properties of such modified resins. In the first place the resin was partially presaturated by treating it with amounts of potassium and calcium below its exchange capacity (1 m.eq. of each to 1 g. of resin), whereas in later experiments it was completely saturated (6 m.eq. to 1 g. of resin), the subsequent behaviour of the modified resins towards sodium chloride solution being observed in each case.

The first experiments showed that the treatment with sodium of a partially saturated resin merely replaces the hydrogen remaining in the resin by sodium, and causes no appreciable replacement of the cation bound during the preliminary treatment. It seems, therefore, that nothing is to be gained by such partial presaturation.

In the second group of experiments the resin was (1) saturated with calcium and then studied as an exchange material *(a)* for sodium, and *(b)* for potassium, calcium, and sodium ions in solution in the relative proportions present in an average meal (with added sodium chloride), (2) the resin was saturated with potassium before being treated with *(a)* sodium and *(b)* potassium, calcium, and sodium as before. The results were as follows:

(1*a*) In first stage, 1 g. of resin exchanged 2·55 m.eq. Ca (100% saturation).

In second stage when 1 g. of calcium saturated resin was treated with 6·0 m.eq. of sodium chloride, the Na uptake was 1·30 m.eq. and the Ca release 1·30 m.eq.—i.e., 51% replacement.

(2*a*) In first stage, 1 g. of resin exchanged 2·30 m.eq. of potassium (92% saturation).

In second stage, when 1 g. of potassium saturated resin was treated with 6·0 m.eq. of sodium chloride, the Na uptake was 1·35 m.eq. and the K release 1·30 m.eq.—i.e., 57% replacement, with a small additional hydrogen exchange as a result of incomplete presaturation.

(1*b*) First stage as in 1*a*.

In second stage, when 1 g. of calcium saturated resin was treated with solution containing 6·0 m.eq. of Na, 1·5 m.eq. of K, and 0·5 m.eq. of Ca, the final solution showed a Na uptake of 0·6 m.eq., a K uptake of 0·4 m.eq., and a Ca release of 1·0 m.eq.—i.e., 39% replacement.

(2*b*) First stage as in 2*a*.

In second stage, when 1 g. of potassium saturated resin was treated with solution containing 6·0 m.eq. of Na, 1·5 m.eq. of K, and 0·5 m.eq. of Ca, the final solution showed a Na uptake of 1·0 m.eq., a K release of 1·2 m.eq., and a Ca uptake of 0·4 m.eq.—i.e., 52% replacement, with an additional hydrogen exchange for calcium sufficient for full saturation of the resin.

It is evident from these few in-vitro experiments that neither calcium nor potassium resins would be quantitatively efficient substitutes for the original hydrogen exchange resin. The effects of the relative affinities for the resin of the three elements studied are clearly demonstrated. It is unfortunate, from the clinical point of view, that the resin's affinity for sodium is so much weaker than for the other metals. It follows that acidosis and deficiencies of potassium and calcium could not be efficiently prevented by preliminary saturation of the resin with these metals.

Effect of Magnesium Trisilicate on Cation Exchange

The idea occurred to me that the problem of acidosis might be solved by adding magnesium trisilicate to the exchange system. Parallel experiments with and without added magnesium trisilicate were therefore performed and the efficiency of the trisilicate as an acid adsorbent was determined by alkalimetric titration of the exchange solution. The results were as follow:

Experiment 1.—1 g. of resin alone, and with 0·2 g. of magnesium trisilicate, was equilibrated with a solution containing 6·0 m.eq. of sodium chloride. With the resin alone, the Na uptake was 2·25 m.eq. and the H release 2·24 m.eq. With the resin + 0·2 g. of trisilicate, the Na uptake was 1·54 m.eq. and the H release 1·35 m.eq.

Experiment 2.—1 g. of resin alone, and with 0·5 g. of magnesium trisilicate, was equilibrated with a solution containing 3·0 m.eq. of potassium chloride. With the resin alone the K uptake was 1·88 m.eq. and the H release 1·88 m.eq. With the resin + 0·5 g. of trisilicate, the K uptake was 1·14 m.eq. and the H release nil.

These experiments show that the trisilicate leads to a serious loss of efficiency of cation exchange. The reason has not been investigated. It may be that a small amount of magnesium is liberated from the trisilicate and competes with sodium or potassium for the resin; or perhaps that, owing to its small particle size and bulkiness, the trisilicate hinders cation exchange mechanically under the conditions of the experiments.

CATION EXCHANGE UNDER GASTRO-INTESTINAL CONDITIONS

The behaviour of the resin has been studied under experimental conditions similar as regards mineral composition to those of the stomach and small intestine.

The mineral content of a simple everyday diet was determined from the analytical data of McCance and Widdowson (1946) and the daily food bulk was assumed to be 2·5 litres. The food meets with a gastric secretion assumed to amount to 500 ml. per day and containing an average of 135 m.eq. of H ion and 40 m.eq. of Na ion per litre at the peak of digestion. The next stage is contact with intestinal secretions of about 3 litres per day; though there are considerable variations in the electrolyte patterns of the several intestinal secretions, the base is essentially sodium at a concentration of 175 m.eq. per litre. These two stages have been imitated in the two phases of the in-vitro experiments.

Setting out the data in a numerical form, we have:

Diet: contains Na 160 m.eq., K 50 m.eq., Ca 20 m.eq. Total cation = 230 m.eq. per day (allowing for additional salt in cooking, &c.). Theoretical resin requirement = 90 g. Food bulk = 2500 ml. per day.

Gastric secretion: 500 ml. per day at peak of digestion, composed of 135 m.eq. of H ion and 40 m.eq. of Na ion per litre.

Intestinal secretions: 3000 ml. per day, containing 175 m.eq. of Na ion per litre.

For experimental purposes it was found convenient to take a hundredth part of each of these amounts.

Phase 1 (Gastric)

Representing food: 25 ml. of solution containing 1·60 m.eq. of Na, 0·50 m.eq. of K, and 0·20 m.eq. of Ca.

Representing gastric secretion: 5 ml. of solution containing 0·70 m.eq. of H ion as HCl and 0·20 m.eq. of Na.

The two solutions, with 0·9 g. of resin added, were put in the mechanical mixer for 3 hours.

At the end of phase 1 the total cation exchange, calculated from a duplicate experiment, was 1·48 m.eq. (uptake of Na 0·93, K 0·35, and Ca 0·20 m.eq.).

Phase 2 (Intestinal)

Representing intestinal secretions: 30 ml. of 0·9% (*w/v*) NaCl, equivalent to 4·61 m.eq. of Na.

This was added to the tube containing the end-products of phase 1, and mixed for an hour.

At the end of phase 2 the total cation exchange was 1·56 m.eq. (uptake of Na 1·13, K 0·23, and Ca 0·20 m.eq.).

These results show that at the end of the final stage the resin has exchanged 1·74 m.eq. of cation per gramme (i.e., 70% of its theoretical saturation). The over-all efficiency of the process, calculated on the original amount of cation in the "food," was 76%; in these experimental conditions, the resin removed 70% of the sodium, 46% of the potassium, and all the calcium. As might have been expected there was an additional exchange on the resin for sodium, accompanied by a release of potassium An experiment of this kind of course cannot determine the effects of intestinal absorption of cation, but the absorption of potassium by the gut should improve the over all uptake of sodium

DISCUSSION

The clinical applications of cation exchange resins have presented some interesting problems to both physician and biochemist These resins are highly efficient under certain conditions—e g , where weak solutions of inorganic salts slowly percolate through beds of the resin The present experiments show that zeo karb 225 cannot efficiently remove cations from solutions if it is presented with a relatively large mass of the salt, except perhaps in the case of salts of metals with exceptionally high exchange potentials The apparently unfavourable exchange properties of the resin studied here, from the clinical point of view, arising from its unduly high affinity for calcium and potassium compared with sodium, are likely to be counterbalanced to some extent by the preponderance of sodium in the alimentary tract

Judging by these in vitro experiments, preliminary saturation of the resin with calcium and potassium will not prevent the possible production of calcium and potassium deficiencies, or of acidosis, when the resin is being used to abstract sodium from the diet after ingestion, because of the quantitatively poor power of sodium to replace these other metallic ions The deficiencies may, on the other hand, be corrected by giving supplementary doses of the metals concerned at suitable times of the day, when they will be absorbed by the gut before they can be acted on by the resin The experiment simulating gastro intestinal conditions suggests that satisfactory results may be attained by giving the resin in somewhat larger doses than are theoretically necessary, or by restricting the patient's sodium intake

The treatment of patients with cation exchange resins will have to be carefully controlled In particular, the state of the renal function should be determined at the outset, and periodical determinations of the plasma alkali reserve, serum calcium and serum potassium, and of the urinary sodium will provide the data needed for assessing the efficiency of the resin

SUMMARY

The cation exchange resin, 'Zeo Karb 225,' has been examined quantitatively with regard to its exchange efficiency towards sodium, potassium, and calcium ions under various conditions

The resin shows a very high relative affinity for calcium, a lower one for potassium, and a much lower one for sodium

Presaturation of the resin with calcium and potassium gave products whose exchange efficiency for sodium was poor

Magnesium trisilicate is capable of eliminating acid produced during cation exchange, but it was found to cause a well marked loss of efficiency of the resin

An in vitro experiment simulating the mineral conditions in the alimentary tract was devised in order to study the effect on cation exchange of the great preponderance of sodium ions

I wish to acknowledge the critical interest and pertinent suggestions of my colleague Dr J S McKinnell during these investigations.

REFERENCES

Irwin L Berger E Y Rosenberg, B Jackenthal R (1949) *J clin. Invest* 28 1403

Kahn S S Emerson K (1950) *Ibid* 29 827

Kraus H (1950) *Ibid* p 829

McCance R A Widdowson E M (1946) Chemical Composition of Foods *Spec Rep Ser med Res Coun Lond* no 235

Morton F (1945) *Analyst* 70 247

Stanford R V Wheatley A H M. (1925) *Biochem. J* 19 710

Treadwell F P Hall W T (1935) Analytical Chemistry London

CONGENITAL INDIFFERENCE TO PAIN

H G FARQUHAR
B.M. Oxfd, M.R C P , D C H
VISITING
PÆDIATRICIAN

T SUTTON
M B N U I
FORMERLY
HOUSE SURGEON

PROVIDENCE FREE HOSPITAL, ST HELENS, LANCS

CONGENITAL indifference to pain has been described by Schilder and Stengel (1931), who saw ten cases and related the symptoms to a lesion of the left supramarginal gyrus Hemphill and Stengel (1940) reported a further case, which followed cerebral trauma and exhibited an indifference to painful stimuli as well as to abnormally strong visual and auditory stimuli and pure word-deafness There was a fracture of the squamous part of the left temporal bone as well as of the left petrous bone Ford and Wilkins (1938) described three cases, two of which showed mild mental retardation, the third patient being apparently of normal intelligence Critchley (1934) recorded one case of his own and cited three others Rubins and Friedman (1948) had four cases all with lesions in or around the supramarginal gyrus and showing various degrees of aphasia Arbuse et al (1949) reported a case with many similarities to the one we are about to describe, and summarised the literature Recently Leys (1950) has also reported a case

A girl, aged 7 years, was brought to hospital because she walked badly, did not talk clearly or play with other children, and had had a cough for five years She was the third of four children, the rest of the family being healthy Her birth had been at full term after a normal pregnancy, and there was no history of birth injury Developmental progress had been slow, and she had only just begun to sit up at the age of 1 year when she had "meningitis," but an accurate report of this illness could not be obtained. She had first spoken at the age of 2, and walked at the age of $2^1/_2$ She had had measles two attacks of pneumonia, and a facial laceration, extending from the angle of the mouth almost to the ear, which had been sutured apparently without causing any pain The mother complained that corporal punishment was useless because the child was apparently insensitive to pain.

Examination revealed abnormalities in both the nervous and the respiratory systems Save for a few words the patient would not talk to adults, though she would talk to children of about half her own age , her speech was then heard to be indistinct She had a coarse tremor of the head and hands, and her gait was slightly unsteady Her pupils were small and oval, and responded very sluggishly to light after she had been in the dark for half an hour , but they responded well to accommodation The other cranial nerves appeared to be normal, as were the superficial and deep reflexes Sensation of light touch position, and hot and cold was accurate but there seemed to be no reaction whatever to pain A pin thrust deeply into the child's back while her attention was diverted produced no reaction , even when her attention was drawn to what was going to be done she evinced no sign of fear or apprehension Pinching the tendo achillis with the utmost force was received with the same equanimity as were both venepuncture and lumbar puncture

Signs of a left basal bronchiectasis were confirmed by bronchography No other abnormality was found The blood Wassermann reaction was negative both before and after a provocative dose of arsenic The cerebrospinal fluid was normal to all routine tests including the Wassermann and gold curve A blood count was normal, as was radiography of the skull The child s intelligence quotient was estimated to be 72

It may be suggested that in the above case the condition is not congenital but due to the illness at the age of 1 year Though this cannot be denied, the history of retarded development before this illness suggests a previous abnormality of the brain An association between indifference to pain and slight mental retardation is evident in many cases previously described, but in the present case that the abnormal reaction to pain is not part of the general mental retardation seems clear from the child's accurate recognition of other sensory stimuli

REFERENCES

Arbuse D I, Cantor M B, Barenberg, P A (1949) *J Pediat* 35, 221
Critchley M (1934) *Brit med J* ii 891
Ford, F R, Wilkins L (1938) *Bull Johns Hopk Hosp* 62 448
Hemphill R E Stengel E (1940) *J Neurol Psychiat* 3, 251
Leys D G (1950) *Proc R Soc Med* 43 250
Rubins, J L, Friedman, E D (1948) *Arch Neurol Psychiat* 60, 554
Schilder, P, Stengel, E (1931) *Arch Neurol Psychiat* 25, 598

CALCIUM METABOLISM IN HYPERTHYROIDISM

THE EFFECT OF THIOURACIL

J GREEN
M.B Glasg, M R C P E

A LYALL
M A, M D Aberd, F R C.P

LECTURERS ON CLINICAL CHEMISTRY IN THE UNIVERSITY OF ABERDEEN

THE occurrence of osteoporosis in hyperthyroidism was known to von Recklinghausen and Askanazy (Hunter 1930) The metabolic studies of Aub et al (1929) and Hunter (1935) showed that calcium is lost in both fæces and urine, the excessive fæcal excretion of calcium was attributed to "intestinal hurry," but the cause of the increased urinary calcium excretion remained obscure The studies of Robertson (1942) pointed to an effect of thyroid hormone on renal epithelium

The effect of thiouracil offers a new approach to this problem (Lundbaek 1947) We have accordingly tried to find whether the disturbance of calcium and phosphorus metabolism in hyperthyroidism is restored to normal by thiouracil treatment, and whether changes in their day to day excretion can be correlated with nitrogen excretion or any other factor

METHOD

Six cases of severe hyperthyroidism were selected five because of their high urinary calcium excretion, and the remaining one for comparison They were kept on ordinary ward diet containing 0 5–0 6 g of calcium per day It was presumed that any variation in urinary calcium excretion due to dietary variation about this level would not affect the significance of the changes observed No complete balance studies were made in this group because of the difficulty of providing duplicate diets

Daily collections of 24 hour samples of urine were made Standard methods were used in the estimation of urinary calcium (Godden 1937), urinary phosphorus (Fiske and Subbarow 1925), urinary nitrogen (Koch and McMeekin 1924), serum calcium (Clark and Collip 1925), and serum phosphorus (Fiske and Subbarow 1925)

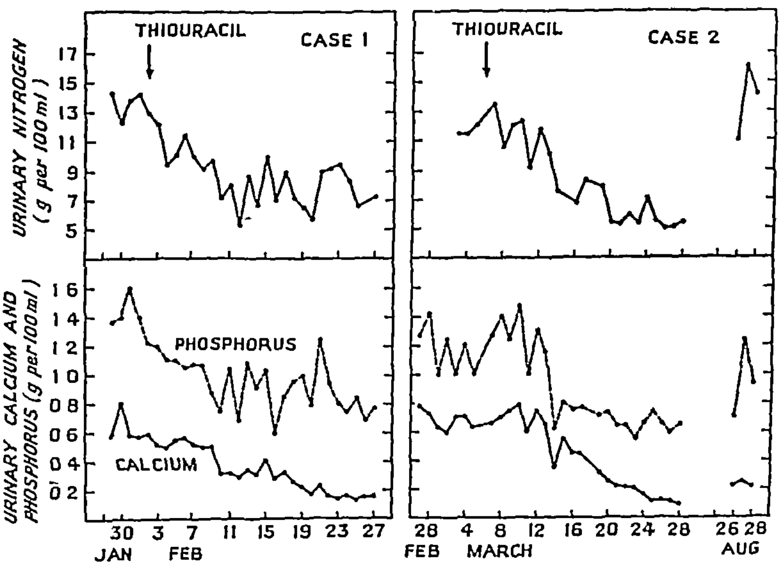


Fig 1—Urinary calcium phosphorus and nitrogen in cases 1 and 2.

CASE RECORDS

Case 1 —A housewife, aged 31, was admitted on Jan. 17, 1949, with 7 months' history of tiredness, excitability, &c She was a typical case of hyperthyroidism, her basal metabolic rate (B M R) being + 22% serum calcium 10·5 mg per 100 ml., serum phosphorus 5 0 mg, and alkaline phosphatase 10 units on Feb 2 Treatment with thiouracil 0 2 g b d was started on Feb 2 She responded well and was put on iodine on March 4, as a prelude to successful thyroidectomy on March 16

Case 2 —A factor, aged 47, was admitted on Feb 24, 1949, with 3 months' history of breathlessness, nervousness, and loss of weight He showed obvious signs of hyperthyroidism, and his B M R on Feb 26, was + 44% His serum calcium was 10 8 mg per 100 ml, serum phosphorus 4 6 mg, and alkaline phosphatase 8 units Treatment with thiouracil 0 2 g t.d.s. was started on March 6 Considerable improvement followed, but thyroidectomy was postponed to allow removal of a nasal polypus The patient was discharged for six months on thiouracil, iodisation and thyroidectomy followed in September, 1949

Case 3 —A farmer, aged 46, had had intermittent dyspepsia for 16 years A barium meal before admission showed a small gastric ulcer (May 9, 1949) Some tremor of hands, exophthalmos, and enlargement of the thyroid were noted, and the B M R on May 15 was + 40% Ten days later the patient developed pyloric stenosis, which precipitated a thyroid crisis, and large doses of iodine were given Thiouracil treatment was started on May 20 Clinical improvement was noted, but the B M R a month later was still +16% The serum calcium at this time was 10 mg per 100 ml, serum phosphorus 3 9 mg, and alkaline phosphatase 6 5 units The patient continued to improve, and on July 13, after preoperative iodine, a successful thyroidectomy was performed

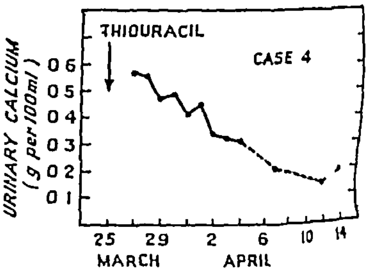


Fig 3—Urinary calcium in case 4.

Case 4 —A fisherman aged 54, was admitted on March 21, 1949, with 6 years' history of intermittent excitability, breathlessness, and loss of weight Exophthalmos, tremor of hands, tachycardia, and enlargement of the thyroid gland were noted, and the B M R was + 47% Treatment with thiouracil 0 2 g b d was started on March 26 Clinical response was rapid, and thyroidectomy was done on May 24 In this patient, only calcium excretion in the urine was estimated, owing to difficulties of collection

Case 5 —A contractor, aged 29, was admitted on Oct 10, 1949, with a history of recent diarrhœa and abdominal pain He was diagnosed as a case of severe hyperthyroidism, his B.M R. being + 90% He also had infected tonsils On Oct 17 his serum calcium was 11 05 mg per 100 ml, serum phosphorus 4 3 mg, and alkaline phosphatase 35 units Treatment with thiouracil 0 2 g t d s was started on Oct 21 The response was excellent and on Nov 20, iodisation was started as a prelude to thyroidectomy on Dec 7

Case 6 —A male nurse aged 49, was admitted on Aug 15, 1949, after he had been diagnosed in March, 1947, as a case of thyrotoxicosis, his B M R then being + 55% He had been given thiouracil for 5 months with good results, but symptoms had recurred each time an attempt was made to stop giving the drug On admission he had had no thiouracil for 2 months, and he showed obvious signs of thyroid overactivity, his B M R on Aug 16 being + 30% He had also

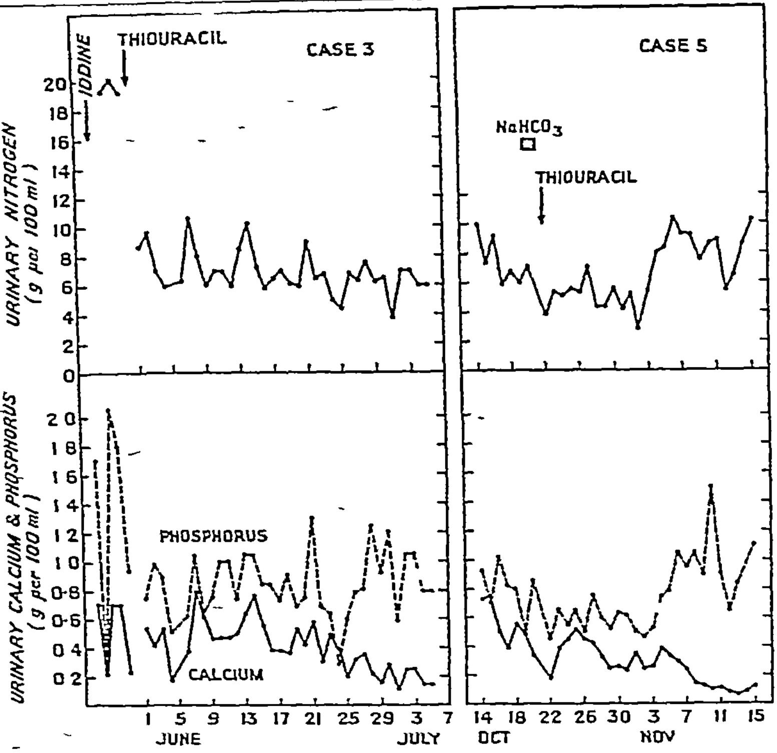


Fig 2—Urinary calcium phosphorus and nitrogen in cases 3 and 5

brief attacks of auricular fibrillation for a few days Treatment with thiouracil 0·2 g b d was started on Aug 22 and thyroidectomy after a course of iodine, was done on Sept 23

RESULTS AND DISCUSSION

The daily levels of urinary excretion of calcium, phosphorus, and nitrogen in our six cases before and during treatment are shown in figs 1–4 Grossly increased excretion of calcium before treatment is shown by cases 1–5, and in cases 1, 2, 4, and 5 a definite decrease in excretion of calcium is apparent about 7 days after the start of thiouracil treatment, and normal levels are attained in another 14 days. These results give more detailed confirmation of Lundbaek's findings (1947)

In case 3 (fig 2) no significant downward trend occurs for 25 days, and levels below 0 2 g of calcium a day are not maintained for another 8 days One may speculate whether the delay in response to thiouracil clinical and biochemical, was due to the initial severity of the disease or to the preceding heavy dosage of iodine

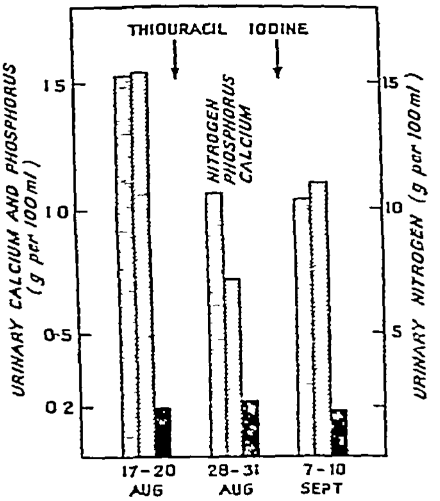


Fig 4—Urinary calcium phosphorus and nitrogen in case 6

These results throw little light on the origin of the increased excretion of calcium in hyperthyroidism If it were due to a direct effect of thyroid hormone on bone katabolism, one would expect it to show a closer relationship to the increase in B M.R , and, if it derived from mobilisation of base to deal with the acidosis of protein katabolism, one would expect a closer relationship to the urinary excretion of nitrogen and phosphorus It is obvious from our data that grossly increased excretion of nitrogen and phosphorus is not necessarily accompanied by increased excretion of calcium, and vice versa

In case 5 two further studies were conducted with a bearing on possible theories fig 5 shows serum calcium and serum phosphorus levels, and urinary calcium levels and totals, before and during treatment If, as Robertson (1942) suggests, the increase in excretion of calcium is due to a direct action of thyroid hormone on renal clearance, there should be an inverse relationship between serum and urinary levels, as he implied In case 5 a direct relationship is shown, a high urinary level accompanying serum calcium and serum phosphorus levels on the high side of normal, a feature also noted in cases 1 and 2

We felt that the rejection by Albright et al (1931) of the hypothesis that disturbance of acid-base equilibrium might be significant was open to criticism Apart from the fact that their argument has an admitted teleological basis, acidosis in hyperthyroidism may be more complex than the loss of fixed base which they studied Ketosis may occur, but, in addition, the production of excessive amounts of carbon dioxide over long periods may strain the buffering capacity of the blood In that event the formula of Rona and Takahashi (1913) could be applied to derive the increase in calcium ions, and in similar situations it is known (Farquharson et al. 1931, Nelson 1928) that the increase in urinary excretion of calcium is out of all proportion to the drain on fixed base

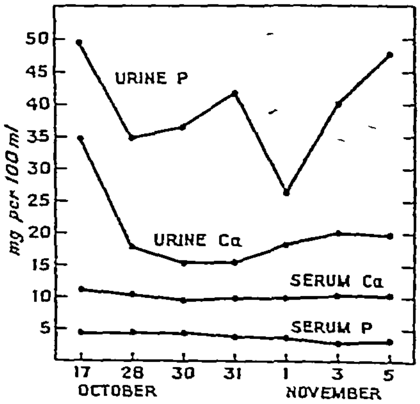


Fig 5—Serum-calcium serum-phosphorus and urinary calcium and phosphorus in case 5

Accordingly case 6 was given sodium bicarbonate 10 g by mouth between Nov 19 and Nov 21 On Nov 22 his urinary calcium had fallen from the previous level of 24–38 mg to 8 8 mg per 100 ml. and his total excretion for the 24 hours to normal limits In view of possible chance variation this finding in a single person is not significant, but this aspect will be studied later

SUMMARY

Six cases of severe hyperthyroidism have been studied before and during treatment with thiouracil

In four of the five cases showing excessive urinary loss of calcium diminution was observed about 7 days after the start of thiouracil treatment, and normal values were attained about 14 days later

The bearing of these and other data on the mechanism of the increased excretion of calcium in hyperthyroidism is discussed

Grateful acknowledgment is made to Sister M E Thomson and the residents and nurses of the metabolic ward, Aberdeen Royal Infirmary, for their coöperation in these investigations, and to Dr Ian Gordon for permission to use one of his cases

REFERENCES

Albright F Bauer W Aub J C (1931) *J clin Invest* 10 187
Aub, J C Bauer W Heath C, Ropes, M (1929) *Ibid*, 7, 97
Clark E P, Collip J B (1925) *J biol Chem* 63, 461
Farquharson, R F Salter W T, Tibbetts, D M, Aub J C (1931) *J clin Invest* 10, 221
Fiske C H Subbarow Y (1925) *J biol Chem* 66, 375
Godden W (1937) Technical Communication no 9 Imperial Bureau of Animal Nutrition
Hunter D (1930) *Lancet* i, 947
— (1935) *Proc R Soc Med* 28 1619
Koch F C McMeekin T L (1924) *J Amer chem Soc* 46, 2066
Lundback K (1947) *Acta med scand* 127 193
Nelson, M V (1928) *Amer J Dis Child* 36 716
Robertson, J D (1942) *Lancet* i 672
Rona P Takahashi D (1913) *Biochem Z* 49 370 Quoted in Peters and Van Slyke's Quantitative Clinical Chemistry Baltimore, 1931

REPAIR OF THE CERVICAL TRACHEA AND LARYNX

EMLYN LEWIS
F R C S
SURGEON, PLASTIC SURGERY CENTRE, ST LAWRENCE HOSPITAL, CHEPSTOW, AND UNITED HOSPITALS, CARDIFF

IN view of the difficulties of reconstructing the trachea (see *Lancet* 1950), the following case is of interest

A boy, aged 16, was referred to the Plastic Surgery Unit, Gloucester, for closure of an opening into the trachea and larynx He had had diphtheria as an infant, and this had necessitated tracheotomy For lack of adequate history, it was assumed that secondary infection had occurred at the time of the tracheotomy, and that this infection had destroyed much soft tissue, the tracheal rings, and part of the thyroid and cricoid cartilages Many operations had been performed on his neck, but treatment, undertaken by Prof T P Kilner and Mr R Battle when he was 8 years old (with the object of restoring patency of the lumen above the tracheotomy) had been interrupted by the evacuation of the hospital in the early days of the war His condition before that treatment is shown in fig 1, above the patent opening into the trachea a median slit communicated with the larynx After that treatment his condition was as appears in figs 2 and 3

Examination

The patient spoke in a whisper, which he achieved by pushing his chin downwards and backwards into his neck He was appalled by his condition and had attempted suicide He was doubtful of the prospect of repair and resistant to treatment In the midline of the front of his neck he had a large opening (fig 2) into his trachea this opening extended down to just above the episternal notch Above, it was estimated that five sixths of the rigid circumference had been lost, and below, it was regarded as tapering off to a loss of a third. At the upper end of the trachea was a transverse ridge (fig 2) which was thought to be made by the remains of the posterior inferior margin of the cricoid cartilage Above this ridge was a second opening (fig 2), which passed into the larynx Both openings were in a shallow pit in the front of the neck, the transverse ridge being more or less continuous with the plane of the skin From this it was assumed that the larynx and the upper end of the trachea had been drawn forwards by scar tissue The opening into the larynx admitted a no 9 endotracheal catheter, and the subglottic region was responsive to touch Direct examination of the larynx corroborated that it was drawn forwards The over all size was smaller than normal, the cords moved with respiration, and a no 7 endotracheal catheter could be passed between them and brought out through the opening in the neck

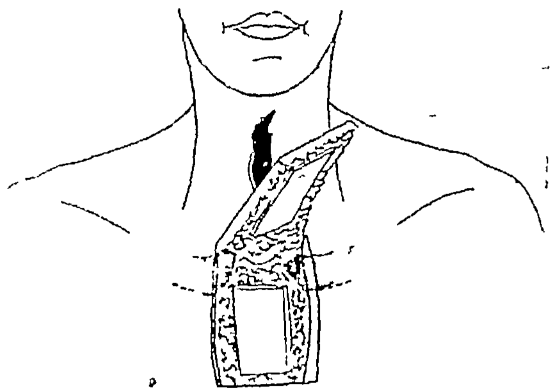


Fig 4—Delayed flap raised from manubrium and turned up to cover openings in neck.

Preparation for Treatment

The boy doubted his ability to breathe properly if these openings were closed by an operation To reassure him my dental colleagues constructed a soft acrylic collar which covered the openings and created an airtight lumen. This appliance worked admirably and convinced the patient of his power to breathe naturally, but it prevented him from pushing his chin downwards and backwards, and consequently he believed he could not speak However, Mr Robert Owen and I got him to make a guttural 'o" sound, this we extended to "Ee," and later to "Mary" Finally, he could speak in more than a whispering tone, in fact he could shout By this time he had become more amenable to surgical repair

The broad requirements were for a rigid skin lining to cover both openings It had to be airtight, and covered by skin to avoid any raw surface on the outside

Surgical Repair

Treatment was carried out in five stages, some of them involving more than one procedure

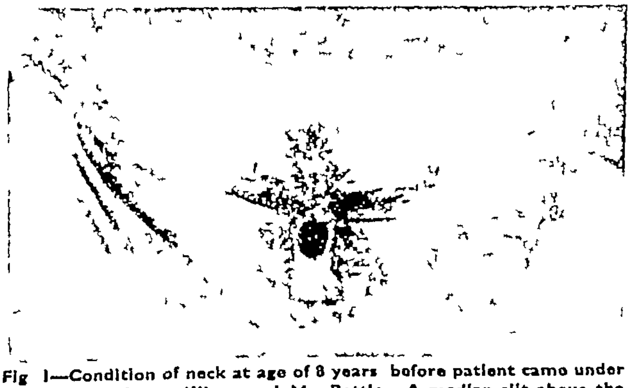


Fig 1—Condition of neck at age of 8 years before patient came under care of Professor Kilner and Mr Battle. A median slit above the tracheal opening communicated with the larynx.

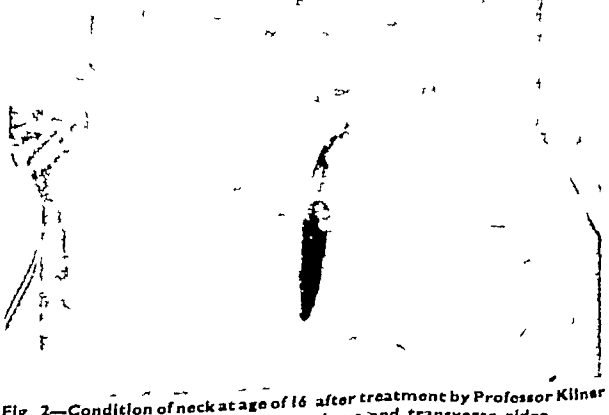


Fig 2—Condition of neck at age of 16 after treatment by Professor Kilner and Mr Battle. Note scar tissue and transverse ridge

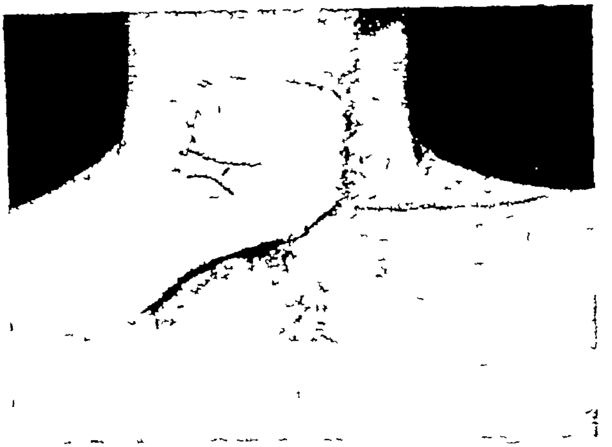


Fig 5—Tubed pedicle detached from left wrist opened for half its length to form a flap and stitched over delayed flap from manubrium Note raw surface on manubrium

Stage I (Oct 25, 1948)—A left abdominal tubed pedicle 4 in wide and 8 in long was prepared, to provide cover for the repair

Stage II (Jan 5, 1949)—The lateral end of the tubed pedicle was divided and attached to the radial border of the left wrist (fig 3) A delayed flap of requisite dimensions was made on the front of the manubrium and sternum (fig 3) The flap was based above the episternal notch and contained on its deep surface a sliver of bone and periosteum from the manubrium and sternum measuring roughly $1^1/_4$ in wide, $1^1/_2$ in long, and $^1/_{16}$ in thick

Stage III (March 24, 1949)—The medial end of the tubed pedicle was detached from the abdomen and implanted on the front of the chest at a selected site (fig 3)

Stage IV (May 5 1949)—Incisions were made on both sides of the openings in the neck and joined by a third incision across the neck above the opening into the larynx The incisions were undermined The delayed flap containing periosteum and bone was then raised from the front of the manubrium and sternum (fig 4), turned up to cover the openings in the neck and sutured to the medial margins of the incisions This flap provided the rigid skin lining Next the tubed pedicle was freed from the left wrist, and from this free end the pedicle was opened for a little more than half its length The flap formed by opening the pedicle was sutured into the lateral margins of the incisions in the neck, with the skin surface superficial (fig 5) It formed a cover flap for the rigid skin lining flap

Stage V (June 9, 1949)—The remaining tubed portion of the pedicle was detached from the chest wall, opened and fixed into the raw surface on the manubrium and sternum (fig 6)

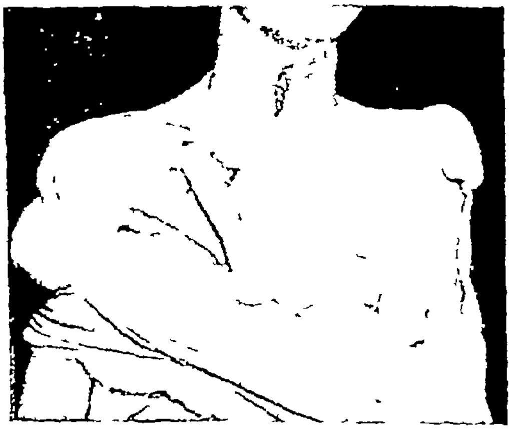


Fig 3—Tubed pedicle attached to front of chest and radial border of left wrist. Note delayed flap over manubrium.

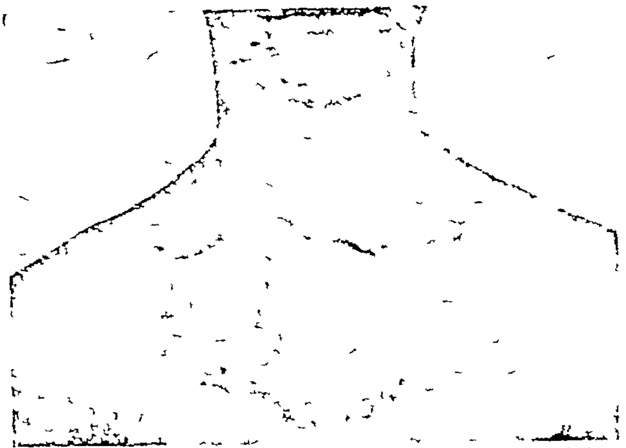


Fig. 6—Repair completed tubed pedicle has been detached from chest, converted into flap and fixed over raw surface on manubrium

The repair proved successful, and a year after completion of surgical treatment the boy was working as an electrician He spoke well, though his voice was slightly husky He could ride a bicycle and run without any difficulty in breathing He could expectorate satisfactorily There was no suction effect on the repair when he took a deep breath The sliver of bone in the neck could still be felt, was much the same in size as originally, and did not hamper movements of the neck

I am indebted to Professor Kilner and Mr Battle for fig 1

REFERENCE

Lancet (1950) i 359

THERAPEUTIC EFFECT OF AN ALLERGIC REACTION TO FOOD ON RHEUMATOID ARTHRITIS

L G Polymenakos
M.D Athens, L M.C Canada
FORMERLY SECRETARY GENERAL, MINISTRY OF HEALTH, TORONTO, ONTARIO

THE therapeutic success of Hench et al (1949) with 'Cortisone' and the adrenocorticotropic hormone (A C T H.) in rheumatoid arthritis indicates that most of the clinical manifestations of this disease can be reversed with the result that the patient feels well again, but the precise actions of the hormones are unknown

A C T H presumably acts by stimulating the adrenal cortex to secrete its hormones but the function and chemical composition of but few of these hormones are known We can separate some of them as glucocorticoids (e g, cortisone and 'Compound F') concerned in the metabolism of sugar, mineralocorticoids (e g, deoxycortone) concerned in the metabolism of sodium, potassium, and water, and the 17 ketosteroids and other steroids, whose actions are synergic with, or antagonistic to those of other endocrine glands, especially the gonads, and play an important part in the resistance of the body against disease

The observation that, in the synovial fluid of patients with rheumatoid arthritis, the concentration of hyaluronic acid and the activity of hyaluronidase are abnormal (Meyer 1947) has led to the suggestion that the enzymes which are responsible for the synthesis of glycogen might similarly play a part in the composition of hyaluronic acid, which is a similar polysaccharide, and probably contain or depend on the glucocorticoids, of which cortisone is one, for the synthesis of hyaluronates or other substances of the intercellular matrix This hypothesis, however, has not been proved

The results obtained by Hench et al (1949) and Thorn et al (1949) with cortisone and A C T H lend

The bearing of these and other data on the mechanism of the increased excretion of calcium in hyperthyroidism is discussed

Grateful acknowledgment is made to Sister M E Thomson and the residents and nurses of the metabolic ward, Aberdeen Royal Infirmary, for their coöperation in these investigations , and to Dr Ian Gordon for permission to use one of his cases

REFERENCES

Albright F , Bauer W Aub, J C (1931) *J clin Invest* 10 187
Aub, J C , Bauer W Heath, C Ropes, M (1929) *Ibid* 7, 97
Clark, E P Collip J B (1925) *J biol Chem* 63, 461
Farquharson, R F Salter W T , Tibbetts D M., Aub J C (1931) *J clin Invest* 10, 221
Fiske C H Subbarow Y (1925) *J biol Chem* 66, 375
Godden, W (1937) Technical Communication no 9 Imperial Bureau of Animal Nutrition
Hunter D (1930) *Lancet* 1, 947
— (1935) *Proc R Soc Med* 28, 1619
Koch F C McMeekin T L (1924) *J Amer chem. Soc* 46, 2066
Lundbaek K (1947) *Acta med scand* 127, 193
Nelson M V (1928) *Amer J Dis Child* 36, 716
Robertson, J D (1942) *Lancet* 1 672
Rona P Takahashi D (1913) *Biochem Z* 49 370 Quoted in Peters and Van Slyke's Quantitative Clinical Chemistry Baltimore, 1931

REPAIR OF THE CERVICAL TRACHEA AND LARYNX

EMLYN LEWIS
F R C S
SURGEON, PLASTIC SURGERY CENTRE, ST LAWRENCE HOSPITAL, CHEPSTOW, AND UNITED HOSPITALS, CARDIFF

IN view of the difficulties of reconstructing the trachea (see *Lancet* 1950), the following case is of interest

A boy, aged 16, was referred to the Plastic Surgery Unit, Gloucester, for closure of an opening into the trachea and larynx He had had diphtheria as an infant, and this had necessitated tracheotomy For lack of adequate history, it was assumed that secondary infection had occurred at the time of the tracheotomy, and that this infection had destroyed much soft tissue, the tracheal rings, and part of the thyroid and cricoid cartilages Many operations had been performed on his neck , but treatment, undertaken by Prof T P Kilner and Mr R Battle when he was 8 years old (with the object of restoring patency of the lumen above the tracheotomy) had been interrupted by the evacuation of the hospital in the early days of the war His condition before that treatment is shown in fig 1 , above the patent opening into the trachea a median slit communicated with the larynx After that treatment his condition was as appears in figs 2 and 3

Examination

The patient spoke in a whisper, which he achieved by pushing his chin downwards and backwards into his neck He was appalled by his condition and had attempted suicide He was doubtful of the prospect of repair and resistant to treatment In the midline of the front of his neck he had a large opening (fig 2) into his trachea , this opening extended down to just above the episternal notch Above, it was estimated that five sixths of the rigid circumference had been lost, and below, it was regarded as tapering off to a loss of a third. At the upper end of the trachea was a transverse ridge (fig 2) which was thought to be made by the remains of the posterior inferior margin of the cricoid cartilage Above this ridge was a second opening (fig 2), which passed into the larynx. Both openings were in a shallow pit in the front of the neck, the transverse ridge being more or less continuous with the plane of the skin From this it was assumed that the larynx and the upper end of the trachea had been drawn forwards by scar tissue The opening into the larynx admitted a no 9 endotracheal catheter, and the subglottic region was responsive to touch Direct examination of the larynx corroborated that it was drawn forwards The over all size was smaller than normal, the cords moved with respiration, and a no 7 endotracheal catheter could be passed between them and brought out through the opening in the neck

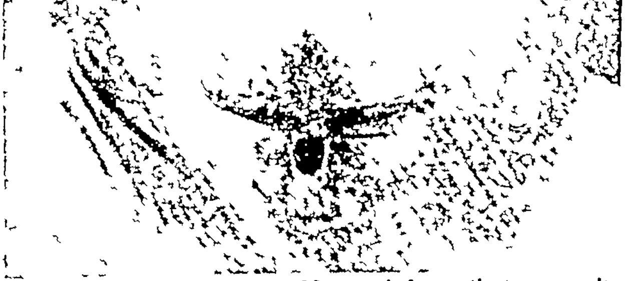


Fig 1—Condition of neck at age of 8 years, before patient came under care of Professor Kilner and Mr Battle A median slit above the tracheal opening communicated with the larynx.

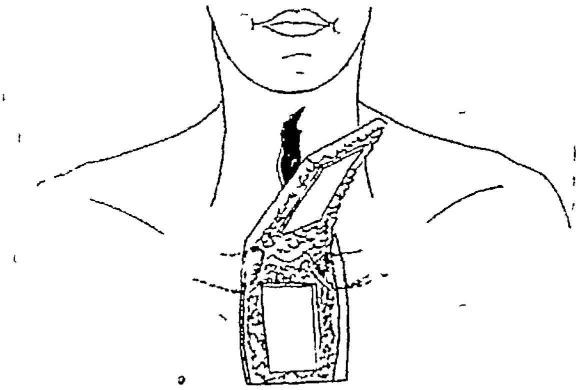


Fig 4—Delayed flap raised from manubrium and turned up to cover openings in neck.

Preparation for Treatment

The boy doubted his ability to breathe properly if these openings were closed by an operation To reassure him my dental colleagues constructed a soft acrylic collar which covered the openings and created an airtight lumen. This appliance worked admirably and convinced the patient of his power to breathe naturally, but it prevented him from pushing his chin downwards and backwards, and consequently he believed he could not speak However, Mr Robert Owen and I got him to make a guttural ' e " sound , this we extended to " Ee," and later to " Mary " Finally, he could speak in more than a whispering tone, in fact he could shout. By this time he had become more amenable to surgical repair

The broad requirements were for a rigid skin lining to cover both openings It had to be airtight, and covered by skin to avoid any raw surface on the outside

Surgical Repair

Treatment was carried out in five stages, some of them involving more than one procedure

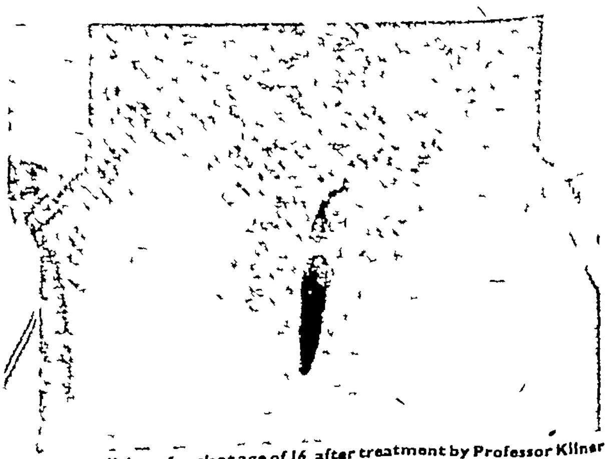


Fig 2—Condition of neck at age of 16 after treatment by Professor Kilner and Mr Battle. Note scar tissue and transverse ridge.

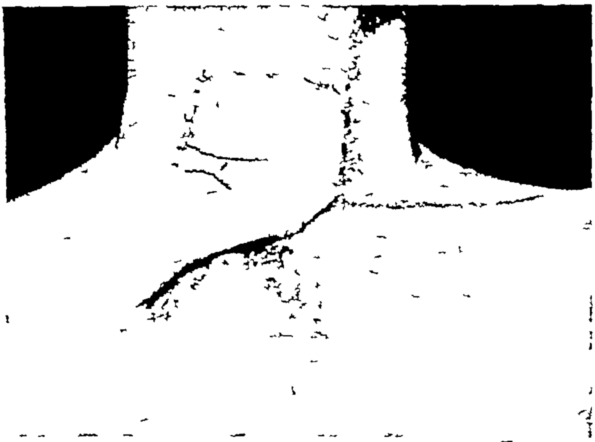


Fig 5—Tubed pedicle detached from left wrist opened for half its length to form a flap and stitched over delayed flap from manubrium Note raw surface on manubrium

Stage I (Oct 25, 1948)—A left abdominal tubed pedicle 4 in wide and 8 in long was prepared, to provide cover for the repair

Stage II (Jan 5, 1949)—The lateral end of the tubed pedicle was divided and attached to the radial border of the left wrist (fig 3) A delayed flap of requisite dimensions was made on the front of the manubrium and sternum (fig 3) The flap was based above the episternal notch and contained on its deep surface a sliver of bone and periosteum from the manubrium and sternum measuring roughly $1^{1}/_{4}$ in wide, $1^{1}/_{2}$ in long, and $^{1}/_{16}$ in thick

Stage III (March 24, 1949)—The medial end of the tubed pedicle was detached from the abdomen and implanted on the front of the chest at a selected site (fig 3)

Stage IV (May 5, 1949)—Incisions were made on both sides of the openings in the neck and joined by a third incision across the neck above the opening into the larynx The incisions were undermined The delayed flap containing periosteum and bone was then raised from the front of the manubrium and sternum (fig 4), turned up to cover the openings in the neck and sutured to the medial margins of the incisions This flap provided the rigid skin lining Next the tubed pedicle was freed from the left wrist and from this free end the pedicle was opened for a little more than half its length The flap formed by opening the pedicle was sutured into the lateral margins of the incisions in the neck, with the skin surface superficial (fig 5) It formed a cover flap for the rigid skin lining flap

Stage V (June 9, 1949)—The remaining tubed portion of the pedicle was detached from the chest wall, opened and fixed into the raw surface on the manubrium and sternum (fig 6)

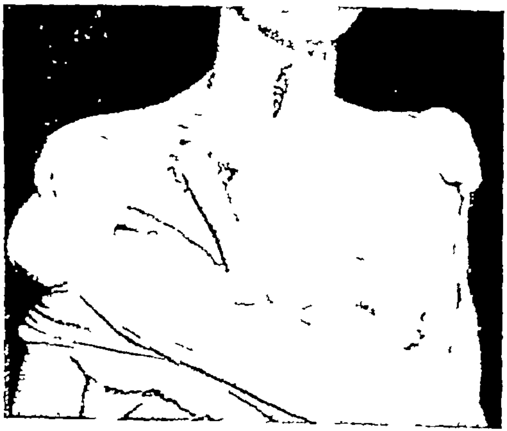


Fig 3—Tubed pedicle attached to front of chest and radial border of left wrist. Note delayed flap over manubrium

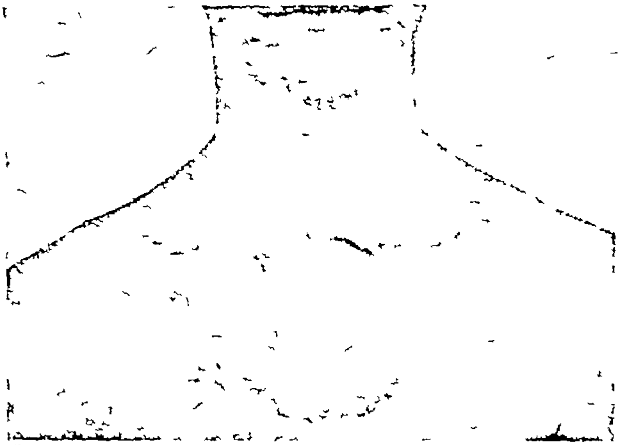


Fig 6—Repair completed tubed pedicle has been detached from chest converted into flap and fixed over raw surface on manubrium

The repair proved successful, and a year after completion of surgical treatment the boy was working as an electrician He spoke well, though his voice was slightly husky He could ride a bicycle and run without any difficulty in breathing He could expectorate satisfactorily There was no suction effect on the repair when he took a deep breath The sliver of bone in the neck could still be felt, was much the same in size as originally, and did not hamper movements of the neck

I am indebted to Professor Kilner and Mr Battle for fig 1

REFERENCE

Lancet (1950) i 359

THERAPEUTIC EFFECT OF AN ALLERGIC REACTION TO FOOD ON RHEUMATOID ARTHRITIS

L G POLYMENAKOS
M D Athens L M C Canada
FORMERLY SECRETARY GENERAL, MINISTRY OF HEALTH, TORONTO, ONTARIO

THE therapeutic success of Hench et al (1949) with 'Cortisone' and the adrenocorticotropic hormone (A C T H) in rheumatoid arthritis indicates that most of the clinical manifestations of this disease can be reversed with the result that the patient feels well again, but the precise actions of the hormones are unknown

A C T H presumably acts by stimulating the adrenal cortex to secrete its hormones but the function and chemical composition of but few of these hormones are known We can separate some of them as glucocorticoids (e g, cortisone and 'Compound F') concerned in the metabolism of sugar, mineralocorticoids (e g, deoxycortone) concerned in the metabolism of sodium, potassium, and water, and the 17 ketosteroids and other steroids, whose actions are synergic with, or antagonistic to, those of other endocrine glands, especially the gonads, and play an important part in the resistance of the body against disease

The observation that, in the synovial fluid of patients with rheumatoid arthritis, the concentration of hyaluronic acid and the activity of hyaluronidase are abnormal (Meyer 1947) has led to the suggestion that the enzymes which are responsible for the synthesis of glycogen might similarly play a part in the composition of hyaluronic acid, which is a similar polysaccharide, and probably contain or depend on the glucocorticoids, of which cortisone is one, for the synthesis of hyaluronates or other substances of the intercellular matrix This hypothesis, however, has not been proved

The results obtained by Hench et al (1949) and Thorn et al (1949) with cortisone and A C T H lend support to the hypothesis that rheumatoid arthritis is one of the "diseases of adaptation" (Selye 1946) The following case record points in the same direction —

CASE RECORD

A man, aged 68, was examined on May 12, 1949, complaining of stiffness of the joints, with aching, pain, redness, swelling, and very limited function Chronic rheumatoid arthritis was diagnosed The patient's blood pressure was 170/95 mm Hg and the erythrocyte sedimentation rate was above normal His urine contained leucocytes and a few red blood cells He had a large prostate and frequency of micturition If he stood up suddenly he felt giddy Radiography showed rarefaction of bone and irregularity of bone surfaces

Treatment —The patient was given a good diet, low in sodium and excluding alcohol, and was ordered to rest Salicylate, iodine, and ascorbic acid were given by mouth in moderate doses To improve the anabolism of the bones, absorption of œdema in the joints, and the strength of the bladder, testosterone propionate 75 mg and thiamine hydrochloride 300 mg were given intramuscularly and 10% calcium gluconate 30 ml intravenously each week

Progress —The patient s condition improved until June 10, 1949, when I was urgently called to see him and found him with œdema of the eyelids and lips, dyspnœa, and itching He said that the previous evening he had had fish for supper, and that the present condition had come on soon afterwards All the symptoms were those of an allergic reaction to food Calcium gluconate, and ascorbic acid were given intravenously and 'Benadryl' by mouth and the patient was told to drink plenty of water When I next visited him I found that not only had his allergic condition improved but also he rose from his bed easily and no longer had any stiffness of his joints For the next five weeks the patient received the same kind of treatment as before but not so intensive A surprising amelioration of his rheumatoid symptoms was the result Six months after his allergic attack, he was still completely free from symptoms Both his hands had the capacity, movement, strength, and appearance of those of a normal person of his age

DISCUSSION

The treatment given in this case helped the patient, but the allergic reaction to food (fish) was the chief cause of the remission of the rheumatoid arthritis The clinical improvement began only fifteen hours after the allergic reaction, and, although the previous treatment was continued, though less intensively, for only five more weeks after the allergic attack, the improvement was very speedy and progressive until complete remission of the disease

The improvement can be explained in terms of the general adaptation syndrome of Selye (1946) The endocrine mechanism came into action because of the excessive stress of the allergic attack, which was an effective stimulus for the production of the "alarm reaction" including increased adrenocortical activity During the alarm reaction an excess of A C T.H can be demonstrated in the blood (Ungar 1944), and the production of adrenal corticoids (e g, cortisone and compound F) is increased, thus augmenting the non specific resistance of the organism

If this explanation is correct, the result in the present case was similar to those obtained by the use of cortisone and A C T H as described by Hench et al (1949) and Thorn et al (1949)

REFERENCES

Hench P S, Kendall E C Slocumb C H Polley H F (1949) *Proc Mayo Clin* 24 181
Meyer, K (1947) *Physiol Rev* 27 335
Selye H (1946) *J clin Endocrinol* 6 117
Thorn G W, Bayles T B Massell B F, Forsham, P H, Hill, S R jun Smith, S III, Wazzen J E (1949) *New Engl J Med* 241 529
Ungar G (1944) *J Physiol* 103, 333

Preliminary Communication

RADIOGRAPHY IN COLOUR

X RAYS and light are both electromagnetic radiations, but the wave lengths which stimulate the retina (visible spectrum) range from about 3200 to 7500 Ångstrom units * (Å) whereas the X ray spectrum extends from 0 06 to 500 Å, the X rays used in diagnosis being those between 0 128 and 0 414 Å

The "hardness" of an X ray beam depends on its wave length, the hardest rays having the shortest wave-lengths, so hardness is closely analogous with colour in a beam of light Raising the kilovoltage passing through the X ray tube shortens the wave length and increases the hardness of its X ray emission—e g, a boundary wave length of 0 414 Å is equivalent to a peak tension of 30 kV, and a wave length of 0 138 Å to 90 kV The penetration of X rays through a given substance depends on their hardness, the short hard rays being most penetrating, on the density of the substance, and on the atomic numbers of the elements of which it is composed Thus by varying the kilovoltage (wave length) of the X ray beam, and therefore its penetrating power, we can take a series of pictures of a part of the body each emphasising different details—for example, if we take two X ray films of the head, one with 45 kV and the second with 90 kV peak tension, the first will show the soft tissues, and the second the bony structure

THEORY

The basis of the three colour theory of colour vision is that all colours, including white, can be matched by mixing the three "primary" spectral colours This premise is not strictly true, for the match is not exact, the colour to be matched, as seen in the solar spectrum, is almost always noticeably more "saturated" than the mixture which imitates it Nevertheless, applications of the theory give good results in practice and almost all natural colour photography is based on it By mixing only two primary colours one can get a more limited range of colour effects, which will be satisfactory for many purposes and may greatly simplify the technique

Colour radiography has something in common with the staining or "tagging" practised in microscopy, as well as with colour photography

Additive Method

A composite picture in pseudo natural colour can be produced by projecting positive films or positive transparencies of three radiograms on to a viewing screen at the same time The positive of the radiogram taken at the lowest kilovoltage can be tagged by projecting it with light of a primary colour, say red, the one taken at the medium kilovoltage with green, and the one at the highest kilovoltage with blue If a more limited spectral range seems sufficient, two films and two primary colours are used A similar effect can be obtained with a chromoscope, in which the three films are illuminated with light in the three primary colours, as before, and are then optically superimposed by the use of partly transmitting and partly reflecting mirrors to form a composite coloured picture

Subtractive Method

Before it can be published, the composite colour radiogram must of course be in the form of a colour print on paper The easiest way to obtain such a print is to treat the radiograms taken at the various kilovoltages as if they were the colour separation negatives of colour photography, and to restrict oneself to two colours I have used a modification of the trichrome carbro process, and the two colours chosen were cyan blue and yellow The composite colour print is made by a "subtractive" method This depends on the filtering, absorption, or subtraction of appropriate amounts of the three primary colours from white light as it passes through the two superimposed colour images to the white paper support and is reflected back again through the colour images. For instance, the cyan blue image absorbs the red rays but reflects the blue and green, whereas the yellow image absorbs the blue but reflects the green and red. Each colour image acts as a colour-filter for the other. This combination gives a composite picture in colour of a limited but satisfactory spectral range. By using an additional image printed in magenta, which absorbs green rays and reflects red and blue, the spectral range can be widened considerably.

---

* The Ångström unit of wave length is a ten millionth of a millimetre (10^{-7} mm.) and a tenth of a millimicron (0 1 mμ)

The rendering of colour on a paper colour print always falls far short of perfection. The trichrome carbro process is among the most popular and most difficult of the indirect processes for making composite colour prints on paper. Very beautiful composite paper colour prints have been made by "subtractive" methods, but their cost and complications have restricted their practical use to a few professional and a very few advanced amateur photographers.

TECHNIQUE

The patient must keep quite still while all the X ray exposures are made. One must get his complete confidence and coöperation by explanation and reassurance beforehand, and see that he is comfortable and relaxed. The recognised methods of the skilled radiologist are used to control unwanted respiratory movement, involuntary swallowing, &c. When some parts are to be examined—e.g., head and neck—the patient must immobilise not only the whole parts but also their components such as the mandible and tongue. Mechanical restraint is sometimes useful here. Needless to say, the radiologist must not waste time over his manipulations.

Markers opaque to X rays should be attached to the part being radiographed, so that indication marks appear on the films. This facilitates exact registration in making the composite colour print. The colour separation positives are adjusted over one another so that the points at which they register are clearly seen.

CONTRAST

The scale of densities in an X ray negative film is greater than in a photographic negative film. The effective photographic range in black and white photography is about 1 to 128. Various factors affect the contrast in an X ray film, such as the length of exposure, the wave length of the beam, the scattering of the beam (diffusion), and the type of intensifying screen.

Monochrome photographic film technique depends on light and tone contrast, whereas colour films depend on colour contrast. Colour-film photography is unsuitable for objects with unusual amounts of contrast, and it is then for the photographer to decide whether the shadows or high lights shall be lost. It is understandable that *the orthodox colour photographers prefer comparatively flat positives.*

The contrast range in orthodox colour photography is only 1 to 4. It should be *emphasised* that the eye is much more sensitive to differences in colour than in brightness. The best method of colour radiography is the projective or chromoscopic one, which gives a nearly perfect contrast range, because the greatest loss occurs in making the composite colour print. It would probably be better to use X ray negatives rather than positives, because as a rule the negatives seem to be more informative.

CONCLUSIONS

A colour radiogram presents its information in an attractive form. In one picture it can convey the information of two or more orthodox radiograms. The total effect is something more than that of the component radiograms. The method shows variations not only in density but also in colour, and the variations in colour may ultimately prove the more important.

Colour radiography will be valuable in studying the details of soft tissue, because it differentiates between degrees of softness inside the tissue as well as defining its outline. When three monochrome radiograms of the soft tissues of a limb are taken at 30, 32, and 34 kV there is a recognisable difference in the details they bring out, and the difference will be usefully accentuated in a composite colour *radiogram made from them.* The same principle applies in the medium and hard X ray bands.

There are no insurmountable difficulties in the way of developing a single-exposure method of colour radiography. Movement of the patient could be prevented by making the exposures in rapid succession with a mechanism adapted from that of serial radiography or direct cineradiography. By means of a mechanical or electronic device, or a combination of both, the kilovoltage and milliamperage of the X ray tube could be adjusted automatically and serially. These methods could also be followed with an indirect cineradiographic technique.

Colour stereoradiography, colour fluoroscopy, colour stereofluoroscopy, colour cineradiography, and colour stereocineradiography are all possibilities for the future.

Colour radiography should stimulate research and have value in diagnostic radiology and other branches of medicine. It is now only in its infancy. Its ultimate value will depend on the ability and enthusiasm with which it is pursued. Research-workers in this field should have a first class knowledge of physics, especially of electronics.

I wish to thank Dr Glyn Jones, consultant radiologist, Swansea General Hospital, for making the X ray negatives *and for his helpful advice and criticism.*

West Glamorgan Health Division
Swansea

G. E. DONOVAN
M.D. N.U.I., D.P.H.

Medical Societies

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE annual congress was held at the Royal Society of Medicine from March 29 to 31, under the presidency of Mr MAURICE H. WHITING. Among the visitors officially welcomed at the opening session were Prof. J. François (Ghent), Dr John D. Blum (Geneva), Dr Noelle Chomé (Lausanne), and Dr P. Mendoza (Philippine Islands).

PRESIDENTIAL ADDRESS

Having chosen Rodent Ulcer as the subject of his presidential address, Mr Whiting was able to draw on his own extensive experience at the Middlesex Hospital for the last quarter of a century. During that period, he said, reports on 1000 sections of rodent ulcer were issued by the Bland Sutton Institute of Pathology, and it was interesting to note that 95% were situated on the face and head, and of these approximately 65% were found adjacent to an eye. In other words more than 60% of all rodent ulcers threaten sight.

Mr Whiting's main thesis was that in properly selected cases, surgical removal is preferable to radiotherapy. He laid stress on the importance of histological examination with a view to differentiating the circumscribed from the infiltrating type of growth, and stated that the chief value of radiotherapy is in the infiltrating variety. Of his series, 81% were cured by surgery at the first attempt, and the percentage of finally uncured cases was only 11, failure being amply explained by the size and perhaps not often enough The terminology used is the B N A. with some lapses, more particularly in the index, where the dura mater encephali is listed both as such and under "brain, hard membrane of" The labelling is always clear, though the script used is sometimes rather fussy and obtrusive Nearly twice as many pages of figures are devoted to the abdomen and pelvis as to any other region, and the series of plates on the female pelvis and perineum, and those on the anterior abdominal wall and inguinal region, are outstanding There are some defects in emphasis the joints are in general rather perfunctorily illustrated, mostly by diagrams from other sources, the eye and orbit are treated in much less detail than the ear, and the tonsil is relatively neglected Most of the variations shown statistically are of importance to the medical graduate (such as those of the appendix, the cystic artery, and the level of termination of the spinal cord), but some are not (including those of the palmaris longus and the pyramidalis muscles) On the other hand, aberrations of many notoriously variable and important structures are not given, thus variations in the nerve-supply of the hand, or in the mode of formation of the brachial plexus, are ignored, and indeed, the main defect of the atlas is that the peripheral nerves, particularly of the limbs, are inadequately figured and their branches inadequately labelled The cutaneous nerves in particular are almost completely neglected, and readers will look in vain for the sural nerve, or for any indication that the obturator nerve, though it appears in some 18 illustrations, has any cutaneous or articular branches The atlas is beautifully produced and bound, and despite the scope of its contents is both portable and convenient to consult

Eternal Eve

HARVEY GRAHAM London Heinemann Medical Books 1951 Pp 699 42*s*

HERE is a book on a subject recognised as "news" The author describes it as the story of women from the Stone Age until today—Myth, Magic, and Medicine—but in fact it is the history of midwifery and everything connected with it, among primitive peoples, in Ancient Greece, Rome, and Byzantium, in the Middle Ages, and so down to the present As we come to more recent times we see clearly the interplay of each new scientific advance in the management of labour The author's knowledge of the by-ways of his vast theme never fails him, and he moves easily in the historical background of the changing scenes from age to age The lying-in chamber dominates the book, though most women will feel that the few hours spent there, during a lifetime, hardly deserve such close, and even gross, attention from a biographer The scholarship and literary skill of the author are beyond dispute, and, this task done, may now perhaps be freed for more attractive uses The section on the modern management of labour shows that his power of engaging his reader's attention need owe nothing to the morbid

Advances in Carbohydrate Chemistry—Vol V

CLAUDE S HUDSON, National Institute of Health, Bethesda, Maryland, SIDNEY M CANTOR, American Sugar Refining Co, Philadelphia New York Academic Press 1950, Pp 322

THESE monographs dealing solely with carbohydrate chemistry are a product of the age of specialisation, but the Anglo-American editors, and the authors, who have been drawn from the United States, Great Britain, and the Commonwealth, have done their best to fulfil the promises made with the first volume—to provide 'critical and integrating reviews, intelligible to the average chemist rather than only to the specialist" The 10 articles in this volume deal with biochemical as well as chemical topics, and the former are more directly of interest to doctors There is a very clear account of the enzymatic synthesis of sucrose through α-D glucose-1-phosphate (the Cori ester) and fructose The fructose apparently does not combine directly with the enzyme and can be replaced by xyloketose or sorbose with the formation of the corresponding non-reducing disaccharides There is an article on enzyme specificity in the domain of carbohydrates, and others on pectases and α-amylases There is a review of the methyl ethers of glucose which have played such a large part in establishing the constitution of this and all the other sugars. The account of the commercial production of crystalline dextrose is likely to interest some doctors, for we must be among its largest users The history of the process, which goes back 150 years, well illustrates how war and the laws of economics will at times interact to produce some highly desirable material The article on xylan makes one wonder whether this substance may not replace inulin or dextran in physiological work, its preparation presents no greater difficulties In short, formidable though some of these articles appear—for example, the one on reductive desulphurisation by Raney nickel, or the one on the anhydrides of the pentitols and hexitols—the book contains much valuable information for advanced students and teachers Probably they will borrow it from a library, but the worker on carbohydrate metabolism will want it for his own bookshelf

---

A Textbook of Gynæcology (8th ed London Adam & Charles Black 1951 Pp 493 40*s*)—A fresh edition of Prof James Young's book follows hot on the heels of the last, but in three years there has been much news among the gynæcologists, particularly on the subject of tumours Besides enlarging this section substantially, he has revised the whole text *and added 17 illustrations including a coloured plate*

Color Psychology and Color Therapy *A Factual Study of the Influence of Color on Human Life* (London McGraw Hill 1950 Pp 284 42*s* 6*d*)—This book is evidently the outcome of much searching in libraries, but Mr Faber Birren seems incapable of separating wheat from chaff, and unaware of the scientific background of the subjects treated in his discursive survey Thus he quotes Gurewitsch's work on mitogenetic radiations as though it had not been discredited, and he often startles the reader by putting the findings of serious workers beside the vapourings of quacks and cranks The theme requires a more critical approach

An Addendum to "King's and Some King's Men" (London Oxford University Press 1950 Pp 201 30*s*)—This, as the title explains, is a postscript to Dr Willoughby Lyle's exhaustive book on King's College Hospital and its medical school *The original volume dealt with the period* 1836–1934, and the object of the addendum is to complete the history of the voluntary hospital period, and bring it up to the day when the National Health Service took over the hospital and when the school became independently incorporated under the wing of the University of London. Like its predecessor the book is divided into chapters dealing with the events and personalities of successive years, with additional chapters on nursing, almoners, physiotherapy, and the like There is also a chapter on the Hambleden family, which did so much, *in successive generations, for the hospital and* school

The account of nursing is particularly instructive few, even of King's men, have remembered that before the Crimean War Florence Nightingale was invited to come to King's and reform the nursing arrangements, or that, even earlier, in 1848 it was four members of the honorary staff of King's who, with the Bishop of London, founded St John's House for the training of nurses, a move which had far reaching effects By relating what happened in the hospital with what happened *in the outer world, Dr Lyle has produced* a work of general interest, and the same thing could usefully be done for other hospitals and schools After all, it was the county histories, and researches into abbeys and manors, that built up so much of modern archæology and of the known history of England Small beer can be condensed into strong and satisfying liquor

Dr Lyle is to be congratulated particularly on two things his accuracy and his objectivity A historian is expected to be accurate, but the expectation is not always fulfilled, and when a mass of minute detail *is found* to be completely trustworthy, one cannot help being grateful (The only questionable statement observed was that Mrs Gamp was addicted to whisky surely it was gin ?) *His* objectivity is olympian, and his generosity to persons for whose memory he has little personal reason to be tender is splendid The book altogether is the crown of a great achievement

THE LANCET
LONDON SATURDAY, APRIL 14, 1951

Ætiology of Diabetes

THE concept that all types of human diabetes arise from disease of the pancreas originated in CAWLEY's paper of 1788[1] and was greatly strengthened by the findings of VON MERING and MINKOWSKI[2] in pancreatectomised dogs a century later. The work of OPIE[3] in 1901 and of SSOBOLEW[4] in 1902 further localised the essential morbid process to the islets of Langerhans, and prepared the way for the discovery of insulin by BANTING and BEST. More recently the picture has been complicated by the studies of extrapancreatic diabetogenic influences, such as those of the anterior pituitary, adrenal cortex, and thyroid gland, and in consequence diabetes is in danger of being degraded from its former position of a clinical entity to that of a mere syndrome with multiple causes.

How far is this change of view justified? According to WILDER,[5] less than 9% of the acromegalics seen at the Mayo Clinic were also diabetics, and in half of these the diabetes had clearly preceded the acromegaly; the diabetes usually disappeared when the acromegaly was treated or burnt itself out. It seems then that in animals growth hormone can produce permanent diabetes,[6] but that it is never present in sufficient quantities in man, even when he is an acromegalic, to produce a lasting diabetes, unless perhaps in exceptional cases of genetic predisposition. Temporary diabetes can also be produced in normal man by A.C.T.H.,[7] but the diabetogenic potency of this hormone cannot be very great, since diabetes is a rare complication of its clinical use, though almost all the other manifestations of Cushing's syndrome are not uncommon as complications. A third pituitary hormone—prolactin—has lately been shown to have diabetogenic properties,[8] but, like growth hormone and A.C.T.H., this seems unlikely to cause permanent diabetes in man. Adrenal cortical diabetes is fairly easily distinguished from pancreatic diabetes, if only because it is insulin resistant and does not occur in a lasting form except in association with the other features of Cushing's syndrome. Removal of the over-functioning adrenal tissue cures the diabetes. In thyrotoxicosis it is not uncommon to find slight glycosuria and a high blood sugar curve, which cannot be entirely accounted for by over-rapid intestinal absorption, though this is present. The formation of glycogen is delayed, and as a result high blood sugar curves are obtained even in intravenous glucose-tolerance tests. These defects disappear, however, when the thyrotoxicosis is controlled. The rare cases of hyperglycæmia resulting from brain injury are not likely to be confused with pancreatic diabetes, for the high blood-sugar depends on the stores of glycogen in the liver and is therefore transient.

Thus, though in animal experiments large doses of the hormones of the anterior pituitary, adrenal cortex, and thyroid gland have produced permanent diabetes or metadiabetes, there is no convincing evidence that they have done so in man. This implies that man normally has such a large reserve of islet-cell function that he can respond to the extra load imposed by acromegaly, Cushing's syndrome, or thyrotoxicosis without exhausting his beta-cells, in the way characteristic of metadiabetes in animals. WILDER[5] suggests that metadiabetes may still be the commonest human type, if obesity is regarded as the load which eventually overwhelms the responsive power of the beta-cells. STETTEN and BOXER[9] have shown that normally dietary glucose is largely converted into fatty acids before being katabolised in the body, and that this conversion mainly depends on insulin. Thus obesity puts extra work on the pancreatic islets, quite apart from the increased metabolic requirements of the superfluous tissue. As in experimental diabetes, early removal of the cause may allow carbohydrate tolerance to return to normal; but after many years of obesity the diabetes may persist, even though the person's weight eventually returns to normal. Since only a minority of fat people eventually develop diabetes, one must assume that, in addition to the diabetogenic effect of obesity, there is an inborn meagreness of the reserves of islet-cell function. Opponents of the single (pancreatic) origin theory of diabetes point to the many necropsy reports on diabetics showing histologically normally pancreatic islets.

In more than a quarter of WARREN's[10] 259 diabetic pancreases the islet tissue was essentially normal, and ROBBINS and TUCKER[11] found pancreatic lesions in only a little over 40% of their 184 necropsies on diabetics. TERBRÜGGEN,[12] on the other hand, with his newer staining methods, has noted that 80% of human diabetics have abnormally small pancreatic islets containing relatively few beta-cells and disproportionately many alpha-cells. Thus, as finer techniques reveal smaller variations from normal in islet-cell appearances, the unexplained gap is narrowing. Abnormal function is perhaps not always associated with abnormal structure; but it is well to remember that in all the experimentally produced forms of metadiabetes definite structural changes were seen in the beta cells. The evidence points to these changes of structure being caused by hyperglycæmia rather than by the inciting agent of the diabetes, for hyperglycæmia alone has produced permanent pancreatic diabetes in partly depancreatised cats—even in one normal cat[13]—and in diabetes induced with A.P.E. (anterior pituitary extract) phlorizin cures the diabetes and reverses the degeneration in the beta-cells,[14] presumably by lowering the blood-sugar Another unifying concept in the ætiology of diabetes is the rôle of the glutathione in the blood and beta-cells in protecting the pancreas from various diabetogenic agents LAZAROW[15] found that glutathione administered before alloxan inhibits or prevents its diabetogenic effect, and that the susceptibility of animals to alloxan varies inversely with the glutathione levels[16] in their blood and tissues Alloxan is rapidly reduced in the body to the relatively innocuous dialuric acid The particular susceptibility of beta cells to the action of alloxan may be due to the higher O/R potential in these cells which must build S–S bridges in the insulin molecule (12% of which is cystine) from —SH compounds Thus a high rate of insulin formation is likely to deplete the glutathione of the beta cells Uric acid, which has been used to produce diabetes in rabbits deficient in thioamino acids,[17] is structurally related to alloxan It is significant then that A C T H both increases the production of uric acid and lowers the blood-glutathione level A P E also lowers the glutathione content of the tissues Thiouracil, which raises the blood glutathione level, prevents rats which have been 95% depancreatised from developing diabetes LAZAROW,[18] however, has introduced a jarring note by producing glycosuria in force fed animals by injecting them with glutathione In the concentrations he used, the glutathione may have partly reduced the S–S linkages of the animals' insulin, thus inactivating it

---

[1] Cawley T Lond med J 1788 9 286
[2] Von Mering J Minkowski O Arch exp Path Pharm 1889-90 26 371
[3] Opie E. L Bull Johns Hopk Hosp 1901 12 263
[4] Ssobolew L. W Virchows Arch 1902 168 91
[5] Wilder R. M. J Amer med Ass 1950 144 1234
[6] Cotes P M. Reid E. Young F G Nature Lond. 1949 164 209
[7] Conn J W Louis L H Johnston M. W Proc Amer diabet Ass. 1945 8 214
[8] Houssay B A Anderson E Endocrinology 1949 45 627
[9] Stetten DeW jun. Boxer G E J biol Chem 1944 156 271
[10] Warren S. Pathology of Diabetes Mellitus. London 1930 p 53
[11] Robbins S L Tucker A. W jun New Engl J Med 1944 231 865
[12] Terbrüggen A Virchows Arch 1945 315 407
[13] Dohan F C Lukens F D W Science 1947 105 183
[14] Lukens F D W Dohan F C. Wolcott M. W Endocrinology 1943 32 475

The main impression gained from the more recent work on human diabetes is that it nearly always arises in the pancreas, and that obesity is the commonest predisposing factor, though it produces the disease only in people with a naturally inferior islet cell reserve

The Body's Iron

Two years ago GRANICK[19] outlined present knowledge of iron metabolism—a field in which he has done much original work For a man weighing 70 kilogrammes the total iron in the body is between 4 and 5 grammes, 60–70% of this iron is in hæmoglobin, 3–5% in the myoglobin of muscle, 15% as ferritin, 0 1% as siderophilin, and 0 1% in hæm enzymes such as cytochrome, while about 10% is not accounted for

Siderophilin and ferritin are comparatively new names and need explanation Siderophilin is a pseudoglobulin protein molecule that can carry iron, oxygen oxidises ferrous to ferric iron, and in the presence of CO_2 a complex of one CO_2 molecule for each ferric atom is attached to the protein molecule In the presence of reducing substances the ferric iron changes to ferrous and becomes detached from the protein All the serum-iron is normally carried by siderophilin Ferritin is a remarkable substance discovered thirteen years ago by LAUFBERGER, it is a protein containing up to 23% of iron, and it is crystallisable because the protein part (apoferritin) is crystallisable Ferritin can be isolated from many tissues, and especially liver, spleen, and bone marrow It has two vital functions it is the normal iron storage protein of the body, and it is a link in the absorption of iron from the alimentary tract and probably in the passage of iron across the placenta from mother to fœtus Hæmosiderin, the microscopically stainable iron seen in histological sections, is a polymerisation product of ferritin but is not a normal storage form The most important function of ferritin is connected with the regulation of iron absorption Iron is only absorbable in the ferrous form, the stomach acid converts the colloidal ferric hydroxide of foodstuffs into monomolecularly dispersed ferric ions which at pH5 (but not at pH7) can be reduced to the ferrous form by ascorbic acid or the sulphydryl groups of protein foods Tracer studies have shown that although iron can be absorbed along most of the gastro intestinal tract, it is normally almost all absorbed from the duodenum just below the pyloric sphincter—i e, in the area where the pH remains about 5 When large amounts of iron, such as therapeutic doses, are taken, the area of absorption spreads perhaps over the whole alimentary tract from stomach to large bowel Nevertheless, there is, as we have explained,[20] a definite early limit to the amount of iron that can be absorbed Repeated experiments have shown that the passage of iron across the intestinal mucosa is one way only, and that the amount of iron passed from the alimentary tract into the blood depends on the presence and extent of anæmia The intermediary substance probably responsible for this regulatory mechanism is ferritin, and GRANICK suggests the following hypothesis When the ferrous iron passes across the intestinal cell, it is converted by the cell enzymes, in the presence of oxygen, into ferric iron and is then attached to apoferritin to form ferritin At the blood stream end of the cell, reducing substances in the cell reconvert the ferric to ferrous iron so that it becomes detached from the ferritin and passes out into the blood, to be taken up by the siderophilin for transport The limiting factors are two (1) the amount of apoferritin is limited, and once it is all converted to ferritin no more iron can be conveyed across the mucosa until some of the ferritin gives up its iron to the blood, and (2) the rate at which ferritin releases its iron depends, not on the level of serum iron, but on the oxygen supply at the blood stream end of the cell, and this is only low enough to permit rapid transit when anæmia is present Possibly the ferritin apoferritin mechanism is not the sole controlling factor, there is quite a lot of evidence[21] that a diet containing excess phosphate may impede iron absorption Such a diet would be rich in foods like meat, fish, and dairy products, so in this country, under present conditions, excess phosphate is unlikely to be troublesome

Proper understanding of iron metabolism and of the steps in iron absorption is important to the physician Iron deficiency anæmia must be one of the commonest diseases in women, and it is more common in men than is supposed The work on iron metabolism has shown that large oral doses are best, but that it is useless to give more than gr 30 (2 g) daily of ferrous sulphate and that ascorbic acid aids absorption of the iron in protein foods It is clear, too, that the iron absorption mechanism efficiently protects the body against excessive absorption of unexcretable

---

[15] Lazarow A *Proc Soc exp Biol N Y* 1946 **61** 441

[16] Lazarow A *Phys Rev* 1949 **29** 48

[17] Griffiths M *J biol Chem* 1948 **172** 853

[18] Lazarow A *Proc Soc exp Biol N Y* 1950 **74** 702

[19] Granick S *Bull N Y Acad Med* 1949 **25** 403

[20] Leading article *Lancet* 1949, i 26

[21] Leading article *Brit med J* Feb 3 1951 p 231

except in hæmochromatosis The introduction
fective iron preparations for intravenous use has
got round the protective absorption barrier,
the question whether continued intravenous
inistration may be harmful has been raised We
that in patients with hæmolytic or aplastic
mia who have received multiple blood-trans-
ons, large amounts of iron are found deposited,
ne form of hæmosiderin, in the liver and spleen,
in the liver may induce fibrosis and damage
mbling that seen in spontaneous hæmochroma-
;[22] Might not intravenous iron do the same sort
hing? Nils Andersson[23] has tried to answer
question. He gave to rabbits a standard intra-
ous iron preparation in doses varying from 12 to
mg Fe per kg body-weight In man the average
l dose for anæmia is 1500–2500 mg Fe, or about
ng per kg Andersson's figures show that at this
l the iron content of the liver and spleen fourteen
s after injection was about four times normal, and
t two to three months later it was still twice normal
greatest absolute amount of iron was in the liver,
weight-for-weight the spleen contained the most
ese increases are not very large, and the iron level
the organs fell steadily after the injection at an
rage rate of 0·13 mg per day Histological examina-
n of the tissues showed a most interesting redistri-
tion of the injected iron. In the liver it was at first
en up by the Kupffer cells, after a week, however,
iron staining was diffused in the cells of the liver
renchyma, and pari passu the iron in the Kupffer
ls diminished. Similarly, in the bone marrow the
n was at first seen in the endothelial cells of the
usoids, but later passed to the stroma Iron
posited in the lungs gradually disappeared in two
eks when a dose of 12 mg per kg was given, no
n could be shown histochemically in the liver after
e month, and last of all it disappeared from the
leen and bone-marrow Where this iron goes to
not clear, but experiments with radioactive iron
ve shown that excretion of iron in the bile is
creased from about thirty days after a parenteral
se Andersson also found that the iron in the bile
his rabbits was increased about three times
of Carl Moore[24] has stated that the excretion
iron is probably greater than has been suspected
d he puts the figures at 1 mg Fe daily for
en, and at 15 mg daily for women of menstrual
e The suggestion that iron can be lost in the
eat has now been denied, but iron is lost
rough desquamated skin cells[25] In order to
t toxic reactions from parenteral iron, Andersson
d to give about ten times the therapeutic dosage,
s conclusions were confirmed when he examined the
gans of a patient who had met with a fatal accident
x weeks after completing a course of 800 mg of
travenous iron No histochemically demonstrable
on was present in the liver, spleen, or kidneys
ndersson's work then, supports the view that
arenteral iron in the present dosage—about 25–40 mg
e for each 1% (0·148 g per 100 ml) hæmoglobin
eficit—is quite safe and unlikely to cause permanent
eposition of hæmosiderin

There have now been many more reports of the therapeutic use of intravenous iron **Horrigan** et al.[26] in the U.S.A confirm that, if single doses are limited to 100 mg Fe, reactions are few **Sinclair** and **Duthie**[27] record 51 cases of rheumatoid arthritis, none of which had responded to oral iron, intravenous administration gave a good result in 38 cases, but in 13 the hæmoglobin remained low In our columns **Scott** and **Govan**[28] have lately reported results in 150 cases of anæmia during pregnancy and the puerperium, they used intravenous iron especially for obtaining a rapid rise of hæmoglobin in pregnant women when time was short, and they, too, regard 100 mg Fe as a safe upper limit for single doses Despite these favourable results, there are some dangers with intravenous iron **Birch** and **Till**[29] have described a case in which the patient developed iron encephalopathy—fortunately not fatal—after receiving altogether 380 mg Fe, the maximum single dose being 75 mg Consequently parenteral iron should not be used as a substitute for oral iron Many patients will respond to adequate doses of oral ferrous sulphate, especially if given in enteric coated tablets to prevent the troublesome gastric disturbance Not until this has failed should parenteral iron be used, the only ground for exception is need for a speedy response, as in pregnancy Repeated courses of intravenous iron are hardly ever necessary With proper precautions, this is a valuable method, and **Andersson**'s results make it clear that the bogy of artificially induced hæmochromatosis need not hamper its use

Tissue Culture and Biophysical Research

Few biological techniques have experienced such fluctuations of fashion as tissue culture In its early days it was exalted almost to the status of a separate science, and such was the elegance of the method and the beauty of the material it produced that more and more people learned to grow cells though they had no particular object in view and had little knowledge of cell biology Papers on the subject became so numerous as to induce a sharp reaction against tissue culture, which led to some notable contributions being overlooked Today, however, thanks to the energy and enterprise of the few American workers who in 1946 founded the Tissue Culture Commission—now the Tissue Culture Association—the technique has been restored to an important position in medical and biological research The years of partial eclipse have had a salutary debunking effect, and tissue culture is taking its rightful place in laboratories as a very valuable experimental method with special advantages and special limitations Tissue growing in vitro has no vascular or nerve-supply and is isolated from the influence of adjacent structures and of the body as a whole, and this is one of the main advantages of the method For this reason however, experiments in vitro can rarely be substituted for experiments in vivo but should be used in conjunction with them For example, if one wants to analyse the complex reactions of the body to some therapeutic agent, such as radiation, an examination of its effects

---

[2] Wyatt J P Mighton H K Moragues V *Amer J Path* 1950 26 583
[3] Andersson N E *Acta med scand* 1950 138 suppl 241
[4] See *Lancet* 1950 ii 407
[5] Adams W S Leslie A Levin M H *Proc Soc exp Biol N Y* 1950 74 46

[26] Horrigan D L Mueller J F Vilter R W *J Lab clin Med* 1950 36 422
[27] Sinclair R J G Duthie J J R *Brit med J* 1950 ii 1257
[28] Scott J M Govan A D T *Lancet* Feb 17 1951 p 367
[29] Birch C A Till M *Brit med J* Jan 13 1951, p 62

on tissues in the body compared with its effects on the same tissues explanted in vitro, will indicate to what extent the changes which appear in vivo are due to the direct action of the agent on the individual cells, and to what extent they are caused by vascular damage and other indirect actions

An excellent account of the main applications of tissue culture is given in the new edition of RAYMOND PARKER's *Methods of Tissue Culture*[1] As he points out, there has been a "gradual development of a system of procedures that has been used to advantage in almost every field of experimental biology and medicine, particularly in cytology, histology, embryology, cell physiology, cell pathology, bacteriology and immunology, and in the study of tumours and viruses" His book gives a full and clear account of many old and new tissue culture techniques and their modifications, JOSEPH P MORGAN contributes an interesting review of recent attempts to make a satisfactory synthetic culture medium, there is a chapter on the thorny question of growth measurements and their interpretation, and concluding sections deal with histological and photographic methods An investigator who wished to undertake tissue culture experiments on a modest scale and with limited space and funds at his disposal might well be daunted by the elaborate procedure and equipment described in the earlier part of the book, and it should be remembered that much useful tissue culture work can be done under far simpler conditions But although *Methods of Tissue Culture* is hardly suitable as a handbook for an impecunious beginner, who might find CAMERON's *Tissue Culture Technique*[2] more helpful, it contains a store of valuable information that makes it an important reference book in any tissue culture laboratory and a useful guide for more experienced workers who wish to employ some of the special techniques described

Though tissue culture is on the whole more widely used and more highly organised in Canada and the United States than in England, it is being practised in an increasing number of centres here It is used at the Strangeways Research Laboratory for studies in cytology, radiobiology, and developmental physiology, at the Chester Beatty Laboratory, and at the Biochemistry Department of Glasgow University, for investigations into the physiology of growth, at the Radiotherapeutic Department of Cambridge University for analysing the action of antimitotic poisons and radiations, and at the Christie Hospital, Manchester, for radiological research, and at various other centres it is being employed on a smaller scale The latest British institution to make extensive use of tissue culture is the Biophysics Unit of the Medical Research Council at King's College, London, where the method is being applied as one of several approaches to problems of cell structure and growth, utilising various optical techniques of infra-red, phase-contrast, ultraviolet, and electron microscopy In general, cells in tissue culture grow in thin flat sheets, and this property is of value in a more quantitative optical approach to the study of the living cell During the last fifty years many theories of mitosis have been proposed, but even today there are very few measurements of the physical aspects of the process which could be used in developing an adequate theory Tissue culture cells, as A HUGHES and others have lately shown, form admirable material for such research

Almost fifty years ago it was discovered that the contents of cell nuclei absorb strongly in the ultraviolet range, and later this characteristic absorption became identified with that of the purine and pyrimidine bases of the nucleic acids It is largely owing to the work of CASPERSSON and his collaborators in Stockholm that the ultraviolet microscope has became an important tool for the study of individual cells, and his recently published lectures[3] give a good idea of how this work developed and of the ideas it has evoked No better example than this field of research could be chosen to illustrate how important it is that physicists, biologists, and biochemists should learn to understand the advantages and limitations of each other's methods The processes of fixation, for example, involve complex chemical problems as yet too little understood, they certainly lead to loss of material from the tissue By the use of cells in tissue culture, the living animal cell may be perhaps most conveniently studied, and it is possible that the physicist can at least assess and approximately distinguish between absorption, refraction, and scattering There can be no doubt that first class biologists and physicists are needed for research in this field, and that the most fruitful additions to biological knowledge can arise only from collaboration between the two groups The expected precision of thought which the physicist brings to his problems is bound to prove useful here

The Budget

IN deciding to charge patients about half the cost of their dentures and spectacles the Government have retreated from the principle that treatment under the National Health Service shall be free of charge, but they have withdrawn only from two salients that were becoming hard to hold For a great many people, better mastication and better vision are of more practical importance than most of the other benefits that medicine can offer, but it has seemed disproportionate that the dental and supplementary ophthalmic services should together absorb £75 million against only £48 million for general practitioner services, and definitely wrong that some 60% of dental expenditure should be on dentures The new arrangements will save some £13 million without, we hope, imposing real hardship With the ceiling of N H S expenditure strictly defined, saving in various other directions will still be necessary in the service, and, with prices rising, all who work in it will have to set their face against every kind of waste if they want to maintain its standards, let alone raise them Against Mr GAITSKELL's background of rearmament, devaluation, and shortage of materials, hardly any prospect pleases, but, in the N H S at least, much improvement is still possible within the limits drawn As doctors we can surely be thankful that the Budget, though it makes large provision for defence, does not create an economy in which the aims of peace are forgotten

---

[1] Methods of Tissue Culture By RAYMOND PARKER 2nd ed London Cassell 1951 Pp 294 57s 6d

[2] Tissue Culture Technique By G CAMERON New York. Academic Press. 1950 Pp 191 $4 20

[3] Cell Growth and Cell Function By T O CASPERSSON New York Norton & Co London Chapman & Hall 1950 Pp 185 28s

Annotations

CHILDHOOD OBESITY

Do fat children grow up to be fat adults? There is a general impression, with no figures to support or refute it, that most people who are fat in childhood and early youth become thin later Nevertheless, the recognised causes of obesity in adults probably operate also in children they are an inherited (familial) tendency, glandular imbalance, affections of the hypothalamus, injuries to the brain, true overfeeding, and the after-effects of infections In the U S.A. there has lately been a reversion to the view that "Fat comes only from food, and obesity results only from eating more than is required to meet the energy requirements of the body"[1] This view has adherents in this country, but Spence[2] and Simpson,[3] among others, doubt whether there is such a simple explanation In Melbourne Graham[4] puts the blame on "defective personality trends leading to increased intake of food and to decreased expenditure of energy" His treatment is based on an assessment of what the child should weigh for its height and age, followed by dietetic control, physical activities, and comparatively large doses of thyroid. But direct mensuration is sometimes misleading, as Brožek and Keys[5] have shown, the evaluation of leanness and fatness is a complicated problem best tackled by indirect methods Then muscular exercise, though uplifting, has disappointingly little effect on body-weight Dodds[6] has calculated that the maximum output of that energy a man can maintain for short periods is about 600 calories an hour At this rate, a half hour game of squash will roughly balance an intake of two slices of bread and butter or a pint of beer

There is a common type of fat boy which does not fit easily into any of the categories so far mentioned, and is often classed as "Froehlich's syndrome" or "Froehlich type" because, besides obesity, the children show delayed development of the penis and testicles and feminisation, with prepuberal fat distribution and a gynæcoid pelvis Simpson[7] analysed some of these cases in detail and coined the term "adipose gynandrism" for them Even without any specific treatment these children ultimately attain a full normal sexual maturity, though they may or may not lose their obesity In Bauer's[8] opinion the overweight child is usually also overgrown, and both conditions result from genetic abnormalities (gigantism), though these abnormalities may manifest themselves at widely different times

Whatever the ætiology of childhood obesity, few pædiatricians in this country would put a fat child under the age of 12 years on a rigorous reducing diet unless there were some exceptional circumstances, and they would be still more chary about prescribing thyroid treatment for such patients

HISTOPLASMOSIS AND PULMONARY CALCIFICATION

It is nearly 50 years since Darling first saw *Histoplasma capsulatum* in the tissues of patients with a disease resembling visceral leishmaniasis but it was not until 1934 that the organism was shown to be a typical filamentous fungus The fungi invade the cells of the reticulo endothelial system, where they appear as round or oval bodies 2–5 µ across, with scattered nuclear material and a refractile edge They are found in various types of phagocytic cells in the blood and bone-marrow as well as in liver and spleen. Histologically, the lesions have a necrotic centre surrounded by granulomatous tissue With disseminated infection there is fever, enlargement of the liver and spleen, and anæmia The disease often simulates tuberculosis, Hodgkin's disease, or carcinoma, and may be associated with them Most of the cases reported have been in America, particularly in the area bordering the Mississippi valley and its larger tributaries, or in South Africa and Java, only very rarely has it been recognised in the British Isles or elsewhere Bunnell and Furcolow[1] in 1945 described 10 patients with the disease in Kansas City, and Furcolow[2] now reports on a further 6 from whom *H capsulatum* was isolated. Of these 6, 2 had laryngeal lesions and 3 had disseminated foci in the lungs visible on radiography Of these 3, 1 healed with miliary calcification, and another with complete disappearance of the lesions, in the 3rd the condition persisted unchanged for two years, when the patient died of an unrelated illness Furcolow groups these 16 cases into (*a*) clear uncomplicated clinical cases, (*b*) cases in which the diagnosis was only probable, and (*c*) cases in which the recovery of *H capsulatum* seems to have been incidental. Of the 16 patients 5 have recovered, and it now seems clear that even overt histoplasmosis is not always fatal as it was once thought to be

Fresh light was cast on this disorder by the discovery that pulmonary calcification was much commoner among troops recruited from the Middle West than from any other part of the U S.A. In 1945 Dr Carroll E Palmer and his associates began a series of epidemiological investigations with histoplasmin, a skin testing reagent used in much the same way as tuberculin in the Mantoux test It was found that many tuberculin negative reactors who had pulmonary calcification reacted to histoplasmin There was also a definite geographical pattern in the prevalence of histoplasmin reactors throughout the country, and a high incidence of lung calcification was found in areas where histoplasmin reactors were numerous In a survey on over 5000 nurses and freshmen at Ohio State University, Prior and Allen[3] found that 75% of residents from the south-western part of the State gave positive histoplasmin reactions, and that the proportion of positives dropped steadily in those coming from the north and east across the area Prior et al.,[4] who surveyed 5000 students by means of chest radiographs and tuberculin and histoplasmin tests, also found that pulmonary calcification in Ohio is more closely associated with histoplasmin sensitivity than with tuberculin sensitivity, indeed there was no obvious relation between calcification and positive tuberculin tests Calcified lung lesions were slightly commoner among male than among female students, and they were also commoner among those from farms than among town dwellers, tuberculin reactors, on the other hand, were commoner among the townsfolk Although many of the calcified lesions brought to light in these surveys were undoubtedly of tuberculous origin, the findings add weight to the increasing evidence that in Ohio and other Middle western States such calcification is usually the result of a benign form of histoplasmosis Most of these large scale surveys have necessarily relied on skin tests, which are convenient but are not necessarily the best tool for such work Possibly infection with an antigenically related organism could give a positive histoplasmin test, but none has yet been found *H capsulatum* has been isolated from dogs and rodents but it is not known whether the organism survives outside the body or how infection is spread to man Until we know more about the epidemiology and pathogenesis of histoplasmosis we can only repeat[5] that the association of pulmonary calcification with histoplasmin sensitivity in certain well defined areas is suggestive, but not conclusive, evidence of a causal relationship

---

[1] Rynearson H E., Gastineau C F Obesity Springfield Ill, 1949 p 13
[2] Spence A W *Proc R Soc Med* 1950 43 340
[3] Simpson S. L Major Endocrine Disorders London 1948 p 133
[4] Graham B H *Med J Aust* 1950 ii 648
[5] Brožek J Keys A *Science*, 1950 112 788
[6] Dodds E C *Proc. R Soc. Med.* 1950 43 343
[7] Simpson S L *loc. cit* (footnote 3) p 64
[8] Bauer J *Arch. pediat.* 1940 57, 631

[1] Bunnell, I L Furcolow M. L *Publ Hlth Rep Wash.* 1948 63 299
[2] Furcolow M L *Ibid* 1950 65 965
[3] Prior J A Allen M. F *Ibid*, 1947 62 1608
[4] Prior J A. Wilce J W Palchanis W *Ibid* 1950 65 1132

SURGERY AND PREVENTIVE MEDICINE

Francis Bacon, that reviver of the experimental method, proposed eight qualities for the scientist They were desire to seek, patience to doubt, fondness to meditate, slowness to assert, readiness to reconsider, carefulness to dispose and set in order, neither affection for what is new nor admiration for what is old, and hatred of every kind of imposture Sir James Learmonth, reviewing, in his Heath Clark lectures of 1949,[6] the contribution of surgery to preventive medicine, likens these precepts to a protracted drip transfusion into British medicine, which did not produce its maximum effect until it distended the veins of John Hunter Considering them in turn, he remarks how variously desire to seek reveals itself, appearing both in those who patiently collect data relevant to an immediate need, and those who, like Charles Darwin, speculate on the data they have collected, so achieving a new synthesis, or are arrested by an exception where another man might be intent upon a rule Patience to doubt, "all too easily taught to recruits in science," brings its own risks, for it is easier to stand back and wait for certainty than to use constructively what is already known In dealing with people, a half plan is sometimes better than no plan When Jenner and Lister made their great contributions, one to preventive medicine, the other to surgery, the science of bacteriology was still unknown They acted resolutely, in a half light

Fondness to meditate is nowadays almost denied the scientist, pressure of work constantly hounds the teachers, and students are not even being prepared for the discipline of meditation Sir James suggests that at some stage in school education simple rules might be introduced by example, and inculcated by practice, to help the student to meditate to some purpose In examinations, he finds, the mark of the candidate who is a stranger to meditation is the phrase "according to X" he only has courage in the opinions of others, and as Arnold Bennett put it "sprinkles a thin powder of dullness over everything" The best method of selecting the worth while men from recruits, Sir James thinks, would be "to propound a presently insoluble problem in the morning and to collect the papers in the evening" Candidates would be free to meditate, and to meet and talk with each other, and with other groups, so that they would receive the stimuli of other minds

Slowness to assert, he says, is a harder precept for surgeons to follow than for those engaged in preventive medicine, fortunately it is always possible to recant a mistaken opinion, and readiness to reconsider ensures that this step can be taken without shame The easiest of the precepts to inculcate should be carefulness to dispose and set in order, and most students nowadays appreciate its purposes at least Recorded observations, they know, often point the way to discovery, as they did for Darwin Order, moreover, includes clear thinking, the forerunner of judgment, and we appraise our great men by their judgment By the use of this very quality the scientist strikes a balance between the new and the old in medicine, and learns to recognise and repulse imposture

Grounded in these precepts, surgery and preventive medicine have supported one another in many ways and Sir James Learmonth foresees future opportunities for collaboration While methods of preventing disease are still being sought the surgeon can offer many temporary expedients Thus he may be able to find methods of access to parts of the body where pathological processes have still to be studied and measured, and he can often eradicate disease in its early stages, prevent the development of some deformities, help to counteract local morbid processes, and suggest indirect ways (e g, by division of sympathetic nerves, or the administration of endocrine preparations) of breaking some link in the chain of pathological processes which cause disease In short, as Sir James said, quoting G M Young, he can help "to conserve and preserve the young and active, so that they can put their strength and vigour at the service of the community, and to preserve the old so that they can put their experience to similar use" But when his colleagues in preventive medicine find ways to break an earlier link in any of the chains, then like a good follower of John Hunter the surgeon will stand back, and cease to operate for a condition which he cannot directly cure

WHY MOSQUITOES BITE

APART altogether from the conditions that bring mosquitoes out in force—darkness and night time, low lying ground, a hot steamy atmosphere, and so on—people living in mosquito infested places seem to show individual differences in their liability to bites The same sort of differences are said to exist elsewhere and in regard to other insects—even our own humble midge In Canada, where most of the country is infested with aedes mosquitoes, Brown[1] and other zoologists at the University of Western Ontario, having spent two years studying the relative attraction of animals for mosquitoes, have lately turned their attention to man—or rather, dummy men—as a subject for study in Ontario and in central Labrador

Their technique is ingenious but simple Two stainless steel tanks, each holding 100 lb of water kept at any desired temperature by electric heaters, represented the human torso For some experiments heads were attached The dummies, dressed in shirts and jerkins of various colours and materials, were set up in a forest glade The number of mosquitoes landing on a dummy in 1 or 2 minutes was then taken as the measure of its attractiveness in the prevailing external conditions of temperature and humidity At air temperatures over 60°F a dummy with moist clothing was found to attract 2–4 times as many mosquitoes as a dry one, but at lower temperatures, and particularly when humidity was high, the dry dummy was the more popular, even though its surface was 1–3°F cooler than the moist one's At air temperatures of 57–74°F, the dummy containing water at blood heat attracted three times as many mosquitoes as one filled with cool water, making its surface 14–24°F colder Clothing both dummies in a felt shirt, which reduced the difference in their surface temperature to 4°F, made them equally attractive, whereas when both dummies were moistened the warm one became twice as attractive as the cool Clothing soaked in water saturated with carbon dioxide was no more attractive than normal wet clothing, but a clean jerkin became twice as attractive when two men rubbed themselves down with it after sweating heavily By affixing a head and passing 10% carbon dioxide out through the dummy's mouth at 2 litres per minute, the attraction of the head and body were raised to half as much again, whereas the apparent exhalation of pure carbon dioxide doubled the attraction of the body and tripled the head's Breathing out ether or petrol vapour also increased a dummy's attraction, ordinary air had no effect, and chloroform vapour repelled the mosquitoes

---

[5] Leading article *Lancet* 1949 ii 228

[6] The Contribution of Surgery to Preventive Medicine London Geoffrey Cumberlege Oxford University Press 1951 Pp 55 12*s* 6*d*

[1] Brown A W A *Nature Lond* 1951 167 202

Turning to colour and texture of clothing, white clothing was not so attractive as black, and either light red or light blue was less attractive than dark shades, light blue was more attractive than pink The mosquitoes liked settling on broadcloths or crepes but not on satin, and certainly not on luminescent satin Finally—and this may well start a new fashion in tropical kit—there was general agreement among the mosquitoes that the traditional cotton shirt and drill trousers made a far better landing ground than woven 'Nylon' Unfortunately, however, nylon fabrics do not absorb perspiration freely as do cotton or wool,[2] and this may make them uncomfortable for next to skin wear in hot climates

THE HEALTH OF WELSH STUDENTS

YOUNG people often reach our universities in haphazard ways Academic ability is not the only quality driving them they may be ambitious, or have ambitious parents, they may wish to share the company of friends, they may enter, and even choose a particular course, in an attempt to solve their personal problems Perhaps only a small proportion are taking an inevitable and fully appropriate step Nevertheless most of them gain from a university training, and many could probably gain more if they were on top of their mental and physical form Recent surveys[3] suggest that this is seldom the case, but it seems, from a pilot survey at Cardiff[4] made in the Lent term, 1950, that students do not suffer more sickness than an equivalent age-group in the general population The survey was conducted by post, and some of the figures for sickness are believed to be artificially low The comparison with non students of the same age, however, was made in terms of the "health index"—that is, the proportion who reported no complaint during the period of the survey Just over half the men, and nearly 46% of the women students, reported such a clean bill of health, for the general population aged 16–24 the comparable figures were roughly 46% and 35% There was slightly more sickness among the women students than among the men, but chronic or continued illness accounted for rather more of the total sickness in men than in women The types of illness were much the same in the two groups, except that men were much more liable than women to chronic nasal catarrh, ear, nose, and throat conditions and skin conditions

The facilities offered by the University for the diagnosis of tuberculosis are good Mass miniature radiography was offered to all students in 1949 only 2 students with active pulmonary tuberculosis were found among 3178 examined, and 5 more were kept under observation There were 20 healed lesions Clinical students at the School of Medicine are offered full size chest X rays at six monthly intervals and among these there were 2 cases of active disease in the period reviewed All medical students are Mantoux tested, and negative reactors are offered B C G vaccination.

General medical and surgical conditions accounted for over a fifth of the chronic illness in both sexes, but by far the heaviest toll was taken by psychological illness, which was responsible for just on half the chronic illness in both groups In the Cardiff survey, 13% of students had major psychological difficulties, and another 20% had minor difficulties, in the five colleges of the university as a whole 37 students in all academic years failed to complete the 1949–50 session through mental ill health Psychoses were rare, and the common disorders were anxiety states, obsessional neuroses, psychosomatic symptoms, and hysterical manifestations Dr R A N Hitchens, Dr G Grant, and Dr E McKnight, who present the report, attribute these disorders to the facts that many students were away from home for the first time, most were in the late stages of adolescence, when emotional instability is common, some had been damped by previous academic or social failure, and others coupled anxiety over their studies with a poor insight into their own ability, unhappy home relationships, including parental discord, affected others, and in some psychological troubles were reinforced by financial anxiety Sexual ignorance and frustration seemed to be at the root of many difficulties, and was relieved by frank discussion, and the report insists on the value of explanation and reassurance in tiding students over emotional crises of any kind A background of general health education was lacking in nearly all the men and three quarters of the women, and this gap should be filled, the writers of the report suggest, before the students leave the university Breakdowns could also doubtless be reduced by appropriate selection procedures, but it is worth remembering that such procedures, if successful, would only keep those liable to breakdown out of the university they would not do away with them altogether It is time we knew a great deal more about adolescent instability—the forms it takes, the outcome to be expected, and what we ought to do about it—whether it crops up in the university, the home, or the juvenile court

AUREOMYCIN INTRAMUSCULARLY

WHEN given by mouth, the usual route, 'Aureomycin' may cause nausea, vomiting, and diarrhœa and irritate the mucous membranes of the mouth and anus Intravenous injection occasionally led to thrombophlebitis in the past,[1] though this risk is said to be eliminated in the present purer products, and intramuscular injections have been too painful for routine use owing to the low pH of the solutions There is an advantage in having a solution which can be injected intramuscularly or subcutaneously, for cases where a rapid effect is needed or swallowing is difficult Seyberlich[2] in France has devised the following preparation which he claims not to be irritating when injected into a muscle He dissolves 2 5 g of aureomycin in 5 ml of olive oil which has previously been washed with alcohol and sterilised He then adds this solution to 10 ml of procaine penicillin in sesame oil with aluminium monostearate Before injection the preparation is warmed and shaken well He explains that the vehicle delays absorption and prolongs the action of the aureomycin, so the dosage can be reduced without loss of effect, his routine is one intramuscular dose every twelve hours Seyberlich has given 300 injections to patients of all ages, and he reports no local reactions, and no complaints of pain He mentions, though without detailed evidence, that the results obtained with his preparation are as good or better than with the usual tablets by mouth He clearly should have included in his paper some blood aureomycin levels after intramuscular doses of this oily preparation Unfortunately, Seyberlich's experience does not conform with that of Whitlock and his co workers[3] in Philadelphia, who used a buffered aureomycin plus 1% procaine and found that injections still caused intense local pain and induration, with febrile reactions This disparity might be worth investigating

Mr A. S BLUNDELL BANKART, consulting orthopædic surgeon to the Middlesex Hospital and consulting surgeon to the Royal National Orthopædic Hospital, died in London on April 8 at the age of 71 or otherwise more expensive ward he can claim from the government the cost of ordinary ward treatment to set against his expenses The scheme is very new and has not yet had time to settle down The Saskatchewan scheme has been going a little longer, since 1947, and again provides ordinary ward treatment It has, however, had two developments of interest in England One is that in order to reduce what appeared to be an excessive demand for medicines a deterrent fee of 20% was put on all prescriptions—i e, the province only paid 80% instead of 100% of the cost of prescriptions The result was that the number of prescriptions ordered dropped by 22% In the south west corner of the province a start has been made in providing a general practitioner service so that the health service is complete This is a very recent development and it is too early to say how the scheme will progress

---

[2] See *Brit med. J* April 7 1951 p 771

[3] See *Lancet* March 31 1951 p 728

[4] Report on the Student Health Service for the Session 1949–50 University of Wales 1951 Pp 52

[1] Hill L M Wright L T, Prigot A Logan M. A. *J Amer med Ass* 1949 141 1047

[2] Seyberlich A *Pr méd* 1951 59 7

[3] Whitlock C M Hunt A D Tashman S G *Pediatrics*, 1950 6 827

Methods of Avoiding the Cost of Inpatient Treatment

The foregoing schemes are all based on accepting the high rate of cost and spreading the payment by insurance Another line of approach has been an endeavour to reduce the demand for inpatient treatment This has been attempted by (*a*) better diagnosis outside the hospital so that admissions for investigations can be cut down, (*b*) the encouragement of early ambulation, (*c*) convalescent care and rehabilitation, and (*d*) treating the patient in his home

IMPROVED DIAGNOSIS

The whole science of diagnosis, particularly in the large private clinics, has been streamlined into a regular business process In the clinics a wide variety of tests are done as a routine, so that the specialist concerned has the results ready to hand when the patient first comes to see him At one large clinic, for instance, the medical staff of 160 see 600 patients a day, every one of whom is fully investigated Extending from this clinic there are various other methods of getting the patient investigated outside the hospital, so that the diagnosis can be made before he reaches hospital and, indeed, partly in the hope that he will be found not to need inpatient investigation or treatment at all

The Pratt Diagnostic Hospital at Boston is perhaps the most developed voluntary method of providing expert diagnosis before deciding whether the patient should be admitted to an acute hospital In this case the patient is admitted to a purely diagnostic hospital, and will subsequently be transferred to an acute hospital or sent home, as the results of the diagnosis indicate

Another process which should be mentioned at this point is that of group practice This varies from the simple doctor's office, where there may be two doctors who between them can afford to have simple equipment for making clinical tests, to the much more elaborate groups run under the ægis of the Hospital Insurance Plan, where some fifty doctors work as a group, half of them being general practitioners and half specialists In this case the general practitioner is able to get all the specialist opinions he may need within his group before sending the patient to hospital This presumably obviates the need to send a patient to hospital with such a diagnosis as ? abdomen, leaving him to occupy a bed while the diagnosis is made

All these are devices which by improving the possibilities of diagnosis, are in fact a welcome relief to hospitals even if that is not their primary object

EARLY AMBULATION

The practice of early ambulation is spreading and the patient is now commonly expected to get out of bed the day after the operation and to go home in a very short time We were given the following as a guide to the time required, after operation, before discharge of a patient appendicectomy 3–4 days, gastrectomy 12 days, abdominoperineal resection of rectum 16 days On the same principle we were told of mothers and babies being sent home on the 6th day The coincidence that a new medical procedure is both financially just what is wanted and also good for the patient is so striking that we felt bound to ask whether, finance apart, the procedure is the best possible for the patient The doctors all agreed that it was, provided the time of discharge was not too rigidly adhered to and could be varied according to the patient's home conditions, general health, and so on Almoners and convalescent superintendents, who know more of the patient as a person, agreed that it was bad for the patient to be left in bed too long, but pointed out that it was possible to get him up too soon Be that as it may, the practice is very widely adopted and eliminates the need for convalescent homes for short term cases On one occasion when we inquired what happened if a patient's home was unsuitable we were told that he was kept in hospital for a little longer

CONVALESCENT CARE

Convalescent homes as a whole appear to be in much the same state in the U S A as they are in England. There is a committee of the United Hospital Fund for New York which is trying to raise standards by arranging meetings of matrons and trustees of convalescent homes, much as the Convalescent Homes Committee has done in Thanet and Brighton The tendency is for the more progressive homes to take patients at an earlier stage of recovery, and since more money is available in America they have been able to adapt themselves more readily than in England

Without going into details of our inquiry, it is sufficient to say that the progressive homes take a much higher percentage of bed cases, and pay a great deal more attention to physiotherapy and dietetics Patients discharged early from hospital on the principle of early ambulation are sent home and not given convalescence Since a short period of convalescence is just what they might be supposed to need, this is curious We could only suppose it was due to a lack of knowledge of the advantages of convalescence, or to financial reasons In practice there is a tendency for homes to get mainly long term cases, noticeably cardiacs and chronics. We were rather surprised to find that more use was not made of these homes, for the saving in the cost of maintenance is very large, hospital costs being in the order of three to four times as much as convalescent homes

In the Master Plan for New York, which is the official building plan approved by the Surgeon General's department for grants under the Hill Burton Act, it is proposed that convalescent homes should actually form part of the hospital building This is an intriguing thought, but as yet it is only an idea on paper In this plan it is suggested that convalescent beds should be provided in the proportion of 25% of the general beds

REHABILITATION

It is generally admitted that England has been leading in rehabilitation, owing to the great strides made by the Royal Air Force during the war However, much thought is being given to rehabilitation in Canada and the U S A In particular we saw institutions for veterans (ex Servicemen) in Toronto and Montreal where the re establishment of men injured in industry was carried to great lengths At the Workmen's Compensation Board Center at Malton, Toronto, they take the view that re establishment to the point that a man can return to light work is no use He must be fit to return to his own work, however arduous, or must be retrained altogether To ensure that a man can return to his own work, the actual implements and materials of his trade are available at the centre and a lumberjack only returns to work after he has been able to hew and handle lumber in the centre. The same applies to railway gangers, dockers, labourers, and so on. Much imagination had been shown in providing both the appropriate work and the incentive to do it so that the speed of recovery was maintained. It was interesting to notice that this particular institution, which is doing outstanding work, is housed in an ex R.C.A.F. camp with no expensive equipment or furnishings. And such of the equipment as is not provided by employers is made by the patients themselves.

In New York perhaps the most outstanding case is the Altro Workshops where people recovering from tuberculosis and compensated heart disease are given work, according to a time schedule laid down by their doctor. They are paid regular rates and the goods are sold on the open market. Anyone who has completed his rehabilitation is discharged, but the principle of sale on the open market is maintained in order to make clear to the patients what they will have to do on return to normal life.

HOME CARE

Interesting experiments are being made by the Montefiore Hospital in New York in extending hospital care to poor patients in their own homes. These arise from the shortage of beds for long-term patients for which the conventional remedy is new buildings. This would involve a heavy cost, and to avoid it these hospitals have hit on the ingenious device of using the patient's bed instead of providing one in the hospital. The patient gets the advantage of staying at home and the hospital is saved the cost of building.

The scheme is intended to provide patients in their own homes with everything they would receive as a hospital inpatient. They are visited by hospital doctors; by district nurses, who aim at training the patient and relatives in all necessary nursing measures; by medico-social service workers (almoners) and, if necessary, by physiotherapists or psychologists. The services of a visiting dietitian are available, and, if patients cannot afford the diet prescribed, the necessary food is provided. If no one is available to buy or cook food, a housekeeper service is provided, generally by a suitable neighbour. If a consultant is necessary, transport to the hospital outpatient department is arranged.

Any necessary furniture, drugs, dressings, or appliances are provided—even a hospital bed if the patient's own is unsuitable. Minor operations are performed in the home.

The service is chiefly suitable for long-term cases; for clearly its money-saving features come into full play when the patient is set up with the necessary equipment, and a routine is started that can largely be maintained by the patient or his friends. The service can, however, be used for simple short-term cases, thus leaving beds free for more serious ones. The hospital maintains that this method saves money to the hospital. Whether it saves the time of the staff was more difficult to determine; but we were told that there should be a saving in nursing staff, since the nurses are sent out to teach the patient's relatives how to look after him rather than to do the nursing themselves.

This scheme has great possibilities, but in New York it is heavily restricted by the need to apply it only to patients who are either indigent or what is termed "medically indigent"—i.e., unable to pay their doctor. As, however, the patient must also have good enough accommodation to enable him to be properly looked after, and these conditions tend to be mutually destructive, the scheme can only be applied on a small scale. As the financial requirements do not now apply in England it seems that schemes of this type may well achieve success here.

ACCOMMODATION FOR MEDICAL STAFF IN HOSPITALS

J. W. D. GOODALL
M.D., F.R.C.P.E.

MEMBER OF TEAM INVESTIGATING FUNCTIONS AND DESIGN OF HOSPITALS (NUFFIELD PROVINCIAL HOSPITALS TRUST AND THE UNIVERSITY OF BRISTOL)

What accommodation is needed in hospitals for the use of the medical staff, and where should it be placed? My comments to these questions are based first on my own observations and secondly on specific details of the accommodation at present provided in 22 hospitals (10 teaching and 12 non-teaching), 4 of which are among the most recently built in the United Kingdom.

Present Position

Sleeping accommodation.—There is a striking similarity in the sleeping quarters in these 22 hospitals. Nearly all of them provide a bedroom or bed-sitting room for each resident doctor, either in a separate block or in flats in the main building. Baths, lavatories, and sometimes a common sitting room are provided nearby. A notable exception is in Glasgow, where in the 2 hospitals studied the residents sleep in quarters attached to their wards. This is considered highly satisfactory by both the doctors and the administrative staff, on the grounds that it enables the resident to give maximum attention to the patients. Women residents are as a rule accommodated in the same way as their male colleagues. In a very few instances they sleep in the nurses' home, but the only usual concession to them is a separate sitting room and bathroom. In maternity hospitals a bedroom near the labour-ward is sometimes provided for the doctor on duty.

Dining rooms.—Commonly there is a residents' mess situated either near the sleeping quarters or centrally in the administrative block, and consisting of a dining room, sometimes with a sitting room attached. It is usual for the mess to have a separate domestic establishment and for the senior visiting staff to have meals there when they want them. As an alternative, some hospitals have a central cafeteria or dining room open to all members of the hospital staff and visitors. This is not always popular; and, in one hospital where this system was instituted, first the senior nurses and then the doctors requested to have separate dining-rooms.

Recreation.—Only 10 of the hospitals possess a medical library, and even fewer have a "quiet room" for reading. A radio, billiards, and tennis courts are often available, the last usually being shared with the nurses. At Great Ormond Street sun bathing was the only recreational activity recorded, apart from the use of a medical library. The Rotunda Hospital in Dublin is very gay, with tennis, squash, croquet, billiards, table tennis, and dancing.

On the ward.—The accommodation for doctors in the wards varies. A doctors' room is provided in almost all teaching hospitals, but rarely in non-teaching hospitals; and the teaching hospitals generally provide a lavatory for the doctors, while the non-teaching hospitals do not. Laboratories or clinical side rooms are found in most of the teaching hospitals and in a few of the others. Demonstration rooms, where patients can be shown to students or where clinical meetings can be held, are sometimes provided in the teaching hospitals. A room for waiting relatives, or relatives of patients requiring an interview with the doctor or sister, is rarely found. Great Ormond Street is exceptional in having a combined waiting and interviewing room attached to each ward. Of the 22 hospitals 9 have what they call treatment rooms, though not in every ward. Among the wards mentioned as having treatment rooms are surgical, gynæcological, mental, and children's wards. In Great Ormond Street there is a treatment room to each 10-bed unit.

happens to be at the time In Bath United Hospital the need for a room in which relatives can be interviewed and in which on occasions a relative may spend the night has been so strongly felt that side-wards have been used for this purpose It has often been suggested that interviews could take place in the doctors' room, but there is no guarantee that this room would be unoccupied when needed Privacy is essential, and experience shows that a separate room with a neighbouring waiting room is desirable The normal 25–30 bed ward produces enough relatives to justify a small interviewing room and waiting room, but these might prove adequate for a unit containing as many as 60 patients

Treatment Room

Only a minority of hospitals have treatment rooms, and these use them in rather different ways At the Royal Victoria Hospital, Newcastle, there has been a treatment room for the past 3 years to which patients are wheeled on a stretcher to have their dressings changed Beds are not wheeled into it and it is not a specially sterile room In one surgical ward in Bristol a treatment room is to be constructed as a ward annexe to which most patients will walk for dressings The Radcliffe Infirmary at Oxford has well equipped treatment rooms which are comparatively new

A treatment room concentrates much of the work of the ward into one "workshop," offers privacy, and removes to a large extent the need for screens Dressing trolleys need no longer be taken round the ward from patient to patient A sterile atmosphere may be provided by air conditioning and the patient is remote from the contaminated dust of the ward Moreover, patients can no longer see the sufferings of their neighbours through cracks in the screens—a sight which is often upsetting

Sir James Spence (1947) visualises a treatment room in each unit, where "all dressings, lumbar punctures and other painful manipulations can be carried out, and where anæsthesia will be frequently used" Bourdillon and Colebrook (1946) point out that "the practice of dressing wounds in a special room designed for that purpose should have considerable advantages, but unless special precautions are taken it must involve the danger of exposing each successive wound to a cloud of organisms disseminated from the dressings of the previous patients" In some hospitals, as for example in Sir James Learmonth's wards in the Royal Infirmary, Edinburgh, patients are taken into the nearby surgical theatre for dressings This is convenient only if the theatre is close to the ward

It is clear that opinions vary as to the purpose and equipment of a treatment room The demand has come principally from surgeons for the dressing of wounds, and perhaps the best example of how this demand has been met can be seen in the burns unit of the Birmingham Accident Hospital

Although less is heard of the physician's need for a treatment room, this undoubtedly exists Medical wards contain many patients whose special treatments are better carried out in a treatment room than in the ward behind screens For example, lumbar puncture, chest aspiration, blood transfusion, sternal puncture, and catheterisation are among the many procedures more suitably carried out in a treatment room There may be a conflict between the conception of a treatment room as a place akin to a small operating theatre with great emphasis on sterility, and the rather different conception of it as a place where most treatments, whether by doctors or nurses, can be done In practice, a treatment room may be used for either purpose The surgeon may treat his wounds or burns, or dress his plastic cases in this room, excluding infected patients if he wishes Since most of his patients will be "clean" this will suit his purpose well The physician, pædiatrician, or gynæcologist may equally well use the same type of room attached to their own wards, for other kinds of cases.

Attention must always be paid to the prevention of cross infection, since concentrated risk may make a treatment room unusable Special ventilation is expensive but necessary in rooms used for the dressing of burns, wounds, and plastic work, and it would be unreasonable to accept a lower standard of antisepsis for other cases One treatment room per ward of 30 patients may be expected to meet the requirements of general medicine because there will be few dressings, and fewer treatments needing the use of a treatment room, its main use would be for diagnostic tests But in surgical wards and in wards admitting special types of patient more than one treatment room may be required

OUTPATIENT DEPARTMENTS

Whether consultations with outpatients should take place in the vicinity of the wards or in a separate outpatient department is still undecided In either case suitable rooms will be needed Fortunately the requirements of different specialists do not, in general, affect the rooms but only their equipment

A consultant needs a room where he may interview patients in privacy, an examination room with a bed or couch, and three dressing rooms (so that one patient can be examined, while the next is undressing and the third is dressing) It is an advantage, particularly in dealing with gynæcological patients or those with cancer, to be able to screen off a part of the consulting room to accommodate a secretary This room should have a wash basin and lavatory nearby

Minor treatments, such as injections, can often be given conveniently in the consulting room, which should be fitted with a steriliser and instrument cabinet Where many tests and treatments are likely to be done it is better to have an additional room for this purpose and in which urines can be tested or specimens taken for laboratory purposes

In the interests of economy different consultants will probably use the same suite of rooms at different times Since more whole-time consultants are likely to be appointed it is worth considering whether each team under a whole-time consultant should not be provided with a suite of rooms for their exclusive use

REFERENCES

Bourdillon, R B Colebrook L (1946) *Lancet* i, 561
Lancet (1949) ii 430
McIntosh T S, Coales H R (1947) *Ibid* i 645
Spence J C (1947) *Brit med. J* i 125
Woodward J (1950) Employment Relations in a Group of Hospitals a report of a survey by the Department of Social Science of the University of Liverpool London

---

CONTROL OF MEDICAL MAN-POWER

Statement by Central Medical War Committee

MANY doctors, and in particular those who have reserve commitments to the Armed Forces, have expressed anxiety about their position and possible liability for active service in the event of war For a long time the Central Medical War Committee has been urging the Government to set up suitable machinery for the provision of advice as to the availability for recall in an emergency of individual doctors with reserve commitments The committee is now authorised by the Ministries concerned to publish the information given below

It will be remembered that during the last war the allocation of medical man power between the various Services was arranged on the advice of a professional committee, the Medical Priority Committee, while the actual recruitment of doctors into the Services was undertaken by other professional committees—the Central

Medical War Committee, the Scottish Central Medical War Committee, and the Committee of Reference, with the advice and assistance of local medical war committees. The Medical Priority Committee, the Central Medical War Committee, and the Committee of Reference have continued, since the end of the war, to organise the recruitment of doctors with national service obligations.

Discussions have now been proceeding for some time between the representative medical organisations and the Ministries on the establishment of new machinery of control designed to take account of the changes in the structure of the health services brought about by the National Health Service Acts. Under these new arrangements, the control machinery will be broadly similar to that now existing; new area committees will be established to deal with the various branches of the medical service—i.e., the general practitioner service, the hospital service, and the public-health medical service. It is hoped that the new machinery will be fully established within the next two or three months.

In the meantime it has become necessary for the Service Departments to begin reviewing the position of doctors with reserve commitments, and to earmark those who would be the first to be recalled to the colours in the early stages of any future war. This procedure is part of a wider review which covers reservists in all walks of life, and is not confined to doctors. Arrangements have been made for the doctors concerned to be "screened", that is to say, for their commitments in civil life to be reviewed so that if the recall of a particular doctor in the early stages of a war appeared likely to prejudice some important branch of the civilian medical service, cancellation or deferment of recall could be considered.

It has now been decided, after consultation with the Central Medical War Committee and the General Medical Services Committee, that the Central Medical War Committee shall undertake the interim "screening" of reservists who are general practitioners, and that the local medical committees, established in accordance with section 32 of the National Health Service Act, 1946, should be invited to assist the Central Medical War Committee in this work, a lay member nominated by the executive council being coopted to the local medical committee for this purpose. In Scotland similar arrangements are being made for the "screening" to be carried out by the Scottish Central Medical War Committee with the cooperation of the local medical committees.

Purely as a stop gap measure, provisional "screening" of doctors in other branches of the medical profession has already been carried out by medical officers of the Health Departments. This "screening" will be reviewed by the appropriate professional committees as soon as agreed machinery for local consultation has been set up.

The "screening" procedure described above is concerned solely with the question of the effect of recall on the civilian medical services. It is not concerned at all with any question of personal hardship, which, in the case of a reservist, whether a medical man or layman, is a matter for the consideration of the Service Departments, to which appeals may be made at the time of recall.

Before Our Time

FRANCISCO DE LA REYNA AND THE CIRCULATION OF THE BLOOD

J. J. KEEVIL, D.S.O., M.A., M.D. Camb., F.S.A. L. M. PAYNE, F.L.A.

FROM time to time in medicine a brilliant guess is made, holds the field for a while, and is forgotten, only to be revived later and established on a basis of scientific evidence. An example is to be found in Francisco de la Reyna's book, published in Spain about 1546, where he asserts, a century before Harvey, that the blood circulates. In Spanish this work is generally known in brief as *Libro de Albeyteria*, but its full title may be rendered in English as follows:

> The Book of the Craft of the Horse leech in which may be seen all illnesses and accidents whatsoever that may befall all manner of animals and their cure. Similarly there will be found the colours and features by which a good horse can be recognised, as well as a good mule. The most extensive that has so far been seen. Expounded by Francisco de la Reyna farrier resident at Zamora.

This work must have been extremely popular among Spanish veterinary surgeons, who could find in it an accurate account of the signs and symptoms of innumerable equine diseases, and of methods of treatment which were in general simple and practical, set out with considerable charm of style. As a result of these qualities it passed through many editions, but its very popularity has been the cause of its great rarity today. Copies were so much used while actually carrying out treatment that they became damaged or worn out.

THE ACCOUNT OF THE CIRCULATION

Reyna divides his book into two parts, the first, which deals with the work of a horse leech, is written wholly by himself, the second, which is concerned with the craft of the farrier, is an enlarged and amended version of the work of Juan de Linuesa. He sets out his views on the circulation of the blood without any particular emphasis, and some of the techniques he advised show that he took it for granted. Thus his technique in phlebotomy differs little from that practised today. He dissected down to the vein with a lancet, lifted it up, and with needle and thread passed two ligatures round it. After bleeding he tied the *lower* ligature and then the *upper*. This order in itself indicates that he did not think that the movement of the blood was a simple pendulum one. Similarly in treating bleeding from the palate he stresses the need to keep the head high.

Towards the end of the book he writes in the form of question and answer, addressing himself to apprentices and beginning each section "If they should ask you . . .", and it is in this part of the book that the following passage occurs:

> "If they should ask you why, when they bleed a horse from the fore legs, or from the hind legs, the blood comes from the lower part and not from the higher. The answer ? In order that you may understand this matter you must know that the main veins emerge from the liver, and from the arteries of the heart, and these principal veins are distributed throughout the limbs in this fashion—in branches and thin membranous vessels through the external parts of the fore legs and hind legs . . . And from there all these membranous vessels turn round to flow through the main veins which ascend from the hoofs through the fore limbs to the interior in such a way that the veins of the exterior have as their function to convey the blood down, and the internal veins have as their function to carry the blood upward in such a way that *the blood travels in a circle* [*torno*] and as a wheel, through all the limbs and veins, it has the function of carrying nourishment to the inner parts right up to the emperor of the body which is the heart, which all the parts obey, and that is the reason [for bleeding coming from the distal end of a deep vein]."

Without in any way anticipating the discovery of the capillary circulation, Reyna appears to recognise the existence of the gap in the closed circulatory system which that discovery was to fill:

> 'Before the blood can enrich itself,' he writes, 'it must first alter into the four humidities; first it changes in order that it may pass from the little veins to infuse itself throughout the limbs and the porous tissues

secondly it changes while it is thus diffused so that it can moisten these tissues Thirdly it changes while it is there so that it may repair and support any wasted parts It travels on and again separates the humours. Fourthly it changes since in any given place it soaks into the limb and takes on its character, that is in order that it may recover and restore, what gave it its heat, and use up the air, and repair the changes caused by a cruel world [i e , by wear and tear] "

TEACHING OF THE TIME

Reyna's anatomical views are highly traditional in most respects, the great exception being those on the circulation of the blood This is the more surprising by comparison with his teaching that the brain is a chimney for the smoke from the heart, expelling it through the eyes, nose, and mouth He describes digestion as taking place in four stages in the mouth, stomach, liver, and tissues , that in the stomach separates waste from nutriment, the latter (chyle) is carried to the liver, where it is coloured and is then distributed to the body according to its needs Blood is formed from the most "temperate" part of the chyle, the other humours from other appropriate portions If any chyle is formed in excess, it must be purged by the bowel, or by bleeding, or by dieting, or by other similar methods of depletion Purgation by the bowel should be regulated as a result of studying the blood removed at bleeding There are two kinds of blood the arterial or vital, and the venous or nutritive The arterial flows from the heart, the venous from the liver The seat of the spirit is the heart , it is vaporous, controlling movement, sensation, and warmth, and it is this spirit which is manifested in all the pulses

His pathological theories were the current humoral ones , he stressed the importance of a knowledge of anatomy in order that the humours responsible for any illness might be easily identified and abnormalities recognised Diseases being seasonal, a knowledge of the qualities of the humours and the seasons was required in order to appreciate the relationship But although the seasons were a factor he attached more importance to any form of excess, whether in eating, drinking, exercise, rest, or exposure to heat and cold The four qualities of heat, cold, wetness, and dryness, and their combinations are discussed in relation to the four humours Health consists of the right balance between qualities and between these and the corresponding humours—e g , heat and wetness, and the blood This concept is related to the four seasons, thus blood is dominant in March, April, and May which were, perhaps arbitrarily, classified as hot and wet—at least in Spain But the actual local quality of the weather at any season does not appear to have affected this seasonal classification

He compares the art of curing illness to the work of a gardener, who, finding an irrigation channel blocked, removes the obstruction and allows the water to flow to the plants He thus appears to subordinate the healer to the *vis medicatrix naturæ*, but in practice he does in fact advise a less passive rôle , this was inevitable in view of the long held and still prevailing view on the treatment of all diseases by the exhibition of their opposites

He was not wholly free from the influence of astrology (horses' tails should not be docked at certain seasons of the moon), or from alchemy (powder of lizards was of value, and so was an ointment made from certain black worms which emerged from the earth in May, June, July, and August, "as long as a finger," and had to be fried in oil), but in general he used such simple dairy produce as eggs and butter for dieting and for surface applications, and such vegetables and grain as would be found on any farm Qualities associating these products with the humours and the seasons indicated their appropriateness for any condition , thus butter is cold and wet, honey is hot and dry, yolk of egg is hot and wet Since all treatment was by opposites the horse-leech had an easy guide to prescribing , he need only remember that hot diseases must have cool medicaments Plethora must be treated by bleeding

Thus, between much that is now known to be error, Reyna believed that the blood circulated, that in the course of that circulation it was diffused in the tissues, that it was associated with the warmth of the body, and that it gave off air Spain has never claimed for Reyna the discovery of the course that the blood followed and it need hardly be stated that no such claim is made for him here Prof H E Sigerist has inveighed with much eloquence against the present tendency, particularly in the English speaking world, to attribute paternity to every advance in medicine, every new discovery If such a protest needs any support, it is surely to be found in such books as the *Libro de Albeyteria* Reyna should be recognised as giving expression to a belief which, if not clearly defined, was evidently fairly widely held in 1546, since his book led to no protest

EDITIONS OF THE BOOK

The book was certainly first printed about 1546, the copyright—which was granted by Pedro de Lovos on behalf of the King of Castile—being dated at Madrid, Nov 21, 1546 The title, *Libro de Albeyteria*, was used again in 1550 by Lopez de Zamora, suggesting that Reyna's book had achieved a success during the previous five years, which Lopez was quick to exploit

Although many editions have been recorded by Palau in his *Manual del Librero Hispano Americano*, there is one edition which has not previously been identified this is the edition of 1556 Palau cites the following editions 1546, 1552, Mondoñedo , 1553, Zaragosa (doubtful) , 1564, Burgos, 1580, Salamanca , 1582, Alcala , 1583, Alcala , 1603, Alcala (first annotated edition) , 1617, Madrid , 1623, Alcala, 1647, Alcala The annotated editions of his work were probably published after his death There are copies of 1603 and 1623 editions in the British Museum The notes are by Ferdinand Calvo, and although he doubtless improved the purely veterinary part of the book, he seems to have regarded Reyna's description of the circulation of the blood as irrelevant He omitted the sentence about the heart being "the emperor of the body" from the 1603 edition and suppressed the whole description from subsequent editions

A copy of the first edition is in New York, in the possession of the Hispanic Society of America, and is stated to have been printed at Burgos Two copies of the Mondoñedo edition have survived, one at the Hispanic Society, the other in the National Library, Madrid , and the British Museum has a copy of the 1580 edition in which the colophon is incorrectly dated 1570 No copy of the doubtful 1553 Zaragosa edition is known In the library of the Royal College of Physicians there is a copy of the edition of 1556, which has never been recorded, and of which this is therefore likely to prove the only surviving copy It is a revised edition, priced at two maravedis a copy Certain pages are missing, but were made up in manuscript in the late eighteenth century, or a little earlier The copyist states that he had before him a Zaragosa edition printed by the Casa de Lorenzo y Diego de Robles hermanos in 1583 , and that he considers the 1623 Alcala edition superior to this 1583 edition, but wishes to use the earliest one available to him

The 1556 edition was unknown to Saenz Egaña when he wrote his *Historia de la veterinaria Española*, which contains a recent (1941) history and bibliography of the early Spanish writers on the circulation of the blood, Montaña de Monserrat and Servetus It is possible that this edition was printed at Baeza in the province of Jaén, the title-page having a coat of arms with two lions and two castles which resembles that of Jaén The earliest surviving book printed in the town of Jaén is dated 1605, but at Baeza there was a printer Juan Bautista Montoya, between 1551 and 1594 He printed another book on horses—*Reglas de la Cavalleria de la Brida* by Federico Grisone (1568)

Reyna gave as his motive for writing the *Libro de Albeyteria* the absence of any reliable work of a similar nature, and the existence of many misleading books which falsely stated that they were based on the teachings of Hippocrates and Avicenna. His book reveals a wise and modest man ,of great experience, sound judgment, and alert observation He quotes Hippocrates, Guido de Cauliaco, Pliny, and Fray Yñigo de Mendoça , he also states that he has translated the works of Albertus Magnus from the Latin into Romance (the vernacular), but found them of little value Reyna has been dismissed by some Spaniards as an ignorant horse leech, but he belonged to a profession of the highest importance at a time when all land transport depended on good horses , before he was 26 he looked after the horses of the great Duke of Alva, who would not have chosen any but a man of reputation When at this early age he published his book he appears to have been regarded as the foremost exponent of the veterinary art of his time, but nothing further is known about him—except that he lived to an advanced age—and eyen his birthplace is uncertain it is thought to have been either Burgos or Zamora

---

Parliament

QUESTION TIME

Increase in Drunkenness

Mr **CHUTER EDE**, the Home Secretary, replying to a question, stated that the convictions for drunkenness in the Metropolitan police district during 1950 were 16,760 The comparable figure for 1946 was 9107 The figures caused him serious concern, and he was investigating the causes which could be assigned to them and what action if any, could be taken to reverse the position

Mr **SOMERVILLE HASTINGS** Is this unfortunate result found only in London or has there been an increase of drunkenness in other large towns?—Mr **EDE** I regret to say that such figures as I have been able to examine as a result of the reports of brewster sessions and so on indicate that this trend is prevalent all over the country

Prostitution in London

Mr **EDE**, replying to a question, said that a deputation, led by the Bishop of London, which he received, left with him a memorandum containing proposals made by the Paddington Moral Reform Council for dealing with the problem of prostitution in London, and he promised that it would be carefully examined. Until the examination was completed he could not say whether further inquiry by a departmental committee would be necessary If he decided to have an inquiry the necessary publicity would be given so that the widest possible range of evidence might be obtained

Mr **SOMERVILLE HASTINGS** Will the Minister make the terms of reference wide enough to include the problem of homosexuality ?—Mr **EDE** I have not yet decided that there shall be a committee but I shall have regard to the terms of reference

Protection against Smallpox from India

Mr **THOMAS REID** asked the Minister of Health what precautions had been taken to prevent the influx of smallpox from Calcutta where deaths from this disease now exceeded 500 a week —Mr **ARTHUR BLENKINSOP** replied Special care is being taken by airport medical officers, and travellers by air are given a warning notice Travellers by sea pass out of the incubation period for smallpox before they arrive Rigorous measures including if necessary the isolation of passengers, would be taken if a ship or aircraft were found to have a case of smallpox on board

Hospital Accommodation for Chronic Sick

Miss **IRENE WARD** asked the Minister of Health what steps he had taken to increase the beds for the chronic sick in the Northern Region —Mr **BLENKINSOP** replied A 30 bed unit has been opened, and the work on providing a further unit of 20 beds is almost finished

Waiting-lists for Sanatoria

Replying to a question Mr **BLENKINSOP** stated that in England and Wales at Dec 31, 1950 the estimated number of patients awaiting admission to sanatoria was 10 400

In England Now

A Running Commentary by Peripatetic Correspondents

WRIDDLE-ME-WREE

My size is small , my gait is of a hopper ,
  My colour brown, it does not catch the eye
My name, though short, is not considered proper
  By the learned, and I often wonder why
Instead, they name me like the high and mighties ,
Troglodytes troglodytes troglodytes

There's botany displayed upon the tanner ,
  On the threepenny bit it urges one to thrift,
As one struggles with a dodecagonal spanner
  To extract it for a pourboire or a gift ,
On the farthing, on the humble widow's mite is
Troglodytes troglodytes troglodytes

Though human kind may all conspire to mock me,
  I can well afford to disregard their sneer ,
The fanciers of song-birds seldom stock me,
  For my voice is inconspicuous though clear
But there are fine games when the nights are Aphrodite's
For *Troglodytes troglodytes troglodytes*

* * *

Stimulated by Dr Ffrangcon Roberts's inquiries into the authorship of *Lancet* articles, I began to wonder what are the causes of the decline in acknowledgments to the family doctor in case-reports published by members of hospital staffs Is the extreme rarity nowadays of such acknowledgments merely a change in medicosocial custom, like the abandonment of the top hat and frock-coat ? Is it a reflection of the lessened financial dependence of hospital staffs on the general practitioner ? Or is it a symptom of a diminished collaboration between the hospital consultant and the G.P ?

These reflections were " pointed up " (as our American colleagues might say) by a recent report of a young man, earning his living and leading what he considered to be a satisfactory married life, who complained of symptoms suggesting a mild anxiety state and whose considerable surgical adventures left him with a prospect of endocrine therapy for the rest of his life—at a total cost to you and me of certainly more than £1000 The long list of acknowledgments at the end of this report did not include any reference to the family doctor, though one would have thought that the social aspects of the case could hardly have been dealt with satisfactorily without his collaboration Anyhow the family doctor will have to " hold the baby " and be primarily responsible for the aftercare—no light task Incidentally the " mild anxiety state " got lost in the general tohu-bohu and was not mentioned again Perhaps it is in the bottle with the other specimens in the pathological museum

The moral seems to be that it will be a pity if hospital staffs are not only going to ' Take the Cash " but " Take the Credit Too ' —if any What I should like to see among the acknowledgments is "　and to Dr XY, the family practitioner, who did his best to keep the patient out of hospital "

* * *

As a registrar in the Department of Anæsthesia, I used to be regarded as (*a*) a member of the F D A (Failed D A) Club, and (*b*) an anæsthetist's mate The latter position is roughly equivalent to a plumber's mate, the main duty being to carry laryngoscopes and endotracheal tubes in the wake of one s chief It came as a surprise to my colleagues and other occupants of this large teaching hospital to discover that, owing to the searching examination for the modern D A., my character had developed some other facets

One of the theatre sisters, for example, collapsed in hysterical laughter when she saw me in the theatre corridor carrying a stethoscope Her comment was illuminating ' I didn t know you had one Can you use it ? ' Similar remarks emanate from the disrespectful medical students one sees around the wards nowadays when I attempt to organise the pre- and post operative care of patients Then the pathologists—defined by a surgical colleague as ' Men who smoke pipes and spit in the sinks "—gather in a bunch, like cartoon characters, and set their scented halls rocking with puckish mirth when I enter to find out just what did happen to that secondly it changes while it is thus diffused so that it can moisten these tissues Thirdly it changes while it is there so that it may repair and support any wasted parts It travels on and again separates the humours. Fourthly it changes since in any given place it soaks into the limb and takes on its character, that is in order that it may recover and restore, what gave it its heat, and use up the air, and repair the changes caused by a cruel world [i e, by wear and tear]"

TEACHING OF THE TIME

Reyna's anatomical views are highly traditional in most respects, the great exception being those on the circulation of the blood This is the more surprising by comparison with his teaching that the brain is a chimney for the smoke from the heart, expelling it through the eyes, nose, and mouth He describes digestion as taking place in four stages in the mouth, stomach, liver, and tissues, that in the stomach separates waste from nutriment, the latter (chyle) is carried to the liver, where it is coloured and is then distributed to the body according to its needs Blood is formed from the most "temperate" part of the chyle, the other humours from other appropriate portions If any chyle is formed in excess, it must be purged by the bowel, or by bleeding, or by dieting, or by other similar methods of depletion Purgation by the bowel should be regulated as a result of studying the blood removed at bleeding There are two kinds of blood the arterial or vital, and the venous or nutritive The arterial flows from the heart, the venous from the liver The seat of the spirit is the heart, it is vaporous, controlling movement, sensation, and warmth, and it is this spirit which is manifested in all the pulses

His pathological theories were the current humoral ones, he stressed the importance of a knowledge of anatomy in order that the humours responsible for any illness might be easily identified and abnormalities recognised Diseases being seasonal, a knowledge of the qualities of the humours and the seasons was required in order to appreciate the relationship But although the seasons were a factor he attached more importance to any form of excess, whether in eating, drinking, exercise, rest, or exposure to heat and cold The four qualities of heat, cold, wetness, and dryness, and their combinations are discussed in relation to the four humours Health consists of the right balance between qualities and between these and the corresponding humours—e g, heat and wetness, and the blood This concept is related to the four seasons, thus blood is dominant in March, April, and May which were, perhaps arbitrarily, classified as hot and wet—at least in Spain But the actual local quality of the weather at any season does not appear to have affected this seasonal classification

He compares the art of curing illness to the work of a gardener, who, finding an irrigation channel blocked, removes the obstruction and allows the water to flow to the plants He thus appears to subordinate the healer to the *vis medicatrix naturæ*, but in practice he does in fact advise a less passive rôle, this was inevitable in view of the long held and still prevailing view on the treatment of all diseases by the exhibition of their opposites

He was not wholly free from the influence of astrology (horses' tails should not be docked at certain seasons of the moon), or from alchemy (powder of lizards was of value, and so was an ointment made from certain black worms which emerged from the earth in May, June, July, and August, "as long as a finger," and had to be fried in oil), but in general he used such simple dairy produce as eggs and butter for dieting and for surface applications, and such vegetables and grain as would be found on any farm Qualities associating these products with the humours and the seasons indicated their appropriateness for any condition, thus butter is cold and wet, honey is hot and dry, yolk of egg is hot and wet Since all treatment was by opposites the horse-leech had an easy guide to prescribing, he need only remember that hot diseases must have cool medicaments. Plethora must be treated by bleeding

Thus, between much that is now known to be error, Reyna believed that the blood circulated, that in the course of that circulation it was diffused in the tissues, that it was associated with the warmth of the body, and that it gave off air Spain has never claimed for Reyna the discovery of the course that the blood followed and it need hardly be stated that no such claim is made for him here Prof H E Sigerist has inveighed with much eloquence against the present tendency, particularly in the English speaking world, to attribute paternity to every advance in medicine, every new discovery If such a protest needs any support, it is surely to be found in such books as the *Libro de Albeyteria* Reyna should be recognised as giving expression to a belief which, if not clearly defined, was evidently fairly widely held in 1546, since his book led to no protest

EDITIONS OF THE BOOK

The book was certainly first printed about 1546, the copyright—which was granted by Pedro de Lovos on behalf of the King of Castile—being dated at Madrid, Nov 21, 1546 The title, *Libro de Albeyteria*, was used again in 1550 by Lopez de Zamora, suggesting that Reyna's book had achieved a success during the previous five years, which Lopez was quick to exploit

Although many editions have been recorded by Palau in his *Manual del Librero Hispano Americano*, there is one edition which has not previously been identified this is the edition of 1556 Palau cites the following editions 1546, 1552, Mondoñedo, 1553, Zaragosa (doubtful), 1564, Burgos 1580, Salamanca, 1582, Alcala, 1583, Alcala, 1603, Alcala (first annotated edition), 1617, Madrid, 1623, Alcala, 1647, Alcala The annotated editions of his work were probably published after his death There are copies of 1603 and 1623 editions in the British Museum The notes are by Ferdinand Calvo, and although he doubtless improved the purely veterinary part of the book, he seems to have regarded Reyna's description of the circulation of the blood as irrelevant He omitted the sentence about the heart being "the emperor of the body" from the 1603 edition and suppressed the whole description from subsequent editions

A copy of the first edition is in New York, in the possession of the Hispanic Society of America, and is stated to have been printed at Burgos Two copies of the Mondoñedo edition have survived, one at the Hispanic Society, the other in the National Library, Madrid, and the British Museum has a copy of the 1580 edition in which the colophon is incorrectly dated 1570 No copy of the doubtful 1553 Zaragosa edition is known In the library of the Royal College of Physicians there is a copy of the edition of 1556, which has never been recorded, and of which this is therefore likely to prove the only surviving copy It is a revised edition, priced at two maravedis a copy Certain pages are missing, but were made up in manuscript in the late eighteenth century, or a little earlier The copyist states that he had before him a Zaragosa edition printed by the Casa de Lorenzo y Diego de Robles hermanos in 1583, and that he considers the 1623 Alcala edition superior to this 1583 edition, but wishes to use the earliest one available to him

The 1556 edition was unknown to Saenz Egaña when he wrote his *Historia de la veterinaria Española*, which contains a recent (1941) history and bibliography of the early Spanish writers on the circulation of the blood, Montaña de Monserrat and Servetus It is possible that this edition was printed at Baeza in the province of Jaen, the title page having a coat-of arms with two lions and two castles, which resembles that of Jaen The earliest surviving book printed in the town of Jaén is dated 1605, but at Baeza there was a printer, Juan Bautista Montoya, between 1551 and 1594 He printed another book on horses—*Reglas de la Caballeria de la Brida* by Federico Grisone (1568)

Reyna gave as his motive for writing the *Libro de Albeyteria* the absence of any reliable work of a similar nature, and the existence of many misleading books

Nevertheless, the use of noradrenaline to combat hypotension in man would seem to be justified for the present on the following grounds

1 Noradrenaline differs from adrenaline in that its administration seems less likely to be followed by a depression of sympathetic vasomotor tone Whereas infusions of adrenaline in man are followed by peripheral vasodilatation,[2] similar infusions of noradrenaline are not followed by vasodilatation (unpublished observations)

2 Studies in this hospital on the effect of noradrenaline in methonium hypotension indicate that its use is not followed by a further fall in blood-pressure (Churchill-Davidson)

3 Noradrenaline increases the blood-pressure by increasing the peripheral resistance, adrenaline by increasing the cardiac output[3] As methonium hypotension is due to decreased peripheral resistance, it would seem reasonable to give noradrenaline rather than adrenaline

4 Pitressin would also elevate the blood-pressure by a constrictor action on the vessels But, as Professor Burn points out, it has the disadvantage of constricting the coronary vessels Its action in this respect is unfortunate, for the object of raising the blood-pressure is to improve the coronary and cerebral blood flow The action of noradrenaline on the coronary vessels in man is not known In animals, however, noradrenaline dilates the coronary vessels.[4]

Sherrington School of Physiology
St Thomas's Hospital
London S.E 1.

H BARCROFT
H C CHURCHILL DAVIDSON
H J C SWAN

DOSAGE OF METHONIUM COMPOUNDS

SIR,—Several correspondents have stated that they start the administration of methonium compounds with an intramuscular injection of 50 mg I have found in one case recently that this was too large a dose since it produced an unpleasantly great fall in blood pressure

Pentamethonium bromide 50 mg was injected intramuscularly into a woman whose initial blood pressure was 260+/135 mm Hg The pressure fell to 120/70 in ten minutes, and to 100/60 in eighteen minutes The patient was recumbent but nevertheless felt faint Adrenaline 5 minims was given intramuscularly on three occasions, and one hour after the injection of pentamethonium the pressure had risen to 145/80, with the patient feeling comfortable

In my opinion, 25 mg is quite enough to give as an initial intramuscular injection in cases with this degree of pressure

It is of interest to note that after the intramuscular injection of adrenaline there was an interval of about three minutes before the pressure rose, and that it fell again within a few minutes after each of the first two injections. After reading Professor Burn's letter in your issue of March 17, I should try pituitary extract, although I should be inclined to inject it intramuscularly since this would be easier and quicker than setting up an intravenous drip

Dorchester J HERBERT BURNS

UNFAIR QUESTIONS

SIR,—The following suggests a line of approach that commonly succeeds when one is confronted with a ridiculous question

I remember being asked in a clinical oral to diagnose a condition which is so rare as not to be mentioned in any of the standard textbooks of medicine Having been told by the patient what he was suffering from, I presented the right diagnosis When he had recovered the examiner not to be outdone, said, how do you treat it ? Not having the slightest idea and playing for time, I replied well, there are several different ideas about the treatment ", to which the examiner rejoined yes, there are some new fangled notions ' 'But I prefer the good old fashioned treatment, ' I retorted, and to my delight the examiner said, " yes so do I, let's go and see the next case " One wonders if the examiner himself knew the answer to his own question.

It is surely high time that oral and clinical examinations were devised to fulfil the purpose for which they were intended—namely, to find out if the candidate is a suitable person to practise medicine, instead of being at best a humorous diversion and at worst an opportunity for the examiner to show off his own knowledge It would be interesting to hear what the examiners themselves have to say

Bournemouth. G V JAFFÉ

CORONARY DISEASE AND MODERN STRESS

SIR,—All your correspondents appear to agree that "modern stress" is a large factor in the ætiology of coronary occlusion Why then is this so much more common in men than in women, as is all occlusive vascular disease ? Surely during the last thirty years, and especially during the war years, women have had more "stress" than men.

Buxton F A BEARN

MYXŒDEMA FROM RESORCINOL OINTMENT

SIR,—Bull and Fraser[1] threw much light on this condition, and several other cases have now been described[2,3] The causation was confirmed by Doniach and Fraser,[4] but was disputed by Klein et al.[5]

The *National Formulary*, 1949, includes (p 100) ung. resorcinol and ung resorcinol co, the first containing 4% and the second 12% resorcinol The unnamed proprietary preparation incriminated by Bull and Fraser[1] and by Hobson[3] contains 4% resorcinol.

I recently performed a necropsy on one such case This was of an elderly woman who had had leg ulcers for 20 years and died of myxœdema with a very large goitre histologically free from any suspicion of colloid Many more cases of this syndrome are to be expected, it can result from the exhibition of sulphonamides, thiocyanates, thiouracil, and cabbage leaves in addition to resorcinol, and perhaps also from other drugs at present unsuspected Would it not be a good idea to remove the two resorcinol containing ointments from the *National Formulary*, and to persuade the manufacturers of the anonymous proprietary preparation to remove resorcinol from their formula ?

St Margaret's Hospital
Epping Essex.

FRANK MARSH

DIPHTHERIA ANTITOXIN IN CORD-BLOOD

SIR,—Miss Barr and her colleagues, in their article of March 31, have produced just such another valuable contribution to our knowledge of infant passive immunity as one would have expected from them

One does, however, feel that they take a slightly pessimistic view of future possibilities in respect of immunisation of the very young infant which possesses quantities of maternally bestowed antitoxin in excess of 0 04 unit per ml Perhaps it would be more correct to say that one finds no particular note of optimism in this respect This may be justified if Miss Barr and her associates are only prepared to think in terms of A P T as the prophylactic to be employed

To those of us who feel that the future of safe and effective immunisation lies in treating the infant of from 2 to 5 months, the mind turns from the use of A P T to a concept of some form of prophylactic which will provide an adequate primary stimulus in the face of fairly considerable quantities of maternally endowed antitoxin The section "Age at which immunisation transthoracic gastrectomy The radiologists (believe it or not) switch on lights and even remove their goggles when I hazard a staccato "Atelectasis, isn't it?" The Director of the Clinical Laboratory actually signed the report himself after I had consigned to his department an ampoule containing the remnants of some intravenous barbiturate solution with a request that he would try to persuade something to grow in it Most surprised of all was the Lecturer in Public Health when I showed desperate interest in the investigation of an outbreak of diphtheria in an institution, or perhaps it was the Biochemist after I had plagued him with questions on abstruse blood-investigations

---

[2] Swan H J C *Ibid* 1951 112 426
[3] Goldenberg M et al *Amer J Med* 1948 5 792
[4] Burn J H. Hutcheon D E *Brit J Pharmacol.* 1949 4 373 Folkow B Frost J Uvnäs B *Acta physiol scand Stockh* 1949 17 201

[1] Bull G M. Fraser R *Lancet* 1950 i 851
[2] Hart F D Maclagan N F *Ibid* March 3 1951 p 530 Young S *Ibid* April 7 1951 p. 798
[3] Hobson Q J G *Proc R. Soc Med.* 1951 44 164
[4] Doniach I Fraser R. *Lancet*, 1950 i 855
[5] Klein F Ottis V Velvart J *Ibid* ii 768

Oh yes, I have grown truly peripatetic in the hospital Every department other than my own now knows me well—I spend more of my time in these others, you see Giving anæsthetics? How naive of you, gentle reader That is the last thing I'd be expected to do I'm trying for a D A

* * *

I was a trifle suspicious when I heard at my outlying surgery that the vicar's wife was asking whether the doctor kept any scales in the surgery When later, from the window of a patient's house in the village, I saw the vicar's wife, accompanied as usual by her two terriers on leash, coming my way, I was certain from the look in her eye that something was afoot Sure enough, as I reached the car, she suddenly turned round from walking aimlessly down the road and said "I see you have some scales in the car I wonder if you should weigh me and then the dogs? You see, they both have worms and I nearly killed them last year by giving them an overdose of medicine"

I am used to casual consultations in the street, but I was taken aback by this calm assumption that dog-weighing is among the facilities offered by the N H S However, being also anxious not to cause speculation in a village notorious for its gossip, I asked "Where shall we go? To your house?" "Oh, no," said the vicar's wife, "here will do quite well" Bemused and a bit abashed I took out the scales and proceeded to weigh the lot She did thank me, so though I wanted to tell her that the Health Service does not cover pets, I held my peace My fee for the roadside consultation came later and in an unexpected form—a pot of lime honey

* * *

After the meeting we left York on time and sped south through the darkness, and well we might since we were pulled by the great Pacific locomotive *Gay Crusader*, worthy namesake of speed in another sphere We covered mile after mile without faltering, then somewhere in the wilds the train gradually slowed down and stopped It was only a blown out headlamp, but rules must be observed even by the famous And it, would have been a trifle undignified if *Gay Crusader* had ignored the fault and gone on to London with only one headlight, for a single light, according to its side, is the sign of either a universal train or ballast train stopping at all stations

* * *

Two Captions for the same Photograph

1 *Zoo Life* (1948, 3, 69) "A tarsier sitting on the ground This photograph shows to good effect its long fingers ending in flattened discs at their tips Note the long tail stretching out behind

2 *Picture Post* (April 7, 1951) "A tarsier, aglow with potential love, takes his soundings of the modern world"

* * *

'Did you see that correspondence in *The Lancet* some weeks back about *trophic* or *tropic*?" "Yes It crops up about every five years They probably start it to get an idea of how many doctors know any Greek nowadays" "H'mm, a sadly diminishing number, I should think" "'Fraid so Did you notice the rather archaic Greek type they used? One imagines the oldest compositor trundling down to the cellars to unearth it"

'Yes, but they managed it with only one misprint—an *omicron* instead of a *sigma* Not bad for the modern subeditor!"

* * *

Aphorism of the Week

Babes stand asphyxia as adults stand decapitation

Letters to the Editor

GENERAL PRACTITIONER AND CONSULTANT

SIR,—On every side one hears of the falling status of the family doctor and general practitioner With this it would appear that a gulf, which is widening rapidly, has developed between the hospital doctor and his colleague in general practice The causes are no doubt multiple and different, but the effect upon medical practice in the future cannot be anything short of disastrous

Many of the immediate difficulties are no doubt related to finance, and many of the suggestions which have been made—suggestions which would go far to improve the present situation—are impracticable I refer particularly to facilities whereby general practitioners would be able to continue the treatment of certain of their own cases in general hospital beds The impossibility of realising this aim for the time being should not deter us from doing what can be done to relieve the threatening situation. With this end in mind, I have wondered whether it might not be possible for consultants and specialists to be placed in a position where they would be able to request a consultation with the patient's family doctor, the consultation to take place in the hospital wards or outpatient department Such an arrangement would frequently be of great value to the patient, and would at the same time introduce the general practitioner to the inside activities of the hospital Before long he would be welcomed by sisters and nursing staff, who would realise, to their own great benefit, the important position which should be held by the family doctor in the general pattern of investigation and treatment.

To put such consultations upon a firm and proper basis, it would be necessary to pay the general practitioner a suitable fee for his services The total cost of such an arrangement would be fully justified, and would before long be paying big dividends in the all round improvement which would result, not only in the care of the patient, but in the relationship between specialist and general practitioner

One would like to go even further than this, and hope that an arrangement might be possible whereby the attendance of general practitioners at domiciliary consultations was also adequately remunerated It is surely no part of the busy and overworked doctor's terms of service that he should devote an hour of his time watching his hospital colleague carry out an extensive neurological investigation upon one of his patients The value of such attendance is obvious enough, but the sacrifice in time should be remunerated Would it be even worth reducing by, say, 25% the consultant's fee, in order to pay the family doctor—if the money cannot be found in any other way?

The threat to medicine by the present difficulties is real and great Unless we are prepared to make some sacrifice in order to neutralise this threat we may find that we are too late These suggestions are put forward with hesitation and humility They appear to be practicable, and likely to go some way towards safeguarding the profession for the future

Winchester

KENNETH ROBERTSON
Consulting Physician
Royal South Hants & Southampton Hospital

NORADRENALINE IN HYPOTENSIVE STATES

SIR,—In his letter of March 17, Prof J H Burn advised against the use of adrenaline to combat hypotension due to methonium compounds, on the ground that its administration is likely to be followed by a further fall in blood pressure due to its ganglion blocking action[1] Noradrenaline is said to have the same action in this respect curve. In the larger series the site of perforation is not discussed, but I believe that the upper part of the stomach is the more commonly injured.

---

[1] J Physiol 1942 101 289

Schindler advises blind and rapid penetration of his instrument to his position I, from which the pyloric antrum can be viewed, on the grounds that the stomach is taken unawares and the gastroscope is not detained in the upper half of the body by hour glass contraction, which may occur if a more cautious descent is made. Since resistance to the passage of the gastroscope cannot be taken as a warning of impending perforation, it must surely be safer to proceed from the cardia to the pyloric end slowly and with caution, despite the long delays that such a technique involves.

Reference is made in both papers to occasional difficulty in overcoming resistance at the pharyngo-œsophageal junction. At the suggestion of Dr W J Walkden, some months ago, when experiencing this difficulty I employed a capsule of amyl nitrite crushed under the patient's nose, and within a few seconds the gastroscope passed effortlessly downwards. I have since used this technique, with success, whenever encountering resistance either at the upper or the lower end of the œsophagus.

Most observers of the British stomach will surely agree with Dr Avery Jones that the appearances "supposed to indicate" gastritis bear no consistent relationship to clinical findings except perhaps in pernicious anæmia.

Wolverhampton J V S A DAVIES

WILL WE NEVER LEARN ?

SIR,—Now that correspondence has been appearing for some weeks, may I ask that the title "Will we never learn ?" shall be corrected to "Shall we never learn"? These foreign idioms in English journals are very confusing for the natives.

Bristol E WATSON WILLIAMS

⁂ But is it a foreign idiom ? The author of this phrase (as we understood him) chose "will" because it conveyed an element of intention—or rather lack of intention. We tried the effect of substituting the pure future form, but "Shall we never learn ?" seemed a trifle anæmic as a heading for what followed.

We take this opportunity of acknowledging a small inaccuracy in a leading article of March 24, in which Scotland was described as England.—ED. L.

BACTERIAL VARIANTS PRODUCED WITH CHLORAMPHENICOL

SIR,—I should like to answer the points raised by Dr Rogers in his letter of March 10.

(a) I certainly agree that non catheter specimens might be contaminated. This is why the alterations in bacterial morphology observed in micro organisms isolated from patients under chloramphenicol treatment were attributed to the drug only after in vitro experiments had proved that similar alterations could be obtained by the combined action of antiserum and this drug. Moreover, although most of the abnormal bacteria were identified as belonging to the same species as the original infecting organism, the need for verification was the only reason for which the in vitro experiments were done.

(b) Dr Rogers wrongly assumes that the serum of the patients had no agglutinins. Case 4, the only one in which serum agglutinins were sought, had a serum agglutinin titre of over 1/800. Dr Rogers also accepts too lightheartedly that cases with urinary infection do not develop agglutinins. Baird,[1] investigating 69 cases of pyelitis, found agglutinins in the serum of 30. He emphasised that the agglutinins were specific for the organism in the urine, and that in most of them the agglutinin titre of the serum was very high (1/2000). When, however, I spoke of "special conditions in the body" this meant any immunological reaction of the serum, of the cells, or of the tissues, as well as any changes that chloramphenicol might have suffered in the body. Indeed this last possibility had been the first to be investigated. However, only the one hypothesis that eventually proved to be right was described, in a serious effort to conceal how "painstaking" this work had been. After Dr Rogers's letter I see how much I have failed in this effort.

(c) Dr Rogers objects to my nomenclature of the variants, but surely it is not wrong to describe the three children of *Bact coli* D433 as variants α, β, and γ. This simply means 1, 2, 3 or a, b, c, and has nothing to do with Stamp and Stone's alpha antigen. Letters of the Greek alphabet are commonly used in all scientific fields. I feel most distressed at the thought that I might be deprived of the use of some letters of my own alphabet because priority might be claimed by workers who have already used them.

Wright Fleming Institute of Microbiology
St Mary's Hospital Medical School
London W 2

A VOUREKA

INDUSTRIAL HEALTH SERVICES

SIR,—In your interesting leading article of March 10, dealing with the Dale report, you say that in the U S A health engineers "are now maintaining that in order to deal with industrial health it is unnecessary to have a medical qualification." This is not in accord with the facts.

The preservation and improvement of the health of workers in industry is a task to which different persons make their contributions—e g, the doctor, the engineer, the welfare worker, the safety officer, and the nurse. It is impossible for a medical officer to deal alone with the prevention of hazards involved in existing and in newly adopted processes in a plant. Equally it cannot be expected that the health engineer shall know where pathological conditions may arise in man owing to such exciting causes as dust, high temperatures, excessive humidity, and the many toxic substances involved in modern industry. Nor can the engineer adequately assess the conditions necessary to maintain optimum health among the workers in any factory.

The advent of the health engineer is a progressive step in the constant endeavour to improve the health of those engaged in industry, and so indirectly to contribute to a higher standard of physical and mental fitness in the population as a whole, and it in no way displaces anyone from the health team. Your article calls attention to the group industrial health services at Slough, to which there has been appointed an industrial health engineer who works in close coöperation with doctors in providing a genuinely preventive industrial health service.

I have an intimate knowledge of the valuable contribution made by the industrial health engineer in the U S A. A conspicuously successful example of the value of such team work is to be seen in the highly successful development of the area controlled by the Tennessee Valley Authority. It would be fatuous to expect a doctor alone to institute the many measures for the prevention of malaria that have been successfully adopted there by teams consisting of doctors, chemists, entomologists, and public health engineers. Similarly, in industry in the U S A the preventive aspects of industrial health have been dealt with successfully by a team consisting of doctor, industrial hygiene engineer, and chemist. Since the maintenance of health is the main problem of the team it is almost invariably the doctor who leads the members of the team, and he is not, as your article suggests, supplanted by the engineer.

In order that the work already being done in this country by some engineers should be even more effective, it is desirable that they should have a specialised academic could be started" defines a limit which I, for one, am not prepared to take lying down I believe that the trouble can, and will, be overcome, and I am working to that end

---

[1] Baird D *J Obstet Gynæc* 1935 42 577

The final paragraph in the summary is perhaps a little ambiguous It runs "The Schick test would give little useful information as to when immunisation could be started in the babies with expectation of success" I presume that this means that simple Schick testing of any given population would be no sure guide, for in the individual infant the answer is not in doubt They regard 0 004 unit per ml as approximately the Schick positive level, while interference with the primary stimulus is stated by them not to occur at levels of about 0 04 You can, of course, immunise infants at any age by first doing Schick tests and then administering prophylactic only to the positives I believe that you can do much more than this

As a piece of thorough and painstaking research on cord blood, this article will be widely welcomed, and the authors are greatly to be congratulated

London S E 5 GUY BOUSFIELD

PSYCHIATRIC ASPECT OF ORGANIC DISEASE

SIR,—In his article last week, Dr Todd states that in treating cases of chronic arthritis "the essence of the doctor's task should be to put the onus of recovery upon the patient," and that "any pre existing ideas" that various forms of physiotherapy "are necessary should be vigorously suppressed" May I suggest that the pre existing idea that the use of the hospital car service is necessary should be included in this vigorous suppression?

St George's Hospital
London, S W 1

B D SPENCER
Almoner

THE ECONOMIC VALUE OF THE DOCTOR

SIR,—Dr Ffrangcon Roberts, by his frightening article (March 24), has performed a signal service in focusing our attention on a problem hitherto suppressed in the minds of many of us

The time has come for everybody, including auxiliary hospital personnel, high powered scientists, and particularly politicians, to answer the question "What is a health service?" It is time, too, for public health officers to admit that, however much they "prevent," somebody, somewhere and some time, will fall ill It is the diagnosis and treatment of the sick individual that should form the basis of any health service—not because the patient is a key man in industry, not because the family may suffer, not because he is a cog in the economic machine of the community, but simply and solely because he (or she) is ill

For let us be quite clear—when a person becomes unwell he turns to the doctor A history has to be taken—a more difficult, skilled, and accurate diagnostic measure than all the chemical and electrical paraphernalia in use today—and then the patient has to be examined In these two procedures lie the knowledge, experience, judgment, and art of medicine Scientific aids to diagnosis are not of the slightest use until the doctor has decided when and where to use them and how to interpret them in relation to the patient Furthermore, therapists, administrators, statisticians, and the rest could stay at home for all the good they would do in the absence of a doctor If one has a patient, a doctor, and—may I add—a nurse (sadly neglected in the scramble for cash and kudos) one has a health service Without these one has nothing Lashings of preventive medicine and statistics, nice filing systems, plenty of equipment, therapists by the dozen, and marvellous diets would become to the sick man worse than a mockery This, then, is the functional and economic position of the doctor—and may no one forget it

Inchture, Perthshire A HUGHES

PUBLICITY IN CANCER

SIR,—In his letter last week Dr Horace Joules refers to the report by Doll and Bradford Hill as "passed *unnoted by the non medical press of this country*, and, in fact, there is evidence to suggest that publicity has been withheld" I am sure that in fairness to the lay press you will allow me to say that this report was in fact referred to in *The Times* of Sept 29, 1950

The Times
Printing House Square,
London, E C 4

ALAN PITT ROBBINS
News Editor

EFFECT OF A C T H ON RENAL GLUCOSE THRESHOLD

SIR,—Adrenocorticotropic hormone (A C T H) has been found to induce glycosuria,[1] and this has been assumed to be caused by a lowered renal threshold for glucose However, no study of the renal threshold for glucose after administration of A C T H in "renal diabetes" has yet been undertaken

We gave two injections of A C T H to a patient with renal diabetes (one day 36 mg and another day 24 mg) Endogenous creatinine clearance, tubular reabsorption of glucose, tubular glucose reabsorption index, and renal threshold for glucose were determined both before injection and 60, 120, 150, 180, 210, and 240 minutes later Analysis of the data revealed a small fall in plasma creatinine, with no consistent change in urinary creatinine, creatinine clearance was increased Tubular reabsorption of glucose, tubular glucose reabsorption index, and renal threshold for glucose were significantly increased by A C T H More consistent changes followed the larger dose of A C T H

These findings do not agree with earlier reports suggesting that A C T H lowers the renal threshold for glucose Additional studies are desirable in order to determine whether our results are related to any particular condition in renal diabetes Further details of this work are to be published in *Folia Endocrinologica*

Institute of Medical Semeiotics
University of Naples

V DE FILIPPIS
A IANNACCONE

THE RISKS OF GASTROSCOPY

SIR,—In your issue of March 24, Dr Avery Jones and his colleagues appear to show that perforation of the œsophagus, particularly in its upper part, is the chief risk of gastroscopy Only 9 cases of gastric perforation were recorded among about 49,000 gastroscopies. Yet in a companion article Dr Boon cites 4 cases out of 4000, 3000 of which (though we do not know how many gastric perforations) are included in the analysis of Dr Avery Jones Dr Boon's gastric perforation rate was at least five times, and possibly nine times, higher than that which is supposed to have occurred in the larger series

This discrepancy, which *must surely* be significant, is open to various interpretations It is improbable that the technique employed by the various other gastroscopists differed materially from that of Dr Boon, or that the cases subjected to gastroscopy were more carefully chosen Dr Boon stresses the difficulty he experienced on two occasions in convincing his surgical colleagues of the fact of perforation Dr Avery Jones himself implies that in his series "mild cases" may have been overlooked, and it may well be that gastric perforation is a far more common complication of gastroscopy than his figures appear to show In the 3 cases of Dr Boon which came to operation, perforation was found in the upper part of the posterior wall close to the lesser

---

[1] Conn J W, Louis, L H, Johnston M W *J clin Invest* 1949 28, 775 Sprague R G, Power, M H Mason, H L, Albert A, Mathieson D R Hench, P S Kendall, E C, Slocumb C H Polley H F *Arch intern Med* 1950 85, 199 Kass E H, Ingbar S H Finland M *Proc Soc exp Biol N Y* 1950 73 669

Public Health

Statistics for 1950

ACCORDING to provisional figures issued by the Registrar-General,[1] the birth-rate in England and Wales during the year 1950 was 15 8 per 1000 home population, this was 0 9 below the rate for 1949 The illegitimacy-rate was 49 per 1000 live births—15 per 1000 below the average for the preceding five years The provisional stillbirth-rate was 22 6 per 1000 total live and still births, compared with 22 7 for 1949

The death-rate was 11 6 per 1000 home population, this was 0 1 less than that for 1949 Infant mortality was 29 8 per 1000 related live births and was the lowest ever recorded in this country, the rate was 2 4 below that for 1949, the previous lowest

Births exceeded deaths by 182,148, the corresponding increase for the preceding year was 210,479, and the average for 1944–48 was 290,783 The estimated total population for the year was 44,020,000—an increase of 235,000 over the estimate for 1949 The estimated home population was 43,830,000 The effective reproduction-rate, corresponding to the births in 1950 and allowing for continuing improvement in survivorship conditions, is provisionally assessed at 0 98, indicating that births were 2% below those required by a par replacement standard This is the first year since 1945 that the rate has fallen below unity

Population Estimates—The Registrar General has issued *estimates of the population of each administrative area at* June 30, 1950[2]

SCOTLAND

In Scotland the birth rate in 1950[3] was 17 9 per 1000 population—0 6 below the rate for 1949 The illegitimacy-rate was 52 per 1000 live births The stillbirth-rate was 27 per 1000 total births—the same as in 1949

The death rate was 12 4 per 1000 population—0 1 above the rate for 1949 Infant mortality amounted to 39 per 1000 live births, this rate, the lowest ever recorded in Scotland, is 2 below that for 1949, and 11 below the five years' average The neonatal death-rate was 23 per 1000—the same as that for 1949, which was also the lowest ever recorded for Scotland. The death-rate from tuberculosis (all forms) was 54 per 100,000 —21 below the five years' average The rate for deaths from respiratory tuberculosis was 47 per 100,000, and from non-respiratory tuberculosis 6 per 100,000, these two rates are 15 and 6 below the five years' average

The natural increase for the year was 28,532, compared with an average of 36,517 for the previous five years

Infectious Diseases in England and Wales

Disease	Week ended March				
	3	10	17	24	31*
Diphtheria	44	46	50	50	46
Dysentery	1364	1449	1672	1257	939
Encephalitis					
Infective	2	2		3	2
Postinfectious	6	1	2	4	2
Food poisoning	87	89	88	45	88
Measles excluding rubella	29 201	29 071	31 841	27 838	31 208
Meningococcal infection	49	44	38	39	58
Ophthalmia neonatorum	57	48	41	34	20
Paratyphoid fever	2	4	5	10	21
Pneumonia primary or influenzal	1253	1027	1107	936	909
Poliomyelitis					
Paralytic	19	9	18	10	19
Non paralytic	9	4		3	4
Puerperal pyrexia and fever	69	86	80	65	62
Scarlet fever	952	1056	1009	927	918
Smallpox					
Typhoid fever	4	11	1	7	7
Whooping-cough	6099	5639	5527	4079	4098

* Not including late returns.

Postinfectious Encephalitis

Up till the end of 1949 encephalitis was notifiable only under the heading "encephalitis lethargica" From the start of 1950, however, encephalitis has been notifiable as either "infective" or "postinfectious", and under the latter heading altogether 71 cases were notified in England and Wales during the year

Reviewing 65 of these 71 cases, Conybeare[1] remarks that in 6 the disorder, was subsequently judged to be poliomyelitis, in 8 the association with an infectious disease could not be substantiated, and in 10 the diagnosis was eventually changed In the 41 remaining cases the associated diseases were as follows measles, 15, mumps, 10, chickenpox, 9, influenza, tonsillitis and pharyngitis, vaccinia, 2 each, and rubella, 1

Campaign Against Diphtheria

In the last ten years over 9 million children in England and Wales have been immunised against diphtheria, and deaths from the disease dropped from 2480 in 1940 to a provisional 85 in 1949 The improvement continued in 1950 and provisional figures show that there were only 32 deaths from diphtheria in the first half of the year compared with 53 deaths in the same period of 1949 These figures would give every reason for satisfaction were it not that this immense reduction in the incidence of the disease has made parents less aware of its dangers This is shown by the fall of 27,000 in the number of immunisations carried out in the first half of 1950 compared with same period in 1949 Drawing attention to this setback in the immunisation campaign, the Ministry of Health have asked all local authorities to arrange for intensive publicity and propaganda to call the attention of the public to the importance of diphtheria prophylaxis, and have set as the target for 1951 the immunisation of 75% of babies—more than 500,000—before their first birthday

Obituary

CHARLES RICHARD BOX

M D B.Sc. Lond, F R C.P, F R.C S.

Dr C R Box, consulting physician to St Thomas's Hospital, the London Fever Hospital, and the Royal Masonic Hospital, died on April 3 at the age of 84

From Dulwich College he entered St Thomas's Hospital in 1884, where he rounded off a brilliant career as a student by taking honours in physiology, medicine, and obstetrics in the M B examination, qualifying in 1892 At St Thomas's he was appointed successively to the posts of medical registrar and resident assistant physician at a time when each was held for three years During these formative years he found time to take the higher qualifications of M.D, M.R C P, and F.R.C.S He was thus exceptionally well qualified when he was appointed to the staff as physician to outpatients with charge of the children's department

[Lafayette

It was then the exigent custom for each assistant physician, as well as attending outpatients on two days a week, to do post-mortems on another two days But Box did even more, for he continued to act as demonstrator in anatomy for some years after he had been appointed to the full staff in 1915 Indeed, he only gave up this work when the department was reorganised after the war This experience formed the basis of his useful and lucid *Manual of Morbid Anatomy and Post Mortem Technique*, which, like all his infrequent writings, was backed by wide experience and accurate observation *Clinical and Applied Anatomy*, which he wrote with McAdam Eccles, was no exception to this rule, for Box lectured at the medical school for many years on anatomy background and should appreciate the health problems involved The postgraduate course in public health engineering which is now being held in London is recognition of the fact that personnel should preferably be trained rather than that they should learn only from experience gained on the job

---

[1] Registrar General s Quarterly Return for England and Wales Quarter ended Dec 31 1950 H M Stationery Office Pp 37 1s

[2] The Registrar-General s Estimates of the Population of England and Wales Populations of Each Administrative Area at June 30 1950 H M Stationery Office Pp 15 6d

[3] Quarterly Return of the Registrar General Scotland Quarter ended Dec 31 1950 H.M Stationery Office. Pp 40 1s

[1] Conybeare E. T *Bull Min Hlth P H L S* 1951 10, 58

London School of Hygiene and Tropical Medicine, London W C 1 — R F Guymer, Rockefeller Tutor

IS OBESITY AN ENDOCRINE PROBLEM?

Sir,—I read with interest your annotation last week Dieting seems the best remedy for obesity, but it is difficult to apply If indeed overeating is associated with personality factors, the nervous breakdowns that occasionally follow dieting may be due to the same factors On the other hand, I have seen undesirable gain of weight rectified during prolonged treatment for severe anxiety state, because of the change of habits following the mental improvement, this implies both less eating and more productive activity Slimming cures such as those on the television programme and in journals differ from ordinary private dieting through the atmosphere of group therapy involved.

London N W 4 — S Lowy

BORSTAL FOR GIRLS

Sir,—May I add some figures to your footnote on Mr Bell's letter last week with regard to the "care and protection" cases that end up in borstal after absconding from an approved school?

According to figures given in the House of Commons by the Home Secretary in May, 1949, there were 23 "care and protection" cases in the girls' borstal institutions, *excluding* those beyond control and those showing criminal tendencies Considering that the daily average population in the girls' borstals in 1949 was only 221, this figure is startling

The Criminal Justice Act gave the Secretary of State the power to establish special approved schools for absconders, whether "care and protection" cases or delinquents The above figures show how urgently needed such a school is in the case of girls

Parliament Mansions
Abbey Orchard Street
London S W 1

W A Elkin
Hon Press Secretary
Howard League for Penal Reform

MATERNITY AND THE ADMINISTRATOR

Sir,—It is very difficult to understand what Professor Nixon means In his letter (March 31) who is "the administrator?" Does he think that the secretary dictates the policy and resolutions of the London Local Medical Committee? Does he know that the majority of the members of the committee are engaged in active general practice? Does he know that the committee at its meeting in February, "gravely concerned at the number of patients who have died in London this year because hospital beds could not be found for them in time," called on the Minister of Health "to take *all* possible steps to remedy the bed shortage" (Unlike the majority of the lay press, The Lancet omitted to quote the main part of the resolution) Does Professor Nixon also know that the committee has asked the consultants' organisation to appoint eight representatives, that only four have been appointed, and that the fact that there are no obstetricians on the committee is therefore entirely due to their own neglect?

Even your brief extract made it plain that the committee regards unsuitable housing conditions, *when properly established*, as warranting the hospitalisation of an obstetrically normal confinement What about the "other conditions" necessary for a home confinement? Cannot the hospitals of London supply the full resources of a modern obstetric service, including a "flying squad?" Lastly, what evidence has Professor Nixon that it is better for a normal confinement to take place in hospital rather than at home?

In its statement to the press this committee pointed out that in the present shortage of beds it was a case of choosing how they should be occupied—by normal confinements or the acutely ill It seems that Professor Nixon has made his choice He asks the age and condition of the patients who died The conditions were chiefly pneumonia and cardiac failure, and admittedly the age of the majority (though not of all) was over 50 Is Professor Nixon saying "let the old people die?" If he is saying so, then let him realise that he is advocating a return to barbarism

Tavistock House
London, W C 1

F Gray
Secretary Local Medical Committee for the County of London.

*** Dr Gray complains that "unlike the majority of the lay press" we published only a brief extract from the committee's resolution The explanation is simple unlike the lay press, we did not receive a copy—*Ed L*

Sir,—Arising from Professor Nixon's warning on this subject, in his letter of March 31, I think that the time has come to measure the maternity services of the country against the ideal visualised by the Royal College of Obstetricians and Gynæcologists, and even against that referred to in section v of the *Development of Consultant Services*[1]

How many of our towns possess any obstetric service worthy of the name? It would be profitable to learn how many hospital groups have only nominal cover of two or three consultant sessions in order to satisfy the administrator's statistics, whilst the consultant himself may reside some distance from the area It is common knowledge that scores of members of the college are without hope of obtaining an appointment suited to their training, whilst their chances of entering general practice are just as remote

Shirley Croydon — J C Miller.

SALICYLATES AND CORTISONE IN RHEUMATIC DISEASES

Sir,—In your leading article last week, I am quoted as saying that salicylate has an effect on healing when judged by standard skin wounds in mice I did not, in fact, say this, and did not give any observations on salicylate at all, as I have never used it Professor Buttle, however, has tried salicylate, using our technique, and found that it does *not* inhibit healing

My observations on γ resorcylate have been quoted correctly

St Thomas's Hospital
London S E 1

Barbara E Clayton

MUNCHAUSEN'S SYNDROME

Sir,—I was interested to read Dr Rosemary Bolam's account of the second patient described by her in your issue of March 31

This man volunteered that his father, an hotelier, served in the Scots Greys He at first stated that he himself was a 4th year medical student, but subsequently revised this estimate to $2^1/_2$ years He said that he had been able to enter Glasgow University "through friends" He "did some hospital work" but was "more or less in laboratories" He could not recall what examinations he took Dr Bolam describes him as an ex Commando, but she omits to mention his transfer from the Royal Artillery to the 1st Airborne Division and his exploits at Arnhem Attaining the rank of sergeant he served in many theatres, including the Near, Middle, and Far East, not to mention Italy, but disliking "red tape," "I threw my medal ribbons into the fire" He said he had travelled to Liverpool from Glasgow by rail via York—an unusually circuitous route, one might think.

Truth is stranger than fiction, but romance, too, has its charm, even if it only reveals the kind of people we should like to have been, and the deeds we would fain have wrought

Liverpool — S Barton Hall

---

[1] H.M Stationery Office, 1950

Notes and News

THE MEDICAL DIRECTORY

As a new and useful item the *Medical Directory 1951* [1] has index to hospitals Previously it was very difficult to find hospital without knowing its area Now the index refers e searcher to the detailed descriptions which are still arranged y areas The Ministry of Pensions hospitals have been nstated as a separate list Otherwise the contents are milar to those of 1950 The medical practitioners listed umber 79,672 against the 77,730 of last year

DISTRIBUTION OF GENERAL PRACTITIONERS

The following amendments have been made to the Medical ractices Committee's classification of executive council reas described last year in our issues of Aug 5 (p 229) and ct 25 (p 545) Schedule IV contains the names of the closed reas

Schedule IV

ADDITIONS

Devon and Exeter —Torrington
Oxford County and City —Chipping Norton
Sussex West —Wittering and Itchenor Districts

DELETIONS

Kent and Canterbury —St Paul s Cray St Mary Cray and the Poverest ward of Orpington U D

University of Durham

On June 29 the honorary degree of D HY will be conferred on Sir John Charles

University of Birmingham

The title of emeritus director of radiological studies in the living anatomy has been conferred on Dr J F Brailsford in recognition of his services to the university

University of St Andrews

On June 29 the honorary degree of D SC will be conferred on Mr Walter Elliot, F.R C.P , F.R.S M.P

University of Aberdeen

On April 5 the following degrees were conferred

M.D —Valerie A Cowie and Helen L D Duguid (with commendation) G B Forbes A A White

M.B , Ch.B —George Adams R. A Andrew B M Barron G W Cruickshank J G Donald R H Duncan J A G Elmslie Mair L Jones R A Kirton Mary R. Kramer, Hectorina Matheson June M Oliver Moira K M Pratt Isobel B A. Shivas William Soutter I D Spark, R A Spark B S Stephen J G Sutherland Dorothy M. McI Sweenie Jean P Watson Marjory I K. Watt R M Youngson

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on April 2, with Mr Walter Galbraith, the president, in the chair the following were admitted fellows of faculty William Dawson Hamilton Conacher Abraham Goldberg, Peter Glyn Griffiths (*qua* physician) Ian Alexander McGregor (*qua* surgeon)

Society of Apothecaries of London

Dr W S C Copeman has been elected to a seat on the court in place of Mr R Ogier Ward who has resigned R J Dodds has been admitted to the freedom of the society by servitude The following were admitted by redemption

C Herbert Gray M. L Formby H J McCurrich, H E Harding Eve G Field D G C Tasker M H Harmer W N Mascall S A Mason Hilda Lloyd K M A Perry A. J Amos C Horace Gray F B Kiernander, W F Dunham G H Newns S Cochrane Shanks D P Lambert.

R K Franklin has been bound apprentice to R H Franklin for seven years The following have been granted the L M S.S.A. upon examination

R E Hazell W Friis I W Turnbull J R C Wallace H G Hexter T R P Coakley G C Stavrakis R F Mottram C E A Thomas C B Alvey P D Black P Howe J E K Moore B L Breeze K. M Stone A Ross A. E H Safeda D G Philipps (Viscountess St Davids) F J Covill G Dixon P B Hughes A L C A M. Bracchi W M Cornelius.

The diploma in industrial health has been awarded to C G Hunter

Crichton Fellowships

Fellowships at the Crichton Royal, Dumfries, have been awarded to Dr P Rowsell and Dr J Harrington

Central Council for the Care of Cripples

The annual general meeting of the council will be held on Friday, April 20, at 2 45 P M. in the Goldsmiths' Hall, Cheapside, London, E C 2, when Mr Hilary Marquand, the Minister of Health, will speak

Shortage of Sulphur

The Ministry of Health has issued the following statement

"Doctors will be aware of the shortage of sulphur and sulphuric acid, both of which are indispensable to the manufacture of a wide range of medical supplies Every effort will be made to maintain supplies at as high a level as possible to meet medical needs, but it is nevertheless essential if shortages of vital products are to be avoided that every economy (consistent with the needs of their patients) should be exercised by doctors both in hospitals and in the general practitioner services in the ordering or prescribing of all substances where sulphur or sulphuric acid are used during manufacture It may not be generally known how wide a field this is Broadly speaking, the types of drugs and medical supplies concerned are antibiotics , barbiturates , bromides , citrates , preparations containing glycerine , hormones lactates , salicylates (including all forms of aspirin) , preparations containing spirit , sulphates of barium, iron, magnesium, and sodium , sulphonamides , tartrates , vitamins , dressings (most types) , and photographic hypo

World Health Organisation

Spain and the German Federal Republic have applied for admission to the World Health Organisation Their request will be placed on the agenda of the fourth World Health Assembly opening in Geneva on May 7 Another candidature, that of Japan will be examined at the same time Total membership of W.H O is now 76, including Southern Rhodesia as an associate member Of these, 10 member States are considered as inactive

Osler Club of London

The following officers have been elected president, Mr Zachary Cope , vice presidents, Dr A P Cawadias and Mr Geoffrey Keynes general secretary, Dr W R Bett , librarian, Mr J Thornton treasurer, Dr A White Franklin , members of council Mr W J Bishop Dr L Carlyle Lyon, and Mrs Hipkins The club is open to students, doctors, and medical library workers, and further information may be obtained from the secretary 11, the Avenue, Chiswick, W 4

Kathleen Schlesinger Fellowship

The Medical Research Council invite applications for this whole time fellowship (£700–£1000 per annum), tenable at the National Hospital for Diseases of the Nervous System, Queen Square, London, W C 1, for work on cysts of the brain Preference will be given to candidates who elect to work on the mechanisms underlying degenerative processes affecting the brain Further information may be had from the secretary of the council, 38, Old Queen Street, London, S W 1, to whom applications should be sent not later than May 31.

Election to G M C

Last Tuesday voting papers were sent to all doctors registered as residing in England Seven vacancies are to be filled by direct representatives of the medical profession in England and these are the following eight candidates to choose from

NOMINEES OF BRITISH MEDICAL ASSOCIATION

Dr R H B Barrow of Winchester member of the G.M.C. and of the central ethical committee of the B.M.A for 6 years.

Dr J A Brown of Birmingham member of the G.M.C since 1947 chairman of the representative body 1949–50 and member of G M.C of the B M.A

Dr O C Carter of Bournemouth member of the G M.C since 1949 and member of council of the B M.A

Dr H Guy Dain F R.C.S of Birmingham member of the G M C since 1934 chairman of the representative body of the B M A 1937–42 and of council of the B M A 1943–49

Dr E A Gregg of London member of the G M.C since 1942, chairman of the representative body of the B M.A 1948 chairman of council of the B M.A since 1949 and chairman of the Insurance Acts Committee 1937–48

Dr J T Ingram F R.C P of Leeds chairman of the Leeds Division of the B M.A 1941–44 chairman of the Leeds Joint Council of Industrial Medicine 1942–47 and clinical subdean of Leeds Medical School since 1945

Dr N E Waterfield O B E F R.C.S of Little Bookham, Surrey member of the G M.C since 1945 chairman of the central ethical committee of the B.M A 1935–47 and member of council of the Medical Defence Union

INDEPENDENT CANDIDATE

Dr Thomas Beaton O B E F R C.P of Portsmouth physician-superintendent of St James Hospital and director of mental health services Portsmouth as well as on medicine Very many St Thomas's men will remember his ward rounds, and in a farewell note the *St Thomas's Hospital Gazette* spoke of his untiring industry as a physician and a teacher "Encyclopædic in his knowledge, practical in its application at the bedside, watchful and critical of the newer movements, he was perhaps a trifle cynical with those of lesser clay" He examined for the Universities of Birmingham and London, and for the Conjoint Board

---

[1] London J & A Churchill 1951 Pp 2768 £3 3s

His retirement from St Thomas's in 1926 did not mean retirement from hospital practice, and he continued to act as physician to the Royal Masonic Hospital and to the London Fever Hospital His experience there was expounded in the admirable section on the infectious fevers which he contributed to Price's *Textbook of the Practice of Medicine* He also chose a subject from this specialty—Complications of the Specific Fevers—for the Lumleian lectures which in 1932 he delivered to the Royal College of Physicians He had been elected F R C P in 1906, and he later served the college as councillor He was also a member of the court of assistants of the Society of Apothecaries, and he was an honorary member of the British Pædiatric Association

R C J writes "During the greater part of Box's long career the physician had to form his own diagnosis chiefly on his own clinical observations, and in this Box was a past master He had an uncanny aptitude for recognising what was the matter with his patient But he was a difficult man to know, for he was not a good mixer Though inclined to hold himself aloof he was always ready to help those who went to him for advice All his interest appeared to centre in his work and he allowed himself little in the way of recreation and hobbies" Even in his holidays he showed the same constancy, and year after year he looked forward to his visit to the Channel Islands

In 1905 he married Miss Marian Thyer, of Bridgwater, who survives him

GÖSTA FORSSELL

TRIBUTES were paid to the memory of Gösta Forssell, the Swedish radiologist, at a recent meeting of the Swedish Medical Society[1] The speakers, who included Prof E G E Berven and Prof Aakerlund, recalled how Forssell was working with his first teacher in radiology, Thor Stenbeck, in 1899, when a case of cancer of the skin was for the first time successfully treated with radium To cure this case 150 treatments were given in the course of nine months As Professor Berven points out, a similar case now needs only one treatment, lasting about one minute

[Nordisk Medicin

With his gift for organisation as well as for original research, Forssell changed radiology from a subordinate ancillary service to an independent discipline He insisted that radiology departments, both diagnostic and therapeutic, must have their own organisation, doctors, and nurses, and all the necessary equipment Under his guidance the cramped radiological quarters at the Serafimer Hospital have since 1906 developed into a chain of some 70 radiological departments, with two large central röntgen diagnosis institutes at the Serafimer and Karolinska Hospitals

Radiumhemmet also owes much to Forssell It started in 1910 as a modest hospital with 16 beds, a primitive röntgen apparatus, and 120 mg of radium Today this small experimental venture has become the King Gustaf V Jubilee Hospital at the Karolinska Hospital, with its three departments, Radiumhemmet and the radiophysical and radiopathological research institutes After two years' work at Radiumhemmet Forssell in 1912 presented a report to the Swedish Medical Society on his treatment of inoperable cancer of the uterus with radium, which is now recognised as a classic in the history of radiology He showed that a high proportion of inoperable and advanced cases had improved and in some instances had become symptom free As a result of this paper a national appeal for funds was made, and more than six million Swedish crowns was collected to build and equip the present Jubilee hospital and its institutes

In 1919, Forssell founded *Acta Radiologica*, of which he remained editor till his death, and he was also the founder of the Scandinavian Association for Medical Radiology. In 1925 he attended the first International Radiological Congress in London, and it was a tribute to him, as well as to the standing of Swedish radiology, that the next international congress was held in Stockholm in 1928 Shortly after the first world war he took the initiative in creating a Swedish Association for Medical Research which received an endowment of over 100,000 Swedish crowns on his 65th birthday Last year he was elected an honorary member of the Royal Society of Medicine On the 80th birthday of King Gustaf V, Forssell was chosen to represent the nation in an address to the King—an honour which he probably valued more than any other He died on Nov 13 at the age of 71

---

[1] *Nord Med*, Feb 28 1951

Appointments

AITKEN W J, M B Glasg D P H appointed factory doctor, Ayr district

BROOKS B E M B Aberd consultant physician (physical medicine), Leytonstone and Romford hospital groups

BROWN JEAN M B St And asst M O H, St Helens

CAMERON A D C S M B Edin, D P H deputy county M O H and deputy school M O North Riding of Yorkshire

FAIRLEE JAMES, B PHARM Lond M R C S asst M O to chief M O London Transport Executive

GREGORY, JAMES, M B Manc D I H asst M O West Midlands Gas Board

JEFFERY C C F R C S consultant orthopædic surgeon, Exeter clinical area

NEWHOUSE MURIEL M B Lond, M R C P consultant general physician, Salvation Army Mothers Hospital London

PARKER, W S, M B Manc, D P H, D I H M O H and school M O, Brighton

TUDWAY, R C, M B Lond F F R, senior consultant radiotherapist Bristol, Bath, South Somersetshire and North Gloucestershire areas

Local Treasury Medical Officers

CLAY A A, M R C S Newport Pagnell, Bucks

CRAWFORD R P L R C P E, D T M & H Taynuilt, Connel and Kilchrenan Argyllshire

GRANT G B M B Durh Jarrow on Tyne co Durham

GROVES J N, D S O, M A M B Camb Ledbury Herefordshire

HANDS A H M D Lpool D T M Maghull Lancs

KENNEDY D B, M B N U I D P H Tisbury, Chilmark, and Swallowcliffe Wilts

MANNING J V M B Lpool D I H Prescot Knowsley Tarbock Green Rainhill, and Whiston Lancs

SHAW, B J, F R C S E Wednesbury and Darlaston Staffs

Births, Marriages, and Deaths

BIRTHS

CHADWICK —On April 3, in Manchester the wife of Dr T H Chadwick—a son

GUTHRIE —On April 2 at Inverness the wife of Dr G A Guthrie —a son

JOLLES —On April 4, at Northampton the wife of Dr Benjamin Jolles—a son

MUNRO ASHMAN —On April 2 the wife of Dr Donald Munro-Ashman—a daughter

SPRIGGS —On March 29 at St Andrews the wife of Dr E A Spriggs—a daughter

YATES —On April 2 at Leicester the wife of Dr Terence Yates—twin sons

MARRIAGES

DINGLEY—JENKINS —On March 31, in London, Anthony Gordon Dingley F R C S, to Margaret Elizabeth Lowther Jenkins

MELVILLE—DAVIES —On March 31 in London K E M Melville, L R C P E to Pamela Rowell Davies

MOWATT—TIERNEY —On March 24 at St. Andrews Keith Stronach Mowatt M B to Joan Brunskill Tierney

POLLOCK—SAYLES —On March 31, at Doncaster John Sprott Pollock M B to Valerie Borrill Sayles

WATSON—KEATINGE —On March 31 at Denby John Smyly Watson M B to Moira Margaret Keatinge

DEATHS

CROSS DE CHAVANNES —On April 1 at West Meon, Hants, Edward Henry Eustace Cross de Chavannes M D Lausanne wing-commander R A F retd

ROBINSON —On April 1 James Salmond Robinson B A, M B Dubl, F R C S E

RUNDALL.—On April 7 at Broxbourne Herts Laurence Rundall, M B Edin captain I M S retd

SALVAGE —On April 5 John Valentine Salvage M D Durh lieut-colonel R A M C retd

SIDDONS —On April 5 Bertram Siddons M B Edin aged 57

◆

Notes and News

THE MEDICAL DIRECTORY

a new and useful item the *Medical Directory 1951*[1] has lex to hospitals Previously it was very difficult to find pital without knowing its area Now the index refers archer to the detailed descriptions which are still arranged eas The Ministry of Pensions hospitals have been ated as a separate list Otherwise the contents are r to those of 1950 The medical practitioners listed er 79,672 against the 77,730 of last year

ISTRIBUTION OF GENERAL PRACTITIONERS

E following amendments have been made to the Medical ices Committee s classification of executive council described last year in our issues of Aug 5 (p 229) and 25 (p 545) Schedule IV contains the names of the closed

Schedule IV

ADDITIONS

on and Exeter —Torrington
ord County and City —Chipping Norton
sex West —Wittering and Itchenor Districts

DELETIONS

it and Canterbury —St Paul s Cray St Mary Cray and the
cest ward of Orpington U D

---

versity of Durham

n June 29 the honorary degree of D HY will be conferred r John Charles

versity of Birmingham

le title of emeritus director of radiological studies in the g anatomy has been conferred on Dr J F Brailsford in gnition of his services to the university

versity of St Andrews

n June 29 the honorary degree of D SC will be conferred Ir Walter Elliot F R.C.P , F.R S M.P

versity of Aberdeen

n April 5 the following degrees were conferred

D —Valerie A Cowie and Helen L D Duguid (with com dation) G B Forbes A A White
B Ch B —George Adams R A Andrew B M. Barron V Cruickshank J G Donald R. H Duncan J A G Elmslie L Jones R A Kirton, Mary R Kramer, Hectorina Matheson e M Oliver Moira K M. Pratt Isobel B A Shivas William ter I D Spark, R A Spark B S Stephen J G Sutherland othy M McI Sweenie Jean P Watson Marjory I K Watt I Youngson

al Faculty of Physicians and Surgeons of Glasgow

t a meeting of the faculty on April 2 with Mr Walter braith the president in the chair, the following were itted fellows of Faculty William Dawson Hamilton acher, Abraham Goldberg, Peter Glyn Griffiths (*qua* sician) , Ian Alexander McGregor (*qua* surgeon)

iety of Apothecaries of London

Dr W S C Copeman has been elected to a seat on the rt in place of Mr R Ogier Ward who has resigned J Dodds has been admitted to the freedom of the society servitude The following were admitted by redemption

Herbert Gray M L Formby H J McCurrich, H E Harding G Field D G C Tasker M H Harmer W N Mascall S A on Hilda Lloyd K M A Perry, A J Amos C Horace Gray Kiernander, W F Dunham G H Newns S Cochrane Shanks P Lambert

R K Franklin has been bound apprentice to R H. Franklin seven years The following have been granted the .S.S.A upon examination

E Hazell W Friis I W Turnbull J R C Wallace H G cter T R P Coakley G C Stavrakis R F Mottram C E A omas (C B Alvey P D Black P Howe J E K. Moore B L eze K M Stone A Ross A. E H Safeda D G Philipps scountess St Davids) F J Covill G Dixon P B Hughes C A M. Brocchi W M Cornelius

The diploma in industrial health has been awarded to G Hunter

ichton Fellowships

Fellowships at the Crichton Royal, Dumfries, have been arded to Dr P Rowsell and Dr J Harrington

Central Council for the Care of Cripples

The annual general meeting of the council will be held on Friday, April 20, at 2 45 P M in the Goldsmiths' Hall, Cheapside, London, E C 2, when Mr Hilary Marquand, the Minister of Health, will speak.

Shortage of Sulphur

The Ministry of Health has issued the following statement "Doctors will be aware of the shortage of sulphur and sulphuric acid, both of which are indispensable to the manufacture of a wide range of medical supplies Every effort will be made to maintain supplies at as high a level as possible to meet medical needs, but it is nevertheless essential if shortages of vital products are to be avoided that every economy (consistent with the needs of their patients) should be exercised by doctors both in hospitals and in the general practitioner services in the ordering or prescribing of all substances where sulphur or sulphuric acid are used during manufacture It may not be generally known how wide a field this is Broadly speaking the types of drugs and medical supplies concerned are antibiotics, barbiturates bromides citrates, preparations containing glycerine , hormones , lactates , salicylates (including all forms of aspirin) , preparations containing spirit , sulphates of barium, iron, magnesium, and sodium , sulphonamides, tartrates, vitamins, dressings (most types) , and photographic hypo

World Health Organisation

Spain and the German Federal Republic have applied for admission to the World Health Organisation Their request will be placed on the agenda of the fourth World Health Assembly opening in Geneva on May 7 Another candidature, that of Japan, will be examined at the same time Total membership of W.H O is now 76 including Southern Rhodesia as an associate member Of these 10 member States are considered as inactive

Osler Club of London

The following officers have been elected president, Mr Zachary Cope , vice presidents Dr A P Cawadias and Mr Geoffrey Keynes , general secretary Dr W R Bett , librarian, Mr J Thornton treasurer, Dr A White Franklin , members of council, Mr W J Bishop, Dr L Carlyle Lyon, and Mrs Hipkins The club is open to students, doctors, and medical library workers and further information may be obtained from the secretary, 11, the Avenue, Chiswick, W 4

Kathleen Schlesinger Fellowship

The Medical Research Council invite applications for this whole time fellowship (£700–£1000 per annum), tenable at the National Hospital for Diseases of the Nervous System, Queen Square London, W C 1, for work on cysts of the brain Preference will be given to candidates who elect to work on the mechanisms underlying degenerative processes affecting the brain Further information may be had from the secretary of the council 38, Old Queen Street, London, S W 1, to whom applications should be sent not later than May 31.

Election to G M C

Last Tuesday voting papers were sent to all doctors registered as residing in England. Seven vacancies are to be filled by direct representatives of the medical profession in England and these are the following eight candidates to choose from

NOMINEES OF BRITISH MEDICAL ASSOCIATION

Dr R H B BARROW of Winchester member of the G M.C and of the central ethical committee of the B.M.A for 6 years.

Dr J A BROWN of Birmingham member of the G.M.C since 1947 chairman of the representative body 1949–50 and member of G M.C of the B M.A

Dr O C CARTER of Bournemouth member of the G M.C since 1949 and member of council of the B.M.A

Dr H GUY DAIN F R.C.S of Birmingham member of the G M C since 1934 chairman of the representative body of the B M.A 1937–42 and of council of the B.M.A 1943–49

Dr E A GREGG of London member of the G.M.C since 1942, chairman of the representative body of the B M.A 1948 chairman of council of the B M.A since 1949 and chairman of the Insurance Acts Committee 1937–48

Dr J T INGRAM F R.C P of Leeds chairman of the Leeds Division of the B M.A 1941–44 chairman of the Leeds Joint Council of Industrial Medicine 1942–47 and clinical subdean of Leeds Medical School since 1945

Dr N E WATERFIELD O B E F R C.S of Little Bookham, Surrey member of the G.M.C since 1945 chairman of the central ethical committee of the B.M.A 1935–47 and member of council of the Medical Defence Union

INDEPENDENT CANDIDATE

Dr THOMAS BEATON O B F F R.C.P of Portsmouth physician-superintendent of St James Hospital and director of mental health services Portsmouth

---

[1] London J & A Churchill 1951 Pp 2763 £3 3s

Course in Plastic Surgery

A weekend course on the immediate application of plastic principles to the treatment of injury is being held at Rooksdown House, Basingstoke, on June 16 and 17 The course is open only to registrars from the eastern area of the South West Metropolitan Region.

Congress of Anæsthetists

The 26th annual Congress of Anæsthetists will be held in London from Sept 3 to 7, at B M.A House Tavistock Square, W C 1 The manufacturers' exhibition of drugs and apparatus will be at St Pancras Town Hall, N W 1 Copies of the programme may be had from the congress secretary, 25, Park Crescent, W 1

Course on Traumatic Surgery

The institute of accident surgery at the Birmingham Accident Hospital is holding a weekend course on April 20, 21, and 22 Further particulars may be had from the director of postgraduate medical studies, Medical School, University of Birmingham

South African Medical Services

Dr Karl Bremer, the new South African minister of health, speaking at a meeting on March 31, advocated the creation of a central organisation for medical services in the Union At present various local bodies all had their own medical services, which led to overlapping Thus some doctors were employed in hospitals run by the provincial administration, while the government also had their district surgeons, as well as the medical staff they employed at health centres, asylums, and tuberculosis and other hospitals Dr Bremer suggested that the large permanent staff already employed by the State should form the nucleus of a combined State medical service

Awards to Blood-donors

On April 3 the Princess Royal visited the Royal College of Surgeons to present badges to 85 blood-donors, each of whom had given blood at least 50 times The presidents of the three Royal Colleges and the Minister of Health were also present

In a broadcast on April 5 Mr Hilary Marquand, the Minister of Health appealed for 200,000 more volunteers for the Blood Transfusion Service He described his own experience as a recent donor, because, he said, "I thought you'd like to know at first hand that there is no pain, no impairment of activity at all, and that if you re one of those people who happen to dislike the sight of blood you need never see it at all from start to finish All you need do is to send a postcard to the nearest centre and give them your name You'll find the address at your post office, or in the telephone book under Blood Transfusion Service"

London School of Hygiene and Tropical Medicine

In his first annual report as dean of the school, Dr Andrew Topping says that in order to maintain contact with old students an association is to be formed which may be joined by anyone who has followed a recognised course of instruction there 'The large numbers of medical men and women from overseas enrolling for the courses in public health and in tropical medicine make it advisable to continue, and in fact extend, the visits abroad of members of the staff who are able to appreciate what is being done in various countries and to assess their needs" Unfortunately, restrictions have prevented the developments contemplated in 1948 when Winches Farm, St Albans was acquired for the establishment of a field station, "but some work has been done there and it is hoped that in 1951 further funds may become available so that the cramped conditions in the school building may be relieved and the important experimental work which has already been planned may be undertaken"

The report expresses great regret at the resignation of Sir George Elliston from the court of governors and the board of management Appointed to the board in 1943, he succeeded Sir Holburt Waring as chairman in 1944 during the difficult period of the war and the trying years of post war reconstruction, he "served the school with unparalleled devotion and members of the staff who sought his help and advice will never forget his unfailing kindness" His place has been taken by Sir Archibald Gray, F R C.P, and at the annual meeting of the court of governors on March 28, Sir Cosmo Parkinson was elected chairman of the court in succession to Lord Milverton, who has resigned

Diary of the Week

APRIL 15 TO 21

Monday, 16th

ROYAL EYE HOSPITAL, St George's Circus Southwark, S.E.1
5 P M Prof Arnold Sorsby Medical Ophthalmology

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray's Inn Road, W C 1
5 P M Dr D B Fry Speech and Hearing

INSTITUTE OF OPHTHALMOLOGY Judd Street W C 1
5 30 P M Mr C D Shapland Recent Advances in the Treatment of Detachment of the Retina

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S E 5
5 30 P M Dr E Stengel Lecture demonstration

HUNTERIAN SOCIETY
8 30 P M (Talbot Restaurant London Wall E C 2) Mr C Robert Rudolf Hunteriana

Tuesday, 17th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
5 P M Dr A R French Medicolegal Aspects of the Practice of Otorhinolaryngology

PADDINGTON MEDICAL SOCIETY
8 45 P M (St Mary's Hospital W 2) Dr B Gottlieb 'Cortisone and A C T H in Modern Treatment.

SOCIETY FOR THE STUDY OF ADDICTION
4 P M (11, Chandos Street W 1) Dr G W Smith Looking Back Fifty Years (Presidential address.)

UNIVERSITY OF EDINBURGH
4 30 P M (University New Buildings) Prof. J S Browne (Montreal) Studies on A C T H and Cortisone in Disease. (Macarthur postgraduate lecture.)

Wednesday, 18th

ROYAL EYE HOSPITAL
5 30 P M Mr J F P Deller The Measurement of Axial Length in the Living Eye

INSTITUTE OF OPHTHALMOLOGY
5 30 P M Prof D Slome Physiology of Vestibular Nystagmus.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28 Portland Place, W 1
3 30 P M Dr W T Donovan Health Problems in Densely Populated Areas.

UNIVERSITY OF GLASGOW
8 P M (Department of Ophthalmology) Dr A. Lindsay Anomalies of the Optic Disc

Thursday, 19th

ROYAL EYE HOSPITAL
5 P M Dr T H Whittington Myopia—Retinoscopy

ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S W 1
4 30 P M Dr Desmond Curran Psychiatry lecture-demonstration

BRITISH INSTITUTE OF RADIOLOGY 32, Welbeck Street W 1
8 15 P M Prof W V Mayneord D SC Radiation Protection (Silvanus Thompson lecture)

LONDON COUNTY MEDICAL SOCIETY
3 P M (St Olave's Hospital, Lower Road, Rotherhithe S.E.16.) Clinical meeting

UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee.) Prof. T N A. Jeffcoate Intersexuality

Friday, 20th

FACULTY OF RADIOLOGISTS
2 15 P.M *Diagnosis section.* (Royal College of Surgeons Lincoln's Inn Fields, W C 2) Dr J B King Sinusitis and Bronchiectasis

BRITISH INSTITUTE OF RADIOLOGY
6 P.M *Medical members* Mr J N Barron Mr N Veall Use of Radioactive Isotopes in Problems Connected With Plastic Surgery Mr Fenton Braithwaite Observations on the Vascular Channels of Tubed Pedicles Using Radioactive Sodium

INSTITUTE OF OPHTHALMOLOGY
5 30 P.M Dr H Davson Nervous Aspects of the Control of the Intra-ocular Pressure

BRITISH ASSOCIATION OF PHYSICAL MEDICINE
11 30 A M (Middlesex Hospital, W 1) Dr A C Boyle, Mr H F Cook, Dr D L Woolf Micro waves (Opening of 2 day meeting)

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION
8 30 P M (Royal Free Hospital School of Medicine W C 1) Dr A. Gibson Clinical Aspects of Modern Bacteriology

Saturday, 21st

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
11 A M (Lenham Sanatorium Lenham Kent) Dr R Livingstone, Dr E R Jones Thiosemicarbazone Dr Ruth Dingley Primary Lesions

---

Dr Ronald Woolmer senior lecturer in anæsthetics in the University of Bristol, is going to Copenhagen this month as senior instructor in charge of the course in anæsthesiology set up by the World Health Organisation The course is open to postgraduates from all European countries

MIND AND MATTER*

W RUSSELL BRAIN
D.M Oxfd, F.R C P
PHYSICIAN TO THE LONDON HOSPITAL

THE problem of mind and matter has been discussed for over 2000 years, and you may well have come here in a mood of gentle scepticism as to the possibility of hearing anything new upon this topic, but I accepted the invitation to speak about it because it seemed to me timely to review the question in the light of two developments of thought which during the last twenty five years have contributed to put it in a new light The first is the great increase in our knowledge of neurophysiology and especially of the electrophysiology of the nervous system The second is the contribution of those philosophers who are particularly concerned with semantics I think they often go too far in supposing that problems are purely verbal, but they have rendered a great service by directing our attention to the large part which verbal confusions play in creating difficulties and have thereby clarified our thought That they have not achieved more is, I think, due to the fact that with the notable exceptions of Eddington (1939), Whitehead (1929), and Russell (1948), to whom, as you will readily detect, I owe much, no modern philosopher seems aware of the importance of the part played by the body in perception and thought, and current philosophies of perception either dispose of such questions as merely verbal or are satisfied with armchair solutions of extreme naïveté

Before I go further let me add two words of explanation This is at best a difficult subject, and I believe that if we are to understand even how the difficulties arise we must depart somewhat from the timeworn paths of approach You must be patient, therefore, if some of the earlier part of this lecture seems to have little relevance to the main problem its significance will appear later Secondly, in a broad survey such as I am now attempting there will not be time to discuss every point in detail, to deal with the history of the subject, or to counter opposing arguments To some extent I can only present conclusions, but I hope to be able to make it clear how they have been reached

THE PHYSIOLOGICAL CONDITIONS OF SENSATION

Let us begin by considering the use of the words "mind" and "matter" Evidently people think that they mean something when they use the words, and they do not think that they are in the habit of using them for the same events Going no deeper than the verbal level, if the distinction between the words "mind" and "matter" means anything we should try to understand what it means, and if it does not mean anything we should be clear about that also

Philosophers and other thinking people who have assumed that there is some distinction between mind and matter have been chiefly concerned with two different questions (1) What is the relationship between those events we call mental and the collection of matter which we call our brains, and (2) Are the things which we perceive with our senses wholly material or, as some have thought, wholly mental, or partly one and partly the other? As we shall see, these questions are intimately related to one another

People sometimes put it in this way Is the matter *really* mental?" or Is the mind *really* a manifestation of the matter of which the brain is composed?" Evidently there is something which they mean by matter which, at first sight at any rate, is different from mind, and conversely—whatever these two terms may turn out to represent when we get to know more about them

Let us, without attempting to define matter, look at some instances of the use of the term If we ask someone to give us some examples of matter he might say that it consists of solids, liquids, and gases—the earth, water, and air of the earlier philosophers—or that it exists in the form of tables and chairs, muscles and bones, nerves and brains If we then say "What do you mean by the mind, or what would you regard as mental?" he might find it more difficult to reply Thought would certainly seem to be mental, for thinking is perhaps the most characteristic function of the mind, as we use the term Feeling and willing? Yes, those would probably also be regarded as mental. But what about sensation? Is there something mental about colours, touches, and sounds? Here we should begin to get into a difficulty, in fact we should find ourselves at once involved in the ancient controversy between the idealist and the realist On the one hand if we regard sensations as a state of consciousness we can make out a case for treating them as mental, assuming that the mind is somehow involved in consciousness, but on the other hand the colour of the table certainly seems to be in some way part of the table, though the sound of a bell is not in quite the same way part of the bell and a touch on my hand seems to come into yet another category, because it is not exactly part of the object touching me nor can it be described as part of my hand

If instead of talking about isolated sensations we think of a solid object which I hold in my hand, what I learn about the object must reach me in the form of touches and pressures, and feelings of heat or cold, together with information derived from the posture of my fingers and the degree of separation of their palmar surfaces from the palm of my hand Are all these sensations mental or are they part of the object? If I feel that a stone in my hand is cold I do so only because it causes a fall of temperature in my skin which makes my fingers colder than they were and excites certain nerve endings Yet I usually speak of the stone and not of my hand as being cold, though I can remember a small child putting his hand in the river and saying "I am going to feel my hand in the water"

Let us leave this question on one side for the moment and turn now to what we call the world of matter How do we know about the tables and chairs, about other people's bodies and brains, and, for that matter, about our own bodies and brains? Let us observe what happens when somebody else, whom we will call A, sees a colour or hears a sound

The physical stimulus, as we call it, excites the appropriate receptor organ and this in turn starts an electrical impulse in the corresponding afferent nerve These nerve impulses differ somewhat in minor details, including the rate at which they are conducted towards the central nervous system, but they are substantially alike and no neurophysiologist believes that differences in the nature of the impulses conducted by the afferent nerves correspond to differences in the kind of sensation which they lead us to experience Thus merely from recording the electrical disturbances which accompany the passage of a nerve impulse and observing their characteristics it is impossible to say whether the sensation with which they are concerned is one of sight, hearing, sound, taste, or touch, and, indeed, it is not until such nerve impulses reach what may be called their end stations, whether these are in the cerebral cortex or the optic thalamus, that we experience a sensation at all It would seem, therefore, that what determines our awareness of a sensation, and also its nature, is the arrival of a nerve impulse, or more probably a series of nerve impulses at the appropriate end station in the brain

We have other evidence in support of this view, for clinical neurology teaches us that it is not necessary for the brain to be excited by the arrival of a nerve impulse from the appropriate sensory organ in order that we may experience the corresponding sensation. The same thing will happen if the appropriate area of brain is excited in some other way. Thus we know that if one of the sensory areas of the cortex is stimulated by the electrical discharge which underlies an epileptic fit, or by the physiological disturbance which constitutes an attack of migraine, the patient will experience a sensation; and we know further that a very wide range of sensations, including sight, smell, sound, taste, touch, and others, can all be reproduced by exciting the appropriate area of the cortex, some of them even by the surgeon using an electrical stimulus. It is true that the sensations produced in this way are usually of a somewhat crude kind; but then the stimulus is of a crude kind; and, when once the principle has been accepted that delivery of a stimulus which is capable of evoking a response in the sensory cortex will produce a sensation, there is no reason to doubt that if we were able to deliver a more refined and complicated stimulus, complicated both in its spatial and its temporal organisation, we could produce more complex kinds of sensation.

---

* A British Postgraduate Medical Federation lecture

What follows from this? We have seen that a physical stimulus excites a sensory receptor, and thus a nerve impulse; that the nerve impulse, which is in no way like the original physical stimulus, sets going a disturbance in the cerebral cortex which is probably in certain respects unlike the nerve impulse and certainly is quite unlike the original physical stimulus; and that it is upon this cortical disturbance that sensation depends. Hence the cortical state which constitutes the physical basis of a sensation is always quite unlike the physical stimulus which impinges upon the body and which has been in one way or another directly set in motion by the external object which we experience. Thus the relationship between the cortical state which underlies the sensation and the physical object of which that sensation makes us aware is merely that the cortical state is the last of a series of events caused by the physical stimulus. Whatever the relationship between the cortical state underlying a sensation and the corresponding awareness of the sensation in consciousness it would seem to follow that the sensation must be quite unlike the physical stimulus originating in the outside world and exciting the sense organs.

It follows also that the experience of a given sensation must always be later in time than the physical event which initiates it. Indeed it must be later in time than the excitation of the receptors on the surface of the body by that physical event. How much later in time than the physical event it is will depend obviously upon the distance from the body of the object concerned and the rate of propagation of the physical stimulus through the intervening medium. The speed of light is so great that only a fraction of a second intervenes between the time when a light wave is reflected from any object on the earth and the time when it strikes the eye of the observer. This interval is so short that for all practical purposes it can be neglected, and we need pay no attention to it. We behave as though we see something happening at the very moment at which it happens. We cannot do this, however, in the sphere of astronomy where years may pass between the moment at which a light wave leaves a star and that at which the eye perceives it. If it takes several years for the light from a star at which I am now looking to reach my eye, the star can no longer be in the position at which I see it; and, indeed, if it had ceased to exist in the interval between the present moment and that at which the light wave left it I should have no means of discovering the fact. Owing to the relatively slow speed of sound this anomaly may become obvious even on the surface of the earth when sound is concerned. The sound of a jet plane comes from a different point in the sky from that at which we see the plane.

So we reach the idea that the only necessary condition of A's seeing colours, hearing sounds, and experiencing his own body is that the appropriate physiological events shall occur in the appropriate areas of his brain. If these are of the right kind sensory experience will occur irrespective of whether they are caused by a local cerebral disturbance or by a long chain of events originating in the external world. But if we ask A where the events he is experiencing are, where he sees the colours, hears the sounds, or feels part of his body, he does not point to his brain, he points to or describes some region of the external world or some part of his body itself external to his brain.

Here, then is a problem. An event in A's brain causes him to experience something—e.g., see a colour outside his brain. This is what neurologists and psychologists often call "projection," but this is not a very good name for it, for projection seems to imply throwing something from one place to another, but the colour A sees is never anywhere else but where he sees it. He is not aware of any process that could rightly be called projection. The general idea that sensations are in this way as it were manufactured by the brain and somehow or other manage to get outside it into the external world is known as "physiological idealism."

Now let us look at the external world as A perceives it. It is hard or soft, coloured, scented, tasty, composed of objects which have position and move about. As we have seen, the time relationships of A's external world are peculiar. If an event in it causes a sound, he hears it, not when the event occurs, but when the sound, as we say, reaches his ear, or, more precisely, a little later, when the nerve impulse from his ear has travelled as far as the auditory cortex of his brain. Similarly, he sees an object, not when the light wave leaves it, but when the visual nerve impulse has reached his brain, and in the astronomical world this may be a thousand years after the event which originates the light wave.

Consider two stars, one 500 and one 1000 light years away. A sees them both at the same time, but the events he perceives on the stars—i.e., the emission of light waves—happened 500 years apart. So events which A perceives simultaneously are not necessarily simultaneous. In fact A's perceptual view is caused by events stretching away into the past in proportion as they are distant from him in space, and which are on one time scale for vision and another time scale for hearing, in proportion to the differences between the speeds of sound and of light.

What about the body? Surely we have a direct and immediate awareness of that? No, the same principle applies. All A's perception of his body is awareness of its immediate past, for he is not aware of any bodily event until after the interval of time necessary for a nerve impulse to travel from the part of the body in which it occurs to his brain.

THE PERCEPTUAL "WORLD" AND THE PHYSICAL "WORLD"

Hence it would seem that A has to deal with two "worlds"—as we may call them for the moment. There is the "world" of his perceptions and another "world" which differs from the "world" he perceives in various respects, one of the most important of which is that events in this other "world" occur at different times from those at which A perceives them. There is one exception to this—his brain; but here we are dealing with a correlation of a different order, for though it is probably true to say that when an event in A's brain causes a conscious experience the two occurrences are simultaneous, yet in such circumstances A is never aware of an event in his brain but of an event somewhere else I propose to distinguish these two "worlds" for the moment by calling them A's perceptual "world" and the physical "world" But, you will say, if A's knowledge of any "world" is limited to his perceptions, how does he ever discover that there is any other "world"? He does so by a process of inference operating in two ways

(i) *He accepts the observations of other people* Almost the whole of our knowledge of the correlation between sensation and brain function occurs to us in this way We stimulate the brain and ask the patient for his sensations or we ask about sensations and the effects produced upon them by disease and then study the brain after death But we can use the sensations of other people in another way—e g, by using another person as an observer of an event and comparing his observations with our own.

(ii) *He can carry out experimental observations* In practice he profits by the observations of scientists, but they are of a kind which given the requisite apparatus and skill he could carry out for himself For example he sees a man hitting something with a hammer He walks away and notices that he hears each blow at an increasing interval after he sees it occur From this he infers the speed of sound Complex physical apparatus enables physicists to infer the speed of light It follows that from the "world" we perceive we are able to infer a 'world' of events of which we are not able to have any more direct knowledge

Each of us has his own perceptual "world" A's 'world" and mine are different both in time and in content If A stands half way between me and a source of sound he hears the sound at a different time from me, hence his perceptual "world" contains a sound when mine does not, and vice versa Similarly A's perceptual "world" may contain a phantom limb or a toothache, which I cannot perceive. But if our inferences are made according to the appropriate rules we shall all agree about the physical "world" Thus there is only one physical 'world," but as many perceptual "worlds" as there are observers.

At this point let us pause to see how philosophical problems may arise out of verbal confusions in describing the facts of which I have just given an account

One source of confusion arises from the fact that we do not in everyday life need to distinguish between our own perceptual "world" and the physical "world" When I see a table, I do not need to distinguish a perceptual table from a physical table, nor when I speak of a table do I need to specify whether I am referring to one or the other or both In fact I pass from one to the other and use the same term for both indifferently

Now we have seen that A's perceptual "world" and my perceptual "world" are entirely distinct, but that we share the same physical "world," so when A and I talk about a table, all goes well as long as it is not necessary to distinguish between them But suppose that A suffers from hallucinations and declares that he sees a table when neither I nor anyone else can see one It is useless to try to persuade A that he is not seeing a table, because his experience is exactly the same as when he has seen a table in the past In other words there exists a table in A's perceptual "world," but there is no table in the physical world" in the appropriate situation and therefore there is no table in the perceptual "world" of any normal person In other words the table in A's perceptual "world" is not caused by a physical table but by something else, and normally a table *in the perceptual "world" is caused by a physical table.*

Hughlings Jackson (1931) makes this point very clearly when he describes a patient who was a cabman and who thought that his bed was a cab Hughlings Jackson said

> 'This patient saw a cab, had that image strongly projected,' his objective state, at a time when I saw a bed, when I had that image strongly 'projected,' my objective state It is of no avail for trustworthy witnesses to assert that the patient '*could not have seen*' a cab, because there is no cab present, and therefore, that the patient 'only fancied,' &c that he saw one Something, not himself, 'got out of' himself the image cab, 'out of' the bystander the image bed It might be said that this doctrine confuses reality and unreality But what reality and whose reality? The image cab was the patient's reality, the image bed was the healthy bystander's reality"

The age long controversy between the realist and the idealist in the sphere of perception is greatly simplified if we realise the part which words play in it If we ask whether the colour of a table is part of the table the answer is "Yes" if by table we mean the table in the perceptual "world" which belongs to each of us, but it is "No" if we mean the table in the physical "world" which is common to all of us Let us suppose that I see a table, decide that it is in the wrong place, and proceed to move it It is true to say that in this process I am aware of what are sometimes called sense data—that is to say colours, touches, pressures and so on It is also true to say that I perceive a physical table We should normally prefer to say that I moved the table rather than that I moved my sense data, but that is a matter of usage We have, in fact, two different ways of describing the same events. No difficulty will arise as long as we remember this, but there will be much confusion if we use the two methods indiscriminately

PERCEPTION AS SYMBOLICAL REPRESENTATION

What, then, is the relationship between them? What is the connection between what I have called a table in my perceptual "world" and a table in the physical "world"? The answer I think is, as I have suggested in more detail elsewhere (Brain 1951), that "if at least what the philosophers call secondary qualities, such as smells sounds, colours, and so on are quite unlike the physical stimuli which give rise to them, then we must regard them as symbols of physical reality and say that the receptive function of the cerebral cortex is to provide us with a symbolical representation of the external world, not only distinguishing objects by their qualities, but also conveying to us the spatial relationships which exist between them, and at the same time giving us similar symbolical information about our own bodies and their relation to the external world"

Let us apply these ideas to the simple experience of seeing a red light Making use of conceptual symbols I know that waves of a certain wave length and frequency start at a certain spot and pass through space to my retina, there initiating a series of impulses of quite different frequency which pass along my visual pathways and set up a disturbance in my visual cortex I then see the red light The red light in my perceptual "world" is a symbolical representation of the events in the physical "world" of which a certain wave length and frequency are the conceptual symbols, but the events in my cerebral cortex which cause me to see the red light are quite different physically from red light itself My perceptual "world" therefore is a kind of map It is not identical with the physical 'world" any more than a map is identical with the country which it represents, but it is able to symbolise it because events in my perceptual "world" *stand for* events in the physical "world"

To some people this idea is difficult because our representation of the physical "world" is a three dimensional one, and they find it hard to understand how each of us can have his own three dimensional perceptual 'world" which is yet different from the three dimensional physical "world" It may make this idea easier to grasp if we go back to our analogy of the map It is true that an ordinary map represents in two the brain to be excited by the arrival of a nerve impulse from the appropriate sensory organ in order that we may experience the corresponding sensation. The same thing will happen if the appropriate area of brain is excited in some other way. Thus we know that if one of the sensory areas of the cortex is stimulated by the electrical discharge which underlies an epileptic fit, or by the physiological disturbance which constitutes an attack of migraine, the patient will experience a sensation; and we know further that a very wide range of sensations, including sight, smell, sound, taste, touch, and others, can all be reproduced by exciting the appropriate area of the cortex, some of them even by the surgeon using an electrical stimulus. It is true that the sensations produced in this way are usually of a somewhat crude kind; but then the stimulus is of a crude kind; and, when once the principle has been accepted that delivery of a stimulus which is capable of evoking a response in the sensory cortex will produce a sensation, there is no reason to doubt that if we were able to deliver a more refined and complicated stimulus, complicated both in its spatial and its temporal organisation, we could produce more complex kinds of sensation.

What follows from this? We have seen that a physical stimulus excites a sensory receptor, and this a nerve impulse; that the nerve impulse, which is in no way like the original physical stimulus, sets going a disturbance in the cerebral cortex which is probably in certain respects unlike the nerve impulse and certainly is quite unlike the original physical stimulus; and that it is upon this cortical disturbance that sensation depends. Hence the cortical state which constitutes the physical basis of a sensation is always quite unlike the physical stimulus which impinges upon the body and which has been in one way or another directly set in motion by the external object which we experience. Thus the relationship between the cortical state which underlies the sensation and the physical object of which that sensation makes us aware is merely that the cortical state is the last of a series of events caused by the physical stimulus. Whatever the relationship between the cortical state underlying a sensation and the corresponding awareness of the sensation in consciousness it would seem to follow that the sensation must be quite unlike the physical stimulus originating in the outside world and exciting the sense organs.

It follows also that the experience of a given sensation must always be later in time than the physical event which initiates it. Indeed it must be later in time than the excitation of the receptors on the surface of the body by that physical event. How much later in time than the physical event it is will depend obviously upon the distance from the body of the object concerned and the rate of propagation of the physical stimulus through the intervening medium. The speed of light is so great that only a fraction of a second intervenes between the time when a light wave is reflected from any object on the earth and the time when it strikes the eye of the observer. This interval is so short that for all practical purposes it can be neglected, and we need pay no attention to it. We behave as though we see something happening at the very moment at which it happens. We cannot do this, however, in the sphere of astronomy where years may pass between the moment at which a light wave leaves a star and that at which the eye perceives it. If it takes several years for the light from a star at which I am now looking to reach my eye, the star can no longer be in the position at which I see it; and, indeed, if it had ceased to exist in the interval between the present moment and that at which the light wave left it I should have no means of discovering the fact. Owing to the relatively slow speed of sound this anomaly may become obvious even on the surface of the earth when sound is concerned. The sound of a jet plane comes from a different point in the sky from that at which we see the plane.

So we reach the idea that the only necessary condition of A's seeing colours, hearing sounds, and experiencing his own body is that the appropriate physiological events shall occur in the appropriate areas of his brain. If these are of the right kind sensory experience will occur irrespective of whether they are caused by a local cerebral disturbance or by a long chain of events originating in the external world. But if we ask A where the events he is experiencing are, where he sees the colours, hears the sounds, or feels part of his body, he does not point to his brain, he points to or describes some region of the external world or some part of his body itself external to his brain.

Here, then is a problem. An event in A's brain causes him to experience something—e g, see a colour outside his brain. This is what neurologists and psychologists often call "projection," but this is not a very good name for it, for projection seems to imply throwing something from one place to another, but the colour A sees is never anywhere else but where he sees it. He is not aware of any process that could rightly be called projection. The general idea that sensations are in this way as it were manufactured by the brain and somehow or other manage to get outside it into the external world is known as "physiological idealism."

Now let us look at the external world as A perceives it. It is hard or soft, coloured, scented, tasty, composed of objects which have position and move about. As we have seen, the time relationships of A's external world are peculiar. If an event in it causes a sound, he hears it, not when the event occurs but when the sound, as we say, reaches his ear, or, more precisely, a little later, when the nerve impulse from his ear has travelled as far as the auditory cortex of his brain. Similarly, he sees an object, not when the light wave leaves it, but when the visual nerve impulse has reached his brain, and in the astronomical world this may be a thousand years after the event which originates the light wave.

Consider two stars, one 500 and one 1000 light years away. A sees them both at the same time, but the events he perceives on the stars—i e., the emission of light waves—happened 500 years apart. So events which A perceives simultaneously are not necessarily simultaneous. In fact A's perceptual view is caused by events stretching away into the past in proportion as they are distant from him in space, and which are on one time scale for vision and another time scale for hearing, in proportion to the differences between the speeds of sound and of light.

What about the body? Surely we have a direct and immediate awareness of that? No, the same principle applies. All A's perception of his body is awareness of its immediate past, for he is not aware of any bodily event until after the interval of time necessary for a nerve impulse to travel from the part of the body in which it occurs to his brain.

THE PERCEPTUAL "WORLD" AND THE PHYSICAL "WORLD"

Hence it would seem that A has to deal with two "worlds"—as we may call them for the moment. There is the "world" of his perceptions and another "world" which differs from the "world" he perceives in various respects, one of the most important of which is that events in this other "world" occur at different times from those at which A perceives them. There is one exception to this—his brain; but here we are dealing with a correlation of a different order, for though it is probably true to say that when an event in A's brain causes a conscious experience the two occurrences are simultaneous, yet in such circumstances A is never aware of an event in his brain but of an event somewhere else. I propose to distinguish these two "worlds" for the moment by calling them A's perceptual "world" and the physical "world." But you will say, if A's knowledge of any "world" is limited to his perceptions, how does he ever discover that there is any other "world"? He does so by a process of inference operating in two ways:

(i) *He accepts the observations of other people.* Almost the whole of our knowledge of the correlation between sensation and brain function occurs to us in this way. We stimulate the brain and ask the patient for his sensations or we ask about sensations and the effects produced upon them by disease and then study the brain after death. But we can use the sensations of other people in another way—e.g., by using another person as an observer of an event and comparing his observations with our own.

(ii) *He can carry out experimental observations.* In practice he profits by the observations of scientists, but they are of a kind which given the requisite apparatus and skill he could carry out for himself. For example he sees a man hitting something with a hammer. He walks away and notices that he hears each blow at an increasing interval after he sees it occur. From this he infers the speed of sound. Complex physical apparatus enables physicists to infer the speed of light. It follows that from the "world" we perceive we are able to infer a "world" of events of which we are not able to have any more direct knowledge.

Each of us has his own perceptual "world." A's "world" and mine are different both in time and in content. If A stands half way between me and a source of sound he hears the sound at a different time from me; hence his perceptual "world" contains a sound when mine does not, and vice versa. Similarly A's perceptual "world" may contain a phantom limb or a toothache, which I cannot perceive. But if our inferences are made according to the appropriate rules we shall all agree about the physical "world." Thus there is only one physical "world," but as many perceptual "worlds" as there are observers.

At this point let us pause to see how philosophical problems may arise out of verbal confusions in describing the facts of which I have just given an account.

One source of confusion arises from the fact that we do not in everyday life need to distinguish between our own perceptual "world" and the physical "world." When I see a table, I do not need to distinguish a perceptual table from a physical table, nor when I speak of a table do I need to specify whether I am referring to one or the other or both. In fact I pass from one to the other and use the same term for both indifferently.

Now we have seen that A's perceptual "world" and my perceptual "world" are entirely distinct, but that we share the same physical "world," so when A and I talk about a table, all goes well as long as it is not necessary to distinguish between them. But suppose that A suffers from hallucinations and declares that he sees a table when neither I nor anyone else can see one. It is useless to try to persuade A that he is not seeing a table, because his experience is exactly the same as when he has seen a table in the past. In other words there exists a table in A's perceptual "world," but there is no table in the physical "world" in the appropriate situation and therefore there is no table in the perceptual "world" of any normal person. In other words the table in A's perceptual "world" is not caused by a physical table but by something else and normally a table in the perceptual "world" *is* caused by a physical table.

Hughlings Jackson (1931) makes this point very clearly when he describes a patient who was a cabman and who thought that his bed was a cab. Hughlings Jackson said:

"This patient saw a cab, had that image strongly 'projected,' his objective state, at a time when I saw a bed, when I had that image strongly 'projected,' my objective state. It is of no avail for trustworthy witnesses to assert that the patient '*could not have seen*' a cab, because there is no cab present, and therefore, that the patient 'only fancied,' &c. that he saw one. Something, not himself, 'got out of' himself the image cab, 'out of' the bystander the image bed. It might be said that this doctrine confuses reality and unreality. But what reality and whose reality? The image cab was the patient's reality; the image bed was the healthy bystander's reality."

The age long controversy between the realist and the idealist in the sphere of perception is greatly simplified if we realise the part which words play in it. If we ask whether the colour of a table is part of the table the answer is "Yes" if by table we mean the table in the perceptual "world" which belongs to each of us, but it is "No" if we mean the table in the physical "world" which is common to all of us. Let us suppose that I see a table, decide that it is in the wrong place, and proceed to move it. It is true to say that in this process I am aware of what are sometimes called sense data—that is to say colours, touches, pressures, and so on. It is also true to say that I perceive a physical table. We should normally prefer to say that I moved the table rather than that I moved my sense data, but that is a matter of usage. We have, in fact, two different ways of describing the same events. No difficulty will arise as long as we remember this, but there will be much confusion if we use the two methods indiscriminately.

PERCEPTION AS SYMBOLICAL REPRESENTATION

What, then, is the relationship between them? What is the connection between what I have called a table in my perceptual "world" and a table in the physical "world"? The answer I think is, as I have suggested in more detail elsewhere (Brain 1951), that "if at least what the philosophers call secondary qualities, such as smells, sounds, colours, and so on are quite unlike the physical stimuli which give rise to them, then we must regard them as symbols of physical reality and say that the receptive function of the cerebral cortex is to provide us with a symbolical representation of the external world, not only distinguishing objects by their qualities, but also conveying to us the spatial relationships which exist between them, and at the same time giving us similar symbolical information about our own bodies and their relation to the external world."

Let us apply these ideas to the simple experience of seeing a red light. Making use of conceptual symbols I know that waves of a certain wave length and frequency start at a certain spot and pass through space to my retina, there initiating a series of impulses of quite different frequency which pass along my visual pathways and set up a disturbance in my visual cortex. I then see the red light. The red light in my perceptual "world" is a symbolical representation of the events in the physical "world" of which a certain wave-length and frequency are the conceptual symbols, but the events in my cerebral cortex which cause me to see the red light are quite different physically from red light itself. My perceptual "world" therefore is a kind of map. It is not identical with the physical "world" any more than a map is identical with the country which it represents, but it *is able to symbolise* it because events in my perceptual "world" *stand for* events in the physical "world."

To some people this idea is difficult because our representation of the physical "world" is a three-dimensional one, and they find it hard to understand how each of us can have his own three dimensional perceptual "world" which is yet different from the three-dimensional physical "world." It may make this idea easier to grasp if we go back to our analogy of the map. It is true that an ordinary map represents in two dimensions something which exists in three. Nevertheless, a map is really a structure in three dimensions since it must have some degree of thickness and you can easily have a map in which a third dimension is represented arbitrarily but conventionally by lines or colours which stand for the contour. But let us extend the analogy. Suppose that instead of a map we have a globe. Here is a symbolical representation of the whole world in three dimensions with a diameter of a few inches or one or two feet. There can be hundreds or thousands of such globes, each of them representing the earth, and there will be plenty of room for them all within the real earth. Now, each of our individual perceptual "worlds" possesses a physical basis in the physical "world"—namely, the brain. The perceptual "world" depends upon complicated events occurring in the brain and caused by other events in the physical "world." The physical events in each physical brain, therefore, underlie for each of us our three dimensional map of the physical "world." There is plenty of room, in the physical "world" for any number of brains, each of which acts as a basis of one of its representations, just as there is plenty of room in the physical earth for any number of globes each of which acts as one of its models. And there is plenty of room for the perceptual "worlds" since, though each of these represents the physical "world" in its entirety, it takes up no more room in it than is occupied by its physical basis in the brain.

Now let us pause while I try to sum up and clarify the position we have reached. There is only one world which from one point of view consists of physical events including the events in our brain. The combination of our sense organs and the nervous system has the peculiar property of creating in various ways symbolical representations of the rest of the world as a result of the impact of physical impulses coming to it from outside itself. Each of these symbolical representations is in its totality private to the observer whose consciousness is related to each particular nervous system. For the sake of convenience we often speak of this perceptual representation also as "the world." This is as valid as it is to speak of John's photograph as John; but many philosophical confusions have arisen as a result of a failure to distinguish between the world and its representation, because so often it seems natural to use the same term for both.

BRAIN AND MIND

We have now reached the crux of our problem concerning mind and matter. Experience and our reflections upon it have led us to the distinction between the physical "world" on the one hand and its perceptual representation on the other. The physical "world" consists of the subject matter of physics and corresponds in general to what people would loosely term matter. Perceptual representation must have a good deal in common with the physical "world"—for example, numerical correspondence—but it also includes much, such as its sensory qualities, which seem to have no counterpart in physics. The physical "world" is common to all observers; the perceptual representation of it is private and subjective. There are also other events which are private and subjective and seem to have much in common with perceptual representation—for example our feelings and our thoughts. Again, though these may have an underlying physical basis there is nothing like them in the "world" of physics. Many people would apply the term "mind" or "mental" to some at any rate of these subjective events. They would probably agree that thinking is mental, and possibly also feeling; but there would be more difficulty in deciding about sensation. It seems to me a mere matter of terminology as to how one employs the terms "mind" and "mental." It is, I think, more important to recognise that the one feature which all these subjective states have in common is that they are actually or potentially conscious, and the question we should next consider is what is the relationship between any of these conscious states, such as sensation, feeling, and thought, and their physical basis in the brain. Here we seem confronted with two main alternatives. We can either take the view that conscious states are not identical with physical brain states. They may be parallel with them, or caused by them, the result of interaction between brain states and something else, but they are not the same. Alternatively we can take the view that we are dealing with events of only one kind. What we call events in the physical brain are happenings about which we may have indirect knowledge inferred from our perception of other people's brains and what they tell us about their experiences, but we have direct awareness of the physical events in our own brains and when we thus perceive them we find them to be thoughts, sensations, feelings, and so on.

Let us consider the arguments for and against these two views. The theory that brain events and conscious states are two aspects of the same happenings is sometimes known as "neutral monism." The chief arguments in favour of it are that the correlation between the two is so close that we have no reason to suppose the occurrence of one without the other, and, that being so, it is a simpler and more economical hypothesis to believe that the distinction is created by our mode of thought. The arguments for dualism are negative in character. There appears to be nothing in the account which physiology gives of the nervous system which can enable us to translate brain events into states of consciousness. As Dr Johnson (1759) put it long ago, "matter can differ from matter only in form, density, bulk, motion and direction of motion: to which of these however varied or combined can consciousness be annexed?" Again, Sherrington (1940) writes: "The search in that (energy) scheme for a scale of equivalence between energy and mental experience arrives at none. The two, for all I can do, remain refractorily apart. They seem to me disparate; not mutally convertible, untranslatable the one into the other." Brain-states consist, neurophysiology tells us, of rapidly moving charges of electrical potential in highly complex chemical structures; how can these, however we look at them, ever be identified with sights and sounds, hopes and fears, falling in love, and discussing the nature of the mind?

It is worth while to point out that the difficulty upon which the dualists lay such stress exists for them in just as tough a form. For there is no doubt that changes in the physiology of the brain produce parallel and proportionate changes in consciousness. It is certainly difficult to see how a pattern of electrical impulses can *be* a pain; but it is equally inexplicable how, if a pain is a state of an independent mind, it can be made much more unpleasant by a lesion of a peripheral nerve or of the optic thalamus, or much less so by prefrontal leucotomy. The problem of the influence of nervous structure upon consciousness remains, whether it is supposed to be exerted directly or at one remove upon an intangible mind.

In conclusion I want to draw attention to the bearing of certain psychophysiological facts upon this, and then to suggest that it looks somewhat less formidable from the philosophical standpoint I adopted in the earlier part of this lecture. I have just mentioned pain. Can we imagine how the passage of electrical impulses along certain nerve fibres to the optic thalamus can result in a sensation of pain? There is evidence that it is impossible to stimulate a single pain fibre, so that even from the periphery a relationship between several fibres conducting impulses is involved in the simplest sensation. There is also evidence that an alteration in the number of pain fibres, either in the peripheral nerves, or in the pathways in the spinal cord, or in the optic thalamus itself, substantially affects the quality of the pain which is experienced Thus, *it could seem that pain is the* state of consciousness which corresponds to a certain *pattern of nerve impulses existing in space and time* There is evidence too that patterns play an integral part in our recognition of objects, in our understanding of words and sentences and in our comprehension of ideas Pitts and McCulloch (1947) have attempted to describe in mathematical terms the electrophysiological processes in virtue of which the brain renders possible the recognition of universals

TWO MODES OF KNOWLEDGE

But, you may rightly object, granting all this, granting that patterns of brain activity in space and time play an essential part in making mental processes possible, the gulf between patterns of electrical impulses and the richness and variety of states of consciousness is as wide as ever In the first part of this lecture I drew attention to what I called the *two kinds of* "world," the perceptual "world" and the physical "world," but I said that of course there is really *only one* world Now for the two kinds of world let me substitute two kinds of knowledge of the single world There is knowledge depending upon perceptual symbols, aroused by stimuli reaching the body from outside itself, and which we call perception, and there is knowledge by means of conceptual symbols derived from perception by a process of inference Our knowledge of the physical world *is* of the second kind When therefore we ask how a pattern of electrical impulses in the brain can *be* a colour what we are really saying is "How can events in the physical world for which we use conceptual symbols involving electricity be represented also by the perceptual symbol of colour?" To be puzzled by this is logically very like asking "How *on earth* can a man called William have a moustache?" The analogy, I admit, is not quite perfect, because there *is* normally no connection between being called William and having a moustache, and there is some connection between neurophysiological patterns and colours, but in the present state of our knowledge there is no explainable relationship *between their conceptual* and perceptual symbols

THE IMPORTANCE OF STRUCTURE

The view which I have been putting forward has many important and interesting *implications with* which I have not now time to deal It illuminates the difference between externality in the perceptual world and externality in the physical world which is at the bottom of the mystery of so called "projection", but those who are interested in this question will find its psycho physiological aspects discussed by Kohler (1930) and its philosophical aspects by Poincaré (undated) and Russell (1948) It throws light on the presence of somatic data in what we call the external world—see Whitehead (1929) and Sherrington (1940) The idea that objects in the perceptual world *contain subjective* elements proves to be important *for the* understanding of primitive animism, magic and art But I will confine myself *in conclusion* to a few brief comments *on the sort of world* we find ourselves in if the ideas I have been discussing are true

First, what is the distinction between *mind and matter?* This is, more perhaps than we have been accustomed to think, a question of terminology If, following *custom* we describe thought and *feeling as mental* I see no *reason to* exclude from that term any conscious state, and I would accept the definition of Russell (1948) who said "I hold that whatever we know without inference is mental" It follows that mental experiences are the events in the universe of which we have the most direct knowledge

But, you may ask, if we accept neutral monism and say that the mind and the brain are two aspects of the same thing, is not this merely old fashioned materialism *brought up to date?* But *if the stuff of the* universe that we know directly is mind, and matter is the same thing known *only by means of the conceptual symbols* created by mind, it would seem at least as reasonable to call it mind as to call it matter And matter, even crude matter, is not what it was It has turned into energy, and the atom has become a pattern and the molecule a pattern of patterns, till all the different physical substances and their behaviour have come to be regarded as the outcome *of the structure of* their primitive components But we have already met with pattern in *the nervous system,* underlying and rendering possible the most fundamental characteristics of the mind And pattern in some mysterious way possesses a life of its own, for it can survive a change in the identity of its component parts as long as its structure remains the same As a wave can move over the sea and remain the same wave, though the water of which it is composed is continuously changing, a pattern can shift over the retina and therefore over the visual cortex and remain recognisably the same pattern The pattern of our personality, though it changes slowly, remains substantially the same, though every *protein molecule* in the body, including the nervous system, is changed three times a year (Dodds 1950) The ingredients have altered but not the structure How are we to envisage the physiological patterns upon which mental activity depends? Pitts and McCulloch have employed complex mathematical formulæ to explain the physiological *basis of abstract* thought, and I do not think that any thing simpler will serve Consider what happens in the visual cortex when *we perceive a circle* As I have said elsewhere (Brain 1946), "we might expect to find that there is something circular about the *events in the* cerebral cortex, for it is these, we are told, which are 'projected' into the outside world when we perceive a circle *Nothing of the sort is true* when we perceive a two dimensional circle we do so by means of an *activity* in the brain which is halved, *reduplicated, transposed,* inverted, distorted and three dimensional." One might add that as no two brains are the same shape, the shape of the physiological disturbance is different in two people looking at the same circle So the comparatively simple process of seeing a circle cannot be explained in terms of the spatial organisation of the corresponding activity in the brain it must, presumably, depend upon the development of complex relationships of these events in space and time which we may find can be expressed only mathematically Once again it is structure, which *is all important* This world surely is very different from the world of the older materialists

One last word Our knowledge, as we have seen, is symbolic our knowledge of the external world is based on perceptions which depend upon the physical structure of the sense organs and nervous system This in itself constitutes a limit to our perceptions, and it is likely enough that *it sets bounds to our* thought also Need we believe that a nervous system evolved to facilitate action upon the physical world is *capable of presenting* the mind with *conceptual* symbols adequate for the whole of reality? He is a bold man who would claim that today

REFERENCES

Brain W R (1946) *Philosophy* 21 133

— (1951) *Brain* (in the press)

Dodds E C (1950) *Brit med J* ii 1237

Eddington A (1939) The Philosophy of Physical Science Cambridge

Jackson J H (1931) Selected Writings London vol i p 384

Johnson S (1759) The History of *Rasselas* Prince of Abissinia London

Kohler W (1930) Gestalt Psychology London

Pitts W McCulloch W S (1947) *Bull math Biophysics* 9 127

Poincaré H (undated) Science and Method London

Russell B (1948) Human Knowledge Its Scope and *Limits* London

Sherrington C S (1940) Man on His Nature Cambridge

Whitehead A N (1929) Process and Reality Cambridge

THE THIGH-NECK CLEARANCE

A SIMPLIFIED RADIOACTIVE TEST OF THYROID FUNCTION

J B Foote
M A , M B Camb
SENIOR REGISTRAR, DEPARTMENT OF CHEMICAL PATHOLOGY, WESTMINSTER MEDICAL SCHOOL

N F Maclagan
M D , D Sc Lond , M R C P , F R I C
PROFESSOR OF CHEMICAL PATHOLOGY IN THE UNIVERSITY OF LONDON, AT THE SCHOOL , HONORARY CHEMICAL PATHOLOGIST, WESTMINSTER HOSPITAL, LONDON

In 1939 Hamilton and Soley first demonstrated the use of radioactive iodine in the investigation of thyroid function Of the techniques since introduced, some are not very suitable for routine use, and others do not clearly distinguish minor variations from the normal The work has been well reviewed by Rawson (1949), Raben and Astwood (1949), Myant et al (1949), Pochin (1950), and Keating et al (1950) The more recent contributions have been concerned mainly with establishing the concept of a thyroid clearance, the theoretical advantages of which are evident from the work of Pochin and his colleagues (Myant et al 1949)

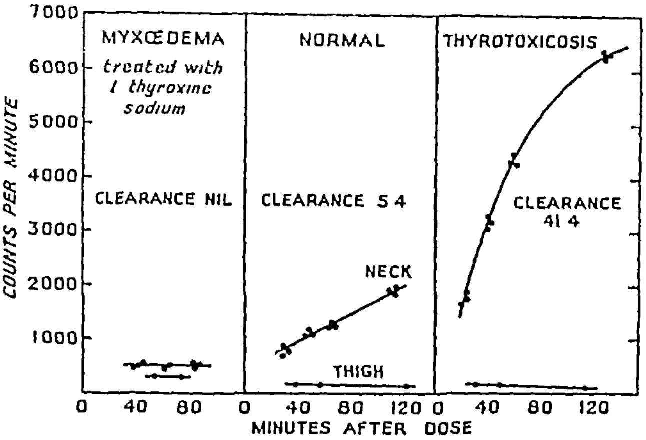


Fig 1—Typical neck and thigh counts after 30 μC of I^{131} by mouth

THIGH NECK CLEARANCE

The plasma iodide clearance as proposed by Myant et al (1949) is not very convenient for routine investigation, because it involves timed venepuncture and the measurement of absolute values of radioactivity, the investigation being spread over two days We have therefore devised a simplified clearance test, which has been reported to the Society for Endocrinology (Foote and Maclagan 1951) As was evident from previous work, changes in thyroid function are well reflected in the neck and thigh counts as shown in the typical results in fig 1 obtained after oral administration of I^{131} It will be seen here that, as one passes from myxœdema through normal to thyrotoxicosis, so the neck uptake curve steepens and the corresponding thigh counts become lower It seemed possible that thyroid function could be estimated by the use of a suitable factor derived from these data, and we have adopted a factor which consists of the rate of uptake in the neck expressed as increase of neck counts per hour, divided by the thigh count, these measurements being made at the time of maximum thigh count This we have called the "thigh neck clearance" The factor is of the nature of a clearance for it relates a rate of increase of thyroid radioactivity to a level of activity in the tissues It must obviously depend on the geometrical conditions of the counting procedure, variations in position of the thyroid gland in the neck, and the relation of thigh to plasma counts , but it seemed to us that these variables might not significantly affect the essential alterations of the factor in abnormal states This hope appears to have been largely realised in practice.

EXPERIMENTAL

Apparatus

The general disposition of the apparatus used is shown in fig 2 The method depends entirely on external

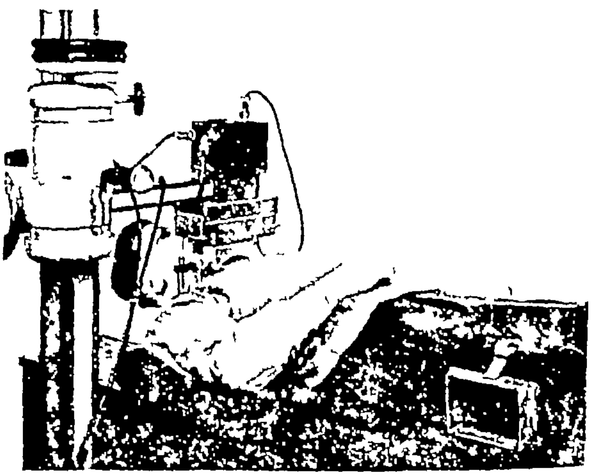


Fig 2—Counting apparatus in use

γ ray counts over the neck and thigh, and occupies about one and a quarter hours The counts were made with a G 10 lead cathode Geiger Muller tube (20th Century Electronics) of diameter 2 5 cm and effective cathode length 8 5 cm operating at 1100 V and having a shielded background count of 39 counts a minute. This was shielded in a housing of lead, with an effective thickness of 2 cm , except for a rectangular aperture, 11 0 by 5 8 cm , situated in a plane 6 cm from the axis of the counter (fig 3)

To avoid heavy lead shielding of the rest of the body, and to enable the patient to lie down, the counter was separated from the neck by a padded aluminium collar (fig 4) so that the axis of the counter lay 11 cm from the

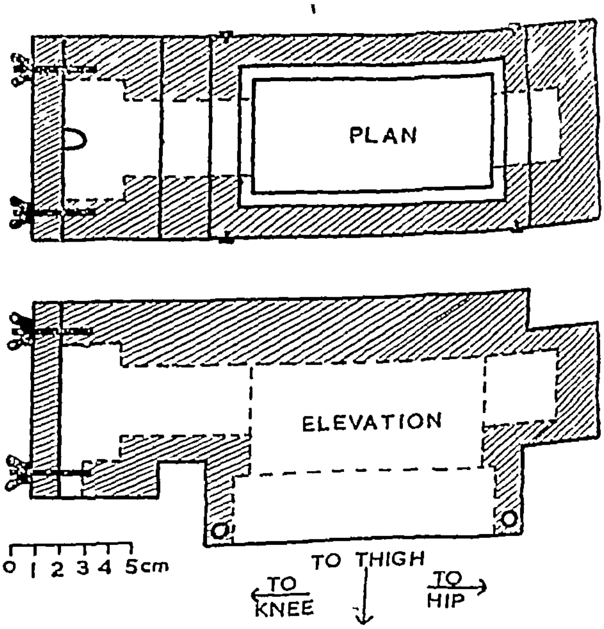


Fig 3—Details of lead counter shielding (made to specification by Stoner and Saunders Ltd. 20, Woodfield Road, W 9)

skin of the neck over the thyroid isthmus. The collar is fixed rigidly to the couch with two adjustable slotted metal supports to which it is attached by hand screws. A similar device was used between the counter and the thigh (fig 2). The anatomical siting over the thigh was standardised by placing the centre of the counter over a point 7·0 cm below the mid-point between the anterior superior iliac spine and the upper border of the patella. To avoid radiation from the opposite thigh a vertical lead block 20 cm square by 2·5 cm, supported on a lead base, was placed between the thighs.

Preparation for Test

For three days before the test the patients studied in this series were not allowed to eat fish, iodised salt, swedes, or turnips, and no drugs or applications containing iodine or goitrogens were given in that period. Although we have no clear evidence to prove that the dietary restrictions were necessary, they seem to be a reasonable precaution on theoretical grounds. Thus, swedes and turnips have been shown to contain goitrogens (see Greer 1950). The omission of iodine-containing medicines or ointments is, however, very important, and neglect of this produced falsely low results in 3 of our cases. The striking effects of goitrogens on iodine uptake are discussed below.

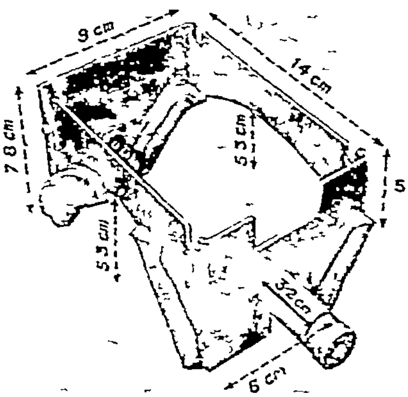
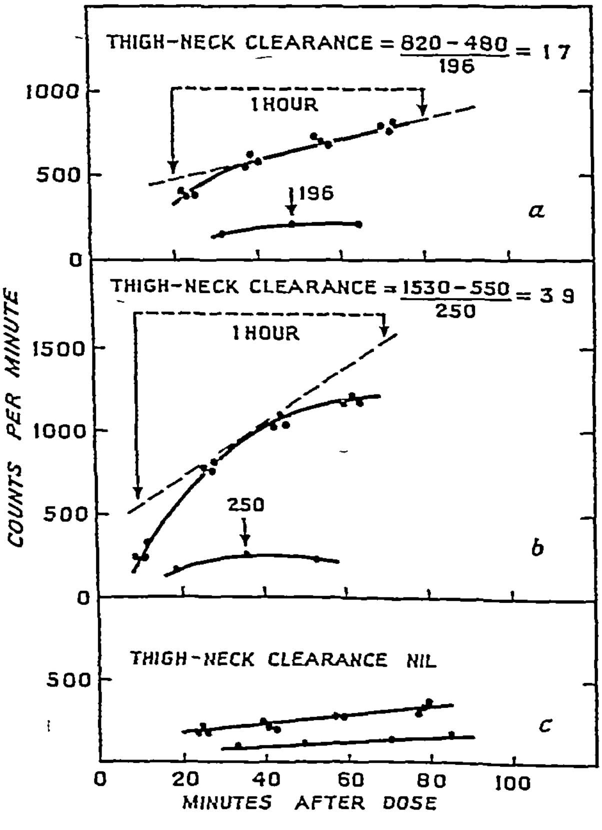


Fig. 4—Neck applicator. Thigh applicator is similarly constructed with a depth of 4 cm. at corners and 2·5 cm. at centre of short sides. Sponge-rubber pads 0·6 cm. thick are placed over surfaces in contact with patient.

Urine iodine levels were estimated in 70 cases and gave results between less than 1 μg per 100 ml. and 72 μg per 100 ml., calculated as iodine, except for the 3 cases noted above. A qualitative test for urinary iodide is a useful check so far as medicines are concerned and should preferably be done as a routine. This is done as follows: 10–20 ml. of urine is clarified, if necessary, by filtration, and 0·5–1 ml. of 20 vol. hydrogen peroxide is added, followed by 1 ml. of 2N sulphuric acid and 0·5 ml. of 1% starch. Mix well and set aside for five minutes. A blue or smoky colour indicates the presence of iodides in concentration greater than 1 mg (as potassium iodide) per 100 ml. A blank experiment omitting the hydrogen peroxide should be performed.



DETAILS OF TEST

The patient is starved for five hours before the test begins. A dose of about 30 μC of carrier free I^{131} is dispensed in 50 ml. of water with 20 μg of inert potassium iodide added. This is drunk and the time recorded. The glass is rinsed, and the dose washed down, with a few millilitres of water. After ten minutes the patient lies down, and the thigh applicator is fitted and remains in position for the remainder of the test. The neck applicator is fitted and three neck counts lasting ½ minute each are made. The collar is then removed and a ten-minute thigh count is made; these procedures are repeated until the maximum thigh count has been passed. This will have been reached within an hour of counting, unless there is much delay in absorption (a rare event). The data, with background and scaler dead time corrections applied, are plotted as a graph, and the calculation, as described above, is made on the best line. Some typical examples of the method of calculation employed are shown in fig 5. A specimen of urine is collected during the test for qualitative iodine tests.

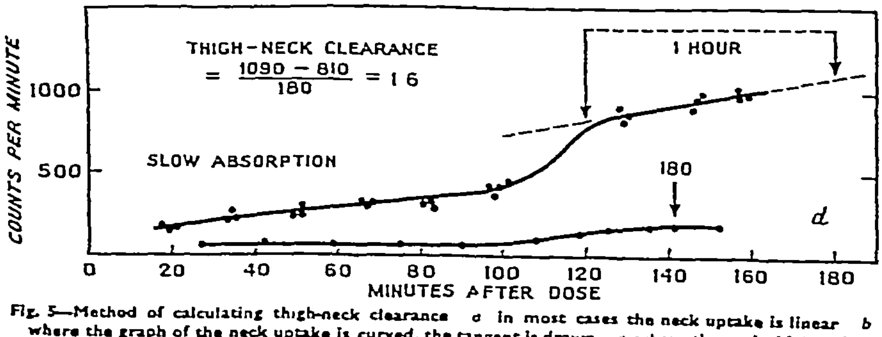


Fig. 5—Method of calculating thigh-neck clearance: *a* in most cases the neck uptake is linear; *b* where the graph of the neck uptake is curved, the tangent is drawn; *c* where the neck thigh ratio is constant for a long time it is not necessary to await the highest thigh count (in a case of Simmonds's disease); *d* occasionally there is delay in absorption from the stomach.

We have standardised the counting distance from the skin over the thyroid at 11 cm. This distance can readily be checked, and with the particular design of collar we have used it is possible to fit all necks so far encountered, except in the shortest and most obese subjects. Variations in the depth of the radiation centre of the gland below the skin surface are more difficult to assess. According to Pochin (personal communication) the radiation centres of thyroid glands lie

2·6 cm below the skin over the thyroid cartilage, with a standard deviation of 1·0 cm. It is therefore possible for the distance from radiation centre to counter to vary between 11·5 and 15·5 cm in extreme cases. The effect of this on the clearance is discussed below.

PLASMA THIGH CORRELATION

To assess the correlation between plasma radioactivity and the corresponding thigh counts we plotted plasma levels against thigh counts in 25 cases two hours after ingestion of the dose, and good correlation was obtained (correlation coefficient = +0·90). In 29 cases a similar graph was prepared for the one hour values and a correlation coefficient of +0·84 was obtained (fig 6). In neither case was it possible to find a correction to the thigh count, based on thigh dimensions, which improved these correlations. It is therefore concluded that the importance of thigh dimensions is slight.

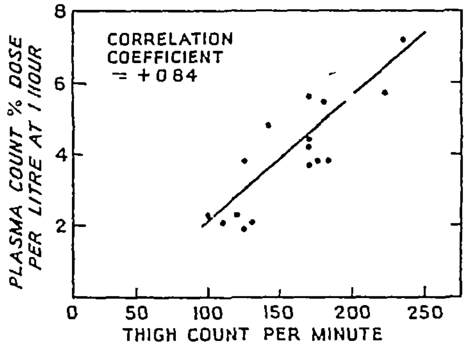


Fig 6—Plasma thigh correlation 1 hr after 30 µC of I^{131} by mouth

It was apparent from a study of the slopes of the regression lines at one and two hours that in this time a considerable diffusion of iodide takes place into the extravascular fluid. To assess the effect of diffusion on the relation between the plasma and thigh counts at the time of the clearance estimate, blood and thigh measurements were made on a heparinised volunteer with an indwelling venepuncture needle. Fig 7 shows that after initial irregularities during the first forty minutes the thigh count followed the plasma count fairly closely until the maximum values had been reached. This is the point at which we calculate the clearance. It is not desirable to calculate the clearance before this time, for it is impossible to be certain of the effect of the non-thyroidal tissue count in the neck until the thigh count has shown that this is no longer rising. At the moment of the maximum thigh count the slope of the neck curve gives an accurate picture of the rate of uptake of radio iodine by the thyroid gland, and the thigh count gives a good estimate of the plasma level. After this time the thigh and plasma counts begin to diverge. The critical moment between the effects due to rising plasma count on the one hand and the extravascular diffusion of iodide on the other is thus easily gauged and the clearance calculated without serious risk of error from these causes. It may be noted that the maximum thigh count is usually reached before forty minutes in thyrotoxic patients.

We have investigated the statistical errors involved in the rather low thigh counts and found that ten minutes is long enough to get a maximal error of 2% in normal persons. The lowest thigh count in our series was subject to a maximum error of 7%. Since, however, several thigh counts are obtained and the best line is drawn, and since the scatter about this line is always very small, probably such a large error as 7% is rarely met with in practice.

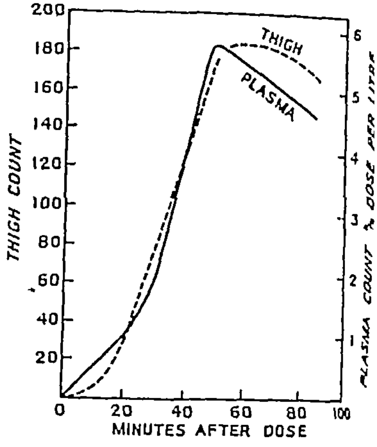


Fig 7—Variation of thigh and plasma counts with time after 30 µC of I^{131} by mouth.

RESULTS

100 persons have been studied by this technique.

24 Normal subjects—Mostly volunteers from the staff of the medical school, with neither history nor signs of thyroid disease and in good health at the time of the test.

14 Thyrotoxics—Patients with definite clinical thyrotoxicosis, whether exophthalmic goitre or toxic nodular goitre.

17 Non toxic goitres—Patients with definite goitres but without any signs of toxicity.

11 Doubtful toxic goitres—Borderline cases of goitre with equivocal symptoms or signs of toxicity.

8 Myxœdemas—5 patients with the fully developed syndrome of myxœdema and 1 of Simmonds's disease with signs of thyroid deficiency (3 of these had been treated with thyroid or thyroxine) and 2 cases of mild hypothyroidism (untreated).

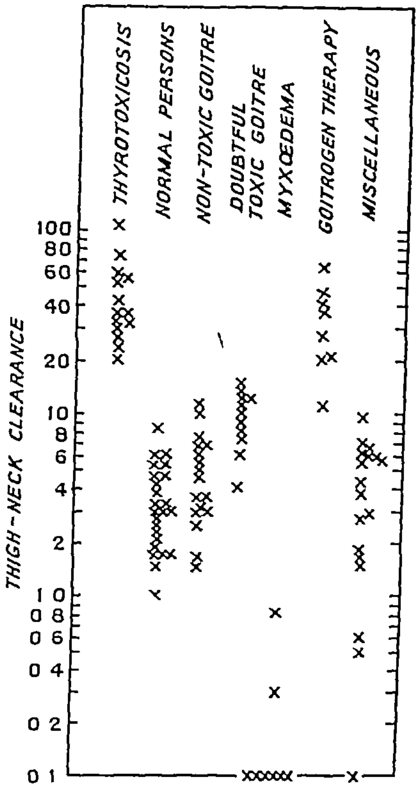


Fig 8—Thigh neck clearance in 100 people. Apparent difference between highest normal clearance (8·6) and lowest thyrotoxic clearance (20·8) is diminished by logarithmic scale used

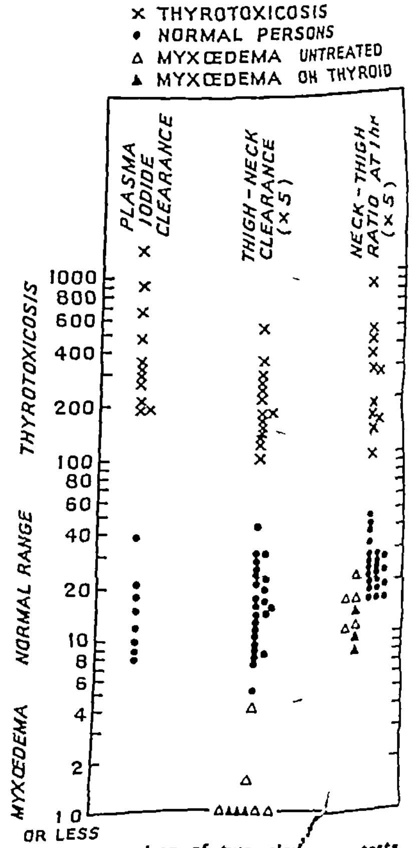


Fig 9—Comparison of two clearance tests and the neck-thigh ratio (Figures for plasma iodide clearance taken from Myant et al (1949))

8 Patients recently treated with goitrogenic drugs (7 with thiouracil, and 1 with resorcinol)

18 Miscellaneous cases —These are further analysed below

The results obtained are given in fig 8 In normal subjects the range was found to lie between 1 and 9 units (mean = 3 5, observed extreme values 1 0 and 8 6) The scatter is such that the logarithms of the values are normally distributed (mean log = 0 49 ± 0 05, standard deviation = 0 23), from which the range ($\pm 2\sigma$) is shown to be 1 1 to 8 9

Patients with definite clinical thyrotoxicosis gave clearances of 21–108 This illustrates the wide separation from the normal range in this disease

17 cases of non toxic goitre showed a slight extension (2 cases) above the normal range Of 11 cases where the diagnosis of toxicity was in doubt clinically, 5 fell within the normal range and 6 were above normal

In 6 cases of myxœdema (3 untreated) no evidence of thyroid activity could be obtained (clearance less than 0 1), 2 mild cases gave clearances below normal

In 8 patients to whom goitrogenic drugs had been given the results were all above normal, in some cases very high In the 7 patients treated with thiouracil it is difficult to be sure whether the thyrotoxicosis was completely controlled, and in addition there is the possibility of a goitrogen withdrawal effect (Vanderlaan and Vanderlaan 1947), since the drug had usually been omitted for at least three days before the test The latter explanation must be accepted in the one case of resorcinol myxœdema which has been reported elsewhere (Hart and Maclagan 1951)

Miscellaneous Cases —3 results below the normal range illustrated the effect of the ingestion of iodide in the lowering of the clearance 1 case of acromegaly was just above normal 14 normal clearances were found in patients with the following conditions neurosis, Simmonds's disease, exophthalmic ophthalmoplegia with no signs of toxicity, obesity, anorexia nervosa, carcinoma of the thyroid without toxic signs, subtotal thyroidectomy, and oligomenorrhœa with obesity

COMPARISON OF RESULTS

We have compared our results with those of Myant et al (1949) in fig 9 To compare the figures directly it was necessary to multiply our results by 5 to equate the normal ranges, which are then seen to be substantially comparable The clearances in our thyrotoxic patients seem to deviate less from the normal than do those of Myant et al, probably because the mean basal metabolism was lower (+ 39%) in our series than in theirs (+ 63%)—i e, our patients were on the average less toxic On the same diagram can be seen a comparison of our clearance figures with the neck thigh ratios one hour after oral dose Though it is true that, to give the latter test a fair trial, it ought to be carried out after intravenous dosage (Pochin 1950), this result shows the poor differentiation between normal and myxœdematous subjects (with overlap) which is its main disadvantage

DISCUSSION

The aim of the investigations has been to simplify the plasma iodide clearance test, eliminating those factors which make it unsuitable for routine use and yet avoiding any major source of inaccuracy The results obtained seem to confirm the value of the simple thigh neck clearance for diagnostic purposes

Provided that the geometrical conditions outlined above are adhered to, there should be no difficulty in reproducing our results in other laboratories The possible sources of inaccuracy in the test are

(1) Variations in the dimensions of the thighs

(2) The effects of extravascular diffusion of radio iodine into the thigh tissue fluids

(3) Variations of the distance of the counter from the radiation centre of the gland in different cases owing to anatomical variations in the position of the thyroid

The first two factors would affect only the plasma thigh correlation, and the results given above show that this correlation was close It is therefore evident that variations in these two factors are relatively unimportant It seems likely that variations in thigh measurement are to some extent compensatory, for bulkier thighs will have a radiation centre further from the counter The third factor is more difficult to allow for As noted above, the greatest range of distances between the counter and the effective radiation centre of the thyroid with our apparatus lies between 11 5 and 15 5 cm These changes will also be to some extent compensatory, for larger goitres will have radiation centres farther from the counter Variations due to all these causes are of course included in our results and have not prevented a wide separation of the normal from the thyrotoxic and myxœdematous groups

It will be seen from the results that the thigh-neck clearance in thyrotoxicosis deviates from normal about as much as the plasma iodide clearance or the neck-thigh ratio It is, however, much superior to the neck-thigh ratio in the diagnosis of myxœdema The thigh-neck clearance is a rapid and relatively simple procedure, suitable for routine use, and does not require much extra labour compared with the neck thigh ratio We feel that this test is worthy of further clinical trial

All methods of this type are open to the objection that the function of the thyroid gland thus measured—i e, iodine uptake—is not necessarily identical with the more important function of secretion of thyroid hormone The results obtained by most workers up to now suggest that the functions are usually closely correlated, except in the case of patients treated with goitrogens of the thiouracil type, where iodide uptake is high with a low output of thyroid hormone The occasional dissociation between the two functions should, however, be recognised as a theoretical possibility in other conditions

SUMMARY

A new test of thyroid function is proposed, depending on alternate neck and thigh counts after oral administration of 30 µC of I^{131} From these counts a factor is calculated which we have called the thigh neck clearance The procedure occupies about one and a quarter hours.

Data are presented on simultaneous thigh and blood radioactivity estimates which indicate a good correlation between the two at the time when the test is performed

The thigh neck clearance gave readings from 1 to 9 in normal subjects, from 21 to 108 in thyrotoxicosis, from 1 5 to 11 5 in non toxic goitre, from 0 to 0 8 in myxœdema, from 1 5 to 14 2 in miscellaneous diseases including cases of questionable toxicity, and from 11 to 63 in patients undergoing goitrogen therapy

The thigh neck clearance showed changes similar to those shown by the plasma iodide clearance in abnormal thyroid states It is superior to the neck thigh ratio in the diagnosis of myxœdema

We are much indebted to Dr E E Pochin for advice, to the physics department of Westminster Hospital for much technical help, to the Tracer Committee of the Medical Research Council for supplies of I^{131} to the normal subjects who so kindly volunteered for the test, and to the medical and surgical staff of Westminster Hospital for referring cases for investigation

REFERENCES

Foote J B, Maclagan N F (1951) *J Endocrinol* (in the press)
Greer, M. A (1950) *Physiol Rev* 30 513
Hamilton J G Soley, M H (1939) *Amer J Physiol* 127, 557
Hart F D Maclagan N F (1951) *Lancet* i 530
Keating F R Haines S F Power M. H Williams M M. D (1950) *J clin Endocrinol* 10 1425
Myant N B Pochin E E Goldie E A G (1949) *Clin Sci* 8 109
Pochin E E (1950) *Lancet* ii 41
Raben M S Astwood E B (1949) *J clin Invest* 28 1347
Rawson R. W (1949) *Ibid* p 1330
Vanderlaan J E Vanderlaan W P (1947) *Endocrinology* 40 403

SYNCHRONOUS COMBINED ABDOMINO-VAGINAL HYSTERECTOMY

JOHN HOWKINS
M D , M S Lond , F R C S , F R C O G
ASSISTANT GYNÆCOLOGIST, ST BARTHOLOMEW'S HOSPITAL, LONDON GYNÆCOLOGIST, HAMPSTEAD GENERAL HOSPITAL, ROYAL MASONIC HOSPITAL, LONDON, AND ST JOHN'S HOSPITAL, LEWISHAM

WHEN a surgeon performs Wertheim's operation he aims to remove a generous margin of vagina below the growth—certainly the upper half, and preferably the upper two thirds The amount actually removed is sometimes disappointing and may spoil an otherwise satisfactory operation The reasons for this inadequate removal are either technical—usually obesity or a deep pelvis—or that the growth has infiltrated the vaginal walls in a downward direction In this latter type of case the point of vaginal section is dangerously near the growth, and it is not surprising that recurrence is first noticed in the new vaginal vault Such a recurrence is particularly distressing to the patient in that it tends to ulcerate and bleed and she is reduced to the original state for which she submitted herself to operation

In assessing the site of recurrence Victor Bonney found that in 25% of cases this was in the track of the vagina and the lower pelvis He states that by his abdominal approach he removes all, or practically all, the vagina (Bonney 1947) This is not disputed, but it should be remembered that he has done more than 500 such operations, a total unlikely to be achieved by any future surgeon

The deeper a surgeon descends into the pelvis in an attempt to remove more vagina, the greater his difficulty in hæmostasis and anatomical definition, especially in a fat patient

A conservative and compassionate surgeon will argue that a third or half of a vagina is better than none, and will justifiably point to those cases in which, after Wertheim's operation, the residuum has performed a useful function Be this as it may, the dangerous presence of a potential source of recurrence is a far weightier argument in favour of its primary and total removal

In discussing the possibilities of a vaginal approach Bonney (1947) admits that " the vaginal route may sometimes be chosen (1) in cases of great obesity, especially in multiparæ , (2) in cases in which, in addition to the primary growth in the cervix, a metastatic nodule is present in the lower inch of the vaginal wall " A consideration of these facts can only lead to one conclusion—that in some cases of carcinoma of the cervix both the abdominal and vaginal routes should be used

This principle having been accepted it was put into practice as a two stage operation, the classical Wertheim being followed in a fortnight's time by the vaginal operation from below Two cases were submitted to this procedure without mishap The obvious criticism of the two stage operation is that the patient is twice subjected to the physical and mental trauma of anæsthesia and surgery, and that her stay in hospital is consequently prolonged A second theoretical objection is that the vagina has been transected through a potentially malignant area by the first operation, and that the surgical ideal of wide block dissection of a malignant area beyond the point of possible local metastases has been transgressed

The next logical step was to borrow the technique of Lloyd Davies (1939) as applied to his synchronous combined operation on the rectum, and to employ two surgical teams working from the abdomen and the vagina simultaneously The advantages of this method are evident (1) time is saved , (2) the extent of the operation is widened , and (3) in those parts of the operation which are notoriously difficult when perf either from above or below, the abdominal and v surgeons, when working together, can give each valuable help in finding planes of cleavage safel rapidly and in the identification of anatomical struc A good example is the dissection of the rectum fro vagina When performed from above this may difficult and bloody procedure, but a gynæcologist possibly several thousand posterior colporrhaphi his credit can reach the pouch of Douglas from perineum safely, quickly, and relatively bloodl The same applies to the separation of the vagina the urethra and bladder

The speed with which the vagina can be disse from the bladder and rectum from below is remark in easy and suitable cases, but it is wise to place more experienced surgeon at the vaginal station the first combined synchronous operation performed Wilfred Shaw and me the vagina was complet separated and freed as far as the cervix by W S bel I, working from above, had tied the uterine arter and the whole operation was completed in forty minutes

PREOPERATIVE TREATMENT

These patients are quite unsuitable for admission nursing homes and the smaller institutions, and shou be transferred to a hospital where the residents a nurses are fully conversant with all the difficulties a complications of major gynæcological surgery Th particularly need an expert pathologist They requ more than ordinary preoperative care, and should b admitted to hospital at least a week before operatio During this period a full and thorough medical examina tion is made, with special reference to the cardiovascula system, and if necessary the opinion of a physician i obtained about their suitability for operation They ar given a high protein diet, special attention being paid to water, salt, and sugar input The blood picture is corrected if faulty, and a blood transfusion is given, so that the hæmoglobin is normal on the day of operation A catheter specimen of urine is collected, and any urinary infection is treated with the requisite drug Special care is taken to obtain an adequate action of th bowels daily without purgation Intravenous pyelo graphy is done in all cases so that a visual picture of renal function and anatomy may be obtained on both sides As soon as possible after admission the patient is examined under an anæsthetic and a biopsy specimen of the growth is obtained The cervix and vagina are best cleaned by frequent douching with dilute hydrogen peroxide or with eusol solution, and between these douches the vagina is packed lightly with acriflavine and paraffin tampons Some patients will need more than a week to build them up to face the operation, and an extra week should never be grudged in these cases It is surprising what a difference such care will make to the ease with which the patient withstands her ordeal. I do not myself employ radiotherapy either before or after operation

ANÆSTHESIA

An experienced anæsthetist is essential, and the choice of the anæsthetic is best left entirely to him

My own preference is slightly in favour of extradural block, since this gives excellent relaxation, minimal bleeding, and absence of large and small bowel in the operation area

INTRAVENOUS DRIP

My present practice is to have a slow drip infusion of glucose saline solution running as a precautionary measure in case intravenous blood is suddenly needed The anæsthetist can then give a blood transfusion a once if need be It is better to transfuse too early and too much than too little and too late

TECHNIQUE

As soon as the patient is anæsthetised, the surgeon passes a metal or glass catheter and empties the bladder. It is unwise to entrust this simple duty to an assistant, since a partially emptied bladder, or one with aspirated air in it, is a great embarrassment to the surgeon and always difficult to rectify during the operation. The patient is then placed in the lithotomy Trendelenburg position, employing the special leg rests of Lloyd Davies (1939). A sandbag under the buttocks is unnecessary. The responsible surgeon should satisfy himself that the patient's position is perfect before he scrubs up.

Abdominal Approach

The abdominal team consists of surgeon, assistant surgeon, and theatre sister or nurse, and has its own complete set of abdominal instruments and swabs bearing a distinctive mark, so that there can be no muddle in the count between the two surgical teams. A long subumbilical midline incision is made, and if necessary this is carried through the umbilicus high enough to give a generous field of operation. After the abdomen has been opened, the ureter is brought into view, the ovario pelvic fold is clamped at its highest possible point, and the round ligament is clamped as far laterally as possible. The peritoneum between these two points is incised, and its mesial leaf is mobilised towards the midline with the ureter. In this way the ureter is identified straight away and followed from above downwards at the very beginning of the operation. The pons asinorum is thus crossed early. The technique of Bonney's classical Wertheim's operation has been followed up to this point, but now comes a modification. The external iliac and obturator glands, plus fat and connective tissue, are swept medially, so that a block dissection of the growth and its glands is made from above downwards and centripetally. This manœuvre enables the uterine artery to be tied in its most proximal part and if necessary the internal iliac artery can be tied at its source. The operation is continued as described by Bonney (1947).

Vaginal Approach

The vaginal operator, meantime with his assistant, his theatre sister, and his own instruments and swabs, makes a circular incision round the vagina in the region of the hymen. This manœuvre is assisted by sewing the labia minora to the skin. A bladder sound can be passed if necessary. The anterior vaginal wall is dissected from the urethra, and the posterior vaginal wall from the perineal body and rectum. When an inch or so has been freed all round, the vagina is lightly but firmly packed with gauze soaked in Bonney's blue and then sewn up with multiple interrupted silk sutures which are left long, and to which is attached a pair of Spencer Wells forceps to act as a tractor. The dissection then proceeds in front, behind, and laterally. In front the bladder is soon reached and stripped from the vagina by sharp and blunt dissection as far up as the cervix. The ease of this dissection depends on the position of the growth, and it is more difficult where the vagina is involved. Posteriorly the rectovaginal space is soon reached as in the operation for posterior colpoperineorrhaphy, and the peritoneum of the pouch of Douglas comes into view. Laterally the puborectalis muscle is inserted through a broad fan like muscular base into the vagina, and this has to be cut with scissors. Certain vessels may require to be tied, and hæmorrhage in this part of the operation is liable to be brisk, hence in some cases it is wiser to proceed by clamp and suture ligature. Quite soon, however, the operator will find his finger above the levator ani muscle and just below the cardinal ligaments. He should now pause and assure himself that all bleeding vessels are secured, and if there is heavy venous oozing, it is best to plug tightly for a few moments until the hæmorrhage abates and individual vessels can be comfortably and safely secured. Diathermy is sometimes useful in such a situation and should always be available. Having reached this point of the vaginal operation, the vaginal and abdominal surgeons should now review the position, and it will usually be found that a common plane of cleavage can be established in the midline, so that the fingers of the two surgeons can meet between the bladder in front and the vagina and cervix behind. The abdominal surgeon will by now have dissected the ureter out of the ureteric canal, and Mackenrodt's ligament can be secured as far out laterally as possible, both from above and below, and cut and tied while the ureter is identified and guarded by the abdominal surgeon. When this has been done on both sides, the two surgeons turn their attention to the peritoneum covering the posterior aspect of Douglas's pouch, which is now incised from above, while the vaginal operator guards the rectum and presses it back with his fingers from below. The uterosacral ligaments are divided by the abdominal operator well back, the rectum being still guarded by the vaginal operator.

In dividing the uterosacral ligaments it is important not to divide them so near the sacrum as to endanger the terminal branches of the superior hæmorrhoidal artery which encircle the rectum in a descending spiral. These vessels are particularly important, because the anastomosis with the middle hæmorrhoidal artery may be poor. Moreover, the middle hæmorrhoidal artery may have been interrupted by the dissection. Damage to the superior hæmorrhoidal artery can therefore cause avascular necrosis of the rectum, with the formation of a fistula. The risk of this type of fistula has been pointed out by Von Peham and Amreich (1934). It is therefore wise not to take the uterosacral dissection farther back than the anterolateral aspect of the rectum.

The vaginal surgeon has now completed his task, and his remaining duty is to deliver the specimen from the vagina, if the uterus is not too big—e.g., when fibroids are present. Having done this he makes a final inspection for the sake of absolute hæmostasis and lightly packs the cavity with flavine and paraffin gauze. Sometimes one or two catgut sutures are passed in front of the rectum through the levatores ani. While he is doing this, the abdominal surgeon completes the peritoneal suture across the floor of the new pelvis. The vaginal surgeon passes and leaves in situ a self retaining catheter, the efflux from which should show a few drops of clear urine. Some surgeons like to dust the cavity from which the vagina has been removed with sulphonamide and penicillin powder and to do the same to the peritoneal floor from above. The abdomen is closed without drainage.

POSTOPERATIVE CARE

The combined operation is a formidable procedure, and even if shock is not present at the time of operation it is liable to come on later. This delayed type of shock is a particular menace in Wertheim's operation, and the surgeon should take precautionary measures against it.

When the patient has returned to the ward she is given morphine gr. 1/4 at intervals of 4–6 hours for the first 24–48 hours and treated along the accepted lines for any major abdominal operation. The surgeon should look out particularly for ileus and peritonitis, because pelvic infection is liable to follow any opening of the vagina, even in a total hysterectomy. For this reason postoperative prophylactic chemotherapy is advised.

The intravenous drip should not be discontinued until the pulse chart fully warrants it and until the oral fluid intake and the activity of the gut are both satisfactory. The vaginal packing is removed with the help of morphine gr $1/_4$ at the end of 48 hours, and thereafter the cavity is lightly packed daily or every second day with acriflavine and paraffin soaked gauze for the next few days The sooner this packing is discontinued the better Some serosanguinous fluid and, later, some seropurulent discharge will be lost from the cavity, and secondary hæmorrhage requiring repacking, though not serious, has been encountered once Although after other operations I encourage my patients to get up as early as possible, after this operation it is probably best to confine the patient's out of-bed activities, for the first 10 days, to sitting in a chair, but no hard and fast rule should be laid down

The treatment of the bowels follows ordinary practice, but only simple rectal washouts are used if there is any distension The bladder will need careful supervision in that, after the removal of the catheter about the 5th day, the patient is always liable to have some residual urine, the presence of which must be ascertained by trial catheterisation after she has emptied her bladder in the ordinary way Residual urine, if present, needs no specific treatment and usually clears spontaneously in about 3 weeks The vaginal cavity may not entirely heal for several weeks, but this need cause no anxiety and can be treated at home by frequent baths and a simple vulval dressing

POSTOPERATIVE COMPLICATIONS

Hæmorrhage —If operative technique is satisfactory and hæmostasis thorough, secondary hæmorrhage should not be a serious complication Oozing from the vaginal bed is largely controlled during the first 48 hours by the vaginal pack, and if anxiety is experienced repacking with or without anæsthetic will dispose of this trouble

Shock —This severe and radical operation is naturally liable to shock the patient, and for this reason blood transfusion should be generously used and oxygen given through B L B mask

Postoperative Retention of Residual Urine and Urinary Infection —The motor nerve supply to the bladder is bound to be damaged if the operation is thorough, and resulting retention of residual urine is to be expected This complication will need initially an indwelling catheter and continuous drainage, and subsequently catheterisation two or three times a day until the bladder regains its tone This usually takes three weeks, but may take longer Recovery is always eventually complete, hence no undue anxiety need be felt Urinary infection is to be expected, and this can be treated by prophylactic chemotherapy as and when it arises

Damage to Bladder and Ureters —In all radical operations for carcinoma of the cervix the bladder and ureters are in peril, especially with the more advanced growths The surgeon should not strip the ureter too thoroughly in its lower reaches, and certainly not for more than two inches, otherwise the danger of avascular necrosis is increased

Damage to Rectum —In the synchronous combined operation the rectum is less in peril than in the classical Wertheim, because the vaginal operator can more easily recognise the pelvic anatomy from below, and Douglas's pouch is opened by both surgeons The question of damage to the superior hæmorrhoidal arteries when the uterosacral ligaments are divided posteriorly has already been mentioned, and its importance in the causation of fistula has been emphasised Such a fistula appears between the 7th and the 14th postoperative days If the rectum is damaged at the operation it should be carefully repaired and a temporary colostomy made

Phlebothrombosis and Pulmonary Embolism —In a few cases of Wertheim's hysterectomy I have tied the common iliac vein on both sides, but I do not yet advise this as a routine, since the results of heparin treatment have been satisfactory

Postoperative Vomiting and Paralytic Ileus —The intravenous drip used for blood transfusion should be kept running with 1/5 physiological saline solution and 4% glucose until the gastro intestinal tract resumes its normal functions Early use should be made of continuous duodenal and jejunal suction if the patient vomits or becomes distended

Peritonitis should be prevented by postoperative chemotherapy, for soiling of the peritoneum is to be expected from the vagina

Slow Obliteration of Vaginal Cavity —This may take six months, but does not require hospital treatment other than frequent supervision in the outpatient department Patients are instructed to take two baths a day, and probably the best results are obtained without any other local treatment Any discharge is absorbed on a sterile vulval pad, changed frequently

SUMMARY AND CONCLUSIONS

Synchronous combined abdomino vaginal excision of the uterus and vagina is described It is a more radical and thorough procedure than the classical Wertheim's operation, and removes a potential site of recurrence—i e, the vaginal residuum This should improve the estimated cure rate obtained by surgery It is particularly suitable for cases where the growth has spread into the vagina

The operation is not technically difficult, and it should be performed as quickly as the classical Wertheim's operation

The bladder and ureters are less likely to be damaged than in the classical Wertheim, since in the difficult part of the operation the two surgeons can assist one another

It is not suggested that the operation should supersede the classical procedure, but that in some cases it will render difficult growths more easily operable.

I wish to acknowledge the valuable help and criticism I have received from my old chief, Mr Victor Bonney, and my senior colleague Mr Wilfred Shaw, also the collaboration of Mr Emlyn Williams, Mr J J O'Sullivan, and Mr S F Hans

REFERENCES

Bonney V (1947) A Textbook of Gynæcological Surgery London, p 377
Lloyd Davies O V (1939) *Lancet*, ii 74
Von Peham H, Amreich J (1934) Operative Gynecology Philadelphia vol ii

DETERMINATION OF HÆMOGLOBIN

VII STANDARDISED OPTICAL DATA FOR ABSOLUTE ESTIMATIONS

R Donaldson R B Sisson
National Physical Laboratory Teddington
E J King I D P Wootton
Postgraduate Medical School of London
R G Macfarlane
Radcliffe Infirmary, Oxford

A UNIVERSALLY available standard to facilitate absolute determinations of hæmoglobin is becoming more than ever necessary with the increase in intercomparison of results for nutritional surveys and other research work Since the final stage of most estimations involves a comparison of optical absorptions or colours, it is desirable that a common optical standard should be available

The absolute accuracy of a result obtained by an optical method depends on two distinct factors (1) the precision or reliability of the estimate, and (2) the accuracy of the relationship between the optical values and the true hæmoglobin content of the blood sample e precision takes account of the random errors asso-ted with the preparation of the solution and its asurement, this has been dealt with in papers III d V of this series Paper IV gave details of the prob ns connected with the determination of hæmoglobin iron analysis, which is regarded as the method that ost nearly gives the total hæmoglobin content Paper II ve a definition of the existing B S Haldane standard terms of hæmoglobin content To complete the formation necessary for accurate determinations, the lationship between optical values and hæmoglobin ust be known This paper gives those optical equivalents at will enable most instruments to be calibrated curately in terms of the agreed hæmoglobin standard

PRINCIPLES OF OPTICAL STANDARDISATION

Optical estimations involve a comparison of colours r absorptions against some kind of optical standard t may be a coloured liquid or glass, as in the Haldane, lkaline hæmatin, and Sahli methods, it may be simply scale of light intensities, as given by a photocell and alvanometer, or for null instruments it may be a ariable diaphragm calibrated in densities, or a neutral edge, which in the M R C photometer is calibrated irectly in % Haldane

When an instrument is used with a material standard he necessity for absolute accuracy of the optical scale s removed, but the results obtained still depend on the ccuracy with which the material standard has been efined Since its optical calibration in terms of hæmo lobin is in itself a very lengthy and difficult procedure, he use of a material standard is often of doubtful value and can lead to significant systematic errors which re only revealed when intercomparisons are made

The alternative is an absolute optical standard of ensity This can be satisfactorily established only by a large scale experiment, such as that described below, where the most modern and reliable methods and equipment have been used to determine optical values and hæmoglobin content by iron analysis The fundamental results for optical standardisation are the spectral absorption curves of the various derivatives These results are, of course, only directly applicable to instruments which use monochromatic light, spectroscopes, or absorptiometers with a line source and isolating filter The large majority of hæmoglobinometers, however, use either a simple colour match or a brightness estimation through a so called monochromatic filter In the latter case, instead of monochromatic light, a band of wave lengths is involved, the components of which are absorbed at different rates However, it is possible to calculate absorption values appropriate to any filter from the fundamental spectrophotometric curves This calculation gives a completely rigorous result and does not just assume that the filtered light behaves as monochromatic corresponding to the peak transmission of the filter Results have been worked out for the commercial green filters generally used in visual and photo electric hæmoglobinometers

With this information, the subsequent calibration of simple hæmoglobinometers is straightforward The improvement of optical apparatus, especially photocells and robust galvanometers, has made possible the production of absorptiometers which can be made to measure optical density with sufficient accuracy Such an instrument can be used to give hæmoglobin values independent of any material standards

PROCEDURE

Iron analyses were made on normal blood samples from 11 males and 10 females Six derivatives from each blood were prepared, and spectrophotometric curves were obtained for each derivative In addition the colour of the carboxyhæmoglobin solution was estimated as a percentage of the B S Haldane standard

Optical data, applicable to various types of hæmoglobinometers, were then derived from the spectrophotometric results

METHODS

Sampling and Iron Analysis —The blood samples were taken and iron analyses were made as described by King et al (1948a)

Hæmoglobin Derivatives —The six derivatives and the method of preparation are described by Macfarlane et al (1948)

Colour and Absorption Measurements —These were made on the N P L colour comparator and spectrophotometer, both of which are described by King et al (1948a)

RESULTS

Spectral Absorption

Absorptions at every 10 mμ throughout the visible spectrum were determined for all six derivatives from each blood sample The absorption peaks were not explored in detail, since all the information necessary for the standardisation of hæmoglobinometers can be obtained from the 10 mμ curves The measured values, being the absorptions of the solution in a 1 cm cell compared with that of water in a similar cell, were reduced to specific extinction coefficients $\left(E^{1\%}_{1\text{cm.}}\right)$ corresponding to a standard concentration of 1 g of Hb per 100 ml. The 21 values of $E^{1\%}_{1\text{cm.}}$ at each wave length, were averaged, and a mean curve was obtained for each of the six derivatives (table I and figs 1 and 2)

These results may be used directly in the measurement of hæmoglobin with a spectrophotometer, providing care is taken to adjust the slits to the correct spectral band-width

Hæmoglobinometers using Monochromatic Light

For instruments which use the mercury green or sodium yellow lines the appropriate absorptions, interpolated from the values in table I, are given in table II

TABLE I—SPECTRAL ABSORPTION, MEAN CURVE, 11 MALES, 10 FEMALES

Wave length (mμ)	Optical density of solution containing 1 g of Hb per 100 ml $\left(E^{1\%}_{1\text{cm.}}\right)$					
	Oxy hæmo globin	Carboxy hæmo globin	Acid hæma tin	Alkaline hæma tin	Cyan hæma tin	Cyan met hæmo globin
430	33 0	35 0	21 2	14 7	39 0	40 0
440	16 1	11 1	19 4	11 1	21 2	20 7
450	9 59	6 42	17 2	8 91	14 2	13 2
460	6 66	4 81	14 2	7 48	10 1	8 83
470	5 05	4 02	11 6	6 53	7 72	6 51
480	4 12	3 60	9 37	5 80	6 39	5 60
490	3 58	3 40	7 94	5 26	5 38	4 84
500	3 26	3 36	7 26	4 77	4 66	4 34
510	3 12	3 74	7 05	4 34	4 65	4 45
520	3 79	5 10	7 02	3 99	5 30	5 26
530	6 41	7 50	6 83	3 80	6 16	6 20
540	8 58	8 61	6 40	3 57	6 47	6 46
550	6 92	7 14	6 13	3 40	6 35	6 25
560	5 16	7 25	5 86	3 34	5 64	5 51
570	7 19	8 57	5 15	3 33	4 74	4 63
580	8 00	4 89	4 03	3 32	3 73	3 63
590	2 25	1 73	3 26	3 28	2 77	2 64
600	0 72	0 80	2 93	3 20	1 90	1 77
610	0 46	0 56	2 73	3 04	1 30	1 16
620	0 35	0 41	2 53	2 72	0 94	0 82
630	0 29	0 32	2 53	2 26	0 74	0 63
640	0 25	0 27	2 72	1 74	0 61	0 50
650	0 21	0 22	3 07	1 26	0 57	0 39
660	0 18	0 18	3 25	0 98	0 53	0 34
670	0 17	0 16	2 99	0 77	0 49	0 29
680	0 16	0 15	2 26	0 64	0 46	0 26
690	0 15	0 15	1 49	0 56	0 43	0 23
700	0 15	0 15	1 0[illegible]	0 51	0 40	0 21

These values can easily be transformed to apply to solutions of any required concentration from blood of any strength—e g at 560 mμ, E for oxyhæmoglobin is 5 16 for a 1 in 200 dilution from blood containing 14 8 g of Hb per 100 ml the equivalent value at 560 mμ is 5 16 × 14 8/200 = 0 382

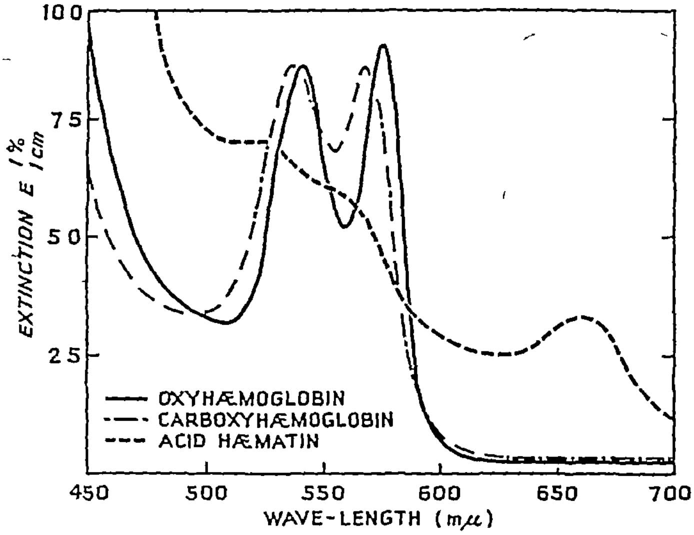


Fig 1—Absorption curves of hæmoglobin derivatives

Here, as in table I, the results are in terms of $E^{1\%}_{1cm}$ but can be transformed to apply to any required concentration

Hæmoglobinometers using a Colour Match

When a hæmoglobinometer operates on a straightforward colour match, the natural optical standard is the trichromatic specification of colour This was the method adopted in the original Haldane specification (Donaldson et al 1943) The only other hæmoglobin derivative which is widely used in colour matching is acid hæmatin, for which a yellow glass is often used as a standard The trichromatic colour specification is essential for an optical calibration of this kind of hæmoglobinometer, because the glass has a different spectral absorption from that of acid hæmatin, although it matches it in colour Only the trichromatic method can show how closely a given glass matches acid hæmatin, the value on the hæmoglobin scale, and whether the match changes seriously on going from daylight to artificial light Details of the trichromatic methods are now available in textbooks, e g, Wright (1944) The colour values of carboxyhæmoglobin and acid hæmatin measured not less than 2 hours after making up are given in table III

Hæmoglobinometers using Monochromatic Filters

A series of results applicable to visual and photo electric hæmoglobinometers using monochromatic filters have been derived from the spectral absorption data of table I and are mathematically consistent with it

The spectral transmissions of the filters were obtained by measurement of a representative selection from the current commercial production The spectral curves are shown in figs 3 and 4

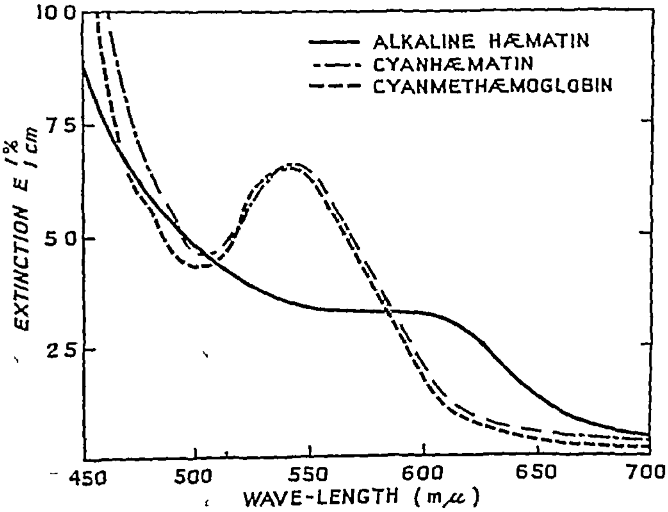


Fig 2—Absorption curves of hæmoglobin derivatives.

Visual Instruments

To get results which apply to a visual instrument one requires, in addition to the properties of the filter and hæmoglobin derivative, the photometric luminosity curve for the eye and the spectral energy of the illuminant It has been assumed that visual instruments are used mostly in daylight, so the illuminant chosen was the colorimetric illuminant B which is equivalent to sunlight

The optical density has been calculated of each hæmoglobin derivative for a visual instrument using brightness matching in filtered light In effect each filter is treated as a band of wave lengths, the result for each wave-length is calculated, and the final result is derived by integration The mathematical processes involved are given in the appendix The results for all seven filters are shown in table IV

Photo electric Instruments

To get similar results applicable to a photo electric instrument the spectral response of the photocell is substituted for the luminosity response of the eye An average response curve was chosen as representative of the selenium barrier layer photocells manufactured commercially in this country The average curve should suit all cells because it is only variations within the waveband of the filters that are significant Photo electric instruments are usually fitted with a tungsten lamp, so the spectral energy of a gas filled projector lamp was taken to represent the illuminant

TABLE II—ABSORPTION FOR MERCURY GREEN AND SODIUM YELLOW LINES, MEAN VALUES, 11 MALES, 10 FEMALES

Wave length (mμ)	Optical density of solution containing 1 g of Hb per 100 ml $\left(E^{1\%}_{1\,cm}\right)$					
	Oxy hæmo globin	Carboxy hæmo globin	Acid hæmatin	Alkaline hæmatin	Cyan hæmatin	Cyan met hæmo globin
546 (Mercury green)	8 10	7 70	6 21	3 45	6 43	6 38
589 (Sodium yellow)	2 64	1 82	3 30	3 29	2 84	2 70

The optical density of each derivative for a photo electric instrument, and variations from Beer's law, have been calculated The results are shown in table IV

Filter Transmissions

Table IV deals with the transmissions of the hæmoglobin derivatives for light which has been filtered by passage through any of the seven filters, but no account is taken of the amount of light transmitted by the filters. Now, although the transmission of any one derivative does not vary by more than 2 to 1 in going from one filter to another, the transmissions of the filters vary over a 20 to 1 range This means that, for any given source, the amount of light reaching the eye or the photocell can vary over this 20 to 1 range, according to which filter is used Other factors being equal, it is obviously desirable to choose the filter which has the highest transmission, since in most instruments an increase in the light available tends towards an increase in precision of measurement

In table V the columns headed "Vis" give for each derivative the values for the percentage of light transmitted by the solution plus each of the filters when used

TABLE III—COLOUR COÖRDINATION OF CARBOXYHÆMOGLOBIN AND ACID HÆMATIN, MEAN VALUES, 11 MALES, 10 FEMALES

(1 in 100 dilution from blood of concentration 100% Haldane —i.e., 14 8 g of Hb per 100 ml)

Hæmoglobin derivative	Colour coördinates		
	x	*y*	*z*
Carboxyhæmoglobin (7 14 mm *)	0 4824	0 3457	0 1719
(B.S.I Haldane standard)	(0 4805	0 3432	0 1763)
Acid hæmatin (7 14 mm)	0 5148	0·4306	0 0546

* Internal diameter of Haldane test tube

The difference in the trichromatic coefficients of the two carboxyhæmoglobin solutions indicates not a difference in strength on the Haldane scale but merely a slight brownness of the present solutions This brownness is probably the result of differences in the methods of making up the solutions. The Haldane standard solution was allowed to stand for some weeks and was then decanted to ensure that a minimum of insoluble matter was present in the measured solution In the present work the solutions to be measured were made up immediately from the whole blood

in visual instruments, the illuminant, as before, is the standard illuminant B In the columns headed "P.E" are tabulated comparable results for photo-electric instruments, the illuminant is a tungsten filament lamp

PRACTICAL TEST OF RESULTS

King et al. (1948b) in paper VI described observations on a later series of blood samples which showed that two M.R.C photometers gave values on an average less than 0 5% different from those obtained by iron analysis These instruments had been calibrated by purely optical methods based on the values in table IV

In the course of this experiment estimations were also made on all six derivatives with a photo electric absorptiometer calibrated in a similar way for use with an Ilford 625 filter The strengths of each of the ten blood samples were estimated by iron analysis, by the absorptiometer, and by the most reliable of all optical methods, the colour derived from spectrophotometric curves The absorption results were expressed as percentages of the 100% value given in table IV the results by iron analysis as percentages of 14 8, and the optical values were then divided by the results by iron analysis and expressed as percentages The mean and standard deviation of all ten quotients for each derivative and method are given in table VI.

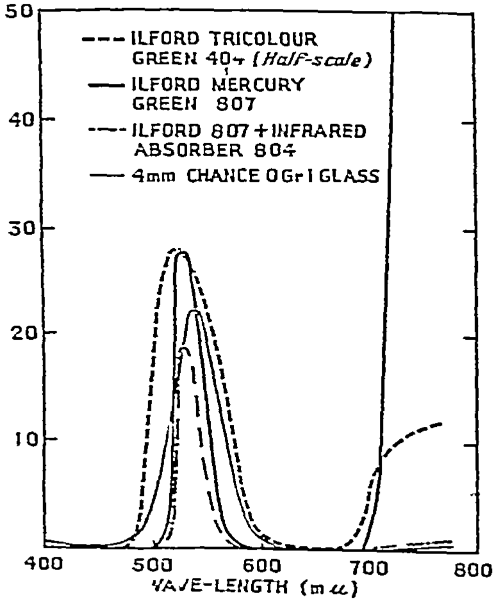


Fig 3—Transmission curves of monochromatic filters.

These results indicate that estimations with a simple absorptiometer, calibrated from table IV without reference to iron determinations, are comparable in precision and accuracy with those made by the most reliable spectrophotometric methods Most of the quotients by each method are in error by less than 1 5% In the case of cyanmethæmoglobin there is probably some systematic difference connected with the making of the solutions, since the standard deviation is less than 1 5, and hence the standard deviation of the mean, so far as measurement is concerned, is less than 0 5%

It is also significant that the standard deviations, as indices of accuracy, are very close to those obtained in paper V as indices of precision. This suggests that the stage has been reached where the uncertainties of optical calibration are less than those associated with the blood itself—the biological variations and the errors in taking the blood and making up the solutions It seems then that any further increase in the accuracy of hæmoglobin determinations now depends primarily on factors other than optical measurement

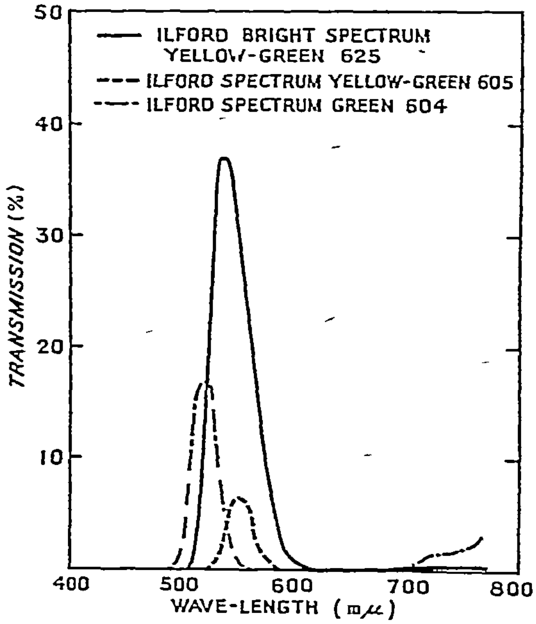


Fig. 4—Transmission curves of monochromatic filters.

DISCUSSION

The tables are intended primarily for the convenience of research-workers and of standardising laboratories undertaking the calibration of hæmoglobinometers, but they will prove useful to any manufacturer or user who wishes to calibrate his own instruments on an absolute basis Tables II and III are of such specialised application that comments on them are outside the scope of this paper Tables IV and V are those which will be more generally useful

The Measuring Instrument

If the instrument is to warrant calibration it must have a satisfactory performance. For a photo-electric instrument this implies that it should give a repeatable reading for a given solution and that there should be no creep, fatigue, or instability as shown by the galvanometer or milliammeter Inconstancy of zero reading and inconstancy of full scale reading are also symptoms of trouble which satisfactory instruments should not have In a visual instrument the readings should be independent of the exact position of the eye, if the field goes out of balance when the eye is moved across the eyepiece, a large spread in readings will result With a good visual photometer the standard deviation ought not to be greater than 0 007 in density—i e, about 1 5% on the Haldane scale. Other features requiring attention are the depth and the shape of the liquid container. Absolute standardisation with circular tubes is very unsatisfactory, and for commercial instruments almost impossible. Cells with flat and parallel sides are essential, located at right angles to a parallel beam of light. The depth of liquid traversed ought to be between 5 and 20 mm. If it is less than 5 mm, the cells are difficult to clean, and if more than 20 mm, the alteration in path length in some instruments may cause errors. There may be departures from Beer's law if the liquid layer is very much greater than the standard 10 mm.

Choice of Filter

If a satisfactory hæmoglobin derivative and a satisfactory measuring instrument have been decided on, there remain the choice of a suitable filter and the calibration of the instrument. It can be seen from table IV that the density depends on the derivative used, the nature of the green filter, and the type of measurement, visual or photo-electric. The table provides not only the absolute density value, but also, in conjunction with table V, the other information necessary for the choice of a suitable filter for any given set of conditions.

For a photo-electric instrument the choice of filter depends on departure from Beer's law and on the amount of light transmitted by the filter and hæmoglobin solution in combination. Although the absorption of a solution is generally proportional to concentration of hæmoglobin for monochromatic light, the proportionality does not necessarily hold exactly when a band of wave-lengths is used, as in the case of the green filters. The departure from Beer's law is due to the fact that the spectrum band of green light passed by the filter is selectively absorbed by the hæmoglobin solution and altered in composition. Now, the alteration in composition of the light varies with different concentrations, hence strict proportionality is not maintained. Ilford 605 is the most nearly monochromatic of the selected filters, and does not show any serious departures from Beer's law. Ilford 807, however, can give serious errors when used in photo-electric instruments, because of its rise in transmission at the red end of the spectrum (fig 3). This characteristic does not upset visual results to the same extent, because the eye is relatively less sensitive than the photocell in the red region, and because there is relatively less red in daylight than in the tungsten lighting used for photo-electric work.

When a filter of narrow bandwidth is selected to minimise the above effect it may have such a low transmission that the instrument becomes unworkable. A transmission of less than 2% in table V makes working conditions difficult, unless there is special provision for high illumination or a highly sensitive galvanometer.

TABLE IV—ABSORPTIONS OF BLOOD DERIVATIVES FOR GREEN-FILTERED LIGHT (100% ≡ 14 8 G OF HB PER 100 ML)

Filter	0 5% Oxyhæmoglobin		0 5% Carboxyhæmoglobin		0 5% Acid hæmatin		1% Alkaline hæmatin		0 5% Cyanhæmatin		0 5% Cyanmethæmoglobin	
	Visual	Photo-electric	Visual	Photo-electric	Visual	Photo-electric	Visual	Photo-electric	Visual	Photo-electric	Visual	Photo-electric
Ilford bright spectrum yellow-green 625												
Density for 100%	0 175	0 170	0 533	0 524	0 453	0 448	0 521	0 522	0 430	0 422	0 195	0 117
Departure from Beer's law at 120%	119 2	119 1	119 6	119 3	119 8	119 7	120 0	120 0	119 7	119 7	119 8	119 8
80%	80 6	80 7	80 0	80 7	80 3	80 3	80 1	80 1	80 2	80 2	80 3	80 1
40%	40 8	41 0	40 7	40 8	40 2	40 3	40 1	40 1	40 2	40 2	40 3	40 4
Colour diff (steps)	1 0		2 3		1 2		1 9		3 4		3 0	
Ilford spectrum yellow-green 605												
Density for 100%	0 199	0 198	0 501	0 502	0 445	0 445	0 500	0 510	0 441	0 440	0 437	0 43[illegible]
Departure from Beer's law at 120%	119 6	119 6	120 1	119 6	120 4	119 7	120 1	120 1	119 8	119 8	119 7	119 6
80%	80 1	80 1	80 6	80 2	80 1	80 0	80 5	79 8	80 2	80 1	80 0	80 4
40%	40 5	40 1	40 3	40 2	40 1	40 1	40 2	40 0	40 2	40 0	40 3	40 1
Colour diff (steps)	1 6		0 7		1 1		0 6		1 8		2 0	
Ilford spectrum green 604												
Density for 100%	0 346	0 330	0 415	0 397	0 511	0 512	0 580	0 580	0 406	0 391	0 401	0 386
Departure from Beer's law at 120%	118 0	118 9	119 2	119 1	119 8	120 0	120 0	119 6	120 0	119 8	120 3	120 3
80%	80 9	80 8	80 8	80 7	79 9	80 1	80 3	80 1	80 1	80 3	80 1	80 6
40%	41 3	41 3	41 1	41 1	40 0	40 0	40 1	41 6	40 2	40 1	40 3	40 6
Colour diff (steps)	1 1		1 3		0 5		1 1		1 3		1 1	
Ilford tricolour green 404												
Density for 100%	0 419	0 383	0 46	0 426	0 457	0 442	0 541	0 541	0 407	0 393	0 400	0 3[illegible]7
Departure from Beer's law at 120%	118 7	118 1	118 8	118 1	119 7	119 2	119 0	119 2	119 7	119 3	120 1	119 3
80%	81 0	81 3	81 0	81 4	80 1	80 6	80 2	80 6	80 3	80 [illegible]	80 6	80 6
40%	41 4	42 0	41 3	42 0	40 3	40 7	40 3	40 7	40 3	40 7	40 5	40 3
Colour diff (steps)	2 3		1 3		1 1		3 2		2 0		2 0	
Ilford mercury green 807												
Density for 100%	0 471	0 342	0 532	0 380	0 480	0 366	0 539	0 443	0 417	0 336	0 441	0 330
Departure from Beer's law at 120%	119 1	115 8	119 8	115 5	119 9	116 0	120 0	116 7	119 9	117 0	120 0	116 8
80%	80 7	82 0	80 6	83 2	80 3	82 1	80 2	82 1	80 1	82 0	80 2	82 [illegible]
40%	40 9	44 1	40 6	44 1	40 1	42 8	40 2	40 0	40 1	42 8	40 3	43 0
Colour diff (steps)	0 8		0 4		1 1		1 5		0 4		0 0	
Ilford 807 + infra-red absorber 801												
Density for 100%	0 17[illegible]	0 40[illegible]	0 530	0 528	0 485	0 48[illegible]	0 511	0 [illegible]44	0 410	0 410	0 447	0 411
Departure from Beer's law at 120%	119 2	119 1	119 8	119 7	119 9	119 9	119 8	120 0	119 0	119 0	120 1	120 0
80%	80 7	80 7	80 5	80 6	80 2	80 2	80 1	80 2	80 1	80 1	80 1	80 2
40%	40 9	41 0	40 5	40 8	40 8	40 1	40 1	40 2	40 1	40 1	40 1	40 2
Colour diff (steps)	0 6		1 2		1 4		1 1		0 0		0 2	
4 mm Chance OGr1 glass												
Density for 100%	0 451	0 431	0 501	0 475	0 450	0 445	0 520	0 532	0 417	0 405	0 441	0 398
Departure from Beer's law at 120%	118 6	118 6	119 1	118 7	119 8	119 6	120 0	120 0	119 7	119 5	119 0	119 0
80%	80 9	81 1	80 8	81 1	80 4	80 1	80 2	80 2	80 3	80 3	80 4	80 0
40%	41 2	41 1	41 2	41 4	40 4	40 4	40 2	40 2	40 3	40 1	40 4	40 0
Colour diff (steps)	0 4		1 5		1 4		2 4		2 0		3 1	

TABLE V—PERCENTAGE OF INCIDENT LIGHT TRANSMITTED BY COMBINATION OF FILTER AND SOLUTION

Filter	0.5% Oxyhæmoglobin		0.5% Carboxyhæmoglobin		0.5% Acid hæmatin		1% Alkaline hæmatin		0.5% Cyanhæmatin		0.5% Cyanmethæmoglobin	
	Vis	P E	Vis	P E	Vis	P E	Vis	P E	Vis	P E	Vis	P E
Ilford bright spectrum yellow-green 625	4.4	4.5	3.9	4.0	4.7	4.7	4.0	4.0	4.9	5.0	5.0	5.1
Ilford mercury green 807	2.3	2.0	2.0	1.8	2.3	1.9	2.0	1.7	2.5	2.0	2.5	2.1
Ilford 807 + 804 (infra red absorber)	1.4	0.8	1.2	0.7	1.3	0.7	1.2	0.6	1.4	0.8	1.5	0.8
Ilford spectrum green 604	1.0	0.6	0.8	0.5	0.7	0.4	0.8	0.4	0.9	0.5	0.9	0.5
Ilford tricolour green 404	10.3	6.5	9.1	5.9	9.4	5.7	7.7	4.6	10.5	6.6	10.7	6.7
Ilford spectrum yellow-green 605	0.5	0.3	0.5	0.2	0.6	0.3	0.5	0.3	0.6	0.3	0.6	0.3
4 mm Chance OGr1 glass	3.3	2.0	3.0	1.9	3.4	2.0	2.8	1.6	3.7	2.2	3.7	2.2

For example if in a visual instrument the field brightness before insertion of the filter and solution is 100 the brightness will be reduced to 2.3 when a solution of oxyhæmoglobin is viewed through an Ilford 807 filter The strength of the solution is given as a percentage of 14.80 g per 100 ml

In choosing a filter, therefore, there must be a compromise between the mutually exclusive qualities of narrow bandwidth and high transmission

To take a specific example, if oxyhæmoglobin is to be estimated photo electrically, table V shows that most light is available with filter 404, then 625, 807, or OGr1 Departure from Beer's law is serious with 807, and not very satisfactory with 404 There is little to choose between 625 and OGr1 on this score, and, since there is twice as much light available when 625 is used (4% against 2% for OGr1), it is the most satisfactory of the selected filters for the purpose

TABLE VI—ACCURACY OF HÆMOGLOBIN ESTIMATIONS

Quotient against iron	Oxyhæmoglobin	Carboxyhæmoglobin	Acid hæmatin	Alkaline hæmatin	Cyan hæmatin	Cyan met hæmoglobin
	Photo electric absorptiometer calibrated by reference to table IV					
Mean	99.7	100.5	98.0	99.8	101.3	102.0
S D	1.51	2.10	1.85	2.79	1.42	1.22
	Spectrophotometer and colour calculation					
Mean	100.3	100.1	101.1	100.8	101.7	102.6
S D	1.17	1.19	2.12	2.71	0.71	1.40

For visual instruments the same factors have to be considered, and there is also, with some combinations of derivative and filter, the problem of colour differences These arise when the filter is used to view adjacent optical fields, one neutral grey and the other illuminated through the derivative They are given in table IV as "steps," each step being the least perceptible difference With oxyhæmoglobin the same four filters permit the greatest amount of light, but there is this time little to choose between them as far as departures from Beer's law are concerned However, colour difference rules out filter 404, and 807 transmits less than is desirable A colour step of one unit in the table is the most that can be tolerated for work of high accuracy, hence either 625 or OGr1 is satisfactory in this respect Since there is more light available with 625 it is the probable choice for visual estimations by the oxyhæmoglobin method

After a decision has been reached on the choice of filter, the instrument has to be calibrated absolutely, since it is desirable that it should provide and maintain its own optical standard independent of any material standard This can best be done by having the instrument calibrated under stipulated conditions at a suitably equipped laboratory such as the National Physical Laboratory The results are usually issued as instrumental readings which are equivalent to, say, 50, 100, and 120% Haldane for the particular blood derivative used

Optical Cell Instruments

Alternatively the worker with an instrument taking optical cells can use an already calibrated neutral grey screen to provide an unvarying reference point This is already a feature of the M R C photometer, and the makers* will also supply glass neutrals for use with any method of hæmoglobinometry Details of green filter, derivative, concentration, cell thickness, and required superficial dimensions should be given in addition to the type of receptor—i e, the eye or photocell. The most convenient density for such a standard is the "100%" value, though other values can be obtained if required for checking linearity The neutral grey screen has to be calibrated for green light, since the absorption curve is never sufficiently flat to justify the assumption that the absorption is the same for white and green light, and it is important to confirm that the optical conditions under which it is calibrated are the same as those which occur in the absorptiometer

The use of such a checking standard gives not only a correction to the instrument readings but also a check on constancy over a period It also shows what is the upper limit of error and gives confidence in the results by removing the possibility of gross hidden errors Once the error at the "100" point has been determined with the neutral glass screen, the errors at other parts of the scale can be checked by neutrals of other known densities, or by using a neutral grey solution at full strength, half strength, &c (Thomson 1946) If a hæmoglobin derivative is used for this purpose, allowance must be made for the departures from Beer's law given in table IV

Test tube Instruments

The calibration of test tube instruments, as mentioned above, is far from straightforward or satisfactory, but

TABLE VII—RESPONSE CURVE OF SELENIUM PHOTOCELL

Wave-length (mμ)	Spectral sensitivity	Wave length (mμ)	Spectral sensitivity
400	619	600	912
410	657	610	844
420	693	620	754
430	728	630	637
440	761	640	509
450	791	650	384
460	820	660	296
470	849	670	172
480	876	680	97
490	903	690	58
500	926	700	39
510	942	710	32
520	955	720	26
530	971	730	21
540	985	740	17
550	992	750	13
560	995	760	10
570	996	770	8
580	986		
590	958		

The values given above are derived from data supplied by Messrs Harding and Preston of the National Physical Laboratory

---

Messrs C Davis Keeler Ltd 39 Wigmore Street London W 1 the following procedure may be used to provide a fairly reliable calibration.

The internal diameter and uniformity of the tubes can be checked by filling them with a strong neutral† or hæmoglobin solution and observing any variation in readings with rotation or interchange. If variations are found, the tube must be used in a fixed orientation and corrections made for differences between tubes. It must be remembered that the difference often depends on the density being measured.

The next stage is to measure in the tubes a neutral solution known to have the same density as the "100%" value of the chosen derivative and filter or, alternatively, a neutral solution to which a definite "% value" has been assigned. For workers with both optical cell and test-tube absorptiometers the neutral solution could be calibrated in the square cell against a standardised glass neutral. The density obtained can then be expressed on the hæmoglobin scale by use of table IV, hence, when the solution is used in the test tube, the scale reading obtained can be correlated with hæmoglobin.

Where these facilities are not available, an already calibrated neutral solution may be obtained from the makers of the glass neutrals. The same details of derivative, filter, &c., should be given.

Measurement of the neutral solution in the test tube provides the instrument reading which would be obtained from a blood of the equivalent strength quoted (or determined) for the neutral. Calibration at other concentrations can then be made by using successive dilutions of the neutral solution. This method does not provide a scale of true optical density, but it gives a reliable scale of hæmoglobin content.

A glass neutral should still be used with test-tube instruments to check constancy over a period. The filter need not be of known density, but its reading in the instrument should be noted during the original calibration, and the value obtained can be checked periodically.

Interconversion of Results

The tables can also be used to correlate the results obtained by different methods or with different filters. Suppose that an M.R.C. photometer is to be used with the carboxyhæmoglobin instead of the oxyhæmoglobin for which it is designed. The Ilford 625 filter fitted to it would give too large a colour difference with carboxyhæmoglobin (2.3 steps), but Ilford 807 would be satisfactory. Table IV gives a density of 0.475 for oxyhæmoglobin with 625, and 0.532 for the carboxy derivative *plus* 807, hence a blood of strength 100% Haldane would be expected to give a reading of 100 × 0.532/0.475 = 112 when estimated by the carboxyhæmoglobin method in an M.R.C. photometer fitted with 807 filter. Thus a correction factor could be applied to the scale readings so that results could be obtained easily on the Haldane scale.

A similar procedure can be followed for photo-electric instruments when a change of derivative or filter is required. Suppose that an absorptiometer has been calibrated for use with oxyhæmoglobin measured via an Ilford 605 filter, and it is found that a scale reading of 0.470 is equivalent to 100%. Then, if estimations by the alkaline hæmatin method are required, the new 100% point can be computed from table IV. The true densities for oxyhæmoglobin and alkaline hæmatin are 0.498 and 0.510 respectively, hence the new scale reading for 100% by alkaline hæmatin is 0.470 × 0.510/0.498 = 0.482.

If the filter is to be changed from 605 to, say, Chance OGr1, the new 100% point for oxyhæmoglobin will be 0.470 × 0.431/0.498 = 0.406.

In this way changes of filter and derivative can be made without the necessity for a lengthy practical recalibration.

Some Variables

Although the data in the tables can be relied on for most work, there are some variables which must be taken into account for work of the highest accuracy. The most important of these concerns the filter. The density values for 100% strength have been calculated on a defined filter transmission curve—the mean of a number of samples of the filter. A filter of the same name will have a transmission curve close to the mean, but may show quite definite differences from it. Unfortunately, these differences are not just due to a variation in the concentration of dye in the filter gelatin. The dye is usually composite, and there are present also variations in the shape of the transmission curve. When the density curve of the hæmoglobin derivative is reasonably flat—e.g., as in the compounds acid or alkaline hæmatin—the variations in filter transmission have a diminished influence on the standard density value. With oxyhæmoglobin or carboxyhæmoglobin considerable variations in density take place even in the range of wave-lengths transmitted by the filter, and consequently any change in the shape of the transmission curve of the filter affects the standard density. This possibility of significant variation in commercial filter production makes the filter the most uncertain element of the absorptiometer when considered as an absolute measuring instrument. If, however, the filter transmission had been measured, and the precise optical densities for a given solution calculated by the method given in the appendix, this doubt is removed. An efficiently working absorptiometer or photometer will then merit comparison with the spectrophotometer so far as that particular coloured solution is concerned.

The energy distribution of the lamp, or the response curve of the eye or the photocell are variables which have relatively little influence on absorptions, but in visual instruments there may be an appreciable change in colour difference with change in illuminant—e.g., from daylight to tungsten filament lamp.

Conclusion

It is realised that this detailed information does not cover all aspects of the choice of a suitable technique of hæmoglobin estimation. There are so many other factors, such as practicability, cost, personal taste, and tradition, which influence the choice, that a judgment on the above-mentioned data alone would not be universally accepted. At the present stage the objective has been limited to showing what can be done by modern optical technique to further hæmoglobinometry, and to indicate the aspects which can be treated with mathematical exactitude.

SUMMARY

The principles involved in the optical standardisation of hæmoglobinometers are discussed.

Tables of the visible spectral absorption of six hæmoglobin derivatives are given, together with calculated data which apply to different types of instrument.

An experiment to test the precision obtainable with purely optical standardisation is described.

The use of the tabulated data is discussed with reference to the selection and routine use of hæmoglobin methods.

The desirable performance of accurate hæmoglobinometers is discussed, and procedures for calibration are given, together with details of a service for providing neutral checking standards.

Tests of instruments calibrated from the tabulated values indicate that any further increase in the accuracy of hæmoglobin determinations depends on technique and biological factors rather than optical factors.

This investigation has been made for the Medical Research Council's subcommittee on analytical methods. The expenses were partially defrayed by a grant from the Medical Research Council, to whom grateful acknowledgment is made. Our thanks are due to Sir Charles Harington, chairman of the subcommittee on analytical methods, for much valuable

---

† A reliable neutral solution of adequate strength is described by Thomson 1946.

advice, and to the patient and willing observers Colour and absorption measurements were made at the National Physical Laboratory on behalf of the Medical Research Council.

Appendix

In deriving the standard optical densities of table IV the following data are required

(1) The spectral transmission, $T\lambda$, of a 1 cm. layer of the hæmoglobin derivative of strength 14 80 Fe per 100 ml. at 1 200 dilution. This is derived from table I by the usual method of first finding the density for the required concentration and thence the transmission. $T\lambda$ is the transmission at wave length λ and is tabulated at wave length intervals of 10 mμ throughout the visible spectrum

(2) The spectral transmission, $t\lambda$, of the green filter at the same wave length intervals These values result from a spectro-photometric measurement of the filter

(3) The spectral energy distribution of the illuminant $E\lambda$. For visual instruments this is taken as daylight, and for photo-electric instruments as a gas filled tungsten lamp of low wattage. The appropriate data have been published by Wright (1944) under the designations "illuminant B" and "illuminant A"

(4) The response curve of the eye, $V\lambda$, and of the photo cell, $S\lambda$. The curve $V\lambda$ or luminosity function is found in Walsh's (1926) book or any other book on photometry. Values for $S\lambda$ are given in table VII. These are characteristic of the usual selenium barrier layer cell The values of $E\lambda$, $V\lambda$, and $S\lambda$ at 10 mμ intervals can easily be found from these references

The magnitude of the eye response before the hæmoglobin solution is interposed is given by

$$\int E\lambda\, V\lambda\, t\lambda\, d\lambda,$$

the range of integration being the visible spectrum 40 μ–76 μ Such an integral can be calculated numerically by the method of summing the ordinates. Each product $E\lambda\, V\lambda\, t\lambda$ is found at each wave-length 0·40, 0 41 0·42 μ, &c, and the results are summed over the range 0 40 μ–0 76 μ. When the solution is interposed, the response is

$$\int E\lambda\, V\lambda\, t\lambda\, T\lambda\, d\lambda,$$

hence the transmission is

$$\int E\lambda\, V\lambda\, t\lambda\, T\lambda\, d\lambda / E\lambda\, V\lambda\, t\lambda\, d\lambda.$$

When a photocell is used, $S\lambda$ is substituted for $V\lambda$. The optical densities for each filter and derivative at strength of 100% Haldane scale are thus found

Similarly the densities for 120 80, and 40% Haldane scale can be calculated to show the departures from Beer's law

The colour differences are found from calculations of a similar type to those given above Instead of $V\lambda$, the luminosity function, there are substituted the three trichromatic colour functions of the eye Full details of this calculation have been given by Wright (1944) and MacAdam (1942)

REFERENCES

Donaldson R Harding H G W Wright, G P (1943) *J Path Bact* 55, 205

King E. J, Gilchrist M. Wootton I D P O Brien J R P Jope H M. Quelch P E, Peterson J M. Strangeways D H Ramsay W N M. (1948a) *Lancet* i 478

— — — Donaldson R Sisson R B Macfarlane R. G Jope H M O Brien J R P Peterson J M. Strangeways D H. (1948b) *Ibid*, ii 563

MacAdam D L (1942) *J opt Soc. Amer* 32 247

Macfarlane R G, King E J Wootton I D P Gilchrist, M (1948) *Lancet* i 282

Thomson L C (1946) *Trans Faraday Soc* 42 663

Walsh J W T (1926) Photometry London

Wright W D (1944) The Measurement of Colour London.

' as science enlarges the area of the known, it is likely to enlarge the area of the unknown even more The more we learn, the less we know should be changed to read 'The more we learn, the more we realise how much more we want to know or need to know It may be more comfortable to be incurious, but the penalty for stifling curiosity is stagnation and eventual retrogression "—Prof E. C STAKMAN, in an address entitled Science and Human Affairs, *Science*, 1951, 113, 137

RADIOLOGICAL DIAGNOSIS OF EMPHYSEMA

J M S KNOTT
M.B Camb, M.R C.P
RONALD V CHRISTIE
M.D Edin., D.Sc Lond., F.R C P
From the Medical Professorial Unit, St Bartholomew's Hospital, London

THE diagnosis of florid emphysema is usually a simple matter, but most physicians would agree that in its early stages the so called physical signs of this condition may be unreliable or even misleading For this reason several special diagnostic procedures have been advocated, but as a rule the one most readily available in hospitals is radiography of the chest It has been claimed that emphysema presents characteristic radiological appearances, and the purpose of the investigation described here was to test this claim

METHOD

Twenty patients, aged 45–60, with a clinical diagnosis of moderate or severe emphysema, were selected from an outpatient clinic Each of these patients had the physical signs of emphysema together with a history of chronic bronchitis for many years and more recently a history of increasing breathlessness on exertion which could not be explained on any basis other than emphysema itself. Each patient was assessed on the basis of physical signs and symptoms and placed in one of two categories, moderate or severe As a control, 20 patients of the same age group were selected in whom there was no evidence of chronic bronchitis, asthma, or any other abnormality of the cardiovascular or respiratory systems In both groups radiograms of the chest were taken in four positions postero anterior and lateral, on full expiration and on full inspiration These were numbered at random and submitted to a physician and three radiologists, all of whom may be considered to have had special experience in this field (Dr P J Kerley, director of the X ray department, Westminster Hospital and the Royal Chest Hospital, Dr R A Kemp Harper, director of the X ray department, St Bartholomew's Hospital, Dr G Simon, assistant radiologist, St Bartholomew's Hospital, and assistant director, radiological department, Brompton Hospital, and Dr. N C Oswald, assistant physician, St Bartholomew's Hospital, and assistant physician, Brompton Hospital) The observers were given a pro forma so that their opinions on the radiological features could be comparably recorded At least one of the observers knew that there was an equal number of controls and patients with emphysema Although this information should not have been given in such an investigation, it does not invalidate the conclusions

The first part of this investigation consisted in the assessment of the postero anterior and lateral films on full inspiration and full expiration on the following criteria

Postero-anterior Chest Films—In emphysema the thoracic cage is usually large and the diaphragm may be low, flat and irregular Hypertrophy of the pectoralis muscles may be seen The ribs may tend to lie horizontally, and the intercostal spaces and subcostal angle may be wide The heart may appear to lie vertically, with a prominent pulmonary conus and exaggerated pulmonary arterial shadows at the lung hila. The medium-sized vessels tend to stand out more clearly but are smaller in calibre than normal The smaller peripheral vessels may also be more clearly visible than normal. The lung fields may show increased translucency, particularly at the lung bases Individual bullæ may be seen, usually at the apices of the lungs

Lateral Chest Films—The thoracic cage is large and there is often kyphosis affecting all the dorsal vertebræ The diaphragm is usually low, and its movements on inspiration and expiration, as well as those of the sternum, may be diminished The space between the sternum and the heart is almost invariably increased In other respects the lateral films confirm the appearances seen in the postero anterior films

RESULTS

Of the 20 patients with emphysema, all four observers made a correct diagnosis in 14 cases, three observers being in agreement on another 4 In 2 cases (nos 20 and 30) three observers were of the opinion that emphysema was not present Of the control group, 4 were diagnosed as having emphysema, in each case by only one of the observers This part of the investigation suggests that a fairly reliable diagnosis of emphysema can be made from postero anterior and lateral films taken on inspiration and expiration, 70% of the emphysema group and 80% of the control group were correctly diagnosed by all the observers Assessment of the degree of emphysema showed a wide divergence of opinion among the four observers (table I)

The provision of both postero anterior and lateral films in full inspiration and full expiration gave the observers more evidence than is commonly available even in the best of departments In most hospitals only a postero anterior film on full inspiration is provided For this reason both patients and controls were assessed again, and on this occasion the only evidence submitted was the postero anterior film on full inspiration The results of this part of the investigation are set out in table II The four observers agreed on the diagnosis of emphysema in 15 cases, three agreed on a further case (no 34) and one diagnosed emphysema in another 3 cases (nos 3, 20, and 40) All were in agreement on the absence of emphysema in 1 case (no 30) There was, however, considerable disagreement on the normal group, no less than 12 of the controls being diagnosed as having emphysema

These results indicate that a diagnosis of emphysema based on a postero anterior film may be misleading 75% of the emphysema group were correctly diagnosed, but only 40% of the controls were passed as normal by all the observers

It is generally agreed that it is often difficult to make a dogmatic clinical diagnosis of emphysema, and consequently the observers might contend that at least 4 of the emphysema cases (nos 3, 20, 30, and 40) had in fact normal chests The relevant clinical and laboratory findings in these 4 cases were as follows

Case 3 —A labourer, aged 60, had had winter bronchitis for fifteen years and dyspnœa, which prevented him from working, for two years

On examination there was no cyanosis, but climbing a flight of stairs caused dyspnœa The chest was barrel shaped, with poor expansion No area of cardiac dullness was apparent. Expiration was prolonged, and there was minimal diffuse bronchospasm The blood pressure was 116/74 mm Hg

Clinical Diagnosis —Severe emphysema

Physiological Data *—Vital capacity, 1700 ml , functional residual air, 4583 ml , mixing efficiency, 40%, residual air (expressed as percentage of total lung volume), 75%, and CO_2-combining power, 74 vol %

Case 20 —A postman, aged 45, had had chronic cough with winter exacerbations for ten years and dyspnœa for four years He could walk only 40 yards

On examination there was no cyanosis, but exertion caused dyspnœa The chest was barrel shaped, with dorsal kyphosis, poor air entry, and moderate diffuse bronchospasm The blood pressure was 106/70 mm Hg

---

*The physiological data were recorded by the methods used by Bates and Christie (1950)

TABLE I—RADIOLOGICAL ASSESSMENT OF DEGREE OF EMPHYSEMA BY FOUR OBSERVERS FROM POSTERO-ANTERIOR AND LATERAL FILMS IN FULL INSPIRATION AND IN FULL EXPIRATION THE OPINION EXPRESSED BY EACH OBSERVER IS REPRESENTED BY HIS INITIAL IN THE APPROPRIATE COLUMN

Clinical diagnosis	Chronic hypertrophic emphysema																				Normal chest*			
Case no	3	5	6	8	12	14	15	17	20	22	23	24	27	29	30	32	34	35	37	40	1	16	21	33
Clinical assessment	+ +	+ +	+ +	+ +	+ +	+	+	+	+	+	+	+ +	+ +	+	+	+	+	+ +	+ +	+				
Radiological assessment Severe generalised emphysema	K	O	K	K	H S K	K	O S K	K		S	S K	H O S	S			S	K	H O S K						
Moderate generalised emphysema	O	S	H O S	O S	O	H O	H	H O		O	H		O	H		H O	S		K	O K				
Slight generalised emphysema	S	H K				S		S	O	H K	O	K	H K	S K	K	K	H O		H O S	S	O	O	S	H
No emphysema	H			H					H S K					O	H O S					H	H S K	H S K	H O K	O S K

*The other 16 controls were recorded as normal by all the observers

TABLE II—RADIOLOGICAL ASSESSMENT OF EMPHYSEMA FROM SINGLE POSTERO-ANTERIOR FILM ON FULL INSPIRATION A RADIOLOGICAL DIAGNOSIS OF EMPHYSEMA IS REPRESENTED BY THE INITIAL OF THE OBSERVER IN THE APPROPRIATE COLUMN

Clinical diagnosis	Chronic hypertrophic emphysema																				Normal chest*											
Case no	3	5	6	8	12	14	15	17	20	22	23	24	27	29	30	32	34	35	37	40	4	7	9	11	13	16	18	21	25	31	33	38
Clinical assessment of degree of emphysema	+ +	+ +	+ +	+ +	+ +	+	+	+	+	+	+	+ +	+ +	+	+	+	+	+ +	+ +	+												
Radiological diagnosis of emphysema	K	H O S K	H O S K	H O S K	H O S K	H O S K	H O S K	H O S K	K	H O S K	H O S K	H O S K	H O S K	H O S K		H O S K	O S K	H O S K	H O S K	K	K	O	O K	K	H K	H	O K	H S K	O	K	S	K

*The other 8 controls were recorded as normal by all the observers

LE III—INCIDENCE OF RADIOLOGICAL FEATURES SAID TO BE ASSOCIATED WITH EMPHYSEMA

adiological feature	Emphysema group (20 patients)		Control group (20 patients)	
	No recorded as positive by all observers	Average no recorded as positive by each observer	No recorded as positive by all observers	Average no recorded as positive by each observer
reased translucency f lung fields	10	13 0	0	0
reased retrosternal pace	11	14·0	2	3 5
llæ	1	4 5	0	0
de rib spaces	3	7 5	0	2 0
creased vascular narkings	6	9 5	0	1 5
creased hilar narkings	4	7 5	0	0
largement of pulmonary conus	1	2 5	0	1 0
phosis	10	10 5	2	4 0
rizontal ribs	3	7 5	0	2 5
lcification of costal cartilages	6	11 5	5	11 0

Clinical Diagnosis—Moderate emphysema

Physiological Data *—Vital capacity, 3320 ml., functional sidual air, 4243 ml., mixing efficiency, 43 5%, residual r as percentage of total lung volume, 51%, and CO$_2$ mbining power, 70 vol %

Case 30—A theatre orderly, aged 46, had had cough with utum and winter bronchitis for fourteen years and dyspnœa n moderate exertion for five years

On examination there was no cyanosis, and the chest was arrel shaped, with no area of cardiac dullness, and with rolonged expiration, moderate diffuse bronchospasm, and attered basal râles The blood pressure was 120/78 mm Hg

Clinical Diagnosis—Moderate emphysema

Physiological Data *—Vital capacity, 1710 ml functional sidual air 2530 ml, mixing efficiency, 32%, residual air s percentage of total lung volume, 55%, and CO$_2$ combining ower, 60 vol %†

Case 40—An electrician, aged 60, had had cough with putum for five years and dyspnœa on exertion for four years

On examination there was no cyanosis, and the chest was arrel shaped, with generalised thoracic kyphosis, no area of ardiac dullness, hyper resonant percussion note, prolonged xpiration, and poor air entry The blood pressure was 120/70 m. Hg

Clinical Diagnosis—Moderate emphysema

Physiological Data *—Vital capacity, 2370 ml, and CO$_2$-ombining power, 69 vol %

This patient died in February, 1948 so further investigaions were not made No necropsy was performed.

The pro formas contained ten radiological signs said commonly to be associated with emphysema, and three of the observers were asked to comment on their presence or absence in the 40 cases. The incidence of these signs is shown in table III, and it is clear that most of them, if taken alone, are of doubtful diagnostic significance, since they may be absent in emphysema and are not infrequently present in those without emphysema

The measurements of diaphragmatic movement in this series showed an average range of 1 5 cm in the emphysema cases and 3 3 cm in the controls These figures are of little diagnostic significance, for 7 controls had diaphragmatic movement of less than 3 cm and 3 emphysema cases had more than 3 cm of movement

The relative importance of the various criteria is of interest because features such as horizontal ribs, wide rib spaces, and calcification of the costal cartilages have been used as radiological evidence for many years and their validity scarcely questioned This investigation shows that many of these features can be seen in people of late middle age who, so far as one can tell from clinical and physiological studies, have not chronic hypertrophic emphysema

DISCUSSION

The diagnosis of chronic hypertrophic emphysema, whether by clinical, radiological, or physiological tests, has always presented great difficulties Cabot (1930) was early to recognise the pitfalls in clinical diagnosis by the so called characteristic physical signs, and thought that emphysema could only be recognised by "careful radiological study" The problem of the radiological diagnosis has received scant attention in radiological textbooks and medical reports Most workers name some features which they consider to be important but make little attempt to analyse the relative significance of features which have been passed from one book to another without comment For example, Köhler (1935) emphasises the diagnostic importance of the increased retrosternal space, Holmes and Ruggles (1931) the hypertranslucency of the lung fields, and Sante (1930) the accentuated peribronchial markings and the formation of a reticular pattern in the peripheral lung fields Fray (1934) has rightly emphasised the importance of fluoroscopy in the diagnosis of emphysema because features such as hypertranslucency of the lung fields and diaphragmatic excursion are more easily appreciated thereby

SUMMARY

A radiological diagnosis of emphysema based on a single postero anterior film on full inspiration is of doubtful significance

A more reliable assessment may be made from films taken in the postero anterior and lateral positions, in both inspiration and expiration, but even on this evidence about 10% of cases will be missed and a few normal persons wrongly diagnosed as having emphysema

The radiological features of emphysema are discussed.

We wish to thank M. P Curwen for statistical advice and assistance

REFERENCES

Bates D V Christie, R V (1950) *Clin Sci* 9 17
Cabot R. C (1930) Physical Diagnosis 10th ed, New York.
Fray W W (1934) *Amer J Roentgenol* 32 11
Holmes G W Ruggles, H. E (1931) Roentgen Interpretation Philadelphia
Köhler, A (1935) Röntgenology 2nd ed London.
Sante L R (1930) The Chest Roentgenologically Considered. New York

COSTAL CHONDRITIS (TIETZE'S DISEASE)

E H W DEANE
M.B Melb
CONSULTANT CHEST PHYSICIAN, MANCHESTER REGION

Tietze (1921) first described, in 5 cases, a condition which was characterised by painful non suppurative swelling of costal cartilages and only slowly resolved It was thought at the time to be related to malnutrition after the 1914–18 war Other cases were subsequently recorded in Germany and Japan, and Gill et al (1942) reported 5, and Acharya (1944) 2, in Service personnel in this country Geddes (1945) described 22 cases in Canadian Servicemen In the Service cases there was no evidence of malnutrition

In most of the more recently reported cases the association of a respiratory lesion has been noted, usually this has been a "cold" or bronchitis, but occasionally a definite pneumonia has been present This association with respiratory infection was first noted by Gill et al (1942) and confirmed by Geddes (1945), who found it in all his patients In no case has a tuberculous lung lesion been noted

The condition is usually called Tietze's disease, but a more anatomical description seems desirable and the term costal chondritis seems suitable

In the past few years I have observed 7 cases (I can also remember 2 earlier cases, though I have no records tion and expiration, as well as those of the sternum, may be diminished The space between the sternum and the heart is almost invariably increased In other respects the lateral films confirm the appearances seen in the postero anterior films

---

† It is of interest that the functional residual air in case 30 is within normal limits and that the mixing efficiency in cases 3 and 20 is higher than has been found in other cases of emphysema

RESULTS

Of the 20 patients with emphysema, all four observers made a correct diagnosis in 14 cases, three observers being in agreement on another 4 In 2 cases (nos 20 and 30) three observers were of the opinion that emphysema was not present Of the control group, 4 were diagnosed as having emphysema, in each case by only one of the observers This part of the investigation suggests that a fairly reliable diagnosis of emphysema can be made from postero anterior and lateral films taken on inspiration and expiration, 70% of the emphysema group and 80% of the control group were correctly diagnosed by all the observers Assessment of the degree of emphysema showed a wide divergence of opinion among the four observers (table I)

The provision of both postero anterior and lateral films in full inspiration and full expiration gave the observers more evidence than is commonly available even in the best of departments In most hospitals only a postero anterior film on full inspiration is provided For this reason both patients and controls were assessed again, and on this occasion the only evidence submitted was the postero anterior film on full inspiration The results of this part of the investigation are set out in table II The four observers agreed on the diagnosis of emphysema in 15 cases, three agreed on a further case (no 34) and one diagnosed emphysema in another 3 cases (nos 3, 20, and 40) All were in agreement on the absence of emphysema in 1 case (no 30) There was, however, considerable disagreement on the normal group, no less than 12 of the controls being diagnosed as having emphysema

These results indicate that a diagnosis of emphysema based on a postero anterior film may be misleading 75% of the emphysema group were correctly diagnosed, but only 40% of the controls were passed as normal by all the observers

It is generally agreed that it is often difficult to make a dogmatic clinical diagnosis of emphysema, and consequently the observers might contend that at least 4 of the emphysema cases (nos 3, 20, 30, and 40) had in fact normal chests The relevant clinical and laboratory findings in these 4 cases were as follows

Case 3 —A labourer, aged 60, had had winter bronchitis for fifteen years and dyspnœa, which prevented him from working, for two years

On examination there was no cyanosis, but climbing a flight of stairs caused dyspnœa The chest was barrel shaped, with poor expansion No area of cardiac dullness was apparent. Expiration was prolonged, and there was minimal diffuse bronchospasm The blood pressure was 116/74 mm Hg

Clinical Diagnosis —Severe emphysema

Physiological Data *—Vital capacity, 1700 ml , functional residual air, 4583 ml , mixing efficiency, 40%, residual air (expressed as percentage of total lung volume), 75%, and CO_2 combining power, 74 vol %

Case 20 —A postman, aged 45, had had chronic cough with winter exacerbations for ten years and dyspnœa for four years He could walk only 40 yards

On examination there was no cyanosis, but exertion caused dyspnœa The chest was barrel shaped, with dorsal kyphosis, poor air entry, and moderate diffuse bronchospasm The blood pressure was 106/70 mm Hg

---

*The physiological data were recorded by the methods used by Bates and Christie (1950)

TABLE I—RADIOLOGICAL ASSESSMENT OF DEGREE OF EMPHYSEMA BY FOUR OBSERVERS FROM POSTERO ANTERIOR AND LATERAL FILMS IN FULL INSPIRATION AND IN FULL EXPIRATION THE OPINION EXPRESSED BY EACH OBSERVER IS REPRESENTED BY HIS INITIAL IN THE APPROPRIATE COLUMN

Clinical diagnosis	Chronic hypertrophic emphysema																				Normal chest*			
Case no	3	5	6	8	12	14	15	17	20	22	23	24	27	29	30	32	34	35	37	40	1	16	21	38
Clinical assessment	+ +	+ +	+ +	+ +	+ +	+	+	+	+	+	+	+ +	+ +	+	+	+	+	+ +	+ +	+				
Radiological assessment																								
Severe generalised emphysema	K	O	K	K	H S K	K	O S K	K		S	S K	H O S	S			S	K	H O S K						
Moderate generalised emphysema	O	S	H O S	O S	O	H O	H	H O		O	H		O	H		H O	S		K	O K				
Slight generalised emphysema	S	H K				S		S	O	H K	O	K	H K	S K	K	K	H O		H O S	S	O	O	S	H
No emphysema	H			H					H S K					O	H O S					H	H S K	H S K	H O K	O S K

* The other 16 controls were recorded as normal by all the observers

TABLE II—RADIOLOGICAL ASSESSMENT OF EMPHYSEMA FROM SINGLE POSTERO-ANTERIOR FILM ON FULL INSPIRATION A RADIOLOGICAL DIAGNOSIS OF EMPHYSEMA IS REPRESENTED BY THE INITIAL OF THE OBSERVER IN THE APPROPRIATE COLUMN

Clinical diagnosis	Chronic hypertrophic emphysema																				Normal chest*											
Case no	3	5	6	8	12	14	15	17	20	22	23	24	27	29	30	32	34	35	37	40	4	7	9	11	13	16	18	21	25	31	33	38
Clinical assessment of degree of emphysema	+ +	+ +	+ +	+ +	+ +	+	+	+	+	+	+	+ +	+ +	+	+	+	+	+ +	+ +	+												
Radiological diagnosis of emphysema	K	H O S K	H O S K	H O S K	H O S K	H O S K	H O S K	H O S K	K	H O S K	H O S K	H O S K	H O S K	H O S K		H O S K	O S K	H O S K	H O S K	K	K	O	O K	K	H K	H	O K	H S K	O	K	S	K

* The other 8 controls were recorded as normal by all the observers

intoxication, hypotonia is apparently most common, but he noted convulsions in 3 cases. Debre has had 2 fatal cases (in children aged twenty and sixteen months who had received respectively 11,200,000 and 18,200,000 units), one apparently due to uræmia and the other to subarachnoid hæmorrhage. In a third case the patient survived with hemiplegia and mental deficiency. Debré concludes that the real dangers are cerebral and renal impairment. THE LANCET (1946) stated that "signs of central nervous system involvement, such as apraxia, aphasia, convulsions, and cerebral vascular accidents, have been noted in the terminal stages of fatal cases." On the other hand, Anning et al. (1948), reviewing the toxic effects of calciferol in 200 cases, do not mention convulsions. Nor does Macrae (1947) in an analysis of 20 hospital cases, although 2 elderly patients suffered severe cerebral damage. It therefore seems that, with severe intoxication, signs of cerebral damage are common but convulsions, in the absence of uræmia or cerebral vascular accidents, are very rare.

CASE RECORD

A man, aged 20, who had been treated continuously since Sept. 17, 1948, with 'High Potency Ostelin' (Glaxo) 150,000 units by mouth daily for papulonecrotic tuberculide, was admitted to the Royal Victoria Hospital on July 8, 1949, after an epileptiform attack, observed by his doctor at home on the previous day. Another general convulsion was observed by the ward sister shortly after his admission. Three weeks previously he had complained of severe pains in the jaws. These had increased in severity but could be partly relieved by aspirin. Shortly after the onset of these pains his parents had noticed that he was becoming increasingly drowsy. At the same time he had complained of anorexia and, shortly before the first fit, of vomiting and colicky abdominal pain.

Previous History.—His birth was normal; there was no history of convulsions in childhood, nor were there any neurotic traits. At no time was he exposed to lead intoxication. He developed papulonecrotic tuberculide about September, 1945.

In October, 1947, radiography of his chest suggested pulmonary tuberculosis, and he rested in bed for 2 months. In January, 1949, he was operated on for gall-bladder empyema and subhepatic abscess.

Family History.—His father, mother, one brother, and one sister were alive and well. One brother had died at the age of 18 with congestion of the lungs. There was no family history of epilepsy, "faints," nervous ailments, or deformities.

On admission he was drowsy, disoriented in time, place, and person, and complained of severe pains in the jaws. His skin was pale and dry. His temperature was 99·5°F, pulse-rate 92, and blood-pressure 140/95 mm. Hg. There had been a short period of amnesia from just before the first convulsion, but he was aware of his surroundings on the day after admission. Except for this abnormal mental state and the presence of bilateral extensor plantar responses no other abnormality was noted. Severe calciferol intoxication was provisionally diagnosed.

Treatment.—The calciferol was stopped and intramuscular soluble phenobarbitone and a low calcium diet were given.

Progress.—The mental state improved slowly until the patient was fully oriented and his normal personality was displayed as that of a cheerful intelligent man. At this time complete formal clinical examination was negative in all respects, apart from his skin condition, despite the fact that his blood calcium level continued to be raised. He was correctly oriented when the first electro-encephalogram (E.E.G.) was recorded. The papulonecrotic tuberculide was not influenced appreciably by the treatment. Apart from an isolated record of 140/95 mm. Hg on admission all subsequent readings of the blood pressure were about 120/80 mm. Hg.

Electro-encephalography was first carried out twelve days after the second and last convulsion. The E.E.G. was abnormal, showing excess of delta and theta activity of moderate amplitude largely replacing the alpha rhythm, which was then at 8 cycles per sec. The serum-calcium level was then 14·5 mg. per 100 ml. Subsequent E.E.G. slowly improved as the blood-calcium level returned to normal four months later (see figure). The last serum-calcium level was 9·8 mg. per 100 ml.; the E.E.G. then showed only occasional theta activity of low amplitude, and the alpha rhythm was 8–12 cycles per sec. There was also occasional low amplitude faster activity at 16–20 cycles per sec. Nothing diagnostic of epilepsy was noted.

Renal Function.—Initially there was slight albuminuria. This cleared completely in nine days, but some months later a faint trace of albuminuria was occasionally noted. Intravenous pyelography on Oct. 7, 1949, was normal. The blood-urea level on July 21, 1949, was 65 mg. per 100 ml., and the blood uric acid level on Jan. 31, 1950, was 4·3 mg. per 100 ml. There is some evidence of slight impairment of renal function seven months after cessation of calciferol therapy. The state of renal function before calciferol was given is not known.

Cerebrospinal fluid on Aug. 5, 1949, was normal.

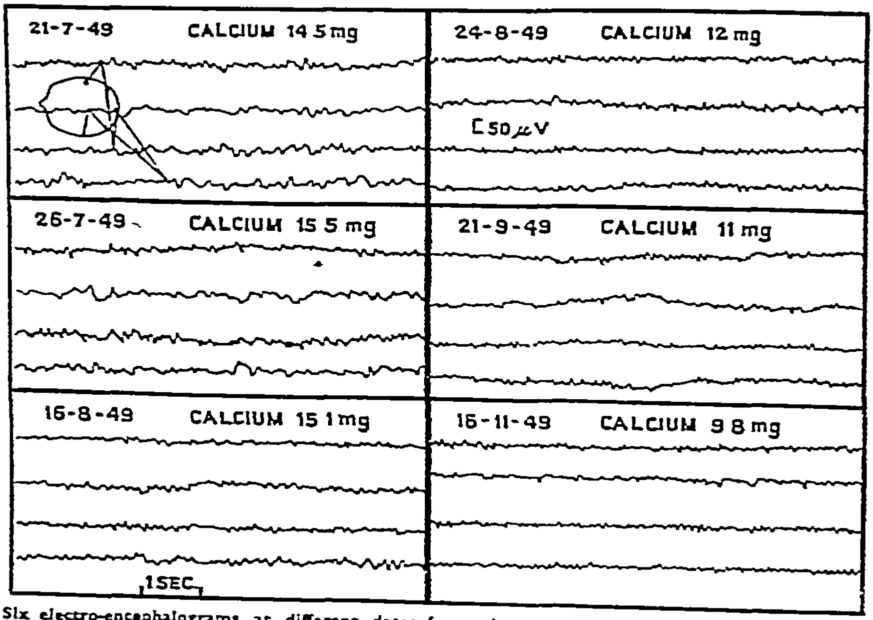
White-cell count on July 15, 1949, showed 9750 leucocytes per c.mm. (neutrophils 83%, eosinophils 1%, basophils 1%, lymphocytes 10%, monocytes 5%).

Wassermann and Kahn reactions were negative.

Radiography of the long bones showed no decalcification, and of the chest showed tuberculous lesions in both upper zones and in the left mid-zone. There was no evidence that calciferol adversely affected the pulmonary tuberculosis.

DISCUSSION

Calciferol was used in this case in the daily dosage recommended by Dowling and Thomas (1945) for lupus vulgaris. Apart from two weeks during which he had been in hospital with gall bladder empyema the patient had taken calciferol continuously, and without routine hospital surveillance, for nine and a half months. So far as we know, he did not at any time exceed a daily dose of 150,000 units.



Six electro-encephalograms at different dates from the same electrode positions as indicated in the first record. These records were made with the eyes closed. There was gradual improvement and return to normal as the blood-calcium level fell.

of them) All the 7 patients were civilians , 5 were males and 2 were females, and their ages ranged from 13 to 46 In 5 there was associated infection of the respiratory tract There was never any evidence that the condition had been caused by injury

CASE RECORDS

Case 1 —A male clerk, aged 40, had a painful swelling of the second right costal cartilage, and the pain was aggravated by a slight cough which he had had for a few weeks Examination revealed a slightly tender swelling of the second cartilage, over which the skin and subcutaneous tissues could be moved freely Deep breathing, coughing, or movement of the right arm caused pain There were no physical signs of a lesion in the lungs, and a chest radiography was clear On the day before the pain and swelling appeared the patient had been erecting a flagpole, but he had no recollection of any injury or strain while so engaged Local application of heat and a sling for the arm were prescribed, and the tenderness and pain decreased and disappeared in three weeks, but some swelling of the cartilage was still present when he was last seen three months later This, however, occasioned no disability

Case 2 —A collier, aged 28, had had for a week a similar painful swelling of the second left costal cartilage There were no associated respiratory symptoms and no history of injury Radiography of chest was clear Tenderness lasted for three weeks, after which the patient returned to work without disability , but some swelling was still present three months later

Case 3 —A painter, aged 30, had had a painful swelling of the second right costal cartilage for four days, without cough or evidence of respiratory infection. Pain disappeared a month later, and he returned to work six weeks after first being seen Some swelling of the cartilage was still present but it did not interfere with his work

Case 4 —A schoolgirl, aged 13, with swelling and pain in the second right costal cartilage, with no cough and no radiographic signs in the chest, had had a sore throat a fortnight before the swelling appeared The pain and swelling gradually subsided, but some thickening of the cartilage was still present three months later

Case 5 —A hawker, aged 46, had had a painful swelling of the second right costal cartilage a day before he attended the clinic The pain decreased and disappeared in four weeks, but there was still slight prominence of the cartilage twelve months later This man had had a tuberculous pleural effusion ten years previously, and radiography showed some hard nodular deposits in his right upper zone , but there was no clinical evidence of an active lesion He had a cough at the time of onset of the swelling, and some scattered rhonchi were heard in both lungs

Case 6 —A farm labourer, aged 25, had had a swelling of the second right costal cartilage for three weeks It had been painful and tender at the onset, but there was little pain and only slight tenderness when he attended the clinic All discomfort has since disappeared, although some swelling remained The patient had had a " cold ' and some cough about the time of the onset, but all evidence of respiratory infection had cleared by the time he came for examination The chest was clear on radiography

Case 7 —A female clerk, aged 28, had had painful swelling of the left second and third costal cartilages for three days She had a cough, and rhonchi were scattered throughout both lungs, but X rays showed no abnormality in the chest, and there was no pyrexia Some swelling and discomfort was still present a month late, but subsiding Catarrhal sounds were still present in the lungs, and the chest remains radiographically clear

DISCUSSION

The cases which have come under my observation have all involved the second costal cartilage, but other workers have reported involvement of any, or in some cases several, cartilages from the first to the tenth Nevertheless the second seems to be involved more often than any other, and in my cases the right was affected more often than the left In only a few cases has a history of injury been obtained, and this may be coincidental rather than causal The swelling is confined to the limits of the costal cartilage, which feels thickened , whether this is due to the swelling of the cartilage or of perichondral tissues is difficult to determine clinically The swelling is sharply demarcated laterally by the costochondral junction, over which tenderness may be more acute than over the cartilage

In all the cases referred to me for an opinion the question of a tuberculous infection was at issue, but in none except case 5 was there any evidence of such an infection, and in this case the pulmonary lesion is regarded as inactive A feature of the condition seems to be that the swelling and pain reach a maximum within a day or two and then gradually subside over three or four weeks Some residual swelling may, however, remain indefinitely Geddes (1945) states that further respiratory infection may cause pain to recur in the cartilage, but this has not been my experience in this small series

Investigation of erythrocyte sedimentation rate, Wassermann reaction, and blood counts has not revealed any significant findings Biopsy has not been done in any of my cases, because it has not been thought justifiable in an essentially benign condition in outpatients, but biopsy in several other cases has shown little beyond a chondral and perichondral hyperplasia In no case has suppuration occurred, and no specific cause for the condition has been found beyond the frequently associated respiratory infection

Costal chondritis is probably more common than has been thought Though the pathological basis has not yet been determined, the patient may be reassured that the lesion is benign No treatment is necessary or likely to shorten the duration of the trouble, but rest of the arm on the affected side and the application of local heat when the swelling is painful give comfort

ADDENDUM

Since this article was completed 3 further cases, similar to those described here, have been observed

REFERENCES

Acharya B S S (1944) *J R Army med. Cps* 83, 148
Geddes A K (1945) *Canad med Ass J* 53 571
Gill, A M , Jones R A Pollak L (1942) *Brit med J* ii, 155
Tietze, A (1921) *Berl klin Wschr* 58 829

EPILEPTIFORM FITS DURING CALCIFEROL THERAPY

J Martin Beare
M.D Belf , M R C P
Assistant,
Department of Dermatology

J H D Millar
M.D Belf , M.R C.P
Principal Neurological
Registrar

ROYAL VICTORIA HOSPITAL, BELFAST

THE more common symptoms of calciferol intoxication include thirst, anorexia, nausea, vomiting, tiredness, malaise, headache, and constipation or diarrhœa. Abdominal pain is a frequent complaint, and patients may be admitted to hospital as abdominal emergencies (Anning et al 1948) Apathy, drowsiness, and coma may occur as late symptoms (Debré et al 1946) Psychic disturbances and confused memory have been recorded (Covey and Whitlock 1946) Convulsions are extremely rare Bell (1949) recorded an example in a boy of 10 years who had taken by mouth a single ampoule of 'Sterogyl' containing 600,000 units of calciferol, in addition to a previously recommended course consisting of 50,000 units of calciferol by mouth twice daily This ampoule of sterogyl had been given a week before the onset of convulsions Dowling in a personal communication (MacKenna 1948) records that among his toxic patients " one child developed signs suggesting meningitis with neck rigidity and photophobia " Debré (1948) states that nervous symptoms may occur with severe

BLOOD CHEMISTRY

Day in hospital	Blood-urea (mg per 100 ml)	Blood-calcium (mg per 100 ml)	Blood phosphorus (mg per 100 ml)	Serum-alkaline phosphatase (King Armstrong units)
4	201			
5	200			
6	137	13 2	6 2	22 7
7	125	14 2	5 0	16 7
8	98	12 2	4 8	
10	102	12 7	5 0	
12	111	13 8	4 9	25 0
14	77	11 2		
15			4 7	34 6
17	72			
21	79	13 9	4 0	50 5
	Serum albumin (g per 100 ml)	Serum-globulin (g per 100 ml)	Alkali reserve (vol %)	Plasma-chlorides as NaCl (mg per 100 ml)
5	3 14	3 16	80 5	
7				514
10	4 05	2 65		
17			105 0	

On examination he looked ill, thin, toxic, and dehydrated, with conjunctival injection. There was diffuse tenderness over the lumbar muscles, particularly on the left side, and over the sacrum and pain in these areas on moving the legs In the abdomen, apart from a palpable pelvic colon loaded with fæces, nothing significant was felt A rectal examination after an enema was normal. There was no abnormality in heart or lungs, and the blood pressure was 145/80 mm. Hg The tendon reflexes were generally diminished, but the central nervous system yielded no other positive findings The retinæ were normal

His hæmoglobin was 13 5 g per 100 ml and the white cell count 12 000 per c mm The differential count showed 11% eosinophils but was otherwise normal. The urine was alkaline, sp gr 1 008, with only a trace of albumin and no cells or casts The blood urea level was 201 mg per 100 ml A fractional test-meal showed achlorhydria Tests for occult blood in the fæces were positive on three occasions and negative once

Treatment and Progress—He was given large amounts of fluid by mouth and intravenously but his blood urea never fell below 70 mg per 100 ml., and his dehydration was never really controlled His urinary output was 3–3$^1/_2$ litres a day, sp gr 1 008–1 010 On the sixth day in hospital his urine was tested for calcium with Sulkowitch's solution and gave a positive reaction. We next investigated his blood chemistry, with the results summarised in the accompanying table

Straight radiography of the abdomen did not demonstrate any renal calcification, and intravenous pyelography showed poor concentration but nothing else abnormal Radiologically there was no gross hypocalcification but in the skull there were several small circumscribed areas of bone absorption, which had moderately well-defined borders and ranged in size up to that of a small pea

Operation—In view of the patient's continued deterioration it was decided to explore the neck for a parathyroid adenoma and three weeks after admission this was done, but with negative result He died a week later without any great change in his general condition.

Necropsy (Dr G Stewart Smith)—There was dense hard infiltration of the stomach wall round a shallow epithelialised ulcer high up on the lesser curvature, and there were several masses of enlarged glands in the vicinity There was no pyloric obstruction Microscopically the growth was a spheroidal celled scirrhous carcinoma

The skull, the sternum, and a femur (the only bones examined) were infiltrated with neoplastic tissue The areas of infiltration in the skull corresponded to the areas of bone absorption shown in the radiogram The kidneys were enlarged the left was pale yellow, the right mottled with red. Corticomedullary definition was poor, and the cortex was swollen. Microscopically the tubules were dilated and there were many intracellular calcium deposits The glomerular tufts were generally swollen, and Bowman's capsule lined with cuboidal epithelium, showing occasional calcium deposits No parathyroid adenoma was found. There were no metastases apart from those in the bones and in the lymph nodes immediately adjacent to the stomach

DISCUSSION

Because of the absence of cardiovascular and retinal changes, and the fact that the patient had had large quantities of alkalis before admission, we originally treated him as a case of prerenal uræmia, but his lack of response soon made it clear that true renal failure was present Albright et al (1934) and subsequent workers have emphasised the importance of searching for a parathyroid adenoma in cases of unexplained renal failure That was why we sought for calcium in the urine and then investigated the blood chemistry We regarded our results as significant, and considered the renal failure sufficient to explain the high blood phosphorus level found instead of the low values usually found in hyperparathyroidism We did not consider that the minimal bone changes and absence of demonstrable calcification in the kidneys on radiography ruled out the diagnosis, for renal failure due to parathyroid adenoma may be present without severe bone changes (Albright et al 1934), and, although in many cases large renal calculi are formed, the deposition may be microscopic and yet lead to renal failure

Although, however, nephrocalcinosis is predominantly associated with hyperparathyroidism, and may be the presenting feature of that disease, it has been described in other conditions Martz (1940) described three cases, and reviewed others described previously, in which nephrocalcinosis occurred in association with hypochloræmia and alkalosis in the persistent vomiting of pyloric obstruction In such cases the blood calcium and blood chlorides levels are both low, and tetany often develops Martz suggests that the alkalosis in these cases is probably the cause of the calcium deposits in the kidneys Although our case does not come into this group, there was, on the two occasions on which it was estimated, an abnormally high alkali reserve, which may have played some part in the deposition of calcium In the two cases of nephrocalcinosis associated with hyperparathyroidism in which the alkali reserve was noted it was within normal limits (Albright et al. 1934, Bellin and Gershwin 1935)

Nephrocalcinosis may also occur in multiple myelomatosis (Perla and Hutner 1930), and may then present difficulties similar to those encountered here There is really no way of proving the presence of a parathyroid adenoma apart from exploratory operation, but we feel that a bone marrow biopsy would serve to exclude such cases as are due to myelomatosis or to a condition such as we have described here

Since seeing this case we have investigated cases of carcinoma with known bone secondaries, but have found none with hypercalcæmia or calcinuria—which suggests that the syndrome only develops in cases in which the bony secondaries are of sufficiently wide distribution or long duration If we assume that this patient's ulcer was malignant at the time of operation, the carcinoma had been present for at least eighteen months without causing local trouble or metastases in organs other than bone Presumably most patients with carcinoma, even with bone secondaries, die from some other cause before nephrocalcinosis has time to develop

The eosinophilia, which we could not otherwise explain, may have been due to the diffuse carcinomatosis of bone—a cause of eosinophilia described by Whitby and Britton (1942)

SUMMARY

A case of renal failure associated with hypercalcæmia is described

Nephrocalcinosis due to parathyroid adenoma was diagnosed but no adenoma was found at operation

At necropsy carcinoma of the stomach with multiple metastases in bones was found associated with nephrocalcinosis

Our thanks are due to Dr R W Luxton, under whose care the patient was to Dr G Stewart Smith, who carried out the

ELECTRO ENCEPHALOGRAPHIC FINDINGS IN 4 PATIENTS UNDER TREATMENT WITH CALCIFEROL

Case no	Sex	Age (yr)	Toxic symptoms	E E G	Serum-calcium level (mg per 100 ml)	Serum phosphorus level (mg per 100 ml)	Blood urea level (mg per 100 ml)
1	M	45	Polyuria and thirst (no bone pain no headache)	Normal	10 7	9 5 1	40
2	M	21	Polyuria and frontal headache (no thirst no bone pain)	Normal	10 8	6 0	60
3	M	10	None	Normal, no change 1 and 2 months after completion of treatment	11 6	6 5	20
4	F	40	None	Normal	10 8	6 0	43

There is no evidence that our patient suffered any cerebrovascular accident, nor was he uræmic Macrae (1947) has suggested that some of the toxic effects of calciferol may be due to immobilisation of lead from the bones There is no evidence of this in the present case Careful inquiries showed that our patient was not at any time exposed to lead intoxication There was no blue line, lead palsy, or abnormality of peripheral blood, and the response to treatment, which included a diet completely free from calcium, was dramatic

The E E G changes suggest a diffuse cortical toxic effect Diffuse changes follow an epileptic fit but usually resolve in a matter of days The first E E G was taken twelve days after the second (last) fit We have not been able to find published reports of E E G changes in hypervitaminosis or in hypercalcæmia Possibly the changes recorded here were due to the hypercalcæmia since the E E G improved as the serum calcium level fell, but the parallel was not exact Electro encephalography was done in 4 other patients under treatment with calciferol for lupus vulgaris (see table) It will be seen that the E E G were normal with and without toxic symptoms and that in each case the serum calcium level was normal Minor deviations of the blood-urea level up to 60 mg per ml cause little change in the E E G The "toxin" must therefore penetrate the blood brain-barrier before E.E G changes occur Since increased concentrations of calcium are known to decrease the frequency of impulses discharged from nerve cells, it is unlikely that hypercalcæmia alone could have caused the fit, but rather the serum calcium levels seem to be a measure of the toxic substance

Toxic symptoms are always associated with an increase in the diffusible (but not the ionised) calcium This increase in the diffusible calcium seems to be due to the presence of a steroid complex to which calcium is linked Possibly this substance is responsible for toxic symptoms (Anning 1949), it has been crystallised by Dawson and Holdsworth (1949)

SUMMARY

A young man had epileptiform fits while taking calciferol 150,000 units daily by mouth for nine and a half months

Full clinical recovery took place Some slight impairment of renal function was present seven months after cessation of treatment

Electro encephalography suggested diffuse toxic effects in the cerebral cortex

We wish to thank Dr Ivan H McCaw and Dr R S Allison for encouragement, and the former for permission to publish details of this case

ADDENDUM

Since this article was written a further case has been seen by us

A woman, aged 20, was admitted to the Royal Victoria Hospital, Belfast, on Feb 21, 1951, in status epilepticus. Twelve convulsions had been observed over a period of a few hours, and the fits were rapidly controlled by intramuscular injections of paraldehyde Later it transpired that she had been treated by her doctor for Bazin's disease with sterogyl 600,000 units orally on Feb 14 and again on the day of admission During the week before admission she had been vomiting, and complaining of pain in the jaws and colicky abdominal pain, which continued for two weeks in hospital.

The blood calcium (Feb 22) was 14 mg per 100 ml. The E E G (Feb 23) was generally abnormal with diffuse slow activity, although the patient showed only slight clouding of consciousness and emotional lability, nothing abnormal was found on neurological examination, the planter reflexes being by this time flexor The trace of albuminuria cleared up on the day after admission, the blood pressure was 110/70 mm Hg, and the blood urea 30 mg per 100 ml.

Two weeks later (March 8) the E E G had improved considerably but was still abnormal, and the blood calcium was 13 mg per 100 ml No cause except calciferol intoxication was found for the fits There was no previous history of epilepsy and all other investigations were negative The patient s mother suffers from epilepsy

We wish to thank Dr J T Lewis for permission to publish the details of this case

REFERENCES

Anning S T (1949) Personal communication
— Dawson J Dolby, D E Ingram J T (1948) *Quart. J Med* 17 203
Bell H (1949) *Brit med J* i 139
Covey, G W, Whitlock H H (1946) *Ann intern Med* 25, 508.
Dawson J Holdsworth E S (1949) See *Lancet* ii 480
Debré R (1948) *Amer J Dis Child* 75, 787
— Thieffry S Brissaud E Trollu L (1948) *Pr Méd* 56, 764.
Dowling G B Thomas, E W P (1945) *Proc R. Soc. Med* 39, 96.
Lancet (1946) ii 872
Macrae D E (1947) *Brit J Derm.* 59 333
MacKenna R M. B (1948) In Tidy, H L, Short, A R The Medical Annual Bristol, p 85

HYPERCALCÆMIC URÆMIA WITH NEPHROCALCINOSIS DUE TO CARCINOMATOSIS

R M Fulton
M B Edin., M.R C.P E, M.R C.P
MEDICAL REGISTRAR

G E Paget
M B Durh, D C.H
RESIDENT CLINICAL PATHOLOGIST

CRUMPSALL HOSPITAL, MANCHESTER

This case is reported because, having correctly diagnosed hypercalcæmic uræmia, we wrongly attributed it to hyperparathyroidism The cause of the hypercalcæmia was widespread secondary carcinomatosis of bone So far as we can discover, this is the first case of its kind to be reported

CASE RECORD

On Jan 14, 1949, a general labourer, aged 25, who had been working until a week before, was admitted to hospital with a fortnight s history of constant low back pain, which radiated to his legs and was unrelieved by treatment Throughout this time he had felt weak and lethargic, his appetite had been poor, and he had vomited twice During the previous year he had lost over a stone in weight He did not complain of urinary disturbance, but had had nocturnal frequency and polyuria for three months He had no symptoms referable to the respiratory, cardiovascular, or central nervous systems.

In September, 1947, he had been admitted to this hospital with acute abdominal pain and rigidity without previous history of dyspepsia At operation a perforated gastric ulcer with some surrounding induration had been found high up on the lesser curvature This was closed he made a good recovery and he had had only occasional slight dyspepsia since There was no previous history of urinary trouble, nor anything relevant in his family history

Thus, while these unicellular sebaceous glands seem to be scattered over the epidermis generally, they are particularly important in the palm of the hand, the sole of the foot, and inner side of the eyelid.

REFERENCE

Masson P (1926) *Ann Anat path* 3, 417

EXCRETION OF THE METHONIUM COMPOUNDS

G. E. MILNE
M.A., B.M. Oxfd, M.R.C.P.

SAMUEL OLEESKY
M.B., B.Sc. Manc., M.R.C.P.

From the Department of Medicine, University of Manchester

THE treatment of hypertension with methonium compounds is not free from danger, and before they can be generally used it is important to know how they are excreted or detoxicated. Zaimis (1950) has developed a chemical method for the estimation of the methonium compounds and has shown that in rabbits 60–70% of an intravenous dose of hexamethonium di-iodide is excreted unchanged in the urine.

We have studied the excretion of hexamethonium compounds in man, and our results (table I) show that in people with normal renal function most of an intramuscular dose is excreted in the urine.

After an oral dose of hexamethonium dibromide, urinary excretion is very low. Our results (table II) show that much of the dose is not absorbed, and that some of this can be recovered from the fæces. Absorption from the alimentary tract varies widely in the same person.

TABLE I—URINARY EXCRETION OF HEXAMETHONIUM DI-BROMIDE (OR IODIDE) GIVEN BY INTRAMUSCULAR INJECTION

Subject	Daily dose injected (mg.)	Urinary excretion (mg. per day)	% excretion
1 (Normal)	95	99	104
	50	43	86
2 (Normal)	100	100	100
3 (Hypertensive)	55	60	109
4 (Normal)	50	37	74

All these subjects had normal renal function.

Certain conclusions can be drawn from these findings. (1) Any of the drug absorbed from an intramuscular depot, and probably from the bowel, is excreted quantitatively in the urine. There seem to be no important destructive agents in the body. (2) In renal failure the drug sometimes accumulates in the blood. This was well shown by one of our patients who was uræmic (blood urea 86 mg. per 100 ml.) and who, on an oral dosage of 1.5 g. per day, developed severe hypotension resistant to 'Methedrine'. The hypotension probably lowered the filtration rate so much that further excretion of the drug was impaired and a vicious cycle developed. She died of uræmia (blood urea 250 mg. per 100 ml.) and still hypotensive. Thus the use of the drug in patients with poor renal function is dangerous. (3) Because of poor absorption from the bowel, large oral doses must be given to have any effect, but the variability of absorption makes this method of administration difficult to control. The actual amount absorbed per day when the drug is taken by mouth can be estimated from the amount present in a 24-hour specimen of urine. Destruction in the bowel may actually take place but gastric juice and trypsin do not affect the compounds.

TABLE II—URINARY EXCRETION OF HEXAMETHONIUM DI-BROMIDE GIVEN BY MOUTH

Subject	Daily dose (g.)	Urinary excretion (mg. per day)	% excreted in urine
1 (Normal)	1.5	34	2.3
3 (Hypertensive, normal renal function)	1.0	26	2.6
	1.0	42	4.2
	1.0	54	5.4
	2.0	105	5.3
	2.0	185	9.3
	3.0	300	10.0
	4.0	520	13.0
5 (Hypertensive, urea clearance 67%, albuminuria)	3.0	227	7.6
	3.0	324	10.8
	3.0	385	12.8
	3.0	437	14.6
	3.0	307	10.2
	3.0	176	5.9
	3.0	121	4.0
	3.0	139	4.6

In case 3 the fæcal excretion was measured on three occasions and found to represent 19–30% of the daily dose.

Thanks are due to Prof. R. Platt for permission to report these findings and for help in this study.

REFERENCE

Zaimis E J (1950) *Brit J Pharmacol* 5 424

STREPTOMYCIN IN LETTERER-SIWE'S DISEASE *

R. P. ARONSON
M.B. Lond., M.R.C.P., D.C.H.

SENIOR PÆDIATRIC REGISTRAR, FARNBOROUGH HOSPITAL, KENT

Letterer (1924) was the first to describe, in a child aged 6 months, a disease characterised by a purpuric rash, enlarged lymph glands, an enlarged spleen, and invasion of the spleen, liver, and bone marrow by endothelial cells. Siwe (1933) reviewed Letterer's cases and added his own, and Abt and Denenholz (1936) published a further case.

CLASSIFICATION OF RETICULOSES

Siwe (1949) classifies the reticulosis found in childhood into three main groups.

1. *Lipoid reticulo-endotheliosis*, of which Hand-Schüller-Christian disease, Gaucher's disease, and Niemann-Pick's disease are examples.

2. *Eosinophilic granuloma*, which is a special form of the non-lipoid reticulosis occurring in one or more bones. The ages of the patients have been between 11 months and 11 years (with a few cases reported in adults). There is a strong tendency for the lesions to heal within one or two years, even in the absence of treatment by curettage. Biopsy of the material shows a granulomatous lesion with eosinophilia, but no foam cells are present. There is no tendency for the lesions to spread.

3. *Non-lipoid reticuloses*, of which Letterer-Siwe's disease is one. In contrast to that of lipoid reticulosis, the onset is always acute, with generalised reactions. The main features are:

(a) A fair degree of enlargement of the liver and spleen.

(b) A hæmorrhagic tendency which manifests itself as petechiæ or purpura.

(c) Generalised enlargement of the lymph glands, which are discrete and not tender.

(d) Localised tumours over bones may be noted, and cyst formations in bones have occurred.

(e) The leucocyte count (total and differential) is normal, and there is a progressive secondary anæmia. There necropsy , to Mr H V Street, who performed the biochemical investigations , and to Dr D M Macartney, medical superintendent, for permission to publish the case

---

* This disease is named after Erich Letterer and S. A. Siwe—not one person (Erich Letterer-Siwe), as some reference books state.—ED. L.

REFERENCES

Albright F Baird P C Cope O Bloomberg, E (1934) *Amer J med Sci* 187, 19
Bellin, D E Gershwin, B S (1935) *Ibid* 190 519
Martz, H (1940) *Arch intern Med* 65 375
Perla D Hutner L (1930) *Amer J Path* 6 285
Whitby, L E H Britton C J C (1942) Disorders of the Blood 4th ed , London

UNICELLULAR SEBACEOUS GLANDS IN THE BASAL LAYER OF THE NORMAL HUMAN EPIDERMIS

EUGENE WOLFF
M B Lond , F R C S
OPHTHALMIC SURGEON, ROYAL NORTHERN HOSPITAL , SURGEON, MOORFIELDS, WESTMINSTER AND CENTRAL EYE HOSPITAL
From the Institute of Ophthalmology, London

IT is always said that the palm of the hand and sole of the foot have no sebaceous glands , and hence presumably the skin of palm and sole is lubricated only by the sweat glands This I now believe to be incorrect

For some time I have been trying to ascertain why the flat yellowish growth known as xanthelasma palpebrarum is found 100 times more often on the inner side of the eyelids than on the skin of the whole of the rest of the body put together Apparently, contrary to all accounts of the condition, it arises as a downgrowth of very interesting cells in the basal layer of the epidermis These cells are distinguished from the other cells of this layer by the fact that they undergo changes similar to those seen in the cells in an ordinary sebaceous gland the nucleus swells, becomes rounded, stains paler, and usually contains one well marked nucleolus , later still it becomes very dark The protoplasm is converted into a network and stains with Scharlach R

Obviously the next step was to see whether these cells were present in the normal epidermis Figs 1–3 illustrate sections of normal skin removed (at operation) from the inner side of the upper eyelid and fixed in 10% formalin Fig 1, from a section embedded in paraffin and stained with Masson's stain, shows how numerous are the special cells here described , fig 2, from the same section under higher power, shows the typical changes in the nucleus and protoplasm , and fig 3, from a frozen section stained with Scharlach R, shows the fat in the basal cells which is stained red The basal cells are birefringent with polarised light and stain purplish with the Liebermann Burchardt reagent (acetic and sulphuric acids) and grey with osmic acid There can be no reasonable doubt then that they are unicellular sebaceous glands

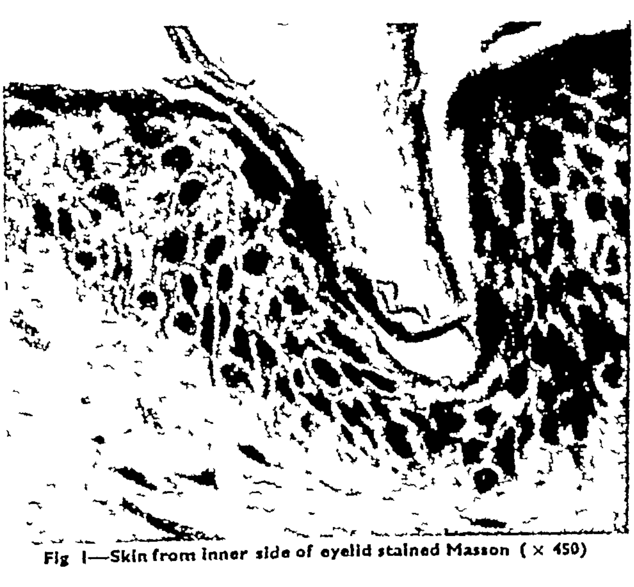


Fig 1—Skin from inner side of eyelid stained Masson (× 450)

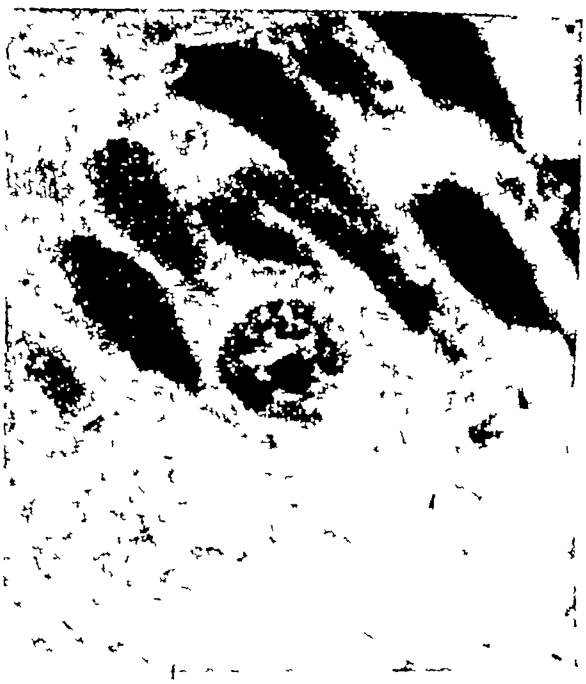


Fig 2—As fig 1 (× 2650)

That sebum forming cells should occur in the basal layer of the epidermis is not really surprising, when we remember that sebaceous glands themselves develop as a downgrowth of this layer These cells are the same as those described by Masson (1926) as *cellules claires* he thought they were derived from Schwann cells and were important in the development of the melanomata

A further examination of the skin from the inner side of the eyelid shows that the few hairs it contains are mostly feeble and have only rudimentary sebaceous glands attached to them, or none at all Probably, then, the numerous unicellular sebaceous glands in the region are there to take the place of ordinary sebaceous glands And the same would no doubt apply to the palm of the hand and sole of the foot, where the ordinary sebaceous glands are absent

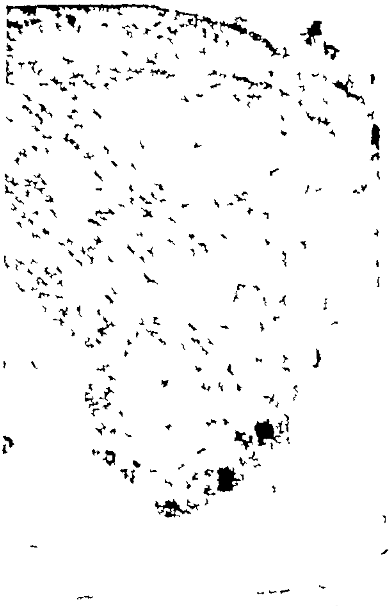


Fig 3—Frozen section stained with Scharlach R (× 532)

Preliminary Communication

EFFECT OF CORTISONE ON PNEUMOCOCCAL BACTERÆMIA

Harvey Cushing,[1] in his classical account of pituitary basophilism, remarked that "the malady appears to leave the patients with a definite susceptibility to infections" Death in the nine fatal cases described was ascribable to, or associated with, multiple cutaneous abscesses and ulcers, intercurrent erysipelas, acute pulmonary complications, intercurrent meningitis, streptococcal phlegmon, and pancreatic necrosis Crooke[2] states that in basophilism "death usually comes rapidly as a result of infection following some trivial injury or manipulation" Kass et al,[3] in a study of the effects of adrenocorticotropic hormone (A C T H) in pneumonia, record a case due to pneumococcus type 8 in which the institution of therapy was followed by bacteræmia which persisted after the clinical crisis

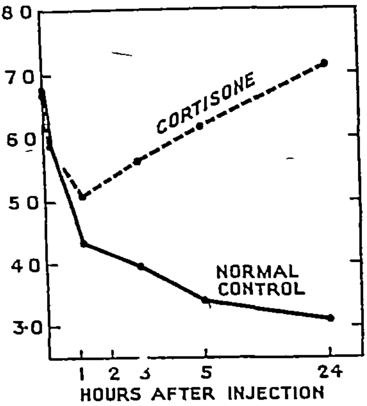


Fig 1—Results in experiment 1

The following experiments were planned as part of a general investigation of the influence of 'Cortisone' on phagocytosis These preliminary findings are presented in order to emphasise one of the possible dangers involved in cortisone therapy

A 24 hour culture of the pneumococcus was used as the test organism Throughout the experiments we adhered strictly to this culture period, in view of the reported influence of the state of encapsulation of the pneumococcus on the course of the initial bacteræmia after intravenous injection of this organism[4] Each experiment was made with a pair of male rabbits of approximately equal weight, maintained under identical conditions of housing and diet One animal served as a control The other received intramuscular injections of a saline suspension of cortisone acetate (Merck), as follows

Relation to injection of pneumococci (hours)	*Dose (mg)*
− 20	20
− 1	15
+ 24	15
+ 48	15

At zero time 1 ml of culture was injected by an ear vein At varying intervals thereafter, 1 ml of blood was withdrawn by syringe from the opposite ear and immediately expelled into nutrient broth containing 0 2% sodium citrate and 0·1% white saponin (B.D.H) The number of organisms in the blood sample was estimated by the pour plate technique, several dilutions were prepared in saponin citrate broth, and the final concentration of rabbit blood in the poured plate was adjusted by the addition of the calculated amount of sterile fresh rabbit-blood. Plates were incubated at 37°C for 48 hours and then counted, after choosing the dilution showing colonies in the range 100–1000 The blood content of pneumococci immediately after injection was calculated from the content of organisms in the 24-hour culture and from the blood volume, taken as 5% of the body weight

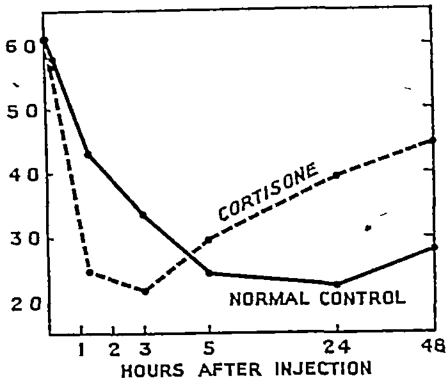


Fig 2—Results in experiment 2

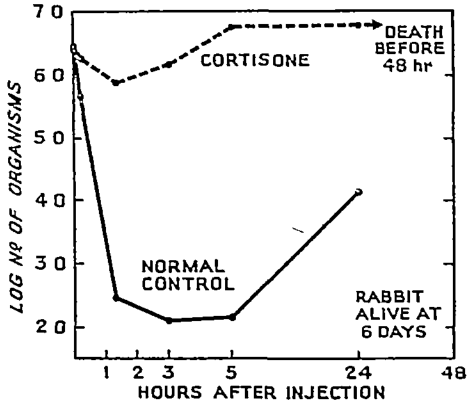


Fig 3—Results in experiment 3

---

[1] Cushing H *Bull Johns Hopk Hosp* 1932 50 137
[2] Crooke A. C Liddle Prize Essay London Hospital 1941–42
[3] Kass E H Ingbar S H Finland M *Ann. intern Med.* 1950 33 1081
[4] Enders J F Shaffer M F Wu C J *J exp Med.* 1936 64 307

RESULTS OF INJECTING CULTURES OF PNEUMOCOCCI IN FOUR EXPERIMENTS, EACH ON ONE NORMAL CONTROL ANIMAL AND ONE ANIMAL TREATED WITH CORTISONE

Time after injection	Expt. 1		Expt 2				Expt 3				Expt. 4	
	Orgs per ml (thousands)		Control		Treated		Control		Treated		Orgs per ml (thousands)	
	Control	Treated	Orgs per ml (thousands)	Rectal temp (F)	Orgs per ml (thousands)	Rectal temp (F)	Orgs per ml (thousands)	Rectal temp (°F)	Orgs per ml (thousands)	Rectal temp (°F)	Control	Treated
Immed	5600 0	4900	1116 0	102 8	1211 0	103 0	2252 0	103 1	2840	103 8	1300 0	1600
10 min	880 0	774	602 0		450 0		470 0		1836		845 0	736
1 hr 20 min	20 7	120	20 2		0 3		0 292		733		32 4	896
3 hr	9 3	414	2 25		0 15		0 128		1440		38 0	830
5 hr	2 5	1400	0 270	105 8	0 9	102 2	0 147	105 0	5700	104 0	41 5	31 500
24 hr	1 2	13 000	0 174	105 8	8 3	102 8	14 2	104 2	6120	104 2	6 228	240,000 *
48 hr			0 618		28 9						1522 8	
72 hr											62 0	

* Post mortem culture

The weights (g) of the control and treated animals in each of the experiments were as follows expt 1, 2150 and 1750, expt. 2, 1750 and 1650 expt. 3 2150 and 1900 expt 4 2200 and 1800

Expt 1—Observation continued 24 hours when both animals were sacrificed for histological examination
Expt 2—Observation continued 18 hours when both animals were sacrificed for histological examination
Expt 3—Observation continued 5 days when control animal was still alive and well Treated animal was found dead at 18 hours.
Expt 4—Observation continued 6 days when control animal was still alive and well Treated animal was found dead at 24 hours

are non lipoid containing macrophages in the spleen and other affected organs

(*f*) The disease is seen only in infants, and ends fatally It is neither hereditary nor familial

(*g*) There is a generalised hyperplasia of the macrophages present in the spleen and other affected organs These cells are large, round (sometimes polygonal), and pale staining, they do not contain lipoid, occasionally multinucleated giant cells are seen, and there is an increase in the reticular fibres The organs that may be affected are the spleen, liver, lymph glands, bones, lungs, skin, thymus, and lymph follicles of the intestine The presence of the enlarged macrophages may cause distortion of the normal architecture of the lymph-glands and spleen, areas of necrosis and hæmorrhages may occur

The case described below seems to fulfil the criteria first laid down by Siwe, although in addition this child had a hæmolytic anæmia, and, unlike all previous cases described, seems to be recovering She is alive and apparently in perfect health more than two years after the onset

Siwe (1933) did not suggest that all the cases he described were due to the same cause Some he regarded as due to infection, but this as a cause has been excluded as far as possible in the case described here

CASE RECORD

A girl, aged 18 months, was admitted to the Leicester Royal Infirmary on Jan 13, 1949 During the past month her mother had noticed that she was becoming paler, was refusing her feeds, and was irritable and fretful Also her urine had been darker than normal The child's birth weight was 7 lb 8 oz, and after being breast fed for a month she had been reared on National Dried Milk Her weight was 22 lb 4 oz She was an only child, both her parents were in good health, and there had been no known contact with tuberculosis or other infectious illnesses She had had no previous illnesses

On examination the infant was a blonde blue eyed baby She had a striking degree of pallor but did not appear jaundiced Very irritable, she keenly resented examination There were scattered petechiæ and purpuric spots all over her body, but chiefly on the trunk Her tonsils appeared healthy, and her tongue furred. There was a mucopurulent discharge from both nostrils Cervical glands were moderately enlarged on both sides, the left tonsillar gland being particularly large It was smooth, soft, not adherent to the overlying skin, and not tender Nothing abnormal was found in the lungs A soft systolic murmur was heard at the apex of the heart The blood pressure was 100/60 mm Hg The liver was palpable one finger breadth below the costal margin The spleen was much enlarged, the angle of the spleen extending to the level of the umbilicus The spleen was smooth and firm and did not seem to be tender The inguinal glands were slightly enlarged *B coli* were present in the urine There was remittant fever ranging between 100° and 103°F and tending to be highest at night

Examination of the blood and bone marrow confirmed that hæmolytic anæmia was present, with Hb 57% The bone marrow was hyperplastic, with large numbers of extremely immature red cells There was some delay in maturation of the leucocytes

Operation—Owing to the rapid rate of hæmolysis a transfusion (1 pint) was given, but the patient continued to hæmolyse her blood and became slightly jaundiced On Feb 13, a further transfusion was given in preparation for splenectomy This operation was performed (Feb 15) because of the pronounced hæmolytic anæmia and because hypersplenism was suspected After splenectomy the hæmolytic process seemed to be arrested, and regeneration of the blood began slowly However, the evening pyrexia was unaltered, the petechiæ continued to appear in crops, the glands in the neck remained enlarged, and the patient remained fretful

The *spleen* was found to be enlarged, with areas of thickened peritoneum covering it Sections were stained with hæmatoxylin and eosin for reticulin, and by Scharlach red, Sudan black, and Nile blue sulphate, and by Schultz test for cholesterol Scattered throughout the medulla were focal collections of large endothelial cells which appeared to be compressed at the periphery and were surrounded by fibroblastic rings The malpighian corpuscles seemed to be compressed and were relatively scanty The cells of the focal collections had a somewhat granular cytoplasm but did not appear to contain lipoid A few cells were undergoing mitosis Sections stained to show lipoid were uniformly negative There was no central necrosis, but apparently some erythrophagocytosis There were occasional giant cells of the mirror image type Though the histology suggested sarcoidosis, the lack of central necrosis and the absence of fibrillary structure were against this diagnosis, and the evidence pointed to a non lipoid reticulosis of the Letterer Siwe type

Streptomycin therapy—A preliminary examination of the spleen had suggested a diagnosis of sarcoidosis, and as sarcoidosis is thought by some to represent an atypical response to the tubercle bacillus, and the response to splenectomy had not been very dramatic it was decided to try streptomycin. The dose used was calculated as 0 02 g per lb of body weight per twenty four hours, given in two doses morning and evening Treatment was begun on Feb 24, 1949, and continued for five weeks

Seven days after streptomycin treatment started, the enlarged cervical glands were no longer palpable, the temperature had begun to settle, and for the first time the body was entirely free from petechiæ On March 7 the Hb was 63% A few days later the temperature had completely settled. In December, 1949, the child was still perfectly well, the hæmoglobin was 83%, the red cells numbered 4,470,000 per c mm, there were no enlarged glands, and the child was gaining weight Seen on April 26, 1950, she was a happy active normal child and a blood count showed red cells 4,520,000 per c.mm, Hb 84%, colour index 0·93, and white cells 11,100 per c mm (polymorphs 51%, lymphocytes 47%, monocytes 2%)

DISCUSSION

This case presented as hæmolytic anæmia but was otherwise typical of the condition described by Letterer and later reviewed by Siwe The diagnosis was not made until histological examination of the spleen had been completed Splenectomy did appear to arrest the hæmolytic process, but otherwise the child's condition was not greatly altered The response to streptomycin, on the other hand, was remarkable the enlarged cervical glands at once began to diminish, and all the other physical signs and symptoms disappeared

The child has remained well now for over two years. All the previous cases reported have progressively deteriorated, the longest survival being two years.

Though the ætiology of Letterer Siwe's disease is unknown, Siwe has suggested that various kinds of sepsis or reactions to as yet undetermined toxins may be factors The favourable response to streptomycin lends some support to this idea Of course, the possibility of a spontaneous remission cannot be ruled out, but remissions are not a feature of the disease

Acknowledgments and thanks are due to Dr Vernon Braithwaite for permission to publish this case, Dr E. Milford Ward, for the pathological report on the spleen, and Dr H S Baar for confirming that the histological appearances of the spleen were those of Letterer Siwe's disease

REFERENCES

Abt A F Denenholz E J (1936) *Amer J Dis Child* 51, 499
Letterer, L (1924) *Frankfurt Z Path* 30, 377
Siwe S A (1933) *Z Kinderheilk* 55 212
— (1949) Advances in Pædiatrics New York, vol 4, p 117

" In my academic pursuits in three universities, I associated with some *learned* men who professed to believe that scholarly achievement is accomplished *only* under the stress of monetary insufficiency—that the church mouse graduate student or fellow invariably out-performs the student with ample funds This is a ridiculous assertion. Many fine minds have been lost by the world of scholarship because its monetary rewards are so poor I personally believe much excellent work has been done *despite* penury and not because of it—Prof DONALD BAUER, of Wisconsin, in *Science*, 1951, 113, 331

Mr Brock went on to talk of mitral stenosis, saying that this was a much more important subject, since only 2% of heart disease was congenital whereas 25% was of rheumatic origin, the condition was, in fact, a national problem The anteromedial cusp of the mitral valve might be said to form the intraventricular part of the aorta, and it must on no account be damaged or split At operation the commissures were split with the finger, *the valve was not merely dilated.* He thought that the best age for operation was between 20 and 40, the oldest patient was aged 50 Fibrillation and embolism were not contra indications, nor was calcification of the valve, which was present in almost half of his series He had so far performed 48 of these operations, 8 patients had died, but all of the last 24 had survived

Dr **Maurice Campbell** observed that the indications for mitral valvulotomy were not clear cut, so far cases had been selected conservatively, only the bad cases being accepted. The operation was chiefly of value where the disorder was essentially mechanical, and this could be expected when the main symptoms were orthopnœa, cardiac asthma and pulmonary œdema, and perhaps recurrent hæmoptysis The main contra-indication was active infection or the chance of this recurring, and for this reason patients under 20 were rarely suitable Slight aortic incompetence or mitral regurgitation should not prevent a good result, but a greater degree of these changes was likely to do so Patients with long standing congestive failure had passed the stage when they could best be helped So far the results had been surprisingly good, even pulmonary hypertension had decreased considerably

In patients with coarctation he found great difficulty in deciding whether to advise operation, many were *able to lead a normal life and kept well for so long that* an operative mortality of 10% with another 10% who could not have an anastomosis done (Gross 1950) was not a justifiable risk unless there were signs that the patient was not doing well

In patent ductus the risk was already much less, and when it was reduced to 1% (as it was in the hands of Professor Crafoord) nearly all cases should be advised to avail themselves of the chance of cure He felt, however, that despite the 10% mortality which might be associated with operations for Fallot's tetralogy this was well justified by the 80% good results, since without operation the outlook was poor He concluded that so far valvulotomy had proved it could produce as successful results as Blalock's operation, though he was not quite sure whether it succeeded in quite so high a proportion of cases *Like Mr Brock, he was doubtful about the results of direct operation for infundibular stenosis,* although this had started so well

---

Reviews of Books

Pharmacology of the Failing Human Heart

JOHN McMICHAEL M D, F.R.C P, professor of medicine in the University of London at the Postgraduate Medical School of London Oxford *Blackwell Scientific Publications* 1950 Pp 63 8*s* 6*d*

THE introduction of cardiac catheterisation and its establishment as a safe method of investigation has been a great stimulus to the study of the circulation In the early days of any new technique, *misleading conclusions are apt to be drawn from insufficient data* at this stage observation is *more* important than interpretation, and working hypotheses may have to be modified to fit in with new facts Professor McMichael's monograph—one of the American Lecture Series—is not so much a guide to treatment as a very able account of the hæmodynamics of cardiac failure and an explanation of how established remedies may work His review is based largely on his own work and on personal discussions with other leaders in this field, and there are generous references to published work The concept of high and low output failure is restated, Starling s law of the heart reconsidered, and the importance of the myocardium emphasised A full discussion of the mechanism of cardiac failure precedes a particular account of the action of mercurial diuretics, and of digitalis and its allies, and the management of individual therapeutic problems is discussed No doubt there are good reasons for the success or failure of digitalis in certain types of patient, but we remain in fundamental ignorance of its ultimate mode of action Many with long clinical experience and knowledge of earlier experimental work will be relieved to learn that perhaps after all the primary action of digitalis is on the heart This book is authoritative and up to date, clearly expressed and well produced

Chemistry and Therapeutics of Synthetic Drugs

J W KEYSER M.SC Lond, A.R I C biochemist, *department of pathology Welsh National School of Medicine* London *Newnes* 1950 Pp 458 42*s*

A BOOK which really lived up to the title of this work would be invaluable, but in attempting to provide a "reference book for medical men, pharmacists, chemists and students' the author has *set himself* an impossible task and has failed fully to satisfy any of his aims. There is a large amount of information, but for whom some of it is intended is not *clear* For instance, a page is used to describe Bratton and Marshall's method of estimation of sulphonamides, which is too much for the general medical reader yet not enough for any worker who wants to perform the examination

No *doses are given, and loose terms* such as "moderate" and 'large" doses are used. The abbreviation *N.F* used throughout the book does not (as might be supposed) indicate the British *National Formulary,* but the American one The description of chemical synthesis varies enormously the synthesis of quinine would be understood only by an experienced organic chemist, and then with difficulty, whereas the synthesis of camphor from pinene, which is well known, is very clearly and graphically expressed If penicillin is included at all in such a work, surely the structure of the six penicillins referred to should be given, and not merely a statement that they exist

The appendix of trade names is useful but cross reference to the body of the work is difficult Thus 'Physeptone' appears in the appendix together with its chemical name, but neither physeptone nor its chemical name appears in the index, and only if the reader already knows that amidone is another synonym can he find the appropriate text page

What is Hypnosis?

Studies in Auto and Hetero Conditioning ANDREW SALTER London Athenaeum Press 1950 Pp 90 8*s* 6*d*

PRESENT-DAY theories of the unconscious owe their origin to the study of hypnosis and this remains the most direct and striking method of psychotherapy although perhaps at the moment the least fashionable No system of psychopathology has yet produced a convincing explanation of its phenomena, although these have been re-described and re-labelled in the language of many systems The objective experiments of Clarke Hall and of Kretschmer have taken much of the mystery out of the subject While these workers have rightly claimed it as material for a wholly scientific approach they have yet hesitated to put forward a theoretical framework to embrace all its features Andrew Salter is a behaviourist who is not lacking in objectivity, he is also human enough to be alive to therapeutic possibilities He points out that hypnotic suggestion has similarities with the process of "conditioning" which produces a conditioned reflex, and feels that the elements of mastery in the hypnotist and dependence in the subject, of which so much has been made in the past, are irrelevant Like Kretschmer and Schultz he has seen the possibilities of teaching the patient to become his own hypnotist, to condition himself The descriptions of his experiments and methods of treatment will ring very true to anyone with practical experience of hypnosis, and they are easily verified in practice In his methods of autohypnosis the author

The results are shown in the accompanying table and in figs 1–4, each representing an experiment with a pair of animals, in each pair the same culture was injected at an interval of 10 minutes, and both animals were followed concurrently

The results agree in demonstrating a striking difference between the course of the bacteræmia in the cortisone treated and in the normal animals In experiments 1 and 2 the number of organisms fell initially in both groups of animals In experiments 3 and 4 this initial fall was slight or absent in the case of the cortisone treated animals At the 3rd hour in experiments 1 and 2, and even earlier in experiments 3 and 4, the number of organisms in the cortisone treated animals began to rise, while in the normal controls the number continued to fall, thereafter, the number of organisms in the cortisone treated group increased rapidly resulting in death within 48 hours in experiment 3, and within 24 hours in experiment 4

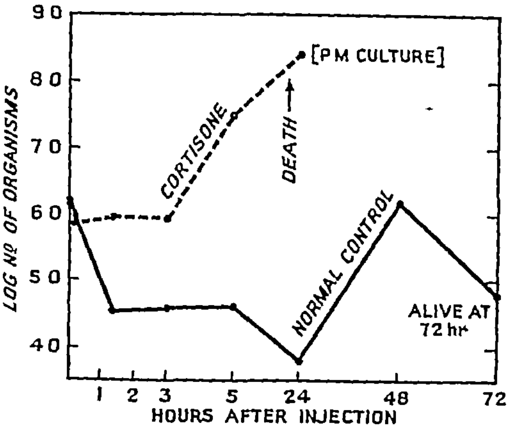


Fig 4—Results in experiment 4.

It would be premature to speculate in detail on the cause of this disastrous effect of cortisone on the course of pneumococcal bacteræmia We are at present engaged in a survey of the effects of cortisone on phagocytosis of bacteria and inert particles, and the results with organisms other than the pneumococcus must not be anticipated In the case of inert particles, Selye [5] has claimed that A C T H markedly increases the phagocytosis of indian ink As regards other bacterial infections, D'Arcy Hart and Rees [6] described an enhancing effect of cortisone on tuberculosis in the mouse, but it is difficult to correlate this with the present work

Cortisone might well be expected to have a deleterious effect on the course of an infective process, in the light of the observation by Bjørneboe et al [7] that antibody production in the rabbit decreases under the influence of cortisone and A C T H But the effects noted by us are demonstrable too early to be attributed to this mechanism Further, the action of cortisone in inhibiting granuloma formation or mitotic division of cells can hardly be relevant, since the clearance of organisms from the blood stream at this early stage of an infection must depend on the already differentiated phagocytes

We are indebted to the Medical Research Council s committee on A C T H, cortisone, and related substances for supplying the cortisone, and to Prof S P Bedson and Prof Dorothy Russell for helpful criticism and encouragement

R G WHITE
B.M. Oxfd
Freedom Fellow Bacteriology Department

A H E MARSHALL
Bernhard Baron Institute

London Hospital

---

[5] Selye H Brit med J 1949 ii, 1129
[6] Hart, P D A, Rees R J W Lancet 1950 ii 391
[7] Bjorneboe, M, Fishel, E E Stoerk H C J exp Med 1951 93, 37

Medical Societies

ROYAL SOCIETY OF MEDICINE

Surgery of the Heart and Great Vessels

THE surgical section of the Royal Society of Medicine met on April 4, under the chairmanship of Sir STANFORD CADE, president of the section, to discuss the surgery of the heart and great vessels

Prof C CRAFOORD dealt chiefly with patent ductus arteriosus and coarctation of the aorta, both of which, he said, though of doubtful ætiology, were essentially due to too little or too much connective tissue reaction after birth at the site of the ligamentum arteriosum Coarctation of the aorta was found once in 7000 births, and 90% of the patients died before the age of 50, mostly through cardiovascular accidents Symptoms started sometimes as early as the age of 5 years, and nearly all patients had symptoms by the age of 25 Some complained of hypotensive effects in the lower limbs, and in many the mental and physical powers were greatly increased by operation The prognosis was unpredictable, and sudden death sometimes took place from acute cardiac failure In most of his 85 cases excision of the stricture with an end to end anastomosis had been performed, and subsequent angiocardiography showed that a lumen which was 60% of normal was adequate Already 24 of his patients were well and at work, 5 years after operation, 17 of these were symptom free As to the age for operation, the limiting factor was arteriosclerosis, he had seen this developing as early as $3^1/_2$ years and as late as 43 years The upper age limit for surgery seemed to be 30 years, but the sooner the patient was operated on, the better

Turning to patent ductus arteriosus, Professor Crafoord said that he had had 282 cases, 16 of which were atypical in that a large right heart and pulmonary hypertension were found Of these 16 patients 8 had died after operation, whereas of the remaining 266 only 2 had succumbed He felt that morbidity and mortality were undoubtedly higher in patients who were not subjected to operation than in those who were operated on, and 90% of the patients were actually better for the operation The optimum time for surgery was at ages between 3 and 12 years When the duct was long enough for a 2 mm gap to be left between the ligatures, the operation of choice was double ligature, failing this, division and suture should be undertaken In all, 4 cases of his had recanalised

Mr R C BROCK said that the surgical approach to heart disease could now be either direct or indirect, and he confined his remarks largely to the former He had performed, in all, 130 intracardiac operations for pulmonary and mitral stenosis The results of the Blalock operation were excellent, and the mortality was low, but the essential lesion—pulmonary or infundibular stenosis—remained and might increase, and thus a direct attack was at least theoretically preferable He was sure that for pure pulmonary stenosis valvulotomy was essential, and here Blalock's operation was absolutely contra indicated He also felt that valvulotomy was the correct procedure for patients with a valvular stenosis in Fallot's tetralogy, but he was as yet less certain that the infundibular punch which he had designed for the treatment of infundibular stenosis, gave as good results as did Blalock's operation He had performed 57 pulmonary valvulotomies with 10 deaths—28 for pure pulmonary valvular stenosis, 29 for Fallot's tetralogy There had been only 1 death in the last 29 cases Infundibular resection had been done in 22 cases with 7 deaths, combined infundibular resection and valvulotomy in 6 cases with no deaths

THE LANCET

LONDON SATURDAY, APRIL 21, 1951

Sisters or Daughters?

A CHIROPODIST writing to us the other day described herself as a member of a junior branch of the medical profession, and complained of a surgeon's action as unseemly in a colleague of the senior branch. What then *is* the medical profession? "The distinction between work which requires and work which does not require a medical qualification is blurred," writes Dr FFRANGCON ROBERTS[1], for we have not only allowed but even initiated and encouraged the dilution of our labour. Clearly, the medical profession proper consists of people who have gone through a full course of training in a medical school—a course intended to fit them not only for the diagnosis and understanding of disease but for the care and understanding of patients. The position of a physicist or biochemist working in medicine is equally plain: he is an honoured colleague from a sister profession making his own contribution to medicine on equal terms. But what about the physiotherapist, the almoner, the dietitian, and the speech therapist? Are they members of sister professions, or are they daughter members of our own? Ought we, perhaps, to enlarge our conception of the Greater Medical Profession to embrace everyone who works in a medical organisation such as the National Health Service? This question arises from the report of the Cope Committees summarised on another page.

We can fairly begin by excluding from professional status a proportion of those who work in the N.H.S.—porters and wardmaids for example. Professionalism is nowadays extending rapidly: hairdressers have been trying to establish a State register for themselves, and any dignified vocation, such as that of butler, tends to describe itself as professional. But, though times change and we with them, it is probably still correct to say, with CARR SAUNDERS and WILSON[2] that no calling is truly a profession which does not require a long specialised intellectual training in its technique. In the typical profession this technique is derived from a basic field of inquiry, and CARR-SAUNDERS and WILSON illustrate this by saying that doctors and dentists are concerned with science whereas nurses and midwives are concerned only with the application of science. But they add that the more the practice of a technique is likely to arouse a sense of personal responsibility, and create a direct and personal relation with clients, the closer will be the approach of a vocation to a profession, and here not only the nurse and midwife have a strong claim, but also many of the other groups who take on part of the care of the patient—the occupational therapist, the almoner, the physiotherapist, and the dietitian. The laboratory assistant in the hospital, or the pharmacist, will see patients less often, but the welfare of these patients may nevertheless depend on his responsible performance of a specialised technique acquired only by years of training. In all these activities the desire for professional status has led to steadily rising standards, both technical and ethical, which is mainly to the good. But Dr ROBERTS paints a dismaying picture of a medical service in which the doctor will hardly get a word in edgeways, and in a letter we publish this week Dr RABSON makes the still more painful suggestion that the doctor's claim to be a doctor, different from the other technicians, has less and less foundation.

The Cope Committees excluded nursing from their purview because nurses already have their own registration councils, but they deal with eight other groups of non-medical staff working in the N.H.S.—almoners, chiropodists, dietitians, medical laboratory technicians, occupational therapists, physiotherapists, radiographers, and speech therapists. Their main report, which is endorsed by the medical members of every committee, accepts the term "medical auxiliaries" for all these diverse callings, pointing out that they all "work for the benefit of the patient under the direct or indirect supervision of the doctor." This conception leads naturally to the proposal that the training and registration of the various groups should be entrusted to a statutory council whose members would be mostly *medical*, and that the professional committee charged with the affairs of each group should be the agents of the main council. The scheme suggested is workable and has conspicuous advantages, but it is based on the idea that the callings in question are junior, ancillary, branches of medicine, which need to be developed paternally as part of the whole. This idea is vigorously challenged in a minority report by two almoners, two occupational therapists, and a speech therapist. They object to the term "medical auxiliary" in relation to their professions, for a profession is a calling having its own standards of training, principles of practice, and professional ethic. They believe that the majority proposals would undermine the sense of responsibility within the professions concerned, and they cannot believe that the Government will accept recommendations which would deny to any profession full responsibility for establishing and maintaining its own standards.

> "We consider that the establishment of a central controlling Council to direct a number of distinct professions, whose diversity is clearly apparent, could only have a stultifying effect on the work of the professions concerned. . . . The recommendations . . . are based on the assumption that doctors can, by virtue of their medical training and experience, satisfactorily plan and control the curricula of training and methods of work of the professions under review. From our experience this is not in accordance with the facts. We agree that members of our professions must work closely with the other specialists in the team treating the patient, of which team the Doctor is the undisputed leader. This, however, presupposes a very different basis of association from that which the Report assumes. Almoners, being primarily social workers, bring into the health services knowledge and experience learned in the social science departments of universities and in fields of social service other than health. Occupational Therapists and Speech Therapists also offer specialised knowledge and skills which can only be acquired outside the field of medicine."

Instead of the single registration council favoured by the majority, this minority propose that each profession should have its own registration board, a small central council being set up, if need be, to advise offers something for the patient who is too proud to surrender all his thoughts to a psycho-analyst or who has at the outset too little hope or leisure to settle down to a prolonged transference relationship The book is short and the author's enthusiasm makes it very readable It is much improved by a foreword by E B Strauss which brings it into relationship with other recent work on the subject of which the author was unaware at the time of writing At a time when the therapeutic efficacy of abreactive methods based on the elastic theories of psycho analysis is much in question, this book may well play its part in the swing of psychotherapeutic fashion towards less interpretative methods The writer has made a good case for regarding the phenomena of conditioning as at least as important as those of transference

---

[1] *Lancet* March 24 1951 p 678

[2] Carr Saunders A M Wilson P A. The Professions Oxford, 1933

Recent Advances in Ocular Prosthesis

J H PRINCE, F B O A, F S M C, F R M S, F Z S Edinburgh E & S Livingstone 1950 Pp 156 20*s*

THIS book is the companion volume of *Ocular Prosthesis* by the same author, and is timely in view of the use of acrylic in the manufacture of the "ocular prosthesis," and the interest aroused by recent work on implants of tantalum and 'Vitallium,' which can be fixed into Tenon s capsule by suturing the rectus muscles and the attachment of the acrylic prosthesis to the implant These advances improve both the comfort and appearance of those who suffer the misfortune of losing an eye Mr Prince gives good descriptions of the technique of making conjunctival impressions, of the chemical and physical properties of methyl-methacrylate, of 8 methods of making an artificial iris, and of the fabrication and processing of acrylic prostheses The illustrations, too, are good It is unfortunate that he has not taken proper advice about anatomical terms, and about some facts in the surgical operation which he has tried to describe, for there are several mistakes and inaccuracies Thus recession of the upper lid is not due to the pull of the superior rectus, but more probably to the downward displacement of orbital fat, and his suggestion that animal conjunctiva might be used to graft a contracted socket shows him to be unaware of the fate of such grafts, and of the reaction of the host to foreign protein Again, no competent surgeon would rob an eyelid of skin to line part of a socket The term orbital cavity is used several times when conjunctival sac is intended For those engaged in making ocular prostheses, however, the book will prove highly valuable

Modern Trends in Neurology

Editor ANTHONY FEILING, M D, F.R C P, senior physician neurological department, St George's Hospital London Butterworth 1951 Pp 717 63*s*

THREE of the twenty articles in this volume are by workers in the United States D E Denny-Brown contributes an exhaustive and admirable account of the physiology and clinical aspects of frontal lobe function, E C Kunkle and H G Wolff give an account of headache based on their experiments, and W J Mixter writes on rupture of the intervertebral disc This last article emphasises the importance of myelography in diagnosis, an investigation largely discarded in this country in the diagnosis of disc protrusions Among the sections by British authors are an outstanding discussion on the conduction of the nervous impulse by W A. H Rushton, a detailed study of intracranial aneurysms by S P Meadows, and a stimulating account of cervical rib and axillary inlet compression syndromes by F M R Walshe In addition to the physiological and clinical articles, radiology of the nervous system is lucidly described by J W D Bull, and Denis Williams discusses the clinical applications of electro-encephalography It is somewhat surprising that there is no section on the nutritional and metabolic aspects of neurological disease, or on the experimental work on the production of demyelination—subjects which have seen definite advances in knowledge in the last few years The production of the book, and the clinical and pathological illustrations and X ray reproductions, are of a very high standard, but there are some inaccuracies among the references We congratulate Dr Feiling on his editing of a valuable book

Human Embryology for Medical Students

S R NAIR, department of embryology, Topiwala National Medical College, Bombay Bombay Popular Book Depot 1950 Pp 364 £2 2*s*

Dr Nair intends his book to serve as a "handy reference" rather than as a textbook of embryology, and it is in fact considerably shorter than most such works Since he covers the usual topics of human embryology, the brevity has been attained by describing in less detail the various developmental processes, and sometimes this tends towards obscurity For example it is unlikely that the student will understand the development of the heart from the description given, unless he supplements it from other sources There are a large number of illustrations, most of them drawings, and all in line generally they are clear and accurate, but their relevance would have been more evident if they had been mentioned in the text On the whole this book will be of more value read as a supplement to lectures than as a textbook in its own right Several existing textbooks are more richly illustrated at a lower cost

Metabolic Interrelations

(Transactions of the Second Conference) January 9-10, 1950 New York Josiah Macy, Jr, Foundation. 1950. Pp 279 $3 95

THE first of these conferences on metabolic interrelations, held in February, 1949, was devoted largely to the biochemistry of bone This second conference was held about a year later, and, since all the papers were about bone, the name "Metabolic Interrelations" is a little misleading The report follows the lines of its predecessor There were eleven papers, some of them frankly physicochemical, such as those on the composition and structure of the bone salt, or on bone as a problem in surface chemistry, others were more biochemical, dealing with the enzymic activity of bone or the effect of hormones and vitamins on its metabolism and calcification A few —such as the one on strontium as an adjuvant to calcium in the remineralisation of the skeleton in osteoporosis in man—were based upon a study of clinical material. They are all rather highly specialised, but none the less interesting to workers in the field of bone metabolism. Sometimes the reports of the discussions exceed the length of the papers themselves, and they are not always very illuminating A little work in the editorial department of the Josiah Macy Foundation would enhance the appeal of their reports

---

Catalogue of Lewis's Medical, Scientific & Technical Library (London H K Lewis 1950 Pp 1152 35*s*)—This catalogue has now been revised to Dec 31, 1949, and readers and librarians alike will be glad to have this new edition for reference The familiar red volume, a little stouter than of old now contains about 27,000 titles In the introduction to the classified index of subjects, there is a mild editorial complaint that this work has been made more difficult by the uninformative and misleading titles which are nowadays often given to 'otherwise serious works" To help the would be reader the initials of authors and the year of publication have been inserted in this part of the catalogue, and a word or two has often been added to show the nature and scope of the book.

Medizinische Psychologie (10th ed Stuttgart Thieme, 1950 Pp 304 D M 24)—This stimulating compendium of Prof Ernst Kretschmer s studies and opinions provides a coherent introduction to psychiatry, but ignores such vast tracts of other men's work that it can hardly be called up to date Professor Kretschmer leans strongly towards the attribution of psychological happenings to cerebral areas, in the manner of Kleist of Frankfurt, and includes in this edition many details of W R Hess s work on vegetative centres in the midbrain. But in this and in his references to the orbital region and its functions he is evidently unaware of the many investigations made in the English speaking countries, nor does he quote French investigators in relevant fields In the main the book remains a vigorous exposition of German medical psychology in its most progressive form unded of other components of the United Nations 'ce, there is no reason to suspect any inadequacy today In comparing the organisation of medicine in Korea th the organisation to which many of us became customed in the late war, the biggest stumbling- ock is terminology A mobile surgical hospital pears to correspond to a C C S with several attached rgical units, but the range of function of separate abulance company, separate collecting company, d separate clearing company is difficult to calibrate the measure of our field ambulance and mobile nbulance column If the employment of armies rawn from many nations becomes common practice iere will no doubt be attempts to introduce some niformity in these things Names matter very little, d we would suggest that the hallmark of an efficient eld medical organisation is intelligent training irected to individual responsibility in small units nd to elasticity sufficient to cope with changes in errain and great fluctuations in the number of ounded Most of the catastrophes of military edicine in this century have been due neither to tupidity nor to callousness but to too much rigidity f direction or equipment In Korea evacuation rom the line has been largely by ambulance as far s railhead, but, owing to the poor state of the oads, ambulance trains have been preferred for transport to the rear Helicopters have been employed for he transport of the seriously wounded from forward reas, and casualties have mostly been removed to Japan r the U S.A. by air, though some have travelled y sea[1]

Among all the changes in surgical practice in the field between 1939 and 1945, "forward" surgery by experts, followed by rapid evacuation, was probably the most revolutionary and the most rewarding It is a principle rather than a drill, and, as applied in Korea, appears to have been gratifyingly successful Figures so far suggest that the mortality among wounded is about $2^{1}/_{2}\%$ as against an over-all average of 4% in the last war Those who remember hoarding a few thousand milligrammes of penicillin in 1943 will smile to hear of the huge supplies of antibiotic drugs available First impressions suggest that 'Terramycin,' because of its "polyvalency," is especially useful in forward areas A novel hazard for the American and British forces has been the cold special clothing has been required, and an interesting experiment is the training of N C O s of all arms to decide the clothing needs of the moment and to recognise the exhausted soldier who must be sent to the "warming tent" for recovery But of casualties due directly to cold less than 10% have had to be evacuated from Korea Keeping the wounded man warm is a problem not yet solved Plastic bags in which the patient and his blankets can be inserted have proved satisfactory, but those in use so far have been too heavy and bulky for forward areas

We have heard those who would excuse war for the advances in medical knowledge which result We cannot agree, but it would be foolish to deny that these advances occur, and it is unlikely that the war in progress will be without benefit in this way Chloroquine is now the standard drug in the U S army for the suppression of malaria and has been found satisfactory The disciplinary advantage of weekly rather than daily dosage is thought to outweigh the risk of relapse, and the treatment of the latter with primaquine, a new product, is under trial Methadone *vice* morphine has also won approval, and in its iso lævo isomer produces less nausea and is better tolerated by those who must make long journeys by air Experience is accumulating in the use of dextran and other plasma substitutes Intramedullary pins have been used largely in the treatment of fractures of long bones, and we shall be glad to hear more of a casein resin splint, lighter and stronger than plaster-of-paris For burns, and with an eye to damage from atomic explosions, a huge water- and bacteria-proof dressing 19 in by 36 in has been used, though effective, it is difficult to hold in place and for this purpose a simple technique for rendering a cotton bandage elastic has been devised All these in their own way seem to promise improvements in surgical technique, and we shall look forward to critical reports in the future In preventive medicine two novelties under trial deserve description Iodine and not chlorine seems to be the active agent in a new water sterilising tablet which is at any rate moderately lethal to cysts of *Entamœba histolytica* It has its failings, it turns starchy foods blue and the water brown, but the taste is no worse than that of chlorinated water Of far more general interest is actidione, a by-product in the making of streptomycin, which is reported to be an effective repellant of rats Such pleasure as this will bring the quartermaster will be negligible compared to that of the farmers and millers of the whole world If the claims for actidione are well founded and it can be produced at a reasonable cost (which it cannot be at the moment) it is a discovery of the first magnitude

It is a common and not unreasonable complaint that war and the threat of war drive the springs of scientific inquiry underground We are therefore unusually grateful to the Office of the Surgeon General in Washington for giving so much news of the doings of his department in Korea It is stimulating to us and can be of no comfort to the enemy

---

[1] Latta R M. *Lancet* Jan 27 1951 p 228 March 31 p 747

Annotations

ADDENDUM TO THE B P

THERE is just enough of the element of surprise in a new pharmacopœia or an addendum to an existing one to arouse in the pharmacologist or pharmacist some of the emotions that other people get from a lottery draw or the Chancellor's Budget speech The *Addendum to the British Pharmacopœia, 1948*, which was published on April 19 and will become official on Sept 1, includes over 40 additions and over 50 amendments to existing monographs The additions sometimes reflect a prompt recognition of the value of some recently introduced drug, like chloramphenicol, and sometimes a more gradual establishment of a drug's status—for example, the anti histamine drugs mepyramine maleate and promethazine hydrochloride ('Anthisan' and 'Phenergan') are now official Other newcomers are D D T, under its previously approved name of dicophane, isoprenaline sulphate (isopropyl noradrenaline), and methacholine chloride (acetyl β methylcholine hydrochloride, or 'Mecholyl') Among the antibiotics, besides chloramphenicol, the addendum includes *streptomycin* (three salts and their injection preparations), and crystalline penicillin G, *officially* known as benzylpenicillin. Procaine benzylpenicillin is also listed and will be dis-on coordination and settle matters in dispute They also disapprove—with reason, we think—the novel proposal to establish statutory registers for purposes of the National Health Service only, which may mean "that more than one standard of basic qualification may be recognised within a single profession"

In bringing his flotilla of committees into port, Commodore **Cope** would no doubt have liked to see the crews unitedly pulling in the same direction Nevertheless, the lack of unanimity is proof of vitality and it usefully displays some rapidly developing stresses in the structure of medicine The minority report we have quoted makes out a good theoretical case, and it is certainly hard to see why almoners and physiotherapists should be offered a lesser degree of professional independence than, for example, nurses On the other hand most of us are convinced that the fragmentation of medicine has already gone too far, and that the time has come, in the interest of patients, to reassert the true doctor's predominance over technicians of whatever kind Which takes us back to Dr **Rabson**'s disturbing letter

Surgery of Mitral Disease

ADVANCES in surgery, like the final chapters of good detective novels, never seem to develop in a way that can be foreseen Mitral stenosis has always offered a challenge to the surgeon, because enlargement of the stenosed opening should relieve most of the symptoms Numerically this is an important problem, in the U S A **Paul White**[1] has estimated that 0 5–1% of the population have valvular disease as a sequel to rheumatic fever, and in Britain the figure can hardly be less

An operation for the relief of mitral stenosis was proposed almost fifty years ago by Sir **Lauder Brunton**,[2] yet it is only in the last couple of years that such an operation has been performed on any scale This latter day progress is due partly to advances in related fields, notably the introduction of new anæsthetic drugs, muscle relaxants, and controlled respiration, the discovery of potent anti biotics, and better understanding of fluid and electrolyte requirements after operation The foundation of the present improved position in cardiac surgery was laid in the middle '20s by **Cutler** and **Beck**[3] in Boston, **Souttar**[4] in this country, and others, who made a direct surgical attack on the stenosed mitral valve The mortality rate proved too high, and during the next ten years cardiac surgery was largely restricted to removal of foreign bodies It was during this decade, however, that investigations into respiration progressed so well that thoracic surgery was robbed of many of its dangers These advances will always be associated particularly with three names **Tudor Edwards** of London, **Edward Churchill** of Boston, and **Crafoord** of Stockholm Subsequently great strides were made in the surgery of congenital defects of the heart and great vessels **Gross** tied the patent ductus arteriosus, **Crafoord** resected coarctation of the aorta, and **Blalock** anastomosed the subclavian and pulmonary arteries to relieve the cyanosis of Fallot's tetralogy Pulmonary stenosis being mainly responsible for the cyanosis in this condition, **Brock** made a direct surgical attack with valvulotomy, and the success of this procedure led him to try a similar operation for mitral stenosis His latest report to the Royal Society of Medicine is summarised on an earlier page of this issue

Brock has performed valvulotomy for mitral stenosis in 48 cases, there have been 8 deaths, but none in the last 24 cases In Philadelphia **Bailey** and his associates,[5] who have proceeded along similar lines, have operated on 50 patients with 8 deaths, they call the operation commissurotomy—a term suggested by **Durant** of Philadelphia From Paris[6] and Montreal[7] come similar accounts of successful operative relief, and in this country and elsewhere many surgeons have been perfecting their operative technique As a result of this rapid progress cardiologists are likely to find themselves called on to decide which cases are most suitable for operation, and Dr **Maurice Campbell** is to be congratulated on his most successful collaboration with Mr **Brock** in this field It has already been shown that younger patients survive valvulotomy best and derive most benefit from it This is probably because they have escaped the changes which accompany long standing back pressure in the pulmonary circulation, one of **Bailey**'s patients who died three days after a commissurotomy[8] was found to have pulmonary changes which accounted for death Patients with Lutembacher's syndrome are known to withstand mitral stenosis well because their atrioseptal defect allows a left to right shunt **Sweet** devised an operation utilising the azygos vein to relieve the pulmonary pressure, and there may still be a place for this type of manœuvre in patients with mitral stenosis of long standing in whom valvulotomy alone is unlikely to be of much help **Blalock**'s operation for making an atrial septal defect may be of use for the same reason

Meanwhile we need some modern **Oliver Wendell Holmes** to devise a word for the new operation, which neither "valvulotomy" nor "commissurotomy" quite describes

Medical Services in Korea

THE opening of the campaign in Korea did not find the medical services of the army of the United States entirely unprepared Equipment for field medical units was in store, assembled and ready for issue, while the garrison in Japan provided personnel enough for three mobile surgical hospitals and an evacuation hospital That these, though hard worked, were just sufficient to handle the casualties of the four U S divisions confined within the Pusan perimeter was due to numerous base hospitals having been already established in Japan, 140 miles away and 45 minutes by air As the number of combatants increased, so did the number of medical units, and, though these have accepted responsibility for the familial allergy, emphysema, nasal allergy with lyposis, and eosinophilia It is thought that aspirin not an allergen per se, but that it combines with dy proteins (perhaps the circulating globulins) to m specific allergens or haptens which evoke the ictions The dangers of aspirin sensitivity should ways be considered when prescribing aspirin for thmatics and allergic subjects

---

[1] White P D Cecil's Textbook of Medicine Philadelphia 1937 p 1107
[2] Brunton L *Lancet* 1902 i 352
[3] Cutler E C Levine S A Beck C S *Arch Surg* 1924 9 689 *Ibid* 1929 18 403
[4] Souttar P W *Brit med J* 1925 ii 603
[5] Glover R P Bailey C P O'Neill T J E *J Amer med Ass* 1950 144 1049
[6] Soulié P O'Neill T J E Servelle M diMatteo J Joly F, Carlotti J Sicot J-R *Bull Soc Méd Hôp Paris* 1950, 66 1665
[7] Cagnon E D *Canad med Ass J* 1950 63 537
[8] Welch K J Johnson J Zinsser H *Ann Surg* 1950 132 1027

A PSYCHODRAMATIC EVENING

GROUP psychotherapy has received increased attention nce the late war, with its large number of psychiatric isualties among Servicemen and civilians, forced sychiatrists to look around for methods of treating ieir patients en masse rather than individually The pproaches have been many, depending largely on the mperament and experience of the proponent they inge from the inspirational, semi revivalistic techniques f L C Marsh at Worcester State Hospital, A A Low ith his "Recovery, Inc" in Illinois, and Alcoholics nonymous, through the educational methods of E W. azell, to the analytical approach of S H Foulkes and Bion—to instance but a few of the pioneers on both ides of the Atlantic

The continued interest of psychiatrists and their co workers in this matter was shown in London on April 9, when a large audience witnessed a demonstration of sychodrama by Dr J L Moreno, presented under the uspices of the Institute of Social Psychotherapy Dr Moreno was one of the first psychiatrists to apply group methods, beginning work with neurotic children n Vienna in 1911, the children were encouraged to ict out their fantasies, and in this way psychodrama evolved Later the method was applied to adult patients ind introduced by Dr Moreno to the U S A., the first psychodrama theatre connected with a hospital was built in 1936 at Beacon Hill, New York, where Dr Moreno's sanatorium and Institute of Sociatry is the headquarters and training school of his movement throughout the U S.A At the meeting Dr Moreno began by recalling that drama had evolved from religious group activities, first one and then more than one participant being pushed forward to enact and voice the group's emotions The hall in which he was speaking conditioned, he said, the response of his audience, for he was on a platform, cut off from his hearers by height and distance His psychodrama theatre or, as he preferred to term it, "spontaneity theatre" had a low, semicircular stage projecting into the auditorium with shallow steps leading down from stage to audience In the front row sat his specially trained assistants who as "auxiliary egos" could be called on by a patient to enact the rôle of the patient himself or of anyone in his emotional story—father, mother in law, wife, child, boss, and so forth Behind the auditorium was a gallery, reserved for "superegos," and useful on one occasion when he had a patient with a remarkable resemblance to Adolf Hitler, moustache and all, who was provided with auxiliary egos to represent the Führer's entourage and was allowed to address the crowd from above This patient, via a mildly homo sexual friendship with his pseudo Goering, eventually made a social recovery

By now Dr Moreno had got into his stride, and was pacing up and down the stage and making sorties into the audience, every muscle in his face and body used with the fluent abandon of the born actor, so that a press photographer and his flashlamp assistant, pussy footing down the aisles were hard put to it to capture his split second gestures They caught one dramatic moment, when Dr Moreno was making believe to strangle the chairman to illustrate what he called mirror acting This was further enacted by Mrs Moreno and a volunteer from the audience In mirror acting the depressed or catatonic patient may be drawn into participation by trained assistants who have studied his case enacting before his eyes the way that he behaves A typical marital problem was acted by a London psychiatrist and Mrs Moreno, starting from the breakfast table squabble over wifely extravagance and hubby's more than professional interest in his secretary, and continuing to the interview of the aggrieved lady with her solicitor—a rôle in which the psychiatrist showed a ready wit and nice opportunism by advising her to consult a psychiatrist Lastly, the importance of the "double" was demonstrated, this being Dr Moreno's term for the imaginary other self with whom each of us carries on a lifelong, not always silent, colloquy This was charmingly and gallantly done by a young newly married Norwegian girl from the audience, ruminating aloud in our foreign tongue on how she expected to feel seeing her parents for the first time since her marriage, with Mrs Moreno skilfully voicing the dubieties and homely aphorisms of her alter ego, and, in the background, Dr Moreno, resourceful as Prospero and lively as Ariel, perpetually darting, prompting, questioning

TUBERCULOSIS IN SCOTLAND

IN Scotland mortality from tuberculosis continued to rise in the years after the end of the late war, but in 1950, as we noted last week,[1] the rate fell to a level 15 per 100,000 below the average for the previous five years In its latest report[2] the Royal Victoria Hospital Tuberculosis Trust observes that definite improvement has taken place "during a period when every public utterance has proclaimed not only the lack of adequate measures for controlling the disease, but the supposed deterioration of facilities which had existed previously" The report draws attention to the epidemic nature of tuberculosis, and rightly attributes the deterioration after 1939 to changes, both mental and physical, in the human soil. It ascribes the failure of the mortality rate to improve in the post war period up to 1949 to the delayed effects of increased infection and morbidity in the war years Infection must also have increased in England and in other countries where mortality, after a war time rise, fell in the immediate post war period, and it seems possible that the main cause of the post war situation in Scotland may have been the less satisfactory pre war conditions, perhaps exaggerated by war time influences In the words of the report "Better developed services in England, particularly better facilities for isolation and treatment, probably influenced the epidemic in that country at an earlier stage" The report attributes the recent fall in mortality to the recession of the epidemic wave initiated by the war, but the fall has coincided with the general introduction of chemotherapy, which may have played an even more important part than the natural recession

It is pointed out that both developmental changes associated with puberty, and recently acquired infection, are important causes of the high mortality among adolescents, especially females, and the high mortality in older men is reasonably attributed to recrudescence of old latent foci, but no mention is made of the "generation" method of analysing mortality rates, to which attention has been drawn in our correspondence columns[3] Such an analysis adequately explains the present high rates of mortality in older males without invoking the "stresses and strains of life and of adverse social and economic factors" These factors, no doubt, are important, as the report says, in determining the general pensed when procaine penicillin is prescribed Other monographs deal with ethinyloestradiol, cetrimide ('Cetavlon'), propylthiouracil, oxyphenarsine, and quinalbarbitone ('Seconal') There are 8 new monographs on preparations of blood, and presumably because of the inclusion of whole blood an appendix has been added on ABO and Rh group testing

---

[1] *Lancet* April 14 1951 p 859

[2] Royal Victoria Hospital Tuberculosis Trust Annual Report 1949–50 Published by the Trust 42 Castle Street Edinburgh.

[3] Daw, R H *Lancet*, 1950, i, 830 Logan W P D *Ibid*, p 926. Springett V H *Ibid* Jacobs A L *Ibid*, p 1019

ANGOR ANIMI

> WHAT a strange force it is that can stir, and with such intensity, a consciousness of the imminence of an event of which there can never have been any actual experience, and yet is so frequently inoperative when death is at hand'

So wrote Dr John A Ryle, assistant physician to Guy's Hospital, in 1928[1] Fourteen years later, and until his death in 1949, Professor Ryle had many opportunities to study in his own person the symptom that had interested him so much Characteristically he noted down his experience, and left the paper to be published in *Guy's Hospital Reports*, as a postscript to his earlier speculations Both papers, and a further postscript written by his son, Dr J C Ryle, have been printed together[2] In both papers, Ryle's concern was to suggest a possible physiological interpretation of the fear of impending death, or more properly the sense of dying, often described as a component of anginal attacks In the earlier paper he noted that those who have studied it closely agree that the sensation is a physical one, Clifford Allbutt referred to it as an "organic sensation" It occurs not only in angina pectoris but also, independently of any demonstrable organic change, in vasovagal attacks, and whereas in angina the sensation is as transient as the pain, in vasovagal attacks it may last much longer, and appear much oftener Ryle had never seen it, in its major form, as a symptom of psychological disease, and he found that though it may be possible to allay the patient's anxiety by assuring him that his feelings are liars, yet the symptom itself cannot be removed by reassurance or by any other psychotherapeutic measure

The associated symptoms, Ryle suggested, give a clue to the site of the physical disturbance In both anginal and vasovagal attacks the patient is unwilling to make the smallest movement, and even his breathing is restricted John Hunter, in his initial attack of angina, found himself not to be breathing at all, and started again by an act of will During vasovagal attacks—of which Ryle reported 13 cases—there was often, he found, coldness, pallor, palpitation, and quickened or sometimes a very slow pulse, the patients might have a sense of unreality and lose consciousness for a time, and many of them complained of pain or discomfort between the precordial area and the left clavicle, with a tugging pain up the left side of the neck Angor animi was present in 11 of these 13 patients, as against only 6 out of his 43 patients with angina pectoris However, he had encountered the symptom in one case each of angina abdominis and angina cruris, in a case of spasmodic Raynaud's disease, and in association with labyrinthine vertigo, and had seen notes of a case associated with a tumour involving the medulla oblongata The common factor in all these conditions, he thought, must be a powerful medullary stimulus of some kind, with physical effects manifested in disturbances of the cardiac, respiratory, and vasomotor functions The sense of dying itself he described as "the aura of a nervous storm having its vortex in those medullary centres upon which the act of living depends" In vasovagal attacks, as in epilepsy and migraine, the origin of the storm is unknown, but in angina and Raynaud's disease it might well be due to impulses arriving from the aorta, or the coronary or peripheral arteries, in moments of arterial stress or spasm, and passing via the medullary nuclei Angor animi, in fact, might be the sensory part of a strong immobilisation reflex intended to protect life and give the distressed heart the best chance of weathering the storm

Ryle's later experience gave him no reason to revise this theory, but he was able to describe in careful detail the sensation of dying and the symptoms associated with it It was most liable to befall him when he had dropped into a pleasant sleep after doing rather too much and increasing his hyperpiesia He was roused abruptly, on these occasions, by a surging sensation behind the sternum, spreading into the head and neck and down the arms, and associated with the indescribable conviction that he was dying There was no feeling of faintness or failure of consciousness, and no pronounced changes in pulse rate or colour He thought the full relaxation accompanying sleep might have resulted in a sudden fall in pressure, which in turn had precipitated the attack, and he found that a few deep breaths cut short the sense of dying Like John Hunter he had to take them deliberately, for his breathing sometimes seemed to be arrested by the attack The heart he suggested, at a time of muscular anoxia, announced its distress by pain and by a secondary arrest of bodily movements, and might induce a reflex respiratory inhibition as well The biological purpose of the whole episode would thus be a warning or protective one Other painful crises—such as renal or biliary colic—"lacking the associated hazard of angina," are not associated with a sense of impending death Nor had he ever found the symptom in hyperpiesia unaccompanied by coronary disease

Among other unanswered questions about this curious sensation, he asked "Will it ever be possible for a keen observer to signify in his last seconds of life whether or not the sense of dying was present?" His son partly answers for him in a final postscript "The symptom of angor animi remained with him up till his third coronary thrombosis about two weeks before his death, thereafter anginal pain was replaced by failure and he did not mention the symptom again During this time he believed with good reason on three occasions that death was imminent, but though perfectly rational did not make any reference to angor animi"

ASPIRIN SENSITIVITY

IT is perhaps not generally realised that aspirin can cause allergic manifestations in susceptible patients Physicians are so used to regarding this as a perfectly safe drug that when prescribing it they rarely pause to consider the possibility of drug allergy Even if they do they are unlikely to remember all the proprietary drug mixtures containing aspirin Bearing in mind the wide use of the drug, sensitivity is rare, but a patient's statement that he cannot tolerate it, and that it may induce asthma or urticaria, should always be heeded Other manifestations of aspirin sensitivity are angioneurotic oedema, allergic rhinitis, and cardiovascular collapse

Fatalities have been reported in bad asthmatics, and many workers have remarked that aspirin sensitivity tends to arise in the most severe and intractable cases of asthma with a poor prognosis, and that skin tests with the drug are often not only negative but highly dangerous In a series of 830 asthmatics Walton and Bottomley[1] observed 22 cases of aspirin sensitivity—an incidence of approximately 2 5%—and half of them had severe asthma Others have described an incidence of 2–10% among all asthmatics, with females more often affected than males In these cases there is a high incidence of familial allergy, emphysema, nasal allergy with polyposis, and eosinophilia. It is thought that aspirin is not an allergen per se, but that it combines with body proteins (perhaps the circulating globulins) to form specific allergens or haptens which evoke the reactions. The dangers of aspirin sensitivity should always be considered when prescribing aspirin for asthmatics and allergic subjects.

---

[1] *Guy's Hosp Rep* 1928 78 371

[2] *Ibid* 1950 99 223

[1] Walton C H A Bottomley, H W *Canad med Ass J* 1951 64 187

A PSYCHODRAMATIC EVENING

GROUP psychotherapy has received increased attention since the late war, with its large number of psychiatric casualties among Servicemen and civilians, forced psychiatrists to look around for methods of treating their patients en masse rather than individually. The approaches have been many, depending largely on the temperament and experience of the proponent: they range from the inspirational, semi revivalistic techniques of L. C. Marsh at Worcester State Hospital, A. A. Low with his "Recovery, Inc" in Illinois, and Alcoholics Anonymous, through the educational methods of E. W. Lazell, to the analytical approach of S. H. Foulkes and J. Bion—to instance but a few of the pioneers on both sides of the Atlantic.

The continued interest of psychiatrists and their co-workers in this matter was shown in London on April 9, when a large audience witnessed a demonstration of psychodrama by Dr J. L. Moreno, presented under the auspices of the Institute of Social Psychotherapy. Dr Moreno was one of the first psychiatrists to apply group methods, beginning work with neurotic children in Vienna in 1911; the children were encouraged to act out their fantasies, and in this way psychodrama evolved. Later the method was applied to adult patients and introduced by Dr Moreno to the U.S.A.; the first psychodrama theatre connected with a hospital was built in 1936 at Beacon Hill, New York, where Dr Moreno's sanatorium and Institute of Sociatry is the headquarters and training school of his movement throughout the U.S.A. At the meeting Dr Moreno began by recalling that drama had evolved from religious group activities, first one and then more than one participant being pushed forward to enact and voice the group's emotions. The hall in which he was speaking conditioned, he said, the response of his audience; for he was on a platform, cut off from his hearers by height and distance. His psychodrama theatre or, as he preferred to term it, "spontaneity theatre" had a low, semicircular stage projecting into the auditorium with shallow steps leading down from stage to audience. In the front row sat his specially trained assistants who as "auxiliary egos" could be called on by a patient to enact the rôle of the patient himself or of anyone in his emotional story—father, mother in law, wife, child, boss, and so forth. Behind the auditorium was a gallery, reserved for "superegos," and useful on one occasion when he had a patient with a remarkable resemblance to Adolf Hitler, moustache and all, who was provided with auxiliary egos to represent the Führer's entourage and was allowed to address the crowd from above. This patient, via a mildly homosexual friendship with his pseudo Goering, eventually made a social recovery.

By now Dr Moreno had got into his stride, and was pacing up and down the stage and making sorties into the audience, every muscle in his face and body used with the fluent abandon of the born actor, so that a press photographer and his flashlamp assistant pussy-footing down the aisles were hard put to it to capture his split second gestures. They caught one dramatic moment, when Dr Moreno was making believe to strangle the chairman to illustrate what he called mirror acting. This was further enacted by Mrs Moreno and a volunteer from the audience. In mirror acting the depressed or catatonic patient may be drawn into participation by trained assistants who have studied his case enacting before his eyes the way that he behaves. A typical marital problem was acted by a London psychiatrist and Mrs. Moreno, starting from the breakfast table squabble over wifely extravagance and hubby's more-than-professional interest in his secretary, and continuing to the interview of the aggrieved lady with her solicitor—a role in which the psychiatrist showed a ready wit and nice opportunism by advising her to consult a psychiatrist. Lastly, the importance of the "double" was demonstrated, this being Dr Moreno's term for the imaginary other self with whom each of us carries on a lifelong, not always silent, colloquy. This was charmingly and gallantly done by a young newly married Norwegian girl from the audience, ruminating aloud in our foreign tongue on how she expected to feel seeing her parents for the first time since her marriage, with Mrs. Moreno skilfully voicing the dubieties and homely aphorisms of her alter ego; and, in the background, Dr Moreno, resourceful as Prospero and lively as Ariel, perpetually darting, prompting, questioning.

TUBERCULOSIS IN SCOTLAND

IN Scotland mortality from tuberculosis continued to rise in the years after the end of the late war; but in 1950, as we noted last week,[1] the rate fell to a level 15 per 100,000 below the average for the previous five years. In its latest report[2] the Royal Victoria Hospital Tuberculosis Trust observes that definite improvement has taken place "during a period when every public utterance has proclaimed not only the lack of adequate measures for controlling the disease, but the supposed deterioration of facilities which had existed previously." The report draws attention to the epidemic nature of tuberculosis, and rightly attributes the deterioration after 1939 to changes, both mental and physical, in the human soil. It ascribes the failure of the mortality rate to improve in the post war period up to 1949 to the delayed effects of increased infection and morbidity in the war years. Infection must also have increased in England and in other countries where mortality, after a war-time rise, fell in the immediate post war period; and it seems possible that the main cause of the post-war situation in Scotland may have been the less satisfactory pre-war conditions, perhaps exaggerated by war-time influences. In the words of the report: "Better developed services in England, particularly better facilities for isolation and treatment, probably influenced the epidemic in that country at an earlier stage." The report attributes the recent fall in mortality to the recession of the epidemic wave initiated by the war; but the fall has coincided with the general introduction of chemotherapy, which may have played an even more important part than the natural recession.

It is pointed out that both developmental changes associated with puberty, and recently acquired infection, are important causes of the high mortality among adolescents, especially females, and the high mortality in older men is reasonably attributed to recrudescence of old latent foci; but no mention is made of the "generation" method of analysing mortality rates, to which attention has been drawn in our correspondence columns.[3] Such an analysis adequately explains the present high rates of mortality in older males without invoking the "stresses and strains of life and of adverse social and economic factors." These factors, no doubt, are important, as the report says, in determining the general

---

1. *Lancet* April 14 1951 p 839
2. Royal Victoria Hospital Tuberculosis Trust. Annual Report 1949–50. Published by the Trust 42 Castle Street Edinburgh.
3. Daw R. H. *Lancet* 1950 i 830; Logan W. P. D. *Ibid* p 926; Springett V. H. *Ibid*; Jacobs A. L. *Ibid* p 1019

level of mortality, but they hardly explain the progressive change in the age distribution of mortality Whilst accepting B C G as of proven value in preventing morbidity and mortality among young adults who have not previously been infected, the report very properly insists that there must be no slackening of efforts to isolate and treat those who have the disease and are infectious Such a reminder is welcome, especially as the Scandinavian countries, from which comes much of the evidence for the value of B C G, have also very efficient services for the identification, isolation, and treatment of sources of infection

NATURAL CAUSES OF SUDDEN DEATH

To the pathologist the cause of sudden death is usually clear, but occasionally it can only be conjectured This is borne out in a series of reports, by Helpern and Rabson,[1–5] on 2030 such deaths from natural causes in the borough of Manhattan during the years 1937–43

The greatest incidence was in the two 5 year age groups between 45 and 54, and diseases of the heart and aorta accounted for 54% of the total[2] Coronary artery disease alone was the cause in 30 4% but a recent thrombus was found in only just over a quarter of these of all the deaths from coronary artery disease only 6% were in women, none of whom was coloured In fact slightly more than 90% in this group were white males and only 3 7% negroes, although the latter formed 14 5% of the male population, and this discrepancy is still great even assuming that all visitors to Manhattan are white males, in which event the negro male population would be 9 4% (By contrast, among negroes deaths from ostial obstruction due to syphilitic aortitis were relatively common, totalling 39% of the deaths from this cause) The incidence of coronary artery disease reached its peak in the 5 year age group between 50 and 54 and then gradually fell Death took place in the street, while at work, or in a public place in 47% of instances Of those who died suddenly at home, half were in bed at the time Hotel deaths usually took place in bed, "though not always following a night of rest and relaxation" In 56% of the cases examined the heart weight exceeded 400 grammes, while more than half of the enlarged hearts exceeded 500 grammes

Diseases of the respiratory tract accounted for 23 2%, and pulmonary tuberculosis for 3 4% of the deaths, tuberculosis provided an appreciable number of the unexpected deaths in middle and later life Diseases of the nervous system were responsible for 18 2% of the deaths, and disorders of the digestive system for 6 5% the urinary tract furnished 2 0%, and the genital system only 1 3% Ruptured tubal pregnancy, however, accounted for 16% of the total female deaths in the age group 20–24, 19% at 25–29, 17 5% at 30–34, 8% at 35–39, and under 6% at 40–44

The third paper[3] deals with subarachnoid hæmorrhage, which was the cause in 4 6% of all the deaths and in 25 7% of those due to diseases of the nervous system, this cause was in fact little less common than cerebral hæmorrhage (30 4%) Fatalities from this disease were most common in late youth and, more especially, middle age In two thirds of the cases an aneurysm was found, the most usual sites being the middle cerebral and anterior communicating arteries Occasionally an aneurysm may produce a misleading picture, as when rupture takes place high up in the fissure of Sylvius and forms a localised hæmatoma between the island of Reil and the overlying cortex this may readily be confused with intracerebral hæmorrhage Sometimes subarachnoid hæmorrhage may rupture into the subdural space and so resemble subdural bleeding from trauma. Of the 95 cases of subarachnoid hæmorrhage, 43 died at home, 10 being found in bed, in 14 cases the subject was walking when the symptoms began Alcohol estimations were sometimes carried out on post mortem material, and positive values were found to exceed the negatives by three to two Possibly the earliest symptoms may have led to the imbibing of alcohol, but Helpern and Rabson believe that alcoholic intoxication may be a precipitating factor, for the resulting active hyperæmia may throw an added burden on the cerebral circulation Alcohol also increases the chances of altercation, and thus the liability to cerebral trauma

As to sudden death in young children,[4] this was rare beyond the age of 3 years, and most of the fatalities were in males This supports the old observation that boy babies are more liable to die in infancy than are girls—a feature which tends to counterbalance the initial preponderance of male over female births The proportion of sudden deaths in negroes in this age-group was far beyond their proportion in the population, this Rabson attributes to their lower economic status Respiratory diseases accounted for almost 80% of the deaths, microscopic studies usually substantiated the diagnosis, but sometimes another cause of death was brought to light, and very occasionally no adequate reason could be found Bronchitis and bronchopneumonia were two and a half times as common in male babies as in females, whereas in older children diseases of the digestive system provided twice as many deaths in girls as in boys, and diseases of the heart and aorta four times as many The majority of the problem cases were of infants between the ages of 4 and 8 months, often no adequate cause of death could be found Asphyxia was not recorded, Rabson believes this to be a rare cause of death in infants found dead in their cribs, for the aspiration of vomitus may complete the lethal circle of an obscure primary condition and mislead the inexperienced (In this connection we remarked last year[6] that "the assumption that infants are easily suffocated is untenable, for all except very young and feeble infants react vigorously to a feeling of impending suffocation, and certainly do not allow themselves to be asphyxiated by turning their face to a pillow") In difficult cases one must avoid invoking status lymphaticus, it is far better to recommend certification of death as "by act of God" In the case of a 5 month old Chinese girl, however, the thymus weighed 77 grammes, and the adrenals, by contrast, only 2 82 grammes She was found dead in her crib lying on her side, just as she had been placed Death was attributed to the enlargement of the thymus, for there was distinct antero posterior compression and narrowing of the lumen of the trachea Why death took place when it did was not clear

An unusual cause of death, judging by experience in the United Kingdom, was malaria in drug addicts The pooling of needles, syringes, and drugs by these unfortunates returning from war is regarded as the reason for the spread of malaria in Manhattan, and in the age-group 20–24 it accounted for 8 3% of the sudden deaths. Pitting scars on the arms and legs usually drew attention to the possibility of this source of infection

Mr ARNOLD WALKER, F R C O G, has been re-elected chairman, and Dr J P HEDLEY, F R C O G, vice chairman, of the Central Midwives Board

Mr JOHN GAY FRENCH, consulting surgeon to the ear, nose, and throat department of the Royal Free Hospital, London, died on April 13 at the age of 79

---

[1] Helpern M., Rabson S M *New York St J Med* 1945 45, 1197
[2] Rabson S M Helpern M *Amer Heart J* 1948 35 635
[3] Helpern, M Rabson S M *Amer J med Sci* 1950 220 262
[4] Rabson, S M *J Pediat* 1949 34 166
[5] Rabson, S M. *Arch intern Med* 1950 86, 361
[6] Leading article *Lancet*, 1950 i 357

Special Articles

POLIOMYELITIS

Some fin-de-saison Reflections

DAVID LE VAY
M S Lond., F.R C S

ORTHOPÆDIC SURGEON, BROOK GENERAL HOSPITAL, LONDON

> "*There is no question that a lot of treatment* (for poliomyelitis) *is still being given undue credit which rightly belongs to the Lord, and not to any orthopædic surgeon or physiotherapist I would not go so far, however, as to say that any sort of treatment is useless* (Steindler 1947)

IT seems likely that major epidemics of infantile paralysis will recur annually in this country in future, and that we shall have to face the situation—which has already existed in North America for a long time—that each succeeding year brings many thousands of fresh cases, a considerable proportion of which are paralytic

In the past, when cases were fewer, it was usual for patients to be retained in fever hospitals until the end of an arbitrary quarantine period, after which, if there was any severe residual paralysis, they were transferred to long stay orthopædic units In view of the trend of the disease these arrangements may now be open to criticism In some cases there may be little or no useful physiotherapy and orthopædic supervision during the all important early quarantine period, when overstretching and contracture begin, the patient's later stay under definitive orthopædic care may be remote from home and family and the main stream of town life, and, as one consequence, practical experience in the management of infantile paralysis is lacking in the ordinary urban hospitals which may now, as the burden increases, have to take their share of this work

Such criticism is admittedly by no means everywhere applicable The system is a natural one and has so far worked fairly well As Clarke (1950) says of orthopædic work in general "a city hospital is unsuited for the treatment of chronic illness The rôle of these hospitals is to act as after care clinics for the collection, treatment, and supervision of outpatients It is important therefore that close working liaison should be established between town and country hospitals" But this is a counsel of perfection We are already hard pressed for hospital beds and services, partly because of the demands made on urban hospitals for the care of the chronic sick and the aged If changes are needed in the immediate future, so far as poliomyelitis is concerned, one reason will be that too few beds are available, *when wanted*, in the old-established peripheral orthopædic hospitals It is vital to ensure that young and valuable members of the community are not discharged prematurely to their homes for lack of those inpatient orthopædic and rehabilitation facilities which are still by no means readily found even for early cases of skeletal tuberculosis

I view this matter in the light of the experience of the management of nearly 200 cases of poliomyelitis of which 140 were paralytic, at the Brook General Hospital during the last three years Until July 5, 1948, this was purely a fever hospital, but since then it has become a general medical and surgical hospital, containing a modern fever unit of 130 beds It was felt that the tradition of early admission to fever hospital and subsequent transfer to a long stay centre should be abandoned, partly because it became increasingly difficult to obtain places in those institutions when they were wanted, but more because the continuity of treatment was broken by such transfer Only 25 of our patients were so transferred, largely because of overwhelming pressure on beds at the height of the epidemic season, or because of the need of education in long term cases in children, or because special facilities, such as large pool therapy, were thought desirable

We sometimes had occasion to regret having made a transfer, and even to readmit patients who had been prematurely discharged from other centres It has been our experience that, except when pressure on beds makes it necessary to use isolation cubicles for their primary purpose only, the need for transfer is negligible when the fever unit works in close liaison with general beds cared for by the same orthopædic and physiotherapy staff, and we now retain our patients until their final discharge home The advantages to them in remaining under the same supervision throughout are obvious

The problem is cumulative Current work includes the victims of the epidemics of the past few years as well as the fresh cases As with another major medicosocial problem, that of pulmonary tuberculosis, the solution—or at any rate a provisional solution—lies in bringing these patients back into the atmosphere of the general hospital Here the fever hospitals, now largely overbedded for their original responsibilities, thanks to the improvement in the public health, may play an important part I agree with James (1951) that these hospitals, largely deprived of their clinical bread and butter by the decline in diphtheria and scarlet fever, should now be used as general hospitals James thinks in terms of a cubicled fever unit, in the charge of a physician experienced in fevers, embedded in a general hospital with provision for pathology, radiology, and surgery He finds that this arrangement works well, that the catholicity of the experience retains medical staff of good calibre and student nurses who might otherwise drift away, and that the greatest benefit is to the patient This is the same as the set up at Brook Hospital, it has worked very well, and is ideal for the city victims of infantile paralysis

Treatment

The routine after admission is for all poliomyelitis patients to be nursed flat on fracture boards Children and light young adults have no pillow or mattress and only four folded layers of blanket over the boards, most adults have a hair mattress and one small pillow A pad behind the knees prevents hyperextension, and bed cradles and sand bags keep the feet from dropping When the deltoid muscles are obviously affected, the arms are fixed with cuff and bandage to the upper bed rail to hold the shoulders abducted

Preliminary *muscle charting* is done as soon as possible, but may be postponed for a few days if need be It is an ordeal in the acute case, and we are reluctant to require any activity which may worsen the paralysis during the early days, even lumbar puncture is not done when the diagnosis is obvious It is realised that this first chart may not be a fair guide, since coöperation is not good when pain and spasm are present, the real starting point may not be obtained until several charts have been made at intervals of a few days and the patient has made a good effort to coöperate After this, charting is done every three or four weeks There is no need here to emphasise the cardinal importance of obtaining some sort of chart, however sketchy, if any idea of progress is to be formed, it is the compass which enables one to guide the patient from stage to stage of his journey With tiny children chart making may require infinite patience perhaps limited to quietly sitting and watching their activities

SPLINTS

In general we think it better to use too few splints than too many, (1) because efficient daily physiotherapy will prevent contractures, and (2) because oversplintage tends to deprive small children of the sense of the use of their limbs When splints are used they are removed for long periods by day so that the patient can do what he likes with his muscles

The main indications for light plaster splints are to maintain abduction for deltoid paralysis in infants who wriggle so much that mere tying of the arm to the bed does not suffice, and to hold the foot at a right angle Elsewhere, elastic splints are used where necessary—e g, the thumb can be comfortably supported in opposition with 'Elastoplast,' when the opponens muscle is paralysed, allowing the first web space to be stretched regularly

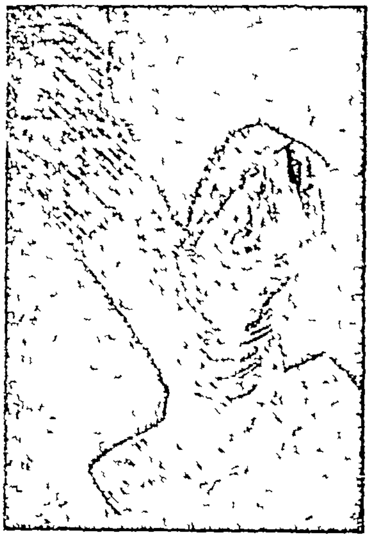


Fig 1—Wooden cross-bar incorporated in foot splint to prevent external rotation of lower leg

Little is to be gained by the use of long arm or leg splints If one wants to hold an elbow at right angles, this can be done efficiently with a collar and cuff, and in the legs it is enough to see that the popliteal pad prevents full extension We have been impressed with the importance of seeing that external rotation of the leg does not produce a chronic strain of the internal lateral ligament of the knee, as may happen insidiously in a flail lower limb when the foot and leg fall outwards As Yachnin (1947) points out, the axis of rotation at the knee is inside the midline of the joint, and the main mass of the limb outside, the joint is more lax when its supporting muscles are paralysed, and when the lower limb falls into external rotation from the hip downwards it is the portion below the knee which rotates abnormally This rotation strains the internal ligament and *may become permanent, with severe pain and* stiffness which may persist for a year or two Such a deformity is easily prevented by incorporating a wooden cross bar in the foot splint (fig 1) When a limb is completely flail, and careful repeated observation shows not the slightest sign of recovery, the splint is discarded and reliance placed merely on passive movements to prevent stiffness and to preserve the proprioception which will be needed later for walking in a calliper But such writing off must be done with caution The deltoid muscles in particular show amazing powers of recovery, which may never take place if the small spark of power is allowed to be extinguished by overfatigue

PHYSIOTHERAPY

This is begun at once, with the following provisos (1) in the very ill patient and in the earliest days it is probably harmful to interfere, and (2) it must be remembered that some cases will continue to deteriorate during the first few days after admission Patients with only mild scattered paresis on the day of admission may develop flail limbs in a few days and be in the respirator by the end of the week Lenhard (1950) says

> "Treatment for the poliomyelitis patient is commonly translated into an urge to do something The more that is done for the patient, the better the therapist feels The greatest need in the early stage is rest for the patient and the muscles involved, they do not require, nor should they have, much physical therapy"

This is true enough, but it is also true that there is an essential minimum of treatment which these patients must have We usually begin treatment before the end of the first week, and at once in those cases where the patient has been ill at home for some days before admission and is obviously ready to recover Only so much attention is given as is needed to keep the joints mobile, and all joints are given a full passive range once daily If every plane of movement is not kept in mind, unexpected contractures may develop—e g, abduction contracture of the hip, with adductor paralysis

TREATMENT OF PAIN AND SPASM

The obstacles to daily movement are pain and spasm, usually, though not always, found in association

What is the source of this pain ? Though it is difficult to answer this question for every patient, we may recognise

1 Painful spasm in the unparalysed or partly paralysed antagonists of completely paralysed muscles

2 Pain due to stretching of the posterior muscles—calves, hamstrings, and erectores spinæ—which are in spasm as part of the meningeal reaction This is not necessarily related to the onset of paralysis and is often most severe in cases which ultimately recover completely

3 Pain arising from the joints and their ligaments, and continuing even when spasm has been relaxed by drugs

4 Secondary pain due to overstrain of ligaments from the faulty position of paralysed limbs

5 Perhaps pain of central origin and *due to inflammation* in the sensory roots and ganglia Against this, however, is the fact that the patient rarely feels pain while lying perfectly still and undisturbed.

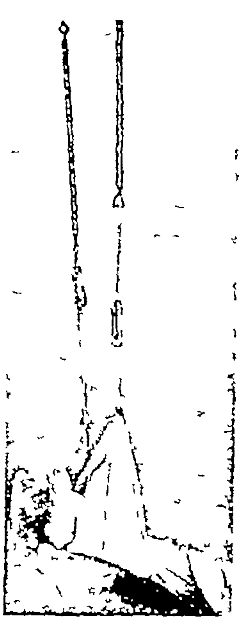


Fig 2—Sling-and spring suspension from ceiling for gross paralysis of lower limbs in an adult.

Spasm embraces

1 Spasm of the antagonists of completely or partly paralysed muscles

2 Primary meningitic spasm of calves and hamstrings, not necessarily related to paralysis

3 A much rarer form occurring during the progress of a limb muscle to complete paralysis We have had only a few cases, always in the quadriceps, where the muscle, capable of little or no active contraction, feels indurated to the touch and gives the sensation of fine fibrillary contractions for 24-48 hours before it becomes soft and functionless

However troublesome pain and spasm may be, they must not be allowed to obstruct daily passive movements. Firmness on the part of the physiotherapist is *essential* —a single decisive movement *may stretch the hamstrings* where more timid attempts fail—but it may be necessary to obtain assistance from drugs

Curare in sufficient dosage will usually relieve most of the spasm and has been vigorously recommended by Dr N S Ransohoff in New Jersey (*Lancet* 1948), but it does not simultaneously relieve the pain Even when the patient has been reduced to flaccidity, movement may remain agonising, and therefore we cannot regard curare as a suitable aid to therapy, apart from its undoubted value in relieving urinary retention due to spasm of the sphincters

'*Priscol*' has been reported on with enthusiasm by Smith *et al* (1950) in New York, but we have not found it of great value, and its effects are less dramatic than those of curare

Intravenous *procaine*, in our hands, has also had only an uncertain effect on pain and spasm, even in large dosage

The veins of small children are not always suited to the administration of these drugs, and the well established relation between intramuscular injections and the site of paralysis in closely following poliomyelitis is a contra-indication to intramuscular injections in the acute phase of the disease We prefer not to give them except into the muscles of completely flail limbs

However, the problem of really serious pain and spasm is not a serious one in this country, where poliomyelitis seems in this respect to differ from the American variety Thus Smith et al. found priscol valuable because it relieved the nurses of the arduous duty of renewing the hot packs in most of his cases Not more than perhaps 10% of our cases are troubled with really severe pain and spasm, and by far the best method of obtaining full motion in such cases is under temporary analgesia-anæsthesia induced with rectal thiopentone or with gas and oxygen Patients in respirators must still be taken out daily for treatment while breathing is maintained with an anæsthetic machine, and this is often just the type of case with the greatest pain

TREATMENT DURING RECOVERY

Once the painful stage is over, or not too troublesome, all the children have daily massage and mobilisation for the back, where rigidity may develop even in non-paralytic cases As recovery proceeds, passive movements give way to assisted active movements, and then to progressively more active exercises against resistance Whenever there is gross paralysis of the lower limbs, return of power in the gluteal and adductor groups is encouraged by sling and spring suspension from eyelet hooks screwed 18 in apart in the ceiling over the bed (fig 2), in the case of young children, these can be attached to double Balkan beams slung across the cot-rails (fig 3) Patients on slings must be taught to perform single deliberate movements with a pause between each phase, or the mere recoil inertia of the apparatus will give the illusion of recovering power The heels need be only just clear of the bed, and then the glutei maximi muscles can be exercised by forcing the feet down on the covers, if these muscles are too weak for this, the patient is turned on his face in the slings for part of the day, so that the springs assist the movement of hyper-extension at the hips As the glutei medii recover, the apparatus can be loaded against them by incorporating a cross spring to make abduction more difficult (fig 2) or by weighting the slings with shot It is important that the exercises should not progress in activity too rapidly, but it is also important to keep slightly ahead of the patient's capacity The sling and springs can also be used for the shoulder if fixed to the overhead bed pulley when the patient has reached the three pillow stage (fig 4)

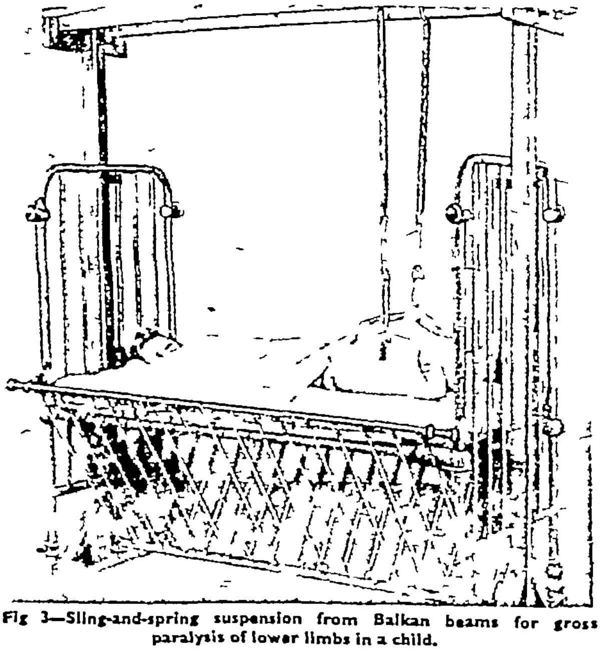


Fig 3—Sling-and-spring suspension from Balkan beams for gross paralysis of lower limbs in a child.

INSTRUMENTATION

Future needs for surgical appliances are foreseen as far as possible, and these are ordered well in advance We prefer to tend to over instrumentation and then are prepared to shed part or all of the appliance when it becomes clear that this is safe The patient who is beginning to get up and about, whether or not with the help of a calliper, is watched more carefully, and charted more often, to ensure that trunk and hip muscles do not deteriorate under the strain If they are evidently holding their own, he is sent home after a few weeks When patients require tendon transplantation or foot-stabilisation operations they are admitted to the surgical wards of this or an associated local hospital, and after operation they return to the unit in plaster

It is important to watch even apparently non paralytic patients for a time in the follow up clinic, because previously undiscovered weaknesses of spinal and trunk muscles may not become obvious for some time Since this hospital draws its poliomyelitis cases largely from a geographically small but densely populated sector of London, many patients live within quite a short distance We have found it an enormous advantage to be able to follow these cases through in close touch with parents and home conditions, it is possible to train them in hospital to deal with replicas of the physical difficulties they will have to surmount at home, to prevent any overfatigue—or overprotection—in the family circle, and to watch over rehabilitation and return to work in consultation with the local resettlement authorities

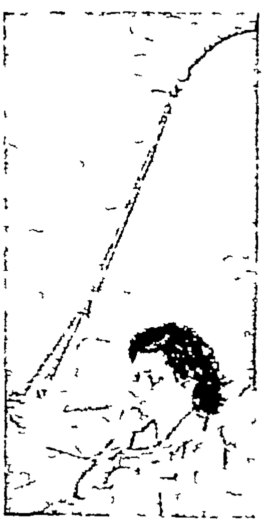


Fig 4—Sling-and-spring suspension from bed pulley for paralysis of shoulder muscles.

Possibilities

The only reasonable outlook for the therapist in poliomyelitis is one of sober pessimism No one can yet cure the disease, and it has been said that the end result after ten years is the same whatever treatment—or if no treatment—is given. While this saying may be true in so far as the sum total of *potential* recovery is concerned, it overlooks the fact that even this potential will not be realised if careless management allows contracture and fatigue to prevent the orderly development of what muscle power exists It is common for a missed case not to be admitted to hospital until some weeks after the acute stage, when prompt improvement occurs in muscle groups relieved from overstrain Would such improvement have taken place without treatment ?

However pessimistic in private, we must be uniformly optimistic in encouraging the patient to make the fullest use of what he possesses, and should err in the direction of the mildest of bullying to prevent self pity and keep his capacities fully extended It is a mistake, for instance, to order a wheel-chair at an early stage for any young adult before he has explored to the limit his capacity to get about unaided and has found a job

The outlook in poliomyelitis is dominated by the rapid development of irreversible changes produced by the virus in the anterior-horn cells of the cord Though specific antibiotics may well be discovered, there will still remain the problem of diagnosing poliomyelitis and exhibiting the antibiotic in the few hours or days before these permanent changes take place In the classical description, the paralysis of this disease is fully fledged at the outset, but we have been greatly impressed by the number of cases which enter hospital without any paralysis at all, or only mild paresis, and then go steadily downhill during the next few days Apart from actual death of neurones from virus toxicity, at least part of the damage must be due to inflammation within the cord —the perivascular cuffing, œdema, and glial infiltration These must be potentially reversible, and Steindler (1947) goes so far as to postulate the essential reversibility of the lesions in the anterior horn cells "Up to a certain point the changes seen in these cells must be reversible, just as the inflammatory glial infiltration and the perivascular lymphocytic exudates are reversible"

This seems to offer hope for the future, now that we are beginning to learn how to control the body's response to injury It was natural to use 'Cortisone' and adrenocorticotropic hormone (A C T H) in the hope of arresting these disabling vascular responses to infection within the cord, since these substances act to a considerable extent by preventing just this defence reaction in other tissues Though a very thorough trial of A C T H by Coriell et al (1950) showed no improvement whatever in paralysis or in mortality over untreated controls and though cortisone produced a severe exacerbation of experimental infections in animals (Schwartzman 1951), it may still prove somehow possible to reverse the inflammation within the cord, and work should continue along these lines

It is a great pleasure for me to acknowledge the devoted care my patients have received from Miss May Cooke, C S P, physiotherapist in charge because the skill and personality of the physiotherapist are far more important in poliomyelitis than anything the doctor can do Both of us have had every possible help and encouragement from Dr John Armstrong, physician superintendent of Brook Hospital

REFERENCES

Clarke H O (1950) *J Bone Jt Surg* **32B** 641
Coriell L L Siegel A C Cook, C D, Murphy I Stokes J jun (1950) *J Amer med Ass* **142** 1279
James E (1951) *Lancet* i 290
Lancet (1948) i 254
Lenhard R E (1950) *J Bone Jt Surg* **32A** 71
Schwartzman G (1951) *New York Times* int ed suppl Jan 28, p 7
Smith E Graubard D J Falcone J Givan T B Rosenblatt P Feldman A (1950) *J Amer med Ass* **144** 213
Steindler A (1947) *J Bone Jt Surg* **29** 59
Yachnin S C (1947) *Ibid* p 415

MEDICAL AUXILIARIES IN THE N H S

REPORTS OF THE COPE COMMITTEES

Two years ago the Minister of Health and the Secretary of State for Scotland set up eight related committees to consider the supply and demand, training, and qualifications of the following groups working in the National Health Service

Almoners
Chiropodists
Dietitians
Medical laboratory technicians
Occupational therapists
Physiotherapists (including remedial gymnasts)
Radiographers
Speech therapists

The majority of members agreed to accept the term 'medical auxiliaries" as a designation for these groups, accepting the view that "however different their duties may be, all medical auxiliaries in the National Health Service have this in common—they work for the benefit of the patient under the direct or indirect supervision of the doctor"

The chairman (Mr V Zachary Cope, F R C S) and two members (Dr G A Clark of the Ministry of Health, and Mr A B Taylor of the Department of Health for Scotland) were common to all eight committees, and with the secretary (Mr T C L Nicole) they have prepared the main report on "matters common to all types of medical auxiliary service"[1] This is followed by the reports of the eight committees Nearly all the members of these committees have approved the main report as well as their own, but there are three minority reports expressing dissent

SUPPLY AND DEMAND

In the main report a distinction is made between "need" and "demand" By "need" is meant the numbers required by the N H S to give the public a full service in all parts of the country "Demand," on the other hand, is defined as the number of vacancies that employing authorities are likely to seek to fill at present or, say, within the next five years

Just as many different factors may limit demand, many other factors may limit supply Most entrants to the medical auxiliary services are drawn from those who pass the School Certificate or some equivalent examination From this pool come nearly all entrants to the professions and a wide range of executives, secretaries, and technical staff in the public services and businesses Any gain in recruitment in one auxiliary service is likely to be made at the expense of recruitment in another auxiliary service—or in some other occupation which may be of national importance and already undermanned, such as teaching or nursing

In some of the medical auxiliary services demand exceeds supply, and the professional associations may seek, severally and independently, to expand their ranks in order to meet it Such competition may defeat itself, and there should therefore be some means of coordinating the relation of supply to demand over the whole medical auxiliary field "The problem of supply is not one of meeting *all* requirements of all kinds as soon as possible, but of advising on a balanced programme of recruitment over a period of time so as to try to spread the available man power over the medical auxiliary services to the best advantage"

Though salaries were not mentioned in the terms of reference, the report says that men and women entering the auxiliary services should be assured of salaries and, so far as possible, of prospects of promotion, similar to those of occupations with comparable standards of training In particular "account should be taken of the effect of salary scales upon recruitment of both men and women when the supply is below the demand"

TRAINING

Some of the services covered fall into groups, either because several types of auxiliaries work together as a team under a hospital consultant or because of affinities in the work done Thus on the one hand there is a "rehabilitation group" consisting of physiotherapists, occupational therapists, and remedial gymnasts, and on the other there is a medical social group which includes almoners with others (outside the terms of reference) such as psychiatric social workers Dietitians and chiropodists cannot readily be grouped with others

The committees sympathise with the view that there should be some common training in basic sciences for some auxiliaries, or at least for those in each distinguishable group, but they note practical difficulties For example, in certain basic sciences, such as anatomy and physiology, the same syllabus will not serve equally well for the speech therapist, the chiropodist, the radiographer, and the physiotherapist Nevertheless the possibility of a common basic course should be kept in mind, especially when new training schools are being set up. And, whether attendance at common lectures is possible or not, students should certainly be given the opportunity of learning about work in related services.

---

[1] Reports of the Committees on Medical Auxiliaries Cmd 8188 H.M Stationery Office 1951 Pp 227 5s

Continuing machinery is needed for joint consultation on the coordination of training wherever such cooordination seems desirable: "we do not think that such coördination should be left entirely, as at present, to the initiative of individual professional associations of medical auxiliaries." Machinery is also needed to ensure that training keeps pace with advances in medical thought and practice. Additional types of medical auxiliaries may seek recognition, and problems of demarcation of function may arise, in which case there must be machinery for giving an authoritative decision.

QUALIFICATION

In the words of the Medical Act 1858, "it is expedient that persons requiring medical aid shall be enabled to distinguish qualified from unqualified practitioners." Similarly, it seems expedient that, as regards the medical auxiliary services, employing authorities should be enabled to distinguish between those qualified and those unqualified to work in the N.H.S.

In the absence of any generally accepted or official scheme of training, groups of able and far-sighted auxiliaries formed their own professional associations, which started training courses or sought to coordinate the content and standards of courses. Often associations grew up in different parts of the country, sometimes with different views on the content of training. In most cases one professional body has emerged for each type of auxiliary service, but for some services there are, in addition to the main recognised bodies, still a number of bodies professing to grant certificates of competence.

Professional associations usually maintain a register of persons who have obtained the certificate or diploma of the association and who comply with the ethical standards it lays down. These registers, however, have their limitations. They have been useful, but only to those who have been able to assess their reliability.

Before the war the British Medical Association set up an independent Board of Registration of Medical Auxiliaries, whose main object was to maintain and publish a register or registers of persons qualified to practise medical auxiliary work. The qualifying bodies that have been recognised by the board are the Association of Dispensing Opticians, the British Dietetic Association, the British Orthoptic Society, the Chartered Society of Physiotherapy, the College of Speech Therapists, the Society of Chiropodists, and the Society of Radiographers. In 1944 the Chartered Society of Physiotherapy resigned from the board, whose registers now contain about six thousand names. The board has done good work in raising the status of the groups of medical auxiliaries on its registers, but by its nature it suffers certain handicaps. It is a voluntary body, dependent for its existence on other voluntary bodies and on subscriptions voluntarily given, and its registers appear to be no more than reproductions of the registers of the constituent professional associations, with the omission of the names of those who do not apply to it for registration. It has exercised care in the approval of training schools, but the inspections made on its behalf have in the main been limited to visits before recognition. "We understand that routine visits to schools and examinations are now to be made, but, in the matter of effecting improvements the Board, as a voluntary body, will find itself at a disadvantage."

The report concludes that a system of statutory registration of medical auxiliaries is desirable to ensure that those employed in the N.H.S. are properly qualified. There should be a separate register for each auxiliary service, and these should be open to all medical auxiliaries qualified for employment in the N.H.S., whether they are already employed therein or not.

At present any recognition of training schools is undertaken by the professional associations concerned: "the final decision is taken by a *professional* association that is representative essentially of the *auxiliary* service concerned." Such arrangements are open to some objection on principle. The associations are—properly—concerned with the standards of competence of their members; but for the maintenance of standards of competence within the N.H.S. the statutory responsibility rests with the two Ministers. Though the associations should continue with their educational activities, they should not have undivided and final responsibility for recognition of training schools and examinations for N.H.S. purposes.

A NEW COUNCIL?

It could be left to the Ministers to take the necessary decisions on the advice of their departments. But non-departmental machinery can be established on a more representative basis and is likely to command more general acceptance.

The committee considered whether the professional associations themselves, or the Board of Registration of Medical Auxiliaries, might undertake the tasks outlined. But "it is no part of the function of a professional association or of the Board to attempt to maintain that broad view of the whole field of the medical auxiliary services in the National Health Service without which most of the tasks cannot be performed." Furthermore, the associations and the board are interested in all qualified persons, whether working in the N.H.S. or outside it, and whether at home or abroad. This range of view is unnecessarily wide for purposes of the N.H.S. "Apart from these considerations, Parliament has from time to time taken the view that the function of the registration of professional qualifications should be separated from the protection of the interests of the members of that profession, and this protective function is an essential element in the work of a professional association, although not necessarily the most important."

A second suggestion was that the machinery should be based on the natural grouping of the medical auxiliary services, and there should be two, three, or even four "group councils" so constituted as to cover the whole medical auxiliary field. To this the main report objects that:

> Independent group councils would be unable to perform all the tasks that we have said will have to be undertaken. The relation of supply and demand has to be reviewed from time to time and correlated over the *whole* medical auxiliary field. Unless this is done, there will be a risk of competition for recruits between groups of medical auxiliaries, just as there is a risk of competition at present between individual auxiliary professions. If a demarcation problem ... arises between services in separate groups where will an impartial and authoritative decision be obtained? Furthermore, it would be difficult to devise machinery for admitting new types of auxiliary service to registration. Which group council would consider an application from a professional association? Who is to decide this question in the event of a difference of opinion? How and by whom are new group councils to be established if there should be a need for them? ... A statutory system of independent group councils seems to us to be too much lacking in flexibility for long term needs."

The conclusion was reached that only a single council would provide the necessary machinery:

> "We admit, and indeed we have stressed, the diversity of the medical auxiliary services. ... We attach much more importance however, to the underlying unity in these services. In the National Health Service all medical auxiliaries are

united in the sense that they all assist the doctor and all have as their objective the welfare of the patient In these two respects they are all on common ground A single council seems to us, therefore, not only to be right in principle, but to provide a better means than a series of independent group councils of promoting a sense of common service among medical auxiliaries and of emphasizing the common objects of medical auxiliary work. If a council is to command respect in the medical and medical auxiliary professions and among the general public, and if its advice is to be of real value to the Ministers, it must be free from any sectionalism We feel that it might be difficult to obtain suitable members able and willing to give this kind of public service unless for a council with a wide field in which to operate Our strongest objection to a system of independent group councils, indeed, is that the medical auxiliary services in the National Health *Service deserve something better* "

Following the precedent of bodies concerned with education and registration in medicine, architecture, and law, the main report proposes a single statutory council of limited size, advised and assisted by professional committees It would be called the Council for the Medical Auxiliary Services in the National Health Service, and in order to cover England, Wales, and Scotland it would be under the ægis of the Privy Council The members might be

Four appointed by the Privy Council of whom one shall be from Scotland and one shall be designated as chairman

Three appointed jointly by the Minister of Health and the Secretary of State for Scotland

Two appointed by the Royal College of Physicians of London

Two appointed by the Royal College of Surgeons of England

One appointed by the Royal College of Obstetricians and Gynæcologists

Two appointed jointly by the Royal College of Physicians of Edinburgh the Royal College of Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow

One appointed by the General Medical Council

Six medical auxiliary members elected by the vice-chairmen of the professional committees from among their own number

They would retire every four years and would not be eligible for reappointment for two years

Each professional committee would as a rule be concerned with a single auxiliary service, and would consist of medical, medical auxiliary, and other members, the medical auxiliary members having a majority (not exceeding, say, three fifths) " It must be a body of experts in its particular field " Its chairman would be appointed by the council, preferably from among the council's members, but the committee would elect its own vice chairman, who would be a medical auxiliary As shown above, the vice chairmen would form an " electoral college " electing six of their number to the council. Having framed its policy, with the advice of the professional committees, the council would rely on the committees to carry it out For example, though the council would have final responsibility for registration and would be the arbiter in the determination of disputes, the committee would have to maintain the appropriate register and implement decisions

Neither the council nor its committees would have power to control the professional associations, which would continue the work they have chosen for themselves under their own constitutions " In particular, we think that it would be unsound for a central Council to attempt either to conduct training courses or examinations " Many associations have members working outside the N H S and would wish to maintain their own registers in order to cover all forms of employment

The council is regarded as essentially an administrative body, dependent on professional committees for information, advice, and executive assistance, and consisting of men and women experienced in judging impartially on evidence laid before them Since Scottish problems and systems differ in some respects, it would be required by statute to meet in Scotland at suitable intervals

As it is important that the registers should contain an up to date record of persons in, or qualified for, employment in the N H S, together with up-to-date information about qualifications, place of residence, and employment, it would be unsatisfactory for the council to take over any of the lists of names in the registers of professional associations All who seek registration by the council will have to make application individually

PROVISION OF TRAINING

At present there is considerable variety in the arrangements for training medical auxiliaries, and considerable variation in the method of financing students The Ministers might themselves be wholly responsible for the provision of training and for financial aid, but this arrangement appears inappropriate, because many medical auxiliaries may not wish to work in the N H S Alternatively, the Ministers might be responsible only for providing the clinical facilities necessary for training; the students would find the money, and would look for assistance to the local education authorities This arrangement is regarded as appropriate, except where this training approximates to an apprenticeship as in the case of medical laboratory technicians

If the Ministers are not to be responsible for more than the provision of clinical facilities, " it would appear that the institutions giving the training should themselves be independent of the hospitals which are under the direct control of the Ministers They would need, therefore, as their governing bodies, *organisations* which would represent all the interests concerned in training We are aware that the general and immediate adoption of this principle might cause undue disturbance, but we consider that new governing bodies of this kind should be adopted for any new schools set up "

MINORITY REPORTS

Two of the three minority reports favour alternative machinery for registration The first wishes to see a statutory registration board established for each profession If necessary, an advisory and coördinating body, to be called the Council for Non medical Professional and Technical Staff in Health Services, could be set up as well This council would have only eight members, not more than two of whom should be medical The signatories of this report regard the term " medical auxiliary " as inapplicable to their professions

The second report recommends grouping of some of the professions A Council for Physical Therapy in the N H S would maintain registers of physiotherapists, occupational therapists, and remedial gymnasts This council, with twenty five members, would be aided by professional committees

The third minority report dissociates itself from the second on the ground that it " gives unbalanced emphasis to the work of the Occupational Therapists in the physical field and completely disregards the psychological aspects of occupational therapy " It also dissents at various points from the report on occupational therapy

REPORTS OF INDIVIDUAL COMMITTEES

Almoners

The evidence suggests that the hospital service in England and Wales alone probably needs 2500–3000 almoners to provide a full service and in Scotland about 500 The probable demand over the next five years is likely to be more limited, but is at least 150 almoners each year The students in training " are hardly enough to make good the wastage and it is evident that unless recruitment is considerably increased it will be impossible to meet even the existing and immediate demands " Publicity in schools and financial assistance to students are recommended as aids to recruitment, but it is recognised that there are too few social science students in the universities to meet the requirements of all the professions for which this training is the basis. The training and qualification given by the Institute of Almoners are suitable for almoners in the N.H.S.

Chiropodists

Only 7.5% of the hospitals have so far appointed chiropodists. As soon as possible there should be chiropodists at every general hospital and in certain hospitals and clinics, and local authorities should be enabled to provide chiropody in the N.H.S. The training and qualifications of the Society of Chiropodists are suitable. Part-time training cannot equal full-time training in value.

Dietitians

In December, 1949, only 139 dietitians had been appointed among 2600 hospitals and convalescent homes in the N.H.S. in England and Wales. Each hospital group will need one or more. Members of the British Dietetic Association are fitted for employment in the N.H.S.

Medical Laboratory Technicians

At the end of 1949, 1602 medical laboratory technicians were employed at hospitals in the N.H.S. in England and Wales and 180 in Scotland. At the same date there were 1898 students in training. At present the supply generally meets the demand but there are local shortages, particularly of trained technicians. The training and qualifications of the Institute of Medical Laboratory Technology are generally suitable.

Occupational Therapists

About 3000 occupational therapists are needed for the N.H.S. The number actually employed is 980. Financial restrictions, &c., are likely to prevent the demand from rising to any extent for some time. Occupational therapists holding the diploma of the Association of Occupational Therapists or that approved by the Scottish Association of Occupational Therapists are fitted for employment in the N.H.S.

Physiotherapists

A year ago there were just over 4000 physiotherapists working whole-time or part-time in the National Health Service in the United Kingdom, and some 1500 more will be required. The present output of trained physiotherapists is over 500 a year and it should be possible to maintain the present numbers in the N.H.S. and gradually build up to the full demand. Supply and demand are fairly evenly balanced. Physiotherapists at present registered with the Chartered Society of Physiotherapy and the Faculty of Physiotherapists are suitable for employment in the N.H.S. The general direction of studies in each school should be in the hands of a medical practitioner, preferably a specialist in physical medicine, and facilities for the training of men should be increased. Part-time training that is wholly in the hands of non-medical teachers and does not include any considerable amount of varied clinical experience is not adequate.

Radiographers

The current output of students should suffice to meet the present demand. The Ministers are invited to consider whether blind assistants could undertake dark-room work so as to relieve radiographers for their specialised duties. Members of the Society of Radiographers are qualified for employment in the N.H.S. Training should be given only in recognised schools able to provide both theoretical and practical training. More men should be trained. Students should pay for their training and, with the possible exception of some nurses, should not receive a salary.

Speech Therapists

There are nearly 300 speech therapists practising in the United Kingdom, and at least 750 are needed both inside and outside the N.H.S. Local education authorities and hospitals should work closely together so as to use the services of speech therapists as economically as possible. Those holding the diploma of the College of Speech Therapists are suitable for employment in the N.H.S.

FREE MEDICAL CARE OF MOTHER AND CHILD IN EIRE

FROM OUR DUBLIN CORRESPONDENT

THE crisis over the scheme for free care of mothers and children in Eire has now been resolved by the resignation of the minister for health, Dr. N. C. Browne. At the end of last month[1] there seemed little prospect of any concessions by the minister to meet the objections of the Irish Medical Association; nor, in fact, were any made by him. Ecclesiastical authorities also objected, on moral grounds, to certain features of the scheme, though they raised no objections to the Social Welfare Bill—very much wider in its scope of social benefits, but on a contributory basis—now before the Dail.

Only in recent weeks did it become clear that well over 80% of the medical profession were opposed to the scheme. The only modification accepted by Dr. Browne was that enabling general practitioners, as distinct from dispensary doctors, to join it should they wish. On April 6, the government instructed Dr. Browne to draw up proposals for a Mother and Child Scheme free from the features to which exception had been taken. He preferred to abide by his own scheme, and resigned on April 11.

Replying in the Dail to an attack by Dr. Browne on his erstwhile cabinet colleagues, Mr. J. A. Costello, the prime minister, said:

> "Every time there was any suggestion of an attempt to meet the minister for health the people who gave in and said that they were willing to come and consult were the medical profession, and every time they were turned down with contumely by the minister for health. . . . I feel it my duty to pay tribute to these men who have done everything they can to see that the mothers and children of this country get a scheme."

Mr. Costello, who enjoys the full confidence of the profession, has himself temporarily taken over the ministry of health, and there seems now no reason why negotiations for a new scheme, which have already started, should not proceed in an atmosphere of mutual good will. In Eire, as in other countries, some means will have to be found of assisting the middle income group to meet the cost of present-day medicine; and any new scheme is sure to provide for this group.

Medicine and the Law

What is "Therapeutic" Treatment?

THE claim of the Royal Victoria Hospital, Dundee, to remain outside nationalisation involved the Court of Session in a discussion of the word "therapeutic." If the treatment afforded was not of a therapeutic character, the hospital might escape being taken over under the National Health Service (Scotland) Act.

For the hospital it was contended that the meaning of the word was limited to treatment designed to cure. As the patients were incurable cases and the treatment and nursing could do no more than alleviate their suffering, the measures taken could not be "therapeutic." On the other side it was argued that the word applied not only to curative treatment but also to measures taken to relieve symptoms and alleviate pain.

After hearing the opinions of medical witnesses, and after recourse to such guidance as dictionaries afford, Lord Blades held that the remedial treatment of disease included the associated relief of suffering. He was unable to apply the test of curability or incurability for the purpose of deciding whether measures to combat illness, relieve symptoms, or alleviate suffering were or were not therapeutic. The main purpose of the hospital, he said, was therapeutic. It did not come within an exception provided by the statute. It was a voluntary hospital within the meaning of the Act, and the Secretary of State for Scotland was entitled to remove it from private hands.

---

[1] See *Lancet*, March 31, 1951, p. 734.

In England Now

A Running Commentary by Peripatetic Correspondents

The signs I find in chests, and plot
So skilfully on diagrams,
Too frequently, alas, are not
Apparent in the skiagrams

Too seldom does the screen disclose
Nor all that barium reveal
The ulcers which I diagnose,
The epigastric lumps I feel

Proof positive, this seems to me,
—*Proof stark and undeniable*—
That radiology must be
Extremely unreliable

* * *

Spring cleaning is about to begin Most of us get used to the discomforts of the weekly turn out of one room at a time, but at this season the process is applied to every room at once, and the only thing is to take all the meals one can at the club and spend one's free time anywhere but in the house, preferably gardening, so as to be within hail when something has to be lifted To complicate the issue in our house the decorators' buckets and steps are always stored in the bathroom Surely this spring cleaning business shouldn't be needed any longer, when we have electrical cleaning devices which do more good in a routine daily session than a complete turn out did of yore? Besides the modern household either has electric or gas fires or no fuel for fires at all, so there can't be anything like as much dust But spring cleaning has become a tradition, like wearing something new at Easter So we may as well resign ourselves to a week or two every year when nothing is where it used to be and there's only the stairs to sit on

* * *

When I qualified, 20 odd years ago, we were expected to know only just enough chemistry to prevent the corks blowing straight out of any bottles we dispensed $-NaHCO_3 + HCl$ that kind of thing But this certainly wouldn't satisfy a modern examiner, and I am beginning to wonder whether we inorganic G P s ought to be allowed to go on prescribing the newer-fangled drugs when we couldn't tell their composition from Adam's if we saw the two side by side Most of us, I suppose, as the years go by, merely lean more heavily on our friend the pharmacist—and *hinc illæ lacrimæ*

In our traditional daily chat I asked our pharmacist if, when I prescribe "phenobarbitone tablets," he dispenses sodium phenobarb or plain phenobarb You'd have thought I'd asked how much hashish he was selling, or something even more shocking When at last he had recovered enough to speak he told me "Plain phenobarbitone, of course, Doctor" "But," said I, putting my foot right in it, "I order them at random, sometimes everybody gets the sodium stuff and sometimes the other, just by chance That means I've ordered some people twice as much hypnotic, or half as much, as I intended" Only then did the full force of my ignorance strike him "The molecular weight of phenobarb being 232," he explained pityingly, "and sodium's atomic weight 23, tacking an atom of sodium on each molecule makes your 1-grain tablet contain about nine-tenths of a grain of phenobarb And as it will be much more soluble, your patient will really find it a good deal stronger hypnotic Good morning"

I see now that the Higher Certificate examiners knew their stuff when they endorsed my certificate "NOT Organic Chemistry"

* * *

It is high time that our Planners turned their attention to pay and status in orchestras All the conductor need possess is a nodding acquaintance with the range of orchestral instruments, an ability to interpret a score, and the nerve to stand up in front of the audience for an hour or two waving a stick in a purposeful manner Ask him to play among the second fiddles, or even to deputise for the tympanist, and he will be out of a job in less time than Menuhin takes to play an A pizzicato Yet it is the conductor who gets all the kudos and most of the cash An obvious effect of this cult of the jack-of-all-trades is to produce few real masters of any All the most promising students of music have conductorship as their goal Why should they spend years learning to beat the triangle with absolute precision when in the end they cannot hope even to see their names on the programme in 6-point italics (*J Jones*) as leaders?

* * *

When the influenza epidemic was at its height one of my colleagues was rung up during his evening surgery and an apologetic voice asked if he could possibly manage a visit that day The caller had fallen in the bathroom that morning, had managed to crawl to his bedroom, and had been lying there ever since, unable to put his foot to the ground He thought his leg was broken He was most emphatic that he was a private patient, and did not want to be treated under the N H S My friend went round and found an irate old gentleman lying on his bed with a Potts fracture When first aid measures had been applied, the patient became quite chatty It seemed that he had just moved into the district, and he had spent all day ringing up the local doctors, but when he told them he was not an N H S patient, each one in turn had flatly refused to visit him—no time to call on private patients was the reply "The old order changeth"

* * *

The art of lecturing is generally accepted as moribund if not actually dead, so it was an unusual experience to hear a lecturer speak for an hour on a fairly complex subject without a single note and without a moment's hesitation or uncertainty Equally surprising to me was the sparsity of the audience! The lecture had, I understood, been well advertised, the subject was one likely to combine welcome instruction with an element of entertainment, and yet when, arriving late, I feared not to find even standing room, I had a whole row of chairs to myself On the other hand, many of the "lectures" I attend consist of the most prosaic textbook material read rapidly to an audience that fills the hall to capacity There must be a reason for this contrast in attendances Presumably some lectures are announced in a way that appeals to the popular taste, some, I dare say, are announced so obscurely that nobody hears of them until afterwards But it does seem strange that we flock to hear somebody read to us what we could very well have read for ourselves at our leisure Maybe this is one more evidence of the persistence of the child in us every child loves being read to, especially if the story is one he knows well—and woe betide the reader who introduces some unorthodox deviation from the familiar text

* * *

The junior nurse was taking the particulars of a new patient, a wizened retiring little man She got his name, address, age, and sex without difficulty, but when she asked for his next of kin he answered "None" "Surely you must have *some* relations?" said the nurse But the little man wouldn't be moved "No," he replied, "None at all." "Well," said the nurse, beginning to get worried, "we must put someone down What about the lady who came with you?", for a large bejewelled woman had accompanied the little man to the door of the ward. "She'll do," the patient replied, "She's my mistress." This took the nurse's breath away (she was very junior), but in the end she said rather shakily, "We really can't put that down, you know, shall I say sister, or cousin perhaps, instead?" The little man seemed shocked "No," he insisted, "she's my mistress" Then the nurse had a brainwave "I know, I'll write 'friend'" "No," said the little man, polite but firm, "as I told you before she's my mistress—I work for her"

And so guileless was the little man that when the nurse had been outside to powder her nose they went quietly on with the next question.

* * *

Aphorism of the Week

Let sleeping tubercle lie

Letters to the Editor

THE ECONOMIC VALUE OF THE DOCTOR

SIR,—The March 24 issue of your journal has just reached here with Dr Ffrangcon Roberts's stimulating discussion of this subject. May I suggest that, in addition to the influence of ancillary personnel in medical practice, another factor is of perhaps greater importance in the attitude of the laity toward our profession. That factor, perhaps better seen in the United States, is the ever lessening gap between the educated layman and the physician.

Formerly, with a low state of formal education in the general population, the physician's training widely separated him from the laity. Today, with secondary schooling almost the rule and college attendance common, the layman has advanced relatively more on the educational scale than the doctor. Premedical and medical training now is largely technical with consequent neglect of the nurturing of the more subtle aspects of the personality of the physician. It is this personality which genuinely distinguishes the doctor from those in other technical callings. The present result is a medical "technician" who, when the technical veneer has been scratched, is appallingly like other "technicians", in short, he is basically a layman. This professional personality inadequacy is well demonstrated in the average doctor's attitude toward death. Death upsets him, and he either acts as if it does not exist, or else regards it as a vicious reflection on his technical skill. His behaviour toward, and at the performance of, necropsy is equally enlightening in exposing the present professional personality pattern.

Perhaps the remedy for the status described by Dr Roberts lies in a revaluation of the role of the doctor so that he may be more than a therapeutic technician among other technicians. In a world advancing toward calamity by a series of technical competitions, I fear this revaluation is impossible.

St. Joseph Hospital Fort Wayne
Indiana U.S.A. S. M. RABSON

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—The experience in this clinic of hexamethonium in the treatment of hypertension confirms that of other investigators, particularly Professor Smirk and his co-workers, in the following respects: (1) if properly administered C6 appears to be an effective agent for reducing blood pressure in the majority of cases, including those with malignant hypertension, (2) oral administration is not so reliable as parenteral, and (3) the patient or a member of the family can be taught to administer the injections and record the blood pressure in the home, thus making long-term therapy feasible. In addition, I would like to suggest certain practical points in management which we have found greatly increase the effectiveness of the drug and reduce the incidence of toxicity.

When doses of C6 were repeated at 4 or 6 hour intervals we observed frequently the rapid development of "tolerance" so that increasing doses were without hypotensive effect. However, if the doses were separated by 12 hour intervals the development of tolerance was delayed or prevented while an increased dose now produced an augmented hypotensive response. Thus, an 8 or 12 hour dosage interval usually was far more effective than a 4 or 6 hour interval. In certain patients the hypotensive response to C6 was not maintained beyond 6 hours, and in these cases various other hypotensive agents were tried in order to prevent the rise of blood pressure. The most effective agent was 1-hydrazinophthalazine ('C5968,' Ciba) in doses of 50–150 mg administered orally midway between the doses of C6. By using such alternating therapy the wide swings of blood pressure frequently were avoided and tolerance to either drug usually was prevented.

Profound hypotensive reactions with collapse occurred almost entirely only after the initial injection of C6, and during continued administration the reduction of blood pressure was more moderate. These severe hypotensive reactions have been avoided since we have utilised the following technique for beginning therapy:

With the patient propped up slightly in bed, C6 was injected intravenously at a rate of 1–2 mg of the ion per minute. An assistant determined the blood pressure at intervals of 30 seconds in the opposite arm. As soon as a significant reduction of blood pressure occurred the injection was halted temporarily until the blood pressure stabilised. If the degree of hypotension was satisfactory the injection was stopped. If not the slow rate of administration was begun again and continued until the desired result was obtained. If despite these precautions, the reduction of blood pressure was excessive it was easily corrected by raising the foot of the bed on 6 in. or 8 in. blocks and elevating and passively exercising the lower extremities. Vasopressor agents, especially epinephrine, were unpredictable, and impressed us as being dangerous.

Having determined the initial effective dose, this amount was administered subcutaneously at 12-hour intervals. If tolerance developed the dosage was raised progressively by increments of 5–10 mg. During such continuous administration of C6 the most common side-effect was constipation, and the most serious was paralytic ileus. Since both of these undesirable effects apparently were due to parasympathetic blockade we have used the urethane of acetyl β methylcholine ('Urocholine,' Merck) in doses of 5–10 mg orally twice per day, along with laxatives such as mineral oil and magnesium hydroxide if necessary.

EDWARD D. FREIS
Chief, Cardiovascular Research Laboratory

Georgetown University Medical Centre
Washington D.C. U.S.A.

SURGICAL TREATMENT OF MÉNIÈRE'S DISEASE

SIR,—In your annotation on this subject (April 7) you stated that "in at least some cases of this disease the essential lesion is an excessive amount of endolymph." If this is so, it is scarcely logical to perform sympathectomy (which should lead to an increased blood supply in the denervated area) for its relief. However, sympathectomy may succeed for other reasons, or in sufferers with no excess of endolymph.

The assertion that the main sympathetic supply to the head and neck comes from D1 is perhaps over-confident. Fibres to the eye emerge at this level, but it is not safe to assume that all the preganglionic vasomotor and sudomotor fibres for the head also emerge at the same level. Brown-Séquard, Claude Bernard, and other early workers in this field thought the vasomotor fibres emerged over a wider area, thus, Brown-Séquard[1] reported that the sympathetic fibres to the blood-vessels of the head come from the cord chiefly through the last cervical and first and second thoracic nerve-roots. More recent observers, such as Hyndman and Wolkin,[2] and Goetz,[3] have suggested that many, and perhaps even the majority, of the preganglionic vasomotor and sudomotor sympathetic fibres for the head and neck are found in the second thoracic nerve-roots and that any more widespread outflow is through lower rather than higher nerve-roots. Thus, assuming that sympathectomy is justifiable in some patients with Ménière's disease, the scope of the operation performed by Mr Passe and Mr Seymour could be defended on anatomical grounds.

Guerrier[4] claimed that preganglionic fibres entering the vertebral plexus emerge through the lower cervical nerve roots, and he suggests they were not discovered earlier because of their deep situation and short course The vertebral plexus is regarded as the main source of sympathetic fibres accompanying the internal auditory artery and supplying the internal ear, and any fibres emerging in the lower cervical roots would escape in the sympathectomy under discussion, or in any preliminary trial injection of the stellate ganglion If section of the main preganglionic outflow through D2 and D3 does in fact interrupt pathways to the head, including the ear (as the surgeons claim), then Hyndman and Wolkin, and Goetz are more likely to be correct than Guerrier If so, this is yet another example of how surgical procedures may assist in anatomical localisation and hodology, and conversely it shows how apparently insignificant anatomical details may be of vital importance in determining correct and scientific treatment

---

[1] Brown-Séquard, C. E. *Philad. med. Examiner*, August 1852, p. 489.
[2] Hyndman, O. R., Wolkin, J. *Arch. Surg.* 1942, 45, 145.
[3] Goetz, R. H. *Surg. Gynec. Obstet. int. Abstr. Surg.* 1948, 87, 417.
[4] Guerrier, Y. Thèse. Montpellier, 1944.

Anatomy Department
University of Manchester G A G MITCHELL

GENERAL PRACTITIONER AND CONSULTANT

SIR,—There are readier means of raising the status and standard of the general practitioner than those suggested last week by Dr Robertson

If laboratory and radiological facilities were extended to general practitioners in all areas they would readily accept the responsibility of pursuing, where possible, a final diagnosis, and would thus have in the eyes of their patients greater authority

The opportunity for a closer acquaintance with modern medical thought can be provided in two ways firstly, by generous use in hospitals of general practitioners as clinical assistants, secondly, by the establishment of clinical societies based on general hospitals where the G P can demonstrate his cases before fellow practitioners and consultant colleagues

If the capitation fee were adequate there would be no desire by the G P to augment his income and certainly not from the sources suggested by Dr Robertson May I add that I still find consultants readily approachable and prepared to lend an ear to the G P and to expand an opinion when requested

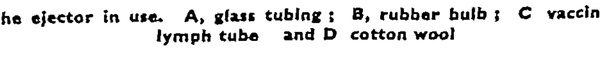
Beckenham Kent D I FINER

IMPROVISED VACCINE-LYMPH EJECTOR

SIR,—Quite a number of practitioners must have been called on to do vaccinations within recent weeks, and some may have been mildly irritated, as I was, by the problem of getting the lymph out of the capillary tube expeditiously and accurately I have found the following simple device, which takes only a very few minutes to make, practical in use and economical of lymph

A firmly fitting rubber bulb is pushed on one end of a glass tube about 8 in. long Into the other end of the tube a small pledget of cotton wool is pushed to act as a bacterial filter In the closed end of the bulb a very small hole is made with the red hot point of a pin. It may be that a black rubber bulb would not show up this hole so well as, say, a red rubber one The device is now ready for use

After the ends of the vaccine capillary tube have been broken off, one of them is pushed through the small hole in the bulb, which grips it (see figure) I have not yet encountered a capillary tube that a small hole in the rubber, made in the way suggested, will not grip I hold the device at the junction of the tube and bulb between the finger and thumb, the bulb can then be angled between the middle and ring fingers of the same hand (with the little finger resting on the patient's limb), so that the distal end of the capillary tube approaches the skin at a convenient angle By gently blowing down the other end of the tube one can extrude small neat drops from the capillary tube, and there is none of the troublesome back suction such as may occur with an ejector worked by finger pressure on a closed rubber bulb Usually four insertions can easily be made, with the help of this device, from one capillary tube It is possible to make up to five or six After a series of insertions the cotton wool can be removed and the glass tubing and bulb boiled



The ejector in use. A, glass tubing ; B, rubber bulb ; C vaccine-lymph tube and D cotton wool

I have been told that the Ministry of Health has never supported the idea of an ejector worked by blowing with the mouth, but I think that this criticism is overcome in my contrivance

Whitley Hospital, Coventry J F GALPINE.

FATE OF A GROUP

SIR,—The B B C broadcast (April 5) on "Taking Stock" of the National Health Service, once again advocated group practice and emphasised how a doctor in a group could follow some special line of his own to the benefit of the practice Almost every authority supports this view I should like to record what has happened in respect of our own group practice

In 1935 we reorganised our surgery accommodation. This involved a certain amount of building, valued today at over £7500, which gave an efficient place for a group to work When the National Health Service came into being the following happened

1 Our dispensary, where three qualified dispensers worked in a costly and well equipped department, became useless and we suffered a dead loss We received no compensation and were unable to sell hundreds of pounds' worth of drugs. The whole balance of the organisation of rooms was accordingly upset

2 Our surgical partner resigned from the firm to become a whole-time surgical consultant Had he not done so he would not have been able to retain his job on the staff of the local hospital

3 Our pædiatrician, by remaining in general practice, was unable to obtain a consultant appointment at the hospital. His hospital appointment was graded S H.M.O, but domiciliary consultations were allowed

4 One of our obstetricians, who had been doing all the emergency obstetrical work at a local authority maternity home, lost his job and was not even offered a G P clinic.

5 All fees and salaries for specialist work had to be cut out of income for the purpose of compensation, and we are to receive nothing at all for this source of income

Reading STANLEY ALCOCK.

MUNCHAUSEN'S SYNDROME

SIR,—The sparkling correspondence on this syndrome reminds me, even in distant Jerusalem, of my two favourite cases, which did the rounds of hospitals in general, and of L C C hospitals in particular, in the years 1936–40 (at least) They are probably very well known to a number of your readers

The first patient stated that he had repeated attacks of hæmoptysis, at intervals of a few weeks He used to appear in casualty late at night with his shirt and jacket covered with blood, but himself remarkably free from dyspnœa and anæmia On some occasions it was proved that the blood covering his clothes was not human blood, but occasionally human blood seemed to be admixed He would be admitted by casualty officers new to the hospital, and usually discharged himself at 6–7 A.M the next day after having had morphine and usually a good meal and a row with the nurses He usually succeeded in getting out before the senior medical officers, who knew him, began their rounds

The second patient, a much younger man, used to give a perfect history of recurrent attacks of appendicitis except that the pain was referred to the left side His abdomen showed operation scars After the senior people had been brought into consultation and he heard the surgeons talk of the possibility of operation, he would begin to insist very firmly that his appendix had been removed and that he was not going to submit to operation. He would then mention the words "transposition of the viscera." The casualty officer examined again and triumphantly proclaimed that the heart was on the right side. He was then brought into hospital and submitted to radiological and electrocardiographic examination and transposition of the viscera was proudly demonstrated by the staff. He was then discharged. But it was too bad to get a call from another hospital in another quarter of London that he had entered there a few hours later with a similar syndrome. We discovered that this patient got board and lodging, comfort, and attention for most months of the year thanks to his masterly presentation of his alleged symptoms.

Hadassah Medical Organisation,
Jerusalem.
ELI DAVIS,
Director.

SIR,—The correspondence following Dr. Asher's most interesting article of Feb. 10 indicates how prevalent this 'syndrome" is. By giving it this name, however, one might be induced to regard these people simply as tricksters, liars, and swindlers, without paying attention to the underlying psychopathology. These patients are invariably severe psychopaths, and their psychopathic personality requires treatment. The extravagant and often purposeless romancing related as facts is, of course, well known as pseudologia phantastica.

Wanstead Hospital,
London, E.11.
ERIC FRANKEL.

PUBLICITY IN CANCER

SIR,—In his letter of March 24, Professor Russ rightly impeaches delay in seeking advice as the greatest handicap to the successful treatment of cancer, while at the same time he sees in this avoidable circumstance the greatest justification for campaigning for wider publicity in the fight against cancer. At any centre where large numbers of patients suffering from cancer are treated, the overwhelming importance of early diagnosis and treatment is all too clearly revealed. The difference in the results of treatment of early and late cases underlines the tragic effects of the patients' *own* delay in seeking advice. Fear, ignorance, and the thought that suffering is inevitable and cancer is incurable are only some of the reasons which hold the patient back until the condition has passed beyond hope of cure. And so the proportion of early cases seeking treatment remains pitifully small, although many thousands of lives could be saved if only the public could be convinced that cancer in the early stages can be cured.

To substantiate this claim Professor Russ deduces, from data supplied by the Christie Hospital and Holt Radium Institute, Manchester, two significant features: (1) an absence of improvement over a long period of years in the percentage of early cases seeking treatment; and (2) the enormous saving of lives which would follow if, through a more enlightened policy of campaign, more patients could be persuaded to seek advice early. Only in this way is the contrast between the numbers of early and late cases undergoing treatment ever likely to be lessened, and it might even become reversed.

On the supposition that the numbers of early and late cases treated at the Radium Institute, Manchester, during the periods specified were reversed, by means of a simple calculation Professor Russ shows that if 1000 patients suffering from cancer of the breast were treated by the methods now in use at that institute 454 would be alive after five years instead of 213—a saving of 241 extra lives. Applying the same formula to the cases treated for cancer of the uterine cervix the corresponding figures would be 630 alive after five years instead of 275—a saving of 355 extra lives. From a purely propaganda point of view this method of presenting the picture is so arresting as to make one wonder how far statistics obtained at other centres, and submitted to the same type of calculation, would support the urgency of the plea for a nation-wide attempt at breaking down the fear of cancer.

With this object I have submitted statistics relating to the radiation treatment of cancer of the breast and uterine cervix at the Marie Curie Hospital to the formula suggested by Professor Russ, and the following points emerge. Of patients treated for cancer of the breast during the period 1932–34, 19.3% were in stage I of the disease. After a lapse of about twelve years, little improvement had taken place, the proportion of stage I cases treated during 1946–48 being 22.6%. In the case of cancer of the uterus for the same years the proportion of cases in stage I increased from 5.5 to 27.7%. Though representing some advance this is far from being a satisfactory state of affairs, and any feeling of satisfaction is quickly dispelled when the position is viewed from the point of view of the lives that could be saved were the proportions of early and late cases reversed. For example, when the above-mentioned formula is applied to cases treated for cancer of the breast during the periods 1932–34 and 1946–48, 687 patients would be alive five years after treatment instead of 134—a saving of 553 extra lives out of a total of 1000. And in the case of cancer of the uterus, 640 patients would be alive five years after treatment instead of 146, a saving of 494 extra lives.

Such emphasis upon the number of *extra* lives which could be saved were patients to seek advice early instead of late should prove a powerful influence in the approach to a problem the gravity of which calls for a more vigorous effort than is known today in the education of the public concerning significant facts about cancer and its treatment.

Marie Curie Hospital,
London, N.W.3.
MARY GILMOUR.

WILL WE NEVER LEARN?

SIR,—Sir Heneage Ogilvie's letter of March 3 draws attention to one of the problems of a United Nations force, where there may be medical units of different nations in the field, and where forward surgery may be performed by surgeons of many different countries. This may lead to different standards and methods of surgical treatment.

The experiences learned in the late war are contained in the *Field Surgery Pocket Book*, a new edition of which was published in 1950 and is on sale (price 4*s*.) at the Stationery Office and through any bookseller. This is issued to our own medical officers and units in Korea, but similar publications are not perhaps available to all members of a United Nations force.

A. G. HARSANT
War Office,
London, S.W.1.
Director of Surgery and Consulting
Surgeon to the Army.

TREATMENT OF DEPRESSION

SIR,—In thanking you for your summary (March 31) of my contribution to the discussion on this subject at the Royal Society of Medicine, may I correct a mistake.

You state that I reported finding: (*a*) during psychoanalytic treatment of depressions, symptoms reminiscent of epilepsy, pointing to (*b*) an instinctive yearning of the patient for shock and convulsive treatment; and (*c*) that previous convulsive treatment was helpful to the progress of psycho-analytic treatment. In my paper I stated (*a*), did not state (*b*), and stated that I had no evidence for (*c*). With regard to (*c*) I said that of 67 depressives interviewed, 9 had had E.C.T. previously. All these were advised psycho-analysis; 5 accepted this treatment, and in none of these was it considered that the previous E.C.T. helped such treatment. In 1 patient it appeared that the memory of the painful electrical stimulus added to the complexity of the treatment.

London, S.W.7.
W. CLIFFORD M. SCOTT.

the vertebral plexus emerge through the lower cervical nerve roots, and he suggests they were not discovered earlier because of their deep situation and short course The vertebral plexus is regarded as the main source of sympathetic fibres accompanying the internal auditory artery and supplying the internal ear, and any fibres emerging in the lower cervical roots would escape in the sympathectomy under discussion, or in any preliminary trial injection of the stellate ganglion If section of the main preganglionic outflow through D2 and D3 does in fact interrupt pathways to the head, including the ear (as the surgeons claim), then Hyndman and Wolkin, and Goetz are more likely to be correct than Guerrier If so, this is yet another example of how surgical procedures may assist in anatomical localisation and hodology, and conversely it shows how apparently insignificant anatomical details may be of vital importance in determining correct and scientific treatment

Anatomy Department
University of Manchester G A G Mitchell

GENERAL PRACTITIONER AND CONSULTANT

Sir,—There are readier means of raising the status and standard of the general practitioner than those suggested last week by Dr Robertson

If laboratory and radiological facilities were extended to general practitioners in all areas they would readily accept the responsibility of pursuing, where possible, a final diagnosis, and would thus have in the eyes of their patients greater authority

The opportunity for a closer acquaintance with modern medical thought can be provided in two ways firstly, by generous use in hospitals of general practitioners as clinical assistants, secondly, by the establishment of clinical societies based on general hospitals where the G P can demonstrate his cases before fellow practitioners and consultant colleagues

If the capitation fee were adequate there would be no desire by the G P to augment his income and certainly not from the sources suggested by Dr Robertson May I add that I still find consultants readily approachable and prepared to lend an ear to the G P and to expand an opinion when requested

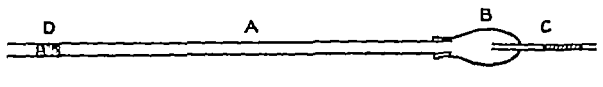
Beckenham Kent D I Finer

IMPROVISED VACCINE-LYMPH EJECTOR

Sir,—Quite a number of practitioners must have been called on to do vaccinations within recent weeks, and some may have been mildly irritated, as I was, by the problem of getting the lymph out of the capillary tube expeditiously and accurately I have found the following simple device, which takes only a very few minutes to make, practical in use and economical of lymph

A firmly fitting rubber bulb is pushed on one end of a glass tube about 8 in long Into the other end of the tube a small pledget of cotton wool is pushed to act as a bacterial filter In the closed end of the bulb a very small hole is made with the red hot point of a pin. It may be that a black rubber bulb would not show up this hole so well as, say, a red rubber one The device is now ready for use

After the ends of the vaccine capillary tube have been broken off, one of them is pushed through the small hole in the bulb, which grips it (see figure) I have not yet encountered a capillary tube that a small hole in the rubber, made in the way suggested, will not grip I hold the device at the junction of the tube and bulb between the finger and thumb, the bulb can then be angled between the middle and ring fingers of the same hand (with the little finger resting on the patient's limb), so that the distal end of the capillary tub approaches the skin at a convenient angle By gentl blowing down the other end of the tube one can extrud small neat drops from the capillary tube, and there i none of the troublesome back suction such as may occu with an ejector worked by finger pressure on a close rubber bulb Usually four insertions can easily be made, with the help of this device, from one capillary tube It is possible to make up to five or six After a serie of insertions the cotton wool can be removed and th glass tubing and bulb boiled



The ejector in use A, glass tubing, B, rubber bulb, C, vaccine lymph tube and D, cotton wool

I have been told that the Ministry of Health ha never supported the idea of an ejector worked by blowing with the mouth, but I think that this criticism is overcome in my contrivance

Whitley Hospital, Coventry J F Galpi

FATE OF A GROUP

Sir,—The B B C broadcast (April 5) on "Tak Stock" of the National Health Service, once again advocated group practice and emphasised how a doctor in a group could follow some special line of his own to the benefit of the practice Almost every authority supports this view I should like to record what has happened in respect of our own group practice

In 1935 we reorganised our surgery accommodation This involved a certain amount of building, valued today at over £7500, which gave an efficient place for a group to work When the National Health Service came into being the following happened

1 Our dispensary, where three qualified dispensers worked in a costly and well equipped department, became usel and we suffered a dead loss We received no compensatio and were unable to sell hundreds of pounds' worth of drug The whole balance of the organisation of rooms was according upset

2 Our surgical partner resigned from the firm to become whole time surgical consultant Had he not done so he woul not have been able to retain his job on the staff of the lo hospital

3 Our pædiatrician, by remaining in general practice, w unable to obtain a consultant appointment at the hospita His hospital appointment was graded S H M O, but domicilia consultations were allowed

4 One of our obstetricians, who had been doing all th emergency obstetrical work at a local authority maternit home, lost his job and was not even offered a G P clinic

5 All fees and salaries for specialist work had to be cu out of income for the purpose of compensation, and we ar to receive nothing at all for this source of income

Reading Stanley Alcoc

MUNCHAUSEN'S SYNDROME

Sir,—The sparkling correspondence on this syndrom reminds me, even in distant Jerusalem, of my two favour ite cases, which did the rounds of hospitals in genera and of L C C hospitals in particular, in the years 1936-4 (at least) They are probably very well known to a numbe of your readers

The first patient stated that he had repeated attacks hæmoptysis, at intervals of a few weeks. He used appear in casualty late at night with his shirt and jack covered with blood, but himself remarkably free from dyspn and anæmia On some occasions it was proved that the blo covering his clothes was not human blood, but occasional human blood seemed to be admixed He would be admitt by casualty officers new to the hospital, and usually discharg himself at 6–7 A M the next day after having h morphine and usually a good meal and a row with the nurs He usually succeeded in getting out before the senior medic officers, who knew him, began their rounds

The second patient, a much younger man, used to give perfect history of recurrent attacks of appendicitis except th the pain was referred to the left side His abdomen show operation scars After the senior people had been broug into consultation and he heard the surgeons talk of t possibility of operation, he would begin to insist very firmly that his appendix had been removed and that he was not going to submit to operation He would then mention the words "transposition of the viscera" The casualty officer examined again and triumphantly proclaimed that the heart was on the right side He was then brought into hospital and submitted to radiological and electrocardiographic examination, and transposition of the viscera was proudly demonstrated by the staff He was then discharged But it was too bad to get a call from another hospital in another quarter of London that he had entered there a few hours later with a similar syndrome We discovered that this patient got board and lodging, comfort, and attention for most months of the year thanks to his masterly presentation of his alleged symptoms

Hadassah Medical Organisation
Jerusalem

ELI DAVIS
Director

SIR,—The correspondence following Dr Asher's most interesting article of Feb 10 indicates how prevalent this "syndrome" is By giving it this name, however, one might be induced to regard these people simply as tricksters, liars, and swindlers, without paying attention to the underlying psychopathology These patients are invariably severe psychopaths, and their psychopathic personality requires treatment The extravagant and often purposeless romancing related as facts is, of course, well known as pseudologia phantastica

Wanstead Hospital
London E 11

ERIC FRANKEL

PUBLICITY IN CANCER

SIR,—In his letter of March 24, Professor Russ rightly impeaches delay in seeking advice as the greatest handicap to the successful treatment of cancer, while at the same time he sees in this avoidable circumstance the greatest justification for campaigning for wider publicity in the fight against cancer At any centre where large numbers of patients suffering from cancer are treated, the overwhelming importance of early diagnosis and treatment is all too clearly revealed The difference in the results of treatment of early and late cases underlines the tragic effects of the patients' *own* delay in seeking advice Fear, ignorance, and the thought that suffering is inevitable and cancer is incurable are only some of the reasons which hold the patient back until the condition has passed beyond hope of cure And so the proportion of early cases seeking treatment remains pitifully small, although many thousands of lives could be saved if only the public could be convinced that cancer in the early stages can be cured

To substantiate this claim Professor Russ deduces, from data supplied by the Christie Hospital and Holt Radium Institute, Manchester, two significant features (1) an absence of improvement over a long period of years in the percentage of early cases seeking treatment and (2) the enormous saving of lives which would follow if, through a more enlightened policy of campaign, more patients could be persuaded to seek advice early Only in this way is the contrast between the numbers of early and late cases undergoing treatment ever likely to be lessened, and it might even become reversed

On the supposition that the numbers of early and late cases treated at the Radium Institute, Manchester, during the periods specified were reversed, by means of a simple calculation Professor Russ shows that if 1000 patients suffering from cancer of the breast were treated by the methods now in use at that institute 454 would be alive after five years instead of 213—a saving of 241 extra lives Applying the same formula to the cases treated for cancer of the uterine cervix the corresponding figures would be 630 alive after five years instead of 275—a saving of 355 extra lives From a purely propaganda point of view this method of presenting the picture is so arresting as to make one wonder how far statistics obtained at other centres, and submitted to the same type of calculation, would support the urgency of the plea for a nation wide attempt at breaking down the fear of cancer

With this object I have submitted statistics relating to the radiation treatment of cancer of the breast and uterine cervix at the Marie Curie Hospital to the formula suggested by Professor Russ, and the following points emerge Of patients treated for cancer of the breast during the period 1932–34, 19 3% were in stage I of the disease After a lapse of about twelve years, little improvement had taken place, the proportion of stage I cases treated during 1946–48 being 22 6% In the case of cancer of the uterus for the same years the proportion of cases in stage I increased from 5 5 to 27 7% Though representing some advance this is far from being a satisfactory state of affairs, and any feeling of satisfaction is quickly dispelled when the position is viewed from the point of view of the lives that could be saved were the proportions of early and late cases reversed For example, when the above mentioned formula is applied to cases treated for cancer of the breast during the periods 1932–34 and 1946–48, 687 patients would be alive five years after treatment instead of 134—a saving of 553 extra lives out of a total of 1000 And in the case of cancer of the uterus, 640 patients would be alive five years after treatment instead of 146, a saving of 494 extra lives

Such emphasis upon the number of *extra* lives which could be saved were patients to seek advice early instead of late should prove a powerful influence in the approach to a problem the gravity of which calls for a more vigorous effort than is known today in the education of the public concerning significant facts about cancer and its treatment

Marie Curie Hospital
London N W 3

MARY GILMOUR

WILL WE NEVER LEARN?

SIR,—Sir Heneage Ogilvie's letter of March 3 draws attention to one of the problems of a United Nations force, where there may be medical units of different nations in the field, and where forward surgery may be performed by surgeons of many different countries. This may lead to different standards and methods of surgical treatment

The experiences learned in the late war are contained in the *Field Surgery Pocket Book*, a new edition of which was published in 1950 and is on sale (price 4s) at the Stationery Office and through any bookseller This is issued to our own medical officers and units in Korea, but similar publications are not perhaps available to all members of a United Nations force

War Office
London S W 1

A G HARSANT
Director of Surgery and Consulting
Surgeon to the Army

TREATMENT OF DEPRESSION

SIR,—In thanking you for your summary (March 31) of my contribution to the discussion on this subject at the Royal Society of Medicine, may I correct a mistake.

You state that I reported finding (*a*) during psychoanalytic treatment of depressions, symptoms reminiscent of epilepsy, pointing to (*b*) an instinctive yearning of the patient for shock and convulsive treatment, and (*c*) that previous convulsive treatment was helpful to the progress of psycho analytic treatment In my paper I stated (*a*), did not state (*b*), and stated that I had no evidence for (*c*) With regard to (*c*) I said that of 67 depressives interviewed, 9 had had E C T previously All these were advised psycho analysis, 5 accepted this treatment, and in none of these was it considered that the previous E C T helped such treatment In 1 patient it appeared that the memory of the painful electrical stimulus added to the complexity of the treatment

London S W 7

W CLIFFORD M SCOTT

DETECTION OF ENTAMŒBA HISTOLYTICA

SIR,—Some of your readers may be interested to know that Pearse's[1] modification of the P A S technique gives beautiful results when used for demonstrating *Entamœba histolytica* in sections These organisms are not always easy to see in ordinary preparations, but with Pearse's technique they stand out as magenta coloured cells which cannot be missed Red blood cells engulfed by the amœbæ are bright orange, contrasting well with the deep red cytoplasm The use of this method is based, of course, on the fact that *E histolytica* is rich in glycogen Ordinary 10% formol saline fixation works perfectly well

Pathological Department
Ashford Hospital Middlesex

C F ROSS

SIZE OF MEDICAL SCHOOLS AND HOSPITALS

SIR,—In his thoughtful and illuminating article of March 17, on the Economic Value of the Doctor, Dr Ffrangcon Roberts uses the term "facultative audit" The need for inquiries of the kind he has in mind is urgent in still other directions The two questions I should like to see submitted to such a technique are (1) what is the optimum size of a medical school ? and (2) what are the most economical sizes of the main varieties of hospital ? Fairly extensive search of the literature has yielded no studies of the completeness that seems requisite

Years ago I started with the Calendar and the annual financial statement of my own medical school, to see whether my fear that we were too big could be justified on statistical grounds, but my knowledge of statistics proved insufficient An answer to the question could, however, be found from the data available Take a preclinical subject as an example—say physiology If the class is about 40, finance may dictate that the professor and one assistant must bear the whole burden of the teaching, and this has disadvantages when so wide a subject is covered It is asking a lot from a physiologist to be so interested in neurophysiology, metabolism, endocrinology, and the rest, that he will *teach* each division efficiently If the class is 220 the staff may comprise a professor, a reader, and seven lecturers or more, and specialisation becomes possible But the personal contact between staff and student is almost lost, while the physical limits of the department may necessitate the shift system for practical classes (The latter, as I know to my cost, imposes a burden on the staff which is far too heavy) What then is the best size of class ? But wait, the answer must also take into consideration the most economical use of the department's space It must be heated, lighted, cleaned, and insured, and its capital value must be amortised What number of students is sufficient to justify the expense ? At what point does overcrowding cause a loss of efficiency or an increase in cost through the need to improvise, or to provide duplicate apparatus ? These are but a few examples of the multitude of variables with which such an inquiry would be concerned, but they are enough to show how complicated would be the integration of numbers of curves, often of opposite trends It would be a fascinating investigation, and I make a present of the idea to anyone who wants a novel thesis subject

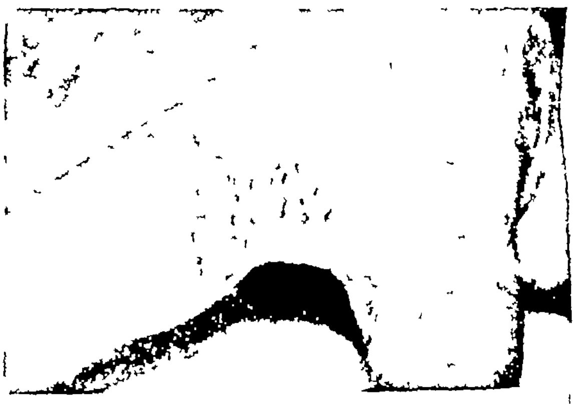
The same type of inquiry is applicable to the clinical side, though here the most important factors are the number of available beds, both general and special, and sometimes the amount of time taken in travelling to different hospitals Many estimates have been made of the best size of hospitals in different circumstances, but none I know of are based on a detailed actuarial and cost accounting basis parallel to the one suggested for medical school size We seem to have been waiting for the catalysis of Dr. Roberts's phrase of the "facultative audit"

"CALCULUS"

PILONIDAL SINUS IN A BARBER

SIR,—I was interested in Mr Jenkins's description (March 31) of this condition Pilonidal sinus is usually regarded as a congenital disorder occurring in association with the spine, and presenting commonly as a dimple in the postanal region

Short hairs are regularly found penetrating the skin of barbers' hands, and all eye departments see as patients hairdressers and barbers who complain of hairs penetrating the conjunctiva Although "cysts" are produced in the skin, these do not grow hair The accompanying figure shows a typical example of multiple sinuses in the web of a barber's hand Each contained a hair, which could readily be removed with forceps This patient has had recurring trouble over many years, and when the sinuses became infected, the cysts they formed needed opening



London W 1

CLARA M WARREN

SIR—I read Mr Jenkins's letter with interest A few hours earlier I had examined a similar case

The patient was a barber, aged 43, who complained of a tender nodule on the radial side of the middle finger, just distal to the web space, which he had noticed for 6 months Later a small sinus had developed from which hairs had been picked When I examined him there was a swelling about 1 cm in diameter with some surrounding inflammation I advised him to allow this to settle down, and to have the cyst excised later

Farnham Hospital, Surrey

S C RAW

HEALTH SERVICE ESTIMATES 1951 52

SIR,—Reading your leading article of April 7 and also p 794 (col 2), I am surprised that you said nothing about the entry which shows an expenditure of £21,144,000, in the hospitals of England alone, on salaries and wages of "other staff" Surely after taking into consideration all the main items—Medical Staff, Nursing Staff, Ward Orderlies, Works Maintenance Staff, Laundry Staff, Farm and Garden Staff, Administrative and Clerical Staff, Professional and Technical Staff, Catering Officers, Cooks, and Kitchen Staff—an item of £21,144,000 for *other* staff should not be allowed to go without comment What other staff can there be left who require nearly as much money as the entire Medical Staff, including specialists ? Such slovenly accountancy seems strange to me, and I think the taxpayer is entitled to more detailed information than we are given here

Attention was drawn to this item by a special correspondent in the *British Medical Journal* of April 7, and I hope that those responsible for the estimates will now throw more light on the subject

HAROLD LEESON

Worthing

---

[1] Pearse A G E *J Path Bact* 1949, 61, 195

Parliament

Trimming Our Coat

In the speech in which he introduced a Budget which he declared to be honest if not popular, Mr Hugh Gaitskell, the Chancellor of the Exchequer, pointed out that the gross estimate for the National Health Service in England, Wales, and Scotland for the year 1951–52 was nearly £470 million Receipts from the Insurance Fund and staff pension contributions brought this figure down to about £398 million This total was £25 million less than the estimate originally submitted to him, which was £30 million above last year's estimate The increase was mostly due to higher prospective expenditure on the hospital services But with all the other burdens to be carried the Government did not feel it reasonable to pass another £35 million on to the Exchequer and therefore on to the taxpayer , so they decided that the health service must be kept within a total of £400 million, which for the time being must be the ceiling The Minister of Health and the Secretary of State for Scotland would make all practicable economies in the course of their administration, but it was plain that the only way to keep within this limit, without reducing the standard of the hospital, family doctor, and consultant services below what was really essential, was to find some other source of revenue The Government had therefore decided, Mr Gaitskell said, to introduce a modest charge for dentures and spectacles In the dental service all extractions and conservation would still be free, but a charge of about half the scale fee would be made in future for all denture work Expectant and nursing mothers would continue to receive free dental treatment, including dentures, from the local-authority services, and children would receive free treatment in schools as now A charge of about half the cost of each pair of glasses would also be made, but there would be no charge for children's spectacles People for whom these charges would be a hardship would be reimbursed, in whole or part, from the National Assistance Board in the ordinary way Legislation would be introduced shortly, and the details of the proposals would then be further explained Mr Gaitskell expected the new charges to yield about £13 million in 1951–52 and about £25 million in a full year The intention to make all practicable economies and to impose these charges had already been allowed for in the estimates lately presented to the House [1]

The Government, Mr Gaitskell admitted, made these changes with regret, but he believed that most people would agree that while it was reasonable to allow a slight increase in expenditure on health—some £7 million above last year—it was also necessary, against the background of our general financial position and remembering the proposed increases in the old-age pensions and on the hospital services, to impose a limit and accept that some charges should be made in the National Health Service The Government thought that they had struck a fair balance between one item of social service and another The charges would not normally fall on those who were seriously ill, such as hospital patients They applied where there was least danger of hardship and perhaps more danger of abuse than anywhere else in the health service

The Debate

In the course of the debate on the Budget Mr John Baird objected to the new charges because they were completely unnecessary and because they involved a major principle People argued that there had been considerable abuses in the health service and that by making a charge for dentures and spectacles we should stop these abuses In his view these abuses, so far as the dental side was concerned, had come, not from the patients, but from the dentists He did not say that every dentist was involved, but a small section of dentists had abused the Act and nothing had been done to stop them. Most of the patients had needed treatment and many of them could not afford to pay for it He therefore hoped that the proposal would be withdrawn During the last year the dental estimates had fallen by something like £10 million, and since the beginning of this year the demand for dentures had fallen, he believed, by about 20% The great demand was now satisfied For instance, last year it was impossible to find a dental mechanic , today in the London area there were 120 looking for work.

He also believed it was wrong in principle to have a ceiling for the health service Why was it necessary, he asked, to have ceilings for great social measures like the food subsidies and the health service where there was none for other forms of expenditure ? Was there no waste in the Service departments ? If the cost of living continued to go up the cost of the health services would go up An ageing population would increase the hospital population and throw further cost on the health service He believed that doctors were asking for more pay, and compared with other branches of the service they could make out a good case But if the cost of the service continued to go up and the ceiling remained at £400 million, what would the next charge be ? Already it had been suggested that we should have a charge for visits to the doctor Perhaps there would soon be a charge for beds in hospitals Let no one imagine this would stop at a charge for false teeth The Government should think again before they jeopardised our free health service for the sake of a mere £13 million.

Mr Richard Ewart agreed that the National Health Service had contributed to the rise in the standard of living of all the people in this country But if there were to be savings he believed the Chancellor had applied those savings in the right direction, where the necessity was non recurrent for several years and might reasonably be expected to be borne An attack on the health service—a charge on consultants' fees, as envisaged by the Opposition, and on medical or hospital services—would mean a reduction in the standard of living of the whole community The Chancellor had taken the right steps to resist this

Mr Ralph Assheton congratulated the Chancellor on his courage in making these charges for the health services A free service had meant that many who most need the health service found themselves pushed aside We all wanted to get the best we could out of the service, but he was not sure that the present system of centralised control over the hospitals was effective, and he thought we should have an independent inquiry The strongest indictment of the health service, he pointed out, came from an unexpected quarter—the Socialist Medical Association's pamphlet *The L S.D of the National Health Service* Had the general practitioner, Mr Assheton asked, any incentive to prescribe economically ? Had the patient any incentive to use the service economically ?

QUESTION TIME

Tuberculosis Treatment in Switzerland

Replying to a question Mr Hector McNeil Secretary of State for Scotland, said that Parliament would shortly be invited to consider legislation enabling arrangements to be made under the National Health Service for giving treatment outside Great Britain to people with respiratory tuberculosis For this year from 150 to 200 beds in Swiss sanatoria would be made available for patients from Scotland, with the necessary transport facilities To minimise the travelling involved the selected patients would normally be people in need of at least six months' sanatorium care but unlikely to require any major surgical operation. Treatment in Switzerland would be offered to persons recommended for sanatorium treatment in the ordinary way where on medical grounds this was considered appropriate by the responsible tuberculosis physicians

Brigadier Frank Medlicott asked the Minister of Health what was the present position of his discussions concerning the possibility of tuberculosis patients being treated in Switzerland under National Health Service arrangements —Mr H. A. Marquand replied Arrangements are now being worked out for the use of about 160 beds in Switzerland for suitable patients from England and Wales suffering from respiratory tuberculosis, and it is hoped to start sending patients out in a few months time

Hospital Registrars

Mr Hugh Linstead asked the Minister of Health whether he would now make a further statement to reassure those registrars whose services were threatened with termination in accordance with circular R H B (50)106 —Mr MARQUAND replied I should prefer to await the outcome of discussions now proceeding

---

[1] See *Lancet* March 31 1951 p 760

Hospital Accommodation for the Chronic Sick in London

Commander A H P NOBLE asked the Minister whether he would give an estimate of the number of chronic sick in London awaiting admission to hospital —Mr MARQUAND replied On Dec 31, 1950, there were 1324 patients on the waiting lists for admission to chronic sick beds in National Health Service hospitals in the county of London

Agenisation of Flour

Mr G C TOUCHE asked the Minister of Food whether his attention had been called to statements made at an inquest at Hull recently regarding the effects of the agenisation of flour, and whether he would make a statement on the subject —Mr F T WILLEY replied I am aware that certain allegations were made which were controverted by expert evidence at the inquest Recently a scientific committee reviewed the subject of flour improvers but was unable to find any evidence that agenised flour is in any way toxic to man

In answer to written questions Mr WILLEY stated that agreement had been reached with the milling industry to stop the use of 'Agene' and the choice of an alternative improver was under consideration Probably about 90% of flour used for human consumption was at present agenised

Doctors and National Insurance

Sir WALDRON SMITHERS asked the Minister of National Insurance if a doctor who worked for the National Health Service was, for the purposes of National Insurance contributions, classed as self employed or employed by the State —Mr H B TAYLOR replied The conditions under which doctors work for the N H S vary, but a general practitioner on the list of an executive council will normally be regarded as self employed for the purposes of the National Insurance Act

Public Health

Bathing in the Thames

WHEN the warmer weather comes many thousands of people will again be bathing in the Thames, and the question arises whether the risk to their health is becoming excessive

The Thames has always received sewage, but formerly the bacterial pollution was relatively slight because the sewage was diluted by a vast volume of flowing water and because river water has some power of self-purification In recent years, however, riverside populations have grown and the amount of sewage discharged into the river has increased in proportion As a result bacterial pollution may be approaching a dangerous level

Two years ago the Windsor baths were closed because of river pollution, but, when the question was raised, the Thames Conservators[1] and the Minister of Health[2] gave assurances that the river was no less safe than it had ever been This year the Eton College authorities, following the example of Windsor borough council, have stopped river bathing, and on April 6 in a letter to the *Times* Mr Cosmo Russell[3] called for an investigation by a "strong departmental committee" to discover ways to remedy the present state of affairs His letter was the subject of a report to the Thames Conservancy Board by its chairman, Sir Jocelyn Bray[4] On this occasion the board did not deny that pollution of the river had increased, but the chairman said that it did not fear the appointment of a committee, as suggested by Mr Russell, for he did not see what a committee could discover that was not already well known No river, said Sir Jocelyn, could possibly be of the standard laid down for swimming-baths by the Ministry of Health Even the "near safe" conditions of a properly constructed swimming-bath could not be produced in a river like the Thames which received large volumes of surface water and effluents Even if all effluents were 100% chemically pure, the river would not be bacteriologically safe, and it was the bacterial pollution which was the cause of apprehension by the Eton College authorities and others In reply to a question the chairman said that there was no definite instance of poliomyelitis or any other disease having been contracted through bathing in the Thames He added that neither in the Hobday report nor in the River (Prevention of Pollution) Bill now before Parliament was any mention made of steps to deal with bacterial pollution Obviously, he said, this was because it was practically impossible to do anything

There seems to be no doubt that pollution of the Thames has increased It is true that there is no proof of disease having been contracted as a result, but, as Albury has said in our columns,[5] it is equally true that there is no disproof While it is generally agreed that the dangers of contracting disease in a properly equipped swimming-bath have been exaggerated[6] it is probable that river water with a high bacterial content is dangerous to bathers Unfortunately, ordinary methods of sewage disposal have little effect on the bacterial content and elaborate methods of sterilisation would be necessary to render it bacteriologically pure Much was expected from the Act of 1948[7] but it is obvious that as far as the Thames is concerned the position is becoming one of urgency

Obituary

KENNETH DOUGLAS WILKINSON

O B E, M D Birm, F R C P

Dr K D Wilkinson, physician to the Birmingham United Hospital and consulting physician to the Children's Hospital, who died at his home in Edgbaston on April 12, had held the chair of therapeutics in the University of Birmingham from 1925 to 1946

He was born in 1886 at High Legh, Cheshire, the son of the Rev H C Wilkinson, and he was educated at Berkhamsted School and the University of Birmingham As a student he already showed both his practical ability and his aptitude for writing, and in 1908 he was awarded the Richardson essay prize, and, when he graduated M B the following year, the senior prize in clinical medicine During the next two years he held house appointments at the Queen's Hospital and at the General Hospital, Birmingham, before he became R M O at the General Hospital In 1912 he took his M D, and the following year he spent some months in London at the Hospital for Sick Children, Great Ormond Street, as a casualty officer On his return to Birmingham he was appointed to the staff of the Children's Hospital, and the following year he also became assistant physician to the General Hospital

[Elliott & Fry

He was thus well embarked on his career when war broke out in 1914 During his service with the R A M C he developed the interest in cardiology, already shown by his early papers on heart block, in his work with G E Gask on wounds of the chest Dr Wilkinson was appointed O B E for these services and mentioned in despatches

On demobilisation he returned to Birmingham to take up again his work as a consultant and teacher In 1920 he was elected F R C P, and the same year he was appointed to his chair As a lecturer he was lucid and incisive He knew how to point his clinical teaching with telling anecdotes, but his students found themselves remembering the principles he described as well as his amusing illustrations He examined for the universities of

---

1 *Times* April 18 1950 p 2
2 *Hansard* May 11, 1950 col 568
3 *Times* April 6 1951 p 5
4 *Times* April 10 1951 p 2
5 Albury M *Lancet* 1950 ii 75
6 *Lancet*, March 10 1951 p 573
7 *Ibid* 1949 ii 1226

Cambridge and Manchester and for the Royal College of Physicians. His continuing interest in cardiology led him to study the problems of rheumatism especially in children, and he chose as the subject of his Ingleby lectures in 1935 Rheumatism and its Results. In 1949 he also gave the St. Cyres lecture in this specialty.

In 1925 his *History of the Birmingham Medical School* appeared, and last year he was joint author of *William Withering of Birmingham*. His profound knowledge of 18th century Birmingham enabled him to set Withering against a vivid and varied background. Of Wilkinson the man, a colleague writes: "He really enjoyed life—his work, his recreations of golf, sailing, and bridge, his family life, and his friendships. Full of anecdotes, an authority on dialect, and a great mimic, he was an entertaining companion. Many of his younger colleagues will remember his generosity."

Dr. Wilkinson was twice married. His first wife, formerly Miss Phebe Homewood, was a sister at the Queen's Hospital, and he leaves three sons and a daughter by this marriage. His second wife, Dr. Agnes Crozier, survives him with a son and two daughters.

ARTHUR SYDNEY BLUNDELL BANKART

M.A., M.Chir. Camb., F.R.C.S.

Mr. Blundell Bankart, who died on April 8, was one of the fathers of British orthopædic surgery, and his influence was felt throughout the world.

Arthur Sydney Blundell Bankart was born in 1879 the son of James Bankart, F.R.C.S., of Exeter. He was educated at Rugby, at Trinity College, Cambridge, and at Guy's Hospital. After qualifying in 1906 he held a resident post at Guy's for a year before he decided to take up surgery. The academic hurdles presented no obstacle, and he became a fellow of the Royal College of Surgeons of England in 1909 and a master of surgery of the University of Cambridge the following year. During this period he came under the influence of two great men, Arbuthnot Lane and Charles Sherrington. From the former he learned the no touch technique that made bone surgery comparatively safe at a time when the aseptic ritual was still at a primitive level, and which he was able later to pass on to others of the now growing band of orthopædic surgeons. But—and perhaps this was more important—he acquired from Sherrington the experimental approach to disease, an attitude of mind that he retained throughout his life.

By courtesy of the Journal of Bone and Joint Surgery

Bankart was attracted from the first by the possibilities that were opening at the borders of the surgical field. His inquiring mind was very ready to turn from the old to the new, and it was natural that he should enter one of the embryo specialties. In 1909 he became the first surgical registrar at the newly formed Royal National Orthopædic Hospital. Dexterous of hand, preferring the operative side of surgery, and well primed with the new Lane technique, he took full advantage of the opportunity. The surgeons of those days took a leisurely two months' holiday each summer, leaving their hospitals deserted and their patients awaiting their return. Bankart loved to tell how, as soon as he was left alone, he emptied all the beds and filled them with new patients whom he could treat without restraint. In 1911 he was appointed assistant surgeon to the Royal National Orthopædic Hospital, and in the same year he became assistant surgeon to the Queen's Hospital for Children and the Belgrave Hospital, and surgeon to the Maida Vale Hospital for Nervous Diseases. This was in the days before the surgical specialties had become a closed shop, and he was practising orthopædics, general surgery, and neurosurgery. This last attracted him greatly and he continued with it almost until the late war. Indeed, stimulated by Campbell Thompson, he carried out much of the neurosurgery at the Middlesex Hospital. Orthopædics, however, was always his first love and it was in this field that he made his chief contributions.

The outbreak of the first world war thus found him already on the honorary staff of four hospitals, and to this burden he added a number of the smaller military hospitals in the London area. Then, shortly after Shepherd's Bush was opened, Bankart joined Robert Jones's team there and this became the busiest time of his energetic career. After the war he was elected to the staff of the Middlesex Hospital as its first orthopædic surgeon. He gave up his appointments at some of the smaller hospitals to be free to devote more of his time to the uphill task of developing a new department in an old-established institution.

His position in the orthopædic world was quickly recognised. In 1913, he became the first honorary secretary of the newly formed subsection of orthopædic surgery of the Royal Society of Medicine, and in 1925 he was elected president of the section. A founder member of the British Orthopædic Association, he was honorary secretary of the association from 1926 to 1931 and president in 1932 and 1933.

P. W. writes: "Bankart is perhaps best known for his operation for recurrent dislocation of the shoulder, a procedure now used by nearly every orthopædic surgeon in the world and out of the hundred or more described for the relief of this condition the only really reliable one. His influence on orthopædics in nearly every field was profound because he had a directness of approach that excluded careless thought and slipshod work, and he was quick to debunk an unsound or superficial argument. His attitude to manipulative work is an example. He saw the good results so often obtained by bonesetters and manipulators and took the trouble to find out what they actually did. He got to know Herbert Barker, watched him work, and followed up his patients. He reduced the claims from 'miracles' to plain facts, showed when manipulation was indicated, made it a 'respectable' procedure, and put it on the orthopædic map, and the culmination of this work was his book, *Manipulative Surgery*, published in 1932.

"He was a shy man and for this reason few of his colleagues knew him well, but those who did loved him greatly. I owe him more than I can say. He took me as a young man, taught me his craft, and made my way easy. He was always helping others, but he did it so unobtrusively that often they would be unaware of what he had done. A connoisseur of the good things of life, he had little use for mediocrity. He liked fine furniture, fine wine, and fine men."

Mr. Bankart married Beryl Winifred, daughter of Mr. A. S. Moss-Blundell, who survives him with one daughter.

ROBERT BROOM

M.D., D.Sc., LL.D. Glasg., F.R.S.

Dr. Robert Broom died on April 6 at the age of 84. His name will for ever be associated with two most important themes in palæontology—the mammal-like reptiles which have provided so much information on the problem of the origin of mammals, and the fossil ape-like creatures of South Africa, the Australopithecinæ, which have contributed such abundant evidence bearing on the origin of man. All these achievements were the product of an amazing energy, mental as well as physical.

Born in 1866, at Paisley, the son of John Broom, a shawl designer and art connoisseur, he studied at Glasgow University where he graduated in science in 1887 and in medicine two years later. During his medical course he came under the influence of John Cleland, professor of anatomy, who was one of the main sources of inspiration for his pursuit of evolutionary studies in later years. He became particularly interested in the question whether mammals had their evolutionary origin from reptilian or amphibian ancestors—a problem which at that time was a matter of active dispute among comparative anatomists. This was one of the reasons why he went to Australia in 1892, for he thought the land of the monotremes might provide important evidence for comparative anatomical studies. During the next few years he published a number of papers dealing with the anatomy of monotremes and marsupials. While in Australia his attention was drawn to the importance of fossil evidence in the elucidation of evolutionary problems His stimulating contact with a remarkable group of biologists who at that time were working together at the University of Sydney—Elliot Smith, J P Hill, Haswell and J T Wilson—led to further contacts by correspondence with biologists in other parts of the world, and it was partly due to the influence of the American palæontologist Osborn that he went to South Africa in 1897 to search for fossil evidence of the evolutionary transition from reptile to mammal The years of productive work which followed were marked by a series of important papers on fossil mammal-like reptiles, many of them reporting the discovery of new types, and on problems of comparative anatomy and vertebrate evolution In 1913 Broom was invited to deliver the Croonian lecture before the Royal Society, in 1920 he was elected to the society, and in 1928 he was awarded one of its Royal medals

To carry out his explorations, Broom engaged in medical practice in out-of-the-way places with the immediate intention of seeking for fossils in the locality Not that he neglected his patients (who in these remote districts were often very few), for according to all accounts he was regarded with great affection by them But he had to live a life of great austerity, not to say poverty, in order to satisfy his scientific interests As a result of his work during these earlier years, he became one of the leading authorities on the mammal-like reptiles Later, Dart's discovery of Australopithecus inspired him to search for more remains of this extinct ape-like form He was convinced that Dart was right in his conclusion that, in spite of the simian proportions of the brain and jaws, Australopithecus showed morphological characters in the skull and dentition which approximated to the Hominidæ rather than to the anthropoid apes With remarkable insight and energy Broom sought, and found, abundant remains of the Australopithecinæ in stalagmitic deposits near Pretoria, and at the time of his death he had discovered, and described, many skulls, jaws, teeth, and limb bones of adults, juveniles, and infants

"Each new discovery," writes W E Le G C, "brought new confirmation of the astonishing mixture of hominid characters with primitive ape like characters in the Australopithecinæ It is not surprising that these discoveries gave rise to acute controversies, indeed, this may be taken as a measure of their importance, for sharp controversies have always accompanied equally important discoveries in the past (It was, for instance, vigorously contended at one time that Pithecanthropus was nothing more than a giant gibbon, or that Neanderthal Man was nothing more than a pathological monstrosity) It is fair to say, however, that almost every authority now recognises the existence in the Australopithecinæ of hominid characters which are not to be found in the anthropoid apes, even though there may be still some difference of opinion as to their precise significance

"Broom used to maintain that the paucity of fossil evidence bearing on human evolution was mainly due to the fact that palæontologists did not look in the right places and did not pursue their searches with enough vigour He himself certainly had a remarkable flair for going to the right places to hunt for fossils But more than that, he possessed a drive and energy which overcame all obstacles and brooked no opposition in his eagerness to find what he was looking for Practically up to the time of his death, he was still working with amazing energy Few men who die at the age of 84 have achieved more in the acquisition of new scientific knowledge than he In his passing we can but feel a deep sense of gratitude for his single-minded devotion in his field of work, and pay our respects to a man who was so outstanding as a discoverer To those of us who knew him personally, his generosity and kindness will be remembered as among the most prominent of his qualities If he permitted his dry Scotch humour to let itself go sometimes in outspoken criticisms of those who threw doubt on the validity of his conclusions—particularly those who did so without having even seen the original fossil specimens—his criticisms were always made with a characteristic twinkle in his eye "

Notes and News

KING EDWARD VII's HOSPITAL FOR OFFICERS

At the request of King Edward's Hospital Fund a consulting staff has been appointed to King Edward VII's Hospital for Officers, Sister Agnes Foundation, Beaumont Street, London, W 1 The council of the hospital are anxious, however, that the specialists and practitioners not on the staff should continue to use the hospital, and the council have laid down that patients may be admitted under any doctor of their own choice The hospital is now for serving, retired, and ex temporary officers of the Forces, and the fees are from 7 to 15 guineas a week according to the nature of the accommodation and subscription rights of patients

CONTROL OF ANTI-HISTAMINES

In this country there have been several fatalities among children who have swallowed tablets containing anti-histamine drugs [1], and last year this group of drugs was added to part 1 of the Poisons List and the first schedule. In the U S.A these compounds are still widely taken as a remedy for the common cold, despite substantial evidence that they have little or no value against this ill [2], and the committee on public health relations of the New York Academy of Medicine states that 8 infants under two years of age are reported to have died from accidental consumption of the tablets, while several others are reported to have had convulsions "Packages of antihistaminic drugs sold to the public," says the committee, "carry directions for dosage, but this is not sufficient protection against accidental over dosage or other hazardous use, especially in children. Allergists have estimated that at least 20 per cent of the people who take anti histamines in the doses recommended will experience undesirable if not dangerous reactions. Several persons are reported to have attempted suicide by taking excessive doses of antihistaminic drugs, and one succeeded "

THE CIBA FOUNDATION

The Ciba Foundation for the Promotion of International Coöperation in Medical and Chemical Research was founded by Messrs Ciba in September, 1947, to encourage study and research in all branches of medicine and its allied sciences. The foundation building was opened in London at 41, Portland Place, W 1, on June 22, 1949, the founders felt that the English language had become the scientific language of the world and that London was the ideal world centre The foundation serves as a meeting place for research workers from all over the world, provides accommodation for foreign visitors, and bestows grants to enable scientists from one country to work in another To begin with it was decided to confine its activities mainly to the international exchange of ideas on the steroid hormones, and a specialist library is being built up on this basis

The first report covers the period June, 1949, to December, 1950 During this time 1800 people, including visitors from 17 countries, have attended meetings at the foundation or have visited research institutions under arrangements made by the foundation It has worked in close coöperation with the medical societies, the University of London, the British Council, the Ministry of Health, and the scientific section of the French Embassy Many of the societies have held meetings at the centre, and one, the Hunterian Society, has held an exhibition at the foundation

The Ciba Foundation lecture for 1949 was given by Prof E C Dodds, F R S, and the lecture for 1950 by Sir Stanton Hicks, University of Adelaide Eight conferences were held, six concerned with the steroid hormones and two with general subjects The proceedings of one of the general meetings have been published in book form, and it is hoped to publish an account of the other meetings shortly The resources of the library have been strengthened by an arrangement whereby guests are allowed to use the library of the Royal Society of Medicine

The trustees of the foundation are Lord Beveridge, Lord Horder, Prof E D Adrian, O M, F R.S, and Mr Raymond Needham An executive council has been set up and is helped by an advisory board consisting of 13 members from Great

---

[1] See *Lancet* 1950 i 28 78, *Ibid*, ii 370

[2] Leading article *Ibid* i 1119

in Australia his attention was drawn to the importance of fossil evidence in the elucidation of evolutionary problems. His stimulating contact with a remarkable group of biologists who at that time were working together at the University of Sydney—Elliot Smith, J. P. Hill, Haswell, and J. T. Wilson—led to further contacts by correspondence with biologists in other parts of the world, and it was partly due to the influence of the American palæontologist Osborn that he went to South Africa in 1897 to search for fossil evidence of the evolutionary transition from reptile to mammal. The years of productive work which followed were marked by a series of important papers on fossil mammal-like reptiles, many of them reporting the discovery of new types, and on problems of comparative anatomy and vertebrate evolution. In 1913 Broom was invited to deliver the Croonian lecture before the Royal Society, in 1920 he was elected to the society, and in 1928 he was awarded one of its Royal medals.

To carry out his explorations, Broom engaged in medical practice in out-of-the-way places with the immediate intention of seeking for fossils in the locality. Not that he neglected his patients (who in these remote districts were often very few), for according to all accounts he was regarded with great affection by them. But he had to live a life of great austerity, not to say poverty, in order to satisfy his scientific interests. As a result of his work during these earlier years, he became one of the leading authorities on the mammal-like reptiles. Later, Dart's discovery of Australopithecus inspired him to search for more remains of this extinct ape-like form. He was convinced that Dart was right in his conclusion that, in spite of the simian proportions of the brain and jaws, Australopithecus showed morphological characters in the skull and dentition which approximated to the Hominidæ rather than to the anthropoid apes. With remarkable insight and energy Broom sought, and found, abundant remains of the Australopithecinæ in stalagmitic deposits near Pretoria, and at the time of his death he had discovered, and described, many skulls, jaws, teeth, and limb bones of adults, juveniles, and infants.

"Each new discovery," writes W. E. Le G. C., "brought new confirmation of the astonishing mixture of hominid characters with primitive ape-like characters in the Australopithecinæ. It is not surprising that these discoveries gave rise to acute controversies; indeed, this may be taken as a measure of their importance, for sharp controversies have always accompanied equally important discoveries in the past. (It was, for instance, vigorously contended at one time that Pithecanthropus was nothing more than a giant gibbon, or that Neanderthal Man was nothing more than a pathological monstrosity.) It is fair to say, however, that almost every authority now recognises the existence in the Australopithecinæ of hominid characters which are not to be found in the anthropoid apes, even though there may be still some difference of opinion as to their precise significance.

"Broom used to maintain that the paucity of fossil evidence bearing on human evolution was mainly due to the fact that palæontologists did not look in the right places and did not pursue their searches with enough vigour. He himself certainly had a remarkable flair for going to the right places to hunt for fossils. But more than that, he possessed a drive and energy which overcame all obstacles and brooked no opposition in his eagerness to find what he was looking for. Practically up to the time of his death, he was still working with amazing energy. Few men who die at the age of 84 have achieved more in the acquisition of new scientific knowledge than he. In his passing we can but feel a deep sense of gratitude for his single-minded devotion in his field of work, and pay our respects to a man who was so outstanding as a discoverer. To those of us who knew him personally, his generosity and kindness will be remembered as among the most prominent of his qualities. If he permitted his dry Scotch humour to let itself go sometimes in outspoken criticisms of those who threw doubt on the validity of his conclusions—particularly those who did so without having even seen the original fossil specimens—his criticisms were always made with a characteristic twinkle in his eye."

Notes and News

KING EDWARD VII's HOSPITAL FOR OFFICERS

At the request of King Edward's Hospital Fund a consulting staff has been appointed to King Edward VII's Hospital for Officers, Sister Agnes Foundation, Beaumont Street, London, W.1. The council of the hospital are anxious, however, that the specialists and practitioners not on the staff should continue to use the hospital, and the council have laid down that patients may be admitted under any doctor of their own choice. The hospital is now for serving, retired, and ex-temporary officers of the Forces, and the fees are from 7 to 15 guineas a week according to the nature of the accommodation and subscription rights of patients.

CONTROL OF ANTI-HISTAMINES

In this country there have been several fatalities among children who have swallowed tablets containing anti-histamine drugs[1], and last year this group of drugs was added to part 1 of the Poisons List and the first schedule. In the U.S.A. these compounds are still widely taken as a remedy for the common cold, despite substantial evidence that they have little or no value against this ill[2], and the committee on public health relations of the New York Academy of Medicine states that 8 infants under two years of age are reported to have died from accidental consumption of the tablets, while several others are reported to have had convulsions. "Packages of antihistaminic drugs sold to the public," says the committee, "carry directions for dosage, but this is not sufficient protection against accidental overdosage or other hazardous use, especially in children. Allergists have estimated that at least 20 per cent of the people who take anti-histamines in the doses recommended will experience undesirable if not dangerous reactions. Several persons are reported to have attempted suicide by taking excessive doses of antihistaminic drugs, and one succeeded."

THE CIBA FOUNDATION

The Ciba Foundation for the Promotion of International Coöperation in Medical and Chemical Research was founded by Messrs. Ciba in September, 1947, to encourage study and research in all branches of medicine and its allied sciences. The foundation building was opened in London at 41, Portland Place, W.1, on June 22, 1949, the founders felt that the English language had become the scientific language of the world and that London was the ideal world centre. The foundation serves as a meeting-place for research workers from all over the world, provides accommodation for foreign visitors, and bestows grants to enable scientists from one country to work in another. To begin with it was decided to confine its activities mainly to the international exchange of ideas on the steroid hormones, and a specialist library is being built up on this basis.

The first report covers the period June, 1949, to December, 1950. During this time 1800 people, including visitors from 17 countries, have attended meetings at the foundation or have visited research institutions under arrangements made by the foundation. It has worked in close coöperation with the medical societies, the University of London, the British Council, the Ministry of Health, and the scientific section of the French Embassy. Many of the societies have held meetings at the centre, and one, the Hunterian Society, has held an exhibition at the foundation.

The Ciba Foundation lecture for 1949 was given by Prof. E. C. Dodds, F.R.S., and the lecture for 1950 by Sir Stanton Hicks, University of Adelaide. Eight conferences were held, six concerned with the steroid hormones and two with general subjects. The proceedings of one of the general meetings have been published in book form, and it is hoped to publish an account of the other meetings shortly. The resources of the library have been strengthened by an arrangement whereby guests are allowed to use the library of the Royal Society of Medicine.

The trustees of the foundation are Lord Beveridge, Lord Horder, Prof. E. D. Adrian, O.M., F.R.S., and Mr. Raymond Needham. An executive council has been set up and is helped by an advisory board consisting of 13 members from Great

---

[1] See *Lancet*, 1950, i, 28, 78. *Ibid*, ii, 370.

[2] Leading article. *Ibid*, i, 1110.

OUR KNOWLEDGE OF THE MENSTRUAL CYCLE, 1910-1950 *

GEORGE W CORNER
M.D , Sc D
DIRECTOR, DEPARTMENT OF EMBRYOLOGY, CARNEGIE INSTITUTION OF WASHINGTON, BALTIMORE

THE founders of the Addison lectureship, Dr Harry Spon and Dr Peter Bishop, challenged the successive speakers not only to convey information upon the topics of their choice, but also to trace the development of the ideas of modern endocrinology, and above all to present a picture of the medical investigator in action, with all the fascination of his problems and his hopes of useful discovery

I am going to try therefore to tell you the story of the development of our knowledge of the menstrual cycle as it has been worked out during the past four decades This is the subject which has chiefly occupied my own energies during that period, and the story will necessarily have a large element of personal reminiscence

INTRODUCTION TO GYNÆCOLOGY

When I entered the Johns Hopkins Medical School in 1909 after a good training in zoology, I was presented almost at once with an opportunity to try my hand at an embryological investigation This involved collecting pig embryos at a nearby abattoir Thus I learned to know the reproductive tract of the pig and something of its embryology at first hand, from the fresh specimens

This work stimulated my interest in gynæcology, and I determined to seek an internship in that specialty I was on the point of obtaining one when Franklin Mall, the professor of anatomy, offered me an assistantship, with the surprising argument that this would be the best pathway to usefulness in the women's clinic He pointed out to me prophetically that the gynæcologists, then basing their superb diagnostic skill and surgical art upon pathology, would soon find themselves involved in physiological problems for which no sound basis of biological knowledge existed Ten years in his laboratory, he said, working at embryology and the physiology of reproduction, would be the best preparation for the new gynæcology

During the one year in which I actually worked with him, Mall set me at the task of describing the sow's corpus luteum during its earliest phases He thought it would be possible to date very early human embryos by histological study of the corresponding corpora lutea This task, incidentally, was not accomplished until many years later, and then in the reverse direction, for our present ability to date the early corpus luteum in primates by microscopical examination was gained largely by studying embryos of known age

At the end of my anatomical year I went into the gynæcology department, and there, although my chief, Howard A Kelly, was one of the best pathologists and surgeons of our country, I saw what Mall meant when he said that gynæcologists did not understand the human cycle Looking back from our present standpoint, one can see that the dawn of the modern physiology of reproduction had begun, but few of its rays were as yet reaching into the gynæcological operating room

THE REPRODUCTIVE CYCLE

That the ovaries are fundamentally necessary to the occurrence of menstruation was first explicitly conjectured by a young Marylander, John B Davidge, in 1793, but this fact did not become a matter of general medical knowledge until the 1860s Meanwhile K E von Baer's discovery of the mammalian ovum in 1847 led to a general exploration of the reproductive cycles of lower (non-menstruating) mammals It became known through the studies of Bischoff, Pouchet, and many others that in domestic animals the ovarian follicles mature and shed their eggs at the time of œstrus, and that the corpora lutea formed after ovulation are contemporaneous with the developing embryos At the end of the 19th century this framework was being filled in with a great mass of detailed information about animal cycles Two English writers had an important part in systematising and summarising this knowledge—Walter Heape of Cambridge, who defined and named the various stages of the œstrous cycle, and another Cambridge don, F H A Marshall, who gave us after the turn of the century an enlightening book, *The Physiology of Reproduction*, which served to introduce many readers to this growing field of study

Marshall's analysis of the dog's and rabbit's cycles, Leo Loeb's studies on the guineapig, J P Hill's on the marsupials, and various other descriptive researches, were beginning to teach us the general picture of the mammalian cycle, characterised by recurrent periods of œstrus, when the follicles shed their ova and are converted into corpora lutea Gustav Born's hypothesis that the corpus luteum has the function of preparing the uterus for the implantation of the embryo, communicated personally to his student, Ludwig Fraenkel, was announced by the latter and demonstrated by experiments on rabbits published in 1903 and 1910 This discovery at last made the cycle understandable in terms of reproductive function.

It had been realised, of course, immediately after von Baer's discovery, that the human menstrual cycle is in some way related to the cycle of ripening and shedding of the egg cell. The precise relation of the human menstrual cycle to the œstrous cycle of non-menstruating animals was, however, still obscure except to a few pioneer investigators at the time I am now discussing—i.e , the second decade of the present century

TWO ERRONEOUS NOTIONS

It was thought by many that the menstrual flow is comparable to the œstrous phase of the animal cycle This fallacy was based upon the assumption that as œstrus is the most conspicuous event of the cycle in lower mammals, and menstruation is the major event in the human species, they must be the same, and also upon a supposed analogy between menstruation and the pro œstrous bleeding that occurs in the cow and the bitch. On the other hand, many pathologists and gynæcologists who had examined human ovaries had failed to find evidence of ovulation at or near the time of menstruation They taught that there is no direct relation between the menstrual cycle and the time of rupture of the successive graafian follicles

These two erroneous notions had to be abandoned as a result of investigations published in the first decade and a half of the 20th century Hitschman and Adler of Vienna showed in 1908 that certain remarkable changes in the glands and stroma of the endometrium which had been classified as " glandular endometritis," and were attributed to inflammatory disease, actually represent a phase of the normal cycle characteristic of the premenstrual stage Three years later Ancel and Bouin proved by brilliant experiments on rabbits that similar changes seen in that species are produced by action of the corpus luteum With these clues, two German gynæcologists who had access to great stores of human material, Schroeder and Robert Meyer, soon worked out the general pattern of the human cycle On the basis of all these investigations, it was established that

---

* Fourth annual Addison lecture, delivered at Guy s Hospital, London, on July 13, 1950

Fellowship of Postgraduate Medicine

The offices of the fellowship and of the *Postgraduate Medical Journal* have been moved Their new address is 60, Portland Place, London, W 1 The telephone number is unchanged (Langham 4260)

Film on Tropical Sprue

The Wellcome Film Unit has produced a film in 16 mm colour, silent (running time 6½ minutes), on tropical sprue It is primarily intended for showing to medical undergraduates, and applications to borrow it (case record no 5) should be sent to the unit, 183–193, Euston Road, London, N W 1

Films on Parasitology

A provisional list of films dealing with human and comparative parasitology has been compiled on behalf of the International Scientific Film Association by Dr Willem de Vogel, c/o Universitaire Film, Catharijnesingel 59, Utrecht, Holland He would be glad to have any additions or corrections, so that a permanent catalogue, with periodical supplements, may be set up

Renal Association

A meeting of this society is to be held at the Ciba Foundation, 41, Portland Place, London, W 1, on Thursday, April 26, at 4 30 P M Prof K J Franklin will speak on the Kidney and the Circulatory System, Dr A H Galley on Spinal Anæsthesia and the Kidney, and Dr Telford Govan on Renal Changes in Obstetric Shock On Wednesday, April 25, at 4 30 P M at the Wellcome Institution a film will be shown on the Kidney in Health and Disease

Diary of the Week

APRIL 22 TO 28

Monday, 23rd

ROYAL EYE HOSPITAL St George's Circus Southwark S E 1
5 P M Prof Arnold Sorsby Detachment of the Retina
INSTITUTE OF OPHTHALMOLOGY Judd Street W C 1
5 30 P M Mr A B Nutt Congenital Ocular Palsies
MEDICAL SOCIETY OF LONDON, 11 Chandos Street, W 1
8 30 P M Dr J H Burn, F R S Dr Richard Doll Effects of Tobacco Smoking

Tuesday, 24th

ROYAL EYE HOSPITAL
5 P M Dr T H Whittington Astigmatism Factors Affecting Binocular Vision Convergence
WESTMINSTER MEDICAL SCHOOL Horseferry Road, S W 1
5 P M (Meyerstein lecture theatre) Clinicopathological meeting on Influenza

Wednesday, 25th

ROYAL EYE HOSPITAL
5 P M Mr R P Crick Buphthalmos
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr L C Thomson Electrophysiology of the Retina
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28, Portland Place W 1
3 30 P.M Dr Henry Yellowlees Hypnotism—Its Uses and Limitations in Medicine
UNIVERSITY OF GLASGOW
8 P M (Department of Ophthalmology) Prof W J B Riddell Emotions and Eye Disease

Thursday, 26th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields, W C 2
3 45 P M Dr L Foulds Experimental Study of the Course and Regulation of Neoplasia (Imperial Cancer Research Fund lecture)
ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P M Major R A Smart Biting Insects in the North
ROYAL EYE HOSPITAL
5 30 P M Miss J M Dollar Ocular Therapeutics
UNIVERSITY COLLEGE Gower Street W C 1
4 45 P M Prof H A Krebs F R.S Energy Transformations in Living Matter (First of four lectures)
MEDICO LEGAL SOCIETY 26, Portland Place W 1
8 15 P.M Dr R Donald Teare Medicolegal Significance of Death following Abortion
HONYMAN GILLESPIE LECTURE
5 P M (Anatomy Theatre University New Buildings Teviot Place, Edinburgh) Dr R H Girdwood Vitamin B_{12} and Folic Acid in the Megaloblastic Anæmias
UNIVERSITY OF ST ANDREWS
5 P M. (Medical School Small's Wynd, Dundee) Prof W C Wilson Circulatory Changes in Surgical Conditions

Friday, 27th

ROYAL EYE HOSPITAL
4 30 P M Mr A J Cameron Surgery of Cataract
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Prof D Slome Sensitivity of Ocular Structures
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASE 11 Chandos Street W 1
8 P M Dr W D Nicol with Dr M Whelen Use of Penicillin in the Treatment of Neurosyphilis

Appointments

BAIRD W A M B Glasg appointed factory doctor, Sandhead Wigtownshire
BURGESS C T A, M B E M A M B Camb, F R C.S consultant general surgeon, Southport General Infirmary Lancs
DALY B G, M B Edin asst psychiatrist, Towers Mental Hospital Leicester
DEARDEN P S, M B Lpool D A consultant anæsthetist, St Helens and Warrington Lancs
FORRESTER H A M B Edin D I H group M O, East Midlands division National Coal Board
GOW J G M B Lpool F R C S consultant general surgeon, Sefton General Hospital, Liverpool
HALL T T S M B E T D M D Belf D OBST D P H deputy county M O H Lancashire
HARRISON B B M B, M RAD Lpool asst radiologist, Broadgreen Hospital Liverpool
* HILSON, DON, M A, M B. Camb M R.C P M R C P L, D C H. consultant pædiatrician, Oldham and Ashton areas Lancs
PATERSON J H M D Lond M R.C P asst physician neurological department St George's Hospital London
ROUILLARD L M F R.C.S E consultant plastic surgeon Norfolk and Norwich Hospital and United Cambridge Hospitals
SHEPHERD J A, V R D M D, M CH St And, F R C.S E consultant general surgeon, North Wirral area Cheshire
SHONE J A V, M R C.S regional blood transfusion officer Leeds.
STOLL B A M R C S, F F R D T M & H consultant senior radiotherapist Liverpool Radium Institute,
WESTHEAD PAMELA M B Brist D A consultant anæsthetist North and South Liverpool areas
WHITEHEAD A S M B, M RAD Lpool asst radiologist, Mill Road Maternity Hospital Liverpool
WRIGHT F B, M B M RAD Lpool asst radiologist North Liverpool and Liverpool and District Eastern Hospital Management Committee groups

Hospital for Sick Children, Great Ormond St., London

CONNOLLY N K M A Camb, M D Harvard, F R.C.S surgical registrar (senior registrar grade)
ERENST M. M, M D Berlin orthopædic registrar (registrar grade)
GILES H M M B Camb M R C P, D C H house physician (senior house officer grade)
OATWAY A W N, M A, M B Camb house physician (senior house-officer grade)
SMITH W D M B N U I house-surgeon orthopædic and plastic surgery departments (senior house officer grade)

Births, Marriages, and Deaths

BIRTHS

BAIRD —On April 10, at Guildford Surrey the wife of Dr J T Baird—a son
FREEMAN —On April 12 in Cardiff the wife of Dr A G Freeman —a son
GREIG —On April 9 at Stornoway Lewis the wife of Dr J C R. Greig—a daughter
HENDERSON —On April 9 at Harpenden, Herts, the wife of Mr R S Henderson F R C S —a son
LLOYD —On April 8 the wife of Dr J T A Lloyd—a son
LUCAS —On March 29 at Stratford on Avon, the wife of Dr D R. Lucas—a son
MACDONALD —On April 12 at Taplow Bucks, the wife of Dr Angus Macdonald—a daughter
PYKE —On April 13 in London, the wife of Dr David Pyke—a son
SMERDON —On April 12, in Liverpool the wife of Dr Geoffrey Smerdon—a daughter
TILL.—On April 11 at Oxford the wife of Mr A S Till, F R C.S.—a daughter

DEATHS

ANDERSON —On April 13 at Bungay Frank Ernest Anderson, M B St. And
BANKART —On April 8 Arthur Sydney Blundell Bankart, M A, M CHIR. Camb F R C S
COMYN —On April 14, at Hythe Kent, Arthur Fitzwilliam Comyn B.A M B Camb, aged 68
ELLIOTT —On April 13 at Wolverhampton, Kenneth Alwyne Elliott, M.R.C.S aged 29
FRENCH —On April 13, John Gay French, M.S Lond F R.C.S, aged 79
GAMES —On April 11 at Eccles Lancs, John Henry Paisley Games, M R.C S aged 62
HART —On April 8, at Ottery St Mary, Devon Henry Percival Hart M C, M B Dubl, lieut-colonel R A M C retd aged 70
MACKENZIE —On April 11 at Drumm Inverness Theodore Charles Mackenzie M D Edin F R C P E
STACPOOLE —On April 12 at Shanklin I o W Henry de Vere Stacpoole L.S A aged 88
WHITEHEAD —On April 9 at Stockport, Cheshire Alfred Whitehead L.R C P E, aged 78
WILKINSON —On April 12, in Birmingham Kenneth Douglas Wilkinson O B E M D Birm, F R C P

Sir George McRobert, F.R C P, is visiting Portugal, under the auspices of the British Council He will lecture at the Institute of Tropical Medicine and at the British Institute in Lisbon, and at the faculty of medicine in the University of Oporto

A booklet on *Appointments in His Majesty's Colonial Service* is obtainable from H.M Stationery Office (pp 125 2s) support by the ovarian hormones No other tissue in the body, so far as we know, ordinarily reacts in any such way to hormone deprivation, nor does the endometrium itself react thus in other mammals Speculation upon the question was more or less sterile until special attention was directed to the endometrial blood-vessels Bartelmez in 1929 declared that his study of the menstruating human uterus revealed no constant factor in menstruation except vascular changes involving rhexis

---

* Amended notice

Much light was thrown on the question by the appearance in 1940 of Markee's remarkable experiments upon rhesus monkeys, in which he transplanted bits of endometrium to the anterior chamber of the eye, where they attached themselves and became vascularised Such implants bleed into the aqueous humour at the time of menstruation, and they respond to hormone stimulation and hormone deprivation exactly as does the endometrium at its normal site Markee was able to watch the process through the cornea, with the microscope His descriptions clearly reveal that the interruption of blood flow through the arteries supplying the endometrium is a basic factor in the menstrual process

In those species of primates which menstruate, these arteries are peculiar in that they are profusely coiled, forming striking spiral bundles as they course toward the free surface of the endometrium Various hypothetical explanations of the menstrual process, some of them crude and others subtle, have been based in recent years upon the coiled arteries, but it has become reasonably certain that the coiling is not itself involved in the periodic constriction of these vessels and the resulting ischæmia of the endometrium that leads to the menstrual breakdown There is no need to go over in this lecture the various hypotheses, some of which postulate a physiological sensitivity of the arteries, or of the vascular system in the endometrium in general, others call for the participation of arteriovenous anastomoses, which it is claimed are specially numerous in the human endometrium, or rest upon peculiarities of the lymphatic drainage of the uterus I have discussed them in the second edition (1947) of my book, *The Hormones in Human Reproduction* None of them has received convincing experimental support

I have myself vainly devoted much time and effort to experiments designed to test a conjecture that menstrual bleeding depends on the action of a hypothetical vasomotor substance to which the endometrial blood-vessels are especially sensitive, and against which they are protected by the ovarian hormones Vasoconstriction and resultant menstrual bleeding would therefore follow a sudden drop in hormone level Such a vasomotor substance might be formed in the endometrium, perhaps as a result of cell damage following hormone deprivation (e g , histamine), or it might be something normally present in the circulating blood (e g , adrenaline) The experiments (admittedly crude in concept and execution) involved direct application of the vasomotor substance to the endometrium, by injection into the uterine cavity through a fine needle In this way a whole series of vasomotor substances has been tried , and as a counter check certain vasomotor substances (e g , antihistaminic drugs) have been given systemically to see if they would inhibit œstrogen-deprivation bleeding

The only substance which has given even a suggestive result is adrenaline In 5 of 8 experiments recorded in my unpublished notes in which 0 5 or 1 ml of 1 1000 adrenaline in oil was injected into the uterine cavity of a laparotomised castrate rhesus monkey under suitable œstrogen stimulation, there was frank external bleeding in one case, and microscopic blood with an occasional clot in the vaginal washings in 4 cases This bleeding was not merely the result of the needle puncture Traumatic blood, or pigment injected with the drug, show themselves in the vagina within a day The bleeding here described did not occur until the third day after the injection I have, however, not as yet had success with the counter experiment of administering anti adrenergic drugs, which might be expected to inhibit œstrogen-deprivation bleeding In view also, however, of G van Wagenen's demonstration some years ago, that lumbar section of the spinal cord is followed by menstruation-like bleeding, one is tempted to cling to the conjecture that some one of the vasomotor substances associated with the nervous system may be involved in the menstrual process

It should be added that in our laboratory the action of neostigmine as an emmenagogue, repeatedly mentioned in American clinical literature for six or eight years past has not been confirmed on monkeys

LABORATORY AND BEDSIDE

These major mysteries of the menstrual cycle must probably be left to the younger generation for solution The older workers whose achievements I have been summarising need not however relax their efforts, for they will remember that Thomas Addison was sixty years of age when he announced the great discovery which we commemorate in this series of lectures Since these older workers began their own youthful efforts, they have seen the once incomprehensible mysteries of the human reproductive cycle yield steadily to the progress of investigation, until at last the gynæcologist is able to analyse his cases of menstrual disorders, of sterility, and of recurrent abortion with a much better understanding of the underlying physiological disturbance and with far greater hope of successful treatment than he could have had forty years ago

Franklin Mall was right when he predicted that gynæcology and obstetrics could be led to new successes by physiological research based upon embryology and the histology of the reproductive cycle The young man, however, whom he persuaded to prepare himself for a gynæcological career by way of the anatomical sciences did not become a gynæcologist, after all In 1915 the women's clinics of the United States had no place open for men who wanted to give research a major claim upon their time Perhaps the chief contribution made by those of us who gave up the satisfaction of being directly helpful to suffering fellow beings in order to embark upon the venture of research, was to reopen the way for the scientific clinician who brings research upon human endocrinology and reproductive physiology to the hospital bedside and the operating room—a pathway long ago taken by Thomas Addison, and now followed with eminent success by some of his successors at Guy's and elsewhere

BIBLIOGRAPHICAL NOTE

The foregoing lecture is not a formal review but rather a sketch of the progress of discovery as seen by one observer No attempt has been made to mention all the contributors systematically The facts discovered are now mostly in the textbooks of embryology, physiology, gynæcology and obstetrics References to the major contributions will be conveniently found in the bibliographies of the following works :

Allen E (1939) Editor Sex and Internal Secretions. Baltimore
Bartelmez, G W (1933) Histological Studies of the Menstruating Mucous Membrane of the Human Uterus *Contr Embryol, Carneg Instn.* 24 141
— Corner G W Hartman C G (1951) Cyclic Changes in the Endometrium of the Rhesus Monkey *Ibid* (in the press)
Corner G W (1947) The Hormones in Human Reproduction Princeton
— Bartelmez G W Hartman, C G (1945) Development, Organization and Breakdown of the Corpus Luteum in the Rhesus Monkey *Contr Embryol. Carneg Instn* 31, 117
Hartman C G (1936) Time of Ovulation in Women. Baltimore
Zuckerman S (1949) The Menstrual Cycle *Lancet*, i, 1031

such bleeding , and (3) that in a castrated female monkey administration of a course of œstrogen, followed by abrupt cessation of the hormone treatment, will cause bleeding These findings were the basis of Allen's "œstrogen deprivation" theory—i e , that natural menstruation results from withdrawal of the effect of œstrogen upon the uterus

Some years later Zuckerman put the deprivation experiments on a more precise quantitative basis, and showed that it is not necessary to cut off the entire supply of œstrogen to cause menstruation like bleeding , a sudden reduction from a high level to a much lower level will have the same effect If the daily dose of injected œstrogen is reduced gradually, instead of suddenly, the endometrium reverts to the castrate condition without hæmorrhage

Some experiments of my own were aimed at testing an obvious deduction from E Allen's deprivation hypothesis In intact monkeys which are having spontaneous menstrual periods it should be possible to prevent or postpone the menstrual flow by giving œstrogen injections so timed as to counteract the hypothetical drop of œstrogen secretion supposed to precede menstruation I was, however, unable to prevent menstruation in this way, with œstrogen injections begun in the latter half of the interval. On the other hand, relatively small doses of progesterone effectively suppress menstruation for many days or even weeks The contrary fact, that removal of a corpus luteum will cause immediate menstruation, had already been learned by clinical observations on women after gynæcological operations

Zuckerman, Hisaw, and I, almost simultaneously but independently, all did the critical experiment A castrated female monkey is given a daily injection of œstrogen in oil, sufficient to build up the endometrium to the level at which sudden œstrogen deprivation would cause menstruation like bleeding The œstrogen is, however, continued, and a course of daily progesterone is added The monkey is now receiving both hormones After ten days the progesterone is discontinued, the œstrogen being continued at the same dosage or even increased The discontinuance of progesterone is always followed after 3–8 days by bleeding, in spite of the continuance of œstrogen in quantities ordinarily sufficient to prevent œstrogen deprivation bleeding We must suppose that the administration of progesterone in some way interferes with the action of œstrogen upon the endometrium An animal receiving progesterone is thus in a sense "deprived" of œstrogen The progesterone is itself able to prevent deprivation bleeding , but when it is in turn discontinued, the monkey is physiologically deprived of œstrogen and literally deprived of progesterone Hence bleeding occurs

The current hypothesis of the rôle of the ovarian hormones in the normal human cycle is based on experiments of this type, for we must suppose that œstrogen is being secreted more or less continuously by the ovaries, whereas the corpus luteum is present and active during a part of the cycle only When it breaks down, the resulting low level of effective hormones causes the menstrual flow This scheme does not of course explain anovulatory menstruation , but there is probably a clue in Hisaw's observation that a surprisingly small single dose of progesterone administered to an intact monkey is usually sufficient to cause bleeding when its effect wears off Possibly anovulatory bleeding results from a recurrent state of the pituitary ovarian system in which a small amount of progesterone or a progesterone-like hormone is secreted by ovarian cells in the absence of a corpus luteum, or by the adrenal cortex, as Zuckerman has suggested

The history of our knowledge of the reciprocal relations between the pituitary and the ovarian hormones, which underlie the cycle in general, would require another lecture , and it would be less complete than the story I have been telling of the interrelation between the ovary and the uterus, because research still lags for want of final purification of the pituitary hormones and of refined methods of assaying them in the circulating blood

This is not to say, however, that our knowledge of the ovarian hormones in relation to the cycle is complete We are, indeed, only now beginning to obtain quantitative knowledge of the blood levels of œstrogen and progesterone in the human female at various stages of the cycle and of gestation The original Allen Doisy assays of œstrogen, refined by many workers, have been supplemented by Browne and Venning's discovery of pregnandiol glycuronidate in the urine and its application as a method of estimating progesterone excretion Very recently Hooker and Forbes, of Yale University, have given us a precise method of estimating progesterone directly in blood and tissue extracts Ultimately such procedures will reveal quantitatively the ebb and flow of the ovarian hormones in the cycle and teach us to study disorders of the cycle far more precisely than has previously been possible

PURPOSE OF MENSTRUATION

Meanwhile many basic problems of the menstrual cycle remain unsolved What, to begin with, is the functional significance of the menstrual flow ? This phenomenon, in its fully developed form, occurs only in certain of the primates—i e , man, the anthropoid apes, and the Old World monkeys Other mammals reproduce their kind without periodic uterine breakdown and hæmorrhage

It was suggested, before the earliest stages of embryonic development were observed in the primates, that the first phases of the menstrual hæmorrhage might serve to provide immediate nourishment for the primate embryo, which was supposed to need special pabulum more promptly than embryos of other orders. The supposition was that menstruation is the end result of a process which serves its real purpose only if the ovum is fertilised In that case the proliferative action of the œstrogen progesterone hormone sequence carries the endometrium on through the progestational (premenstrual) stage and to a point at which the tissues are ready to provide pabulum in the form of free blood, extravasated around the implanting embryo , A further degree of hæmorrhage is inhibited by the continued activity of the corpus luteum of pregnancy In the non pregnant cycle, this preparation for useful localised extravasation goes on, when the corpus luteum retrogresses to the frank breakdown state of menstrual bleeding

The chief evidence for such a conjecture is the occurrence of localised hæmorrhage in the vicinity of the embryo about 16 days after ovulation, and the consequent appearance of erythrocytes or even of microscopic blood in the vagina at about the same time—i e , the "placental sign" of Hartman There is, however, room for doubting whether such local bleeding around the embryonic mass is to be homologised with the general necrosis and extravasation of the menstrual period Anovulatory menstruation, moreover, seems to elude any such conjectural explanation Yet this is the one hypothesis that is at all plausible in the light of present knowledge, and if it is rejected we have not the slightest notion as to what usefulness, if any, appertains to the menstrual flow

BEHAVIOUR OF PRIMATE ENDOMETRIUM

A less philosophical but more practical problem, and one which is all the more baffling because it seems momentarily awaiting solution, is why the endometrium of the higher primates should bleed when deprived of

Case 5.—A housewife, aged 21, had had winter bronchitis since childhood and mild asthmatic attacks for two years. She was six months pregnant when admitted with a staphylococcal pneumonia She developed a synpneumonic empyema, the responsible *Staph aureus* being penicillin sensitive Aspiration on seven occasions removed 77 oz. of pus. The empyema was loculated, and the last specimen of pus obtained still contained scanty organisms The patient became apyrexial in fourteen days and was discharged in six weeks A week later she coughed up a small residual empyema and was readmitted. The pleural pus still grew a *Staph aureus* Penicillin was injected into the pleural space on one occasion only Pregnancy proceeded normally

Follow up—A year and a half later radiological evidence of tuberculosis appeared in the other lung Two and a quarter years later the patient had a very occasional cough Physical examination was normal, and the affected lung was normal on radiography The tuberculous lesion was quiescent Bronchography was not done

Case 6—A labourer aged 68 was admitted six days after the onset of an extensive pneumococcal pneumonia He developed toxic delirium extensive purpura, and a pleural effusion. This was aspirated on seven occasions and 36 oz. was removed, the fluid eventually becoming thick pus Pneumococci disappeared from the fluid after the first aspiration. The patient was discharged from hospital in seven weeks, and has not been traced for follow up

Case 7—A labourer, aged 60, was admitted on the seventh day of his pneumonia with a synpneumonic empyema. The thin stinking pus grew an anaerobic streptococcus Twelve aspirations removed 84 oz. of pus Culture became sterile in four days and smears negative in twenty six days. The patient became apyrexial in ten days, was discharged in seven weeks and returned to work eleven weeks after admission.

Follow up—Two years later he was rather emphysematous and had mild winter bronchitis Chest movement and circumference were equal on both sides The costophrenic angle was obliterated and a bronchogram normal.

Case 8—A housewife aged 35, was admitted with a post-pneumonic pneumococcal empyema. Twelve aspirations removed 9 pints of pus Culture became sterile in three days, and smears negative in ten days, and the patient s temperature became normal in five days She was discharged after six weeks and had returned to full household duties three weeks later

Follow up—Eighteen months later the only abnormality was 1 in. diminution in circumference of the affected chest, expansion appearing equal Radiography and bronchography were normal.

Case 9—A man, aged 27, was admitted with a pneumococcal pneumonia and a turbid effusion. Seven aspirations removed 47 oz., thick pus developing while intrapleural penicillin was continued Culture was sterile but smears showed gram positive cocci on two occasions The patient was discharged in eight weeks and returned to work seventeen weeks after admission

Follow up—Eighteen months later he had a slight smoker s cough as before this illness The affected chest was $^1/_2$ in. greater in circumference than the other Radiography and bronchography were normal.

Case 10—A man aged 27, had lost his sight and both hands in 1941 He was admitted with a pneumococcal pneumonia and sterile effusion. He was unhappy and discharged himself against advice still with an effusion. A fortnight later he was readmitted, coughing up copious foul pus and was considered to have a bronchopleural fistula The aspirated pus was also foul and contained gram positive cocci but was sterile on culture Ten aspirations removed 48 oz. of pus The fistula closed in a few days and the patient became apyrexial in three weeks. He was discharged after eight weeks

Follow up—Sixteen months later he was well There was slight impairment of percussion note at the affected base, but no other signs Radiography showed the costophrenic angle obliterated. A bronchogram was normal

Case 11—A housewife aged 26, was admitted with lobar pneumonia and a small sterile effusion. No intrapleural medication was given but after three and a half weeks a small empyema had formed The thick pus contained *Staph. aureus* and only 20 ml was obtained at two aspirations The patient improved steadily thereafter and was discharged eleven weeks after admission, having been delayed a month in waiting for a vacancy at a convalescent home

Follow up—Since then she has had a few bouts of cough and purulent sputum. Fourteen months after her discharge there was very slight diminution in expansion and a shrinkage of $^3/_4$ in on the affected side Radiography was normal, but a bronchogram showed a minute area of bronchiectasis in the posterior basic segment of the lower lobe

Case 12—A boy, aged 19, had had severe pneumonia in childhood. He had remained well, but in 1948 had had an isolated hæmoptysis In March, 1949, he was admitted with a right-sided pneumonia and a sterile but polymorphonuclear effusion. Nine aspirations withdrew 22 oz., penicillin being given each time and the fluid changing to thick pus The patient was discharged in seven and a half weeks and returned to work in twelve weeks. He remained well until April, 1950, when he was admitted with an abscess in the posterior basic segment of the right lower lobe This healed completely with medical treatment A bronchogram showed bronchiectasis of the right middle lobe and anterior basic segment of the lower lobe Re-examination of the 1948 films showed an opacity corresponding to the affected anterior basic segment. In July, 1950, the patient had only slightly diminished movement of the right side, the circumferences being equal He is awaiting lobectomy

All these patients had pus in the pleural cavity Other patients, whose fluid in the pleura, though containing polymorphs and organisms, did not constitute frank pus, have been excluded from this series though they did equally well

DISCUSSION

Aspiration, however efficiently performed, cannot remove the last trace of pus and debris Natural repair and absorption seem to be capable of clearing up the remainder This seems surprising, but lobar pneumonia is known to resolve rapidly, even though fibrin covers the lung at one stage Even with rib resection no-one can be sure that the sucker has cleared every fragment of fibrin

CONCLUSION

On the evidence of these cases there seems good reason for treating some cases of empyema with penicillin and aspiration only It is not suggested that all cases should be so treated None of the present cases was very chronic, and all had organisms sensitive, or likely to be sensitive, to penicillin There may be chronic empyemas which have reached the stage where surgery is essential. However, since twelve unselected consecutive cases made satisfactory recoveries, it suggests that this form of treatment may be more often used than hitherto, especially with the increasing number and power of new antibiotics The obvious advantages of the method are that the cavity is kept closed and that there is no wound to heal Secondary infection is less likely, and in this series a transient secondary invader was only found in four cases (*Bact coli* in two cases, *B proteus* in one case, and *Strep viridans* in one case) towards the end of treatment, and no complication ensued therefrom Frequent aspirations are no great hardship if done by an experienced man, and are probably no more discomforting than the changing of tubes and dressings which surgery requires Also there are less smell, less soiling, and less work for the nurses Perhaps very large empyemas would respond less well to this treatment In the present series the largest amount of pus removed at one aspiration was 42 oz and the largest total amount aspirated altogether was 270 oz

We are most grateful to Dr Frank Pygott for his help with the radiograms and Dr Keith Ball for his advice and criticism

REFERENCES

Brock R. C (1947) *Proc R Soc. Med* 40 645
Fatti L Florey M E Joules H, Humphrey, J H, Sakula, J.
(1946) *Lancet*, i 257 295

EMPYEMA THORACIS TREATED WITH PENICILLIN AND ASPIRATION ONLY

RICHARD ASHER
M D Lond , M R C.P
PHYSICIAN

DEWI DAVIES
M.D Lond , M R C P
REGISTRAR

CENTRAL MIDDLESEX HOSPITAL

IT is important, in judging the effectiveness of a treatment, to decide not only whether it should work but also whether it does work There are good reasons why aspiration and penicillin alone should not cure empyema, and sound theory in favour of surgical drainage All the same, if penicillin alone does work it has certain advantages Here are described twelve consecutive cases of empyema admitted under one medical firm between October, 1947, and April, 1949 All were treated with systemic and intrapleural penicillin without drainage except repeated aspirations

Brock (1947) says

> " Many of the cures of empyema by aspiration are really cures of early pleural infection It is much less likely that a mature or nearly mature empyema can be cured by aspiration alone, simply because of the adverse mechanical factors present in the thick exudate, rigid or partially rigid walls, and massive fibrin clots Penicillin is not a scavenger, it cannot clear up the battlefield the correction of the mechanical effects of infection is too much for the bodily resources To delay or to withhold surgical help to clear up the battlefield is to harm the patients, at the least, increasing the morbidity of his illness and often causing his death "

Such authoritative and logical opinion is not to be lightly disregarded, but some cases of empyema receiving penicillin as a preliminary to drainage appeared to be progressing so well that it seemed reasonable to wonder if it was true that " the correction of the mechanical effects of infection is too much for the bodily resources " It seemed justifiable to follow John Hunter's famous suggestion " Why think ? Why not try the experiment ? "

TECHNIQUE

Pus or infected fluid being encountered, the pleural cavity was aspirated with a 20 ml syringe and two-way tap as completely as possible and penicillin 500,000 units injected into it In addition systemic penicillin 200,000 units was given eight hourly Subsequent aspirations with intrapleural penicillin 200,000–500,000 units were usually done at intervals of 1–3 days, depending on the clinical and radiological evidence of further pus formation and the response of the patient's fever and general health Aspirations were repeated at lengthening intervals until no pus could be obtained and the patient appeared fit Breathing exercises were performed throughout treatment

FOLLOW UP

One patient could not be traced The other eleven have been followed as outpatients and at the time of writing have all reattended for questioning, chest measurements, straight radiography, and bronchography The length of follow up varies from sixteen months to thirty three months

RESULTS

There were no deaths among the twelve patients, most of whom showed a rapid improvement in fever and ymptoms from the first aspiration Fever usually ttled in fourteen days The pus became sterile on ure in about seven days (penicillinase was not used) rganisms persisted in smears for about fourteen days us disappeared (or, more accurately, none could be d by aspiration) after an average of forty days est time pus persisted to be found was seventy s, and the shortest seven days

The most striking features at follow up were the absence of symptoms and the normality in size, shape, and expansion of the affected hemithorax compared with its fellow

At the follow up ten patients had apparently recovered completely, both clinically and radiologically Case 12 undoubtedly had bronchiectasis before he developed his empyema, therefore its detection afterwards is not significant Case 11 developed a minute area of bronchiectasis She had by far the smallest empyema in the series, but a rather severe pneumonia It is difficult to believe that surgical drainage would have prevented the development of bronchiectasis in her case

The length of stay in hospital was $4^{1}/_{2}$–11 weeks, the mean being $7^{1}/_{2}$ weeks

Since none of these cases had a sinus to heal, the length of illness cannot fairly be compared with figures given by Fatti et al (1946), where recovery was judged complete when the sinus healed—i e , a mean of fifteen weeks for empyemas treated purely surgically, and seven weeks for cases treated with penicillin via intercostal drain

Some indication of the rate of recovery is shown by the interval between admission to hospital and return to normal work, which in this series was 9–17 weeks, the mean being 12 weeks

CASE RECORDS

Case 1 —A labourer, aged 57, developed a pneumonia which did not respond to sulphonamides After a fortnight he was admitted to hospital with a large empyema. Culture of the pus grew a non hæmolytic streptococcus, and eighteen aspirations removed 270 oz of fluid The aspirated pus became sterile on culture after five days, and organisms disappeared from the smear by the fourteenth day The patient became apyrexial in six days He was discharged from hospital after eight and a half weeks, and returned to work sixteen weeks after admission

Follow up —Two and three quarter-years later he was quite well There was slightly diminished movement of the affected chest, but the circumference of each side was equal. Radiography showed slight pleural thickening, and a bronchogram was normal

Case 2 —A man, aged 26, was admitted with a post-pneumonic empyema in the fourth week of his illness The pus grew a penicillin sensitive *Staph aureus* The chest was aspirated on nine occasions and 34 oz of pus removed. Culture became sterile in sixteen days and smears negative in twenty six days The patient's temperature became normal in thirteen days He was discharged in six and a half weeks, and returned to work twelve weeks after admission.

Follow up —He was well two and a half years later, and the affected side was $^{1}/_{2}$ in greater in circumference than the other The costophrenic angle was obliterated, and a bronchogram normal

Case 3 —A man, aged 67, a month before admission developed a lobar pneumonia and was treated with sulphonamides He relapsed and was admitted with a pneumococcal empyema His hæmoglobin was 48 % His chest was aspirated on eight occasions and 36 oz of pus removed Culture became sterile in seven days and smears negative in ten days The patient was discharged in four and a half weeks, and returned to work ten weeks after admission

Follow up —Two and a quarter years later he was at work and had a mild cough, as before his empyema. There was slightly diminished expansion of the affected side, but the circumferences were equal Straight radiography and bronchography were normal

Case 4 —A man aged 54, had pneumonia a month before admission. He relapsed after three weeks and was admitted with an empyema, which consisted of thick pus which grew *Strep viridans* Seven aspirations removed 60 oz of pus Culture was sterile in four days and smear negative in twenty days The patient became apyrexial in three weeks, was discharged after eight weeks, and returned to work twelve and a half weeks after admission

Follow up —Two and a quarter years later he was well, apart from a slight morning cough which he had had for many years Physical examination was negative, the costophrenic angle obliterated, and a bronchogram normal ase 19), is not at variance with the findings of other orkers (Marvin and Pastor 1925, Hill 1932, 1933, Weiss nd Baker 1933)

All the cases in which electrocardiographic abnormalities ere observed are summarised in the table

DISCUSSION

Manipulation of the Abdominal Viscera

No alteration in the heart rate, or in the configuration of the cardiograms, was evident in the 11 cases in which traction was applied to abdominal viscera (stomach 8, gall bladder 1, spleen 1, pelvic colon 1) It is clear that if appreciable changes had been recorded, the significance of the findings during manipulation of the vagus nerves would be difficult to evaluate, since some degree of visceral displacement must obviously be associated with this procedure The literature shows that such alterations are always slight and are neither constant, specific, nor predictable In a total of 110 cases Lennox et al (1922) and Marvin et al (1925) observed no abnormal responses On the other hand, alterations in the heart-rate, and the occurrence of an occasional auricular or ventricular extrasystole, have been reported (Ressinger 1927, Maher et al. 1934, Widenhorn et al. 1938, Hodge and Messer 1948) Such changes are particularly prone to follow manipulation of the upper abdominal viscera, the peritoneum, and the mesenteries and uterine attachments Rovenstine and Hershenson

SUMMARY OF ABNORMAL EXPERIMENTAL FINDINGS IN 36 OPERATIONS

Case no	Sex	Age	Cardio-vascular state	Operation	Premedication					Anæsthetic					Remarks	Operative manipulation	Electrocardiogram
					Omnopon (gr)	Morphine (gr)	Scopolamine (gr)	Atropine (gr)	Premedication induction interval (min)	Thiopentone (g)	Nitrous oxide	Cyclopropane	Ether	Curare (mg)			
5	F	73	Dyspnœa on exertion. Aortic systolic murmur B.P 160/90	Laparotomy	1/3		1/200		60	0 5	+	+		15		Traction on rt. post. vagus in abdomen (large trunk)	Sinus arrhythmia, slight bradycardia ventricular extrasystoles and diminution in amplitude of P waves
13	F	8	Patent ductus arteriosus	Ligation of ductus arteriosus				1/100	80	+	+		+		Thiopentone 1 4 g per rectum 65 min before opn.	Injection of procaine into left vagus ligation of ductus	Increase in cardiac rate following injection No change during ligation
17	M	65	Normal B P 140/80	Œsophagectomy	1/3		1/150		90	0 8		+		10		Incision of pleura Traction on right vagus related to posterior aspect of lung hilum	No change A ventricular extrasystole during traction
19	M	43	Atheroma. B.P 160/90	Block dissection glands of neck	1/3		1/150		90	0 5	+		+		Chloroform also administered	Traction on left vagus in neck	Immediate bradycardia (88 to 64 per min. within 4 beats)
20	F	71	Normal B.P 110/80	Œsophagectomy		1/6		1/100	50	0 9		+	+	10		Division of ant and post trunks of vagus over lower third of œsophagus after injection of procaine	Occasional ventricular extrasystoles in control electrocardiograms After division of nerves ventricular extrasystoles every 4th beat
21	M	53	Normal B.P 120/80	Partial gastrectomy	1/3		1/150		95	0 5			+	15		Traction on large trunk of vagus in abdomen, above division into ant. and post.	No change A ventricular extrasystole during traction
23	M	68	Normal B.P 100/60	Trans thoracic gastrectomy		1/6		1/100	60	0 9		+		19		Traction on left ant. vagus ¹/₂ in. below œsophageal opening of diaphragm	Auriculoventricular dissociation with premature beats in all recordings Died 4 days after operation from bronchopneumonia
24	M	71	Essential hypertension B P 200/100	Block dissection glands of neck	1/3			1/100	75	0 25	+	+				Traction on left vagus in neck	No change in electrocardiogram Sudden onset of hypotension during traction (160/100 to 65/50)
25	M	68	Normal B.P 140/100	Thoracotomy—inoperable œsophageal carcinoma		1/6		1/100	50	0 7		+	+	11		Manipulation of mediastinum Traction on œsophagus	Auriculoventricular dissociation with premature beats in all recordings Died during operation
26	M	46	Normal B.P 120/80	Partial gastrectomy	1/3		1/150		75	0 8		+		21		Traction on stomach traction on right post. vagus in abdomen (large trunk)	No change in electrocardiogram Hypotension during traction (120/80 to 95/45)

ELECTROCARDIOGRAPHIC FINDINGS DURING OPERATIVE MANIPULATION OF THE VISCERA AND VAGUS NERVES *

A G FREEMAN
M.A , M D Camb
REGISTRAR, MEDICAL UNIT, CARDIFF ROYAL INFIRMARY , LATE PATHOLOGICAL REGISTRAR, BRISTOL ROYAL INFIRMARY

IN recent years operative surgery has offered more scope for studying how the heart beat is affected by manipulation of the viscera and the vagus nerve Profound cardiac irregularities, and even cardiac arrest, have been observed after manipulation of the intrathoracic contents, especially those involving the myocardium and the pericardium, and the pleura and hilar region of the lung (Beck and Mantz 1937, Cullen and Rovenstine 1938, Dunlop 1939, Rovenstine and Martin 1941, Burstein 1946, 1949, Burstein and Alexander 1947) It is believed that arrhythmias are commoner when adequate premedication with atropine sulphate is omitted, and to prevent or mitigate them it has been recommended that procaine hydrochloride be injected intravenously, or else be infiltrated into the hilar region or the vagus nerve (Leigh and Belton 1946, Bittrich and Powers 1948, Dennis et al 1948, Burstein et al 1949)

Although electrocardiographic findings following operative manipulation of the vagus have been reported by many workers, most of them have limited their investigations to the supracardiac portion of this nerve in the neck and thorax Seeing that vagotomy for peptic ulcer was firmly established by Dragstedt and Owens in 1943, and that by 1948 the American Gastro enterological Association estimated that 8000 vagotomies had been performed (Colp et al 1948), it is remarkable that so few references have been made to its effect on the cardiovascular system

Bradycardia and circulatory failure have been recorded during manipulation of the right vagus over the lower third of the œsophagus (Weeks et al 1946) the patient, a man aged 55, with no previous symptoms or signs of cardiac disease, died almost immediately after the nerve was divided Moore et al (1946) thought that the death of one of their patients forty eight hours after operation may have been due to irritability of the autonomic nervous system setting up vasovagal reflexes

Noble (1947) stated that "the potential hazards of the new vagotomy operation for peptic ulceration must be considered as vagal inhibition is a real threat" Cole et al (1947) also held that the most serious reaction associated with vagotomy is cardiac and respiratory paralysis, and Allen (1947), Lahey (1947), and Moses (1947) have also commented on this effect A sudden fall in blood pressure and a raised pulse rate during vagal resection has been described by Colp et al (1948), while Tanner (1948) reported tachycardia in the twenty four hours following the operation.

On the other hand, some authorities hold that the risk has been exaggerated In 200 transabdominal vagotomies performed by Dragstedt et al (1948) no alterations were noted in the blood pressure, pulse, or respiration rate which might have indicated vagal reflex effects, and Warren (1947) and Colp et al (1948) found that vigorous manipulation of the vagus did not produce bradycardia or cardiac arrest

It is evident that cardiac arrhythmias occasionally follow resection or manipulation of the vagus in the region of the diaphragm, and when they are slight or transient they may remain undetected Accordingly, I decided to investigate the electrocardiographic findings during operative manipulation of the œsophageal and, more particularly, the gastric branches of the vagus This investigation was encouraged by a leading article in THE LANCET (1947) reviewing the possible dangers of tampering with the vagus nerve during vagotomy "The question arises," it reads, "whether handling of the vagus has repercussions on the heart, and it would be interesting to know whether cardiographic studies during dissection of the vagi have been done."

METHODS AND FINDINGS

Using the continuous recording electrocardiograph, it was possible to take tracings before, during, and after any specific operative procedure, and thus to estimate the type and degree of cardiac arrhythmia caused by drugs, anæsthetic agents, and other factors

At first a Cambridge Standard Electrocardiograph was used, but as this machine provides records for only 5 sec. it proved difficult to synchronise the readings with the manipulation Later a Hellige Portable Electrocardiograph was obtained, and a continuous recording up to 50 feet (6 min.) could then be taken if desired

The three classical limb leads were attached to the patient Copperplate electrodes were made, and the leads were long enough to enable the electrocardiograph to be placed in a far corner of the theatre, away from the operation field. Every effort was made to limit interference from nearby electrical appliances, but at times some interference could not be prevented Between each set of recordings the instrument was standardised by applying a potential of 1 millivolt across the input, which produced a standard beam deflection of 10 mm The actual position of the galvanometer beam could be watched during the operation through an observation window

The electrocardiographic study had to be limited to one limb lead, and on the experience of previous observers, it was decided that lead II was the most satisfactory An attempt was made to obtain control recordings immediately before visceral or vagal manipulation was begun. In cases where the effect of vagal manipulation was under study, traction on the nerve was applied with Spencer Wells forceps or non toothed dissecting forceps

Electrocardiograms were obtained during 36 operations, as follow

Partial gastrectomy	17
Laparotomy	4
Ligation of patent ductus arteriosus	3
Œsophagectomy	3
Block dissection of glands in neck	2
Transthoracic gastrectomy	2
Partial gastrectomy and vagotomy	1
Total gastrectomy	1
Gastropexy	1
Heller's operation for achalasia of cardia	1
Thoracotomy	1

The procedures during which electrocardiograms were taken were

Visceral Manipulation	
Traction on stomach	8
Traction on œsophagus	4
Ligation of patent ductus arteriosus	3
Traction on gall bladder	1
Traction on spleen	1
Traction on pelvic colon	1
Paracentesis pericardii	1
Incision of pleura	1
Vagal Manipulation	
Traction on right posterior abdominal vagus	10
Traction on left anterior abdominal vagus	8
Traction on anterior œsophageal vagus	3
Traction on posterior œsophageal vagus	2
Division of anterior and posterior œsophageal vagi	1
Division of left anterior abdominal vagus	1
Division of anterior and posterior abdominal vagi	1
Traction on abdominal vagus above anterior and posterior trunks	1

Electrocardiograms were obtained in the 3 cases of patent ductus arteriosus during the injection of procaine into the left vagus where the nerve crosses the aortic arch In 1 of these (case 13 in accompanying table) the injection caused a transient rise in heart rate from 120 to 143 per minute

In a further 2 cases the effect of traction on the left vagus in the neck was studied during block dissection of malignant lymph glands It is clearly not practical to base any conclusions on two isolated cases, but it may be said that the onset of severe hypotension in one patient (case 24), and of bradycardia in the other

---

* Part of a thesis for the degree of M.D in the University of Cambridge, March, 1950

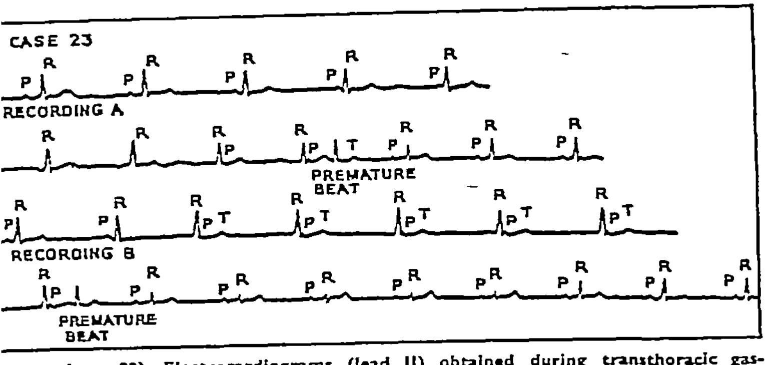


Fig 2 (case 23)—Electrocardiograms (lead II) obtained during transthoracic gastrectomy (A) Continuous recordings before and during traction on the left anterior vagus half an inch below œsophageal opening in the diaphragm. (B) Continuous recording obtained during traction on the nerve and after release of traction.

In all recordings the P waves were upright and normal in appearance, and the P–P intervals were constant (1 36 sec), it is thus apparent that a regular sinus rhythm existed. The R–R intervals excluding those preceding and following the premature beats, were also remarkably constant, and at a faster rate (1 32–1 34 sec) A diminution in amplitude of some of the R waves which followed the premature beats was present The premature beats may have arisen from a focus near the A.V node, as they were almost ‘ pure ” in form.

Conclusion : auriculoventricular dissociation with idioventricular rhythm and premature beats noted in all recordings.

procaine into the vagus sheaths in the neck, abolished the heart block. The observers attributed the arrhythmia to the direct pressure of the diverticulum on the vagus Burstein et al (1949) have reported an A V conduction defect during a transthoracic vagotomy, and this arrhythmia coincided with manipulation of the vagus nerve just above the diaphragm.

In the case under discussion it appears that a summation of effect may have resulted from vagal manipulation during cyclopropane anæsthesia.

Manipulation of the Œsophageal and Gastric Branches of the Vagus Nerve

Experiments on animals have shown that profound disorders of cardiac rate, rhythm, and conduction follow electrical or mechanical stimulation of the cervical and supracardiac portion of the vagus Appreciable changes have rarely followed manipulation of the nerve in the region of the diaphragm

Burstein et al. (1944) made repeated observations in anæsthetised cats and dogs as to the effect of electrical stimulation of the vagus nerves at fixed levels throughout their course They found that the stimulus required to produce a minimal fall in blood pressure when applied to the vagus nerves in the abdomen produced immediate cardiac arrest when applied to the upper thoracic portion of the nerves

Changes in the electrocardiogram on stimulation of the right abdominal vagus nerve in 29 dogs, anæsthetised with cyclopropane, were studied by Martin et al. (1942) Sinus tachycardia with a decrease in the P–R interval, and a diminution in the amplitude of the P and R waves were noted Less frequently, bradycardia, auricular extrasystoles, and auricular flutter occurred

Gullickson et al (1949) have described the findings in dogs during bilateral vagotomy between the pulmonary plexus and the stomach No premedication was given, and endotracheal ether anæsthesia was employed. Bradycardia, changes in amplitude or inversion of the P waves, variations of the P–R intervals, dissociation phenomena, and sino auricular block were noted These electrocardiographic changes were thought to have been specifically related to vagal manipulation but these writers admitted that similar and other, variations also occurred without any definite relation to visceral or vagal stimulation.

Comparable studies in man have seldom been undertaken Martin et al. (1944) have stimulated electrically the right and left cœliac ganglia in patients anæsthetised with cyclopropane or nitrous oxide and ether Bradycardia or other signs of vagal stimulation were seldom seen, in spite of the close proximity of vagal fibres in the region of the cœliac plexus Warren (1947) seems to have been the first to study the electrocardiographic findings during vagotomy In an unspecified number of cases, he found that vigorous manipulation of the nerves failed to alter the recordings. Dennis et al. (1948) also found persistent cardiographic changes no more common after vagotomy than after any other surgical procedure

Since I began my investigation, electrocardiographic findings during transthoracic and transabdominal vagotomy have been published by two independent groups of workers

Burstein et al (1949) found changes in 2 of 9 patients during transthoracic vagal resection. In one case an auriculoventricular conduction defect appeared each time the nerve was manipulated before its division just above the diaphragm In the other case this manœuvre resulted in bradycardia and occasional ventricular extrasystoles These workers believe that these reactions were minimal (1) because procaine was injected into the nerve before its manipulation, and (2) because they were divided as near to the diaphragm as possible

Gullickson et al. (1949) took continuous recordings during bilateral vagotomy (5 transabdominal and 1 transthoracic) Changes apparently related to vagal manipulation and limited to an increase in the P–R interval occurred in 2 cases

I obtained electrocardiograms during manipulation of the œsophageal or gastric branches of the vagus in 22 patients, 29 experiments being conducted The electrocardiographic abnormalities noted after vagal manipulation are of course significant only if absent from the immediate control tracings Thus an isolated ventricular extrasystole in case 21 (see table) may well be due to other causes, such as the anæsthetic Again, the A V dissociation with idioventricular rhythm and premature beats in case 23 (fig 2) evidently bore no specific relation to vagal traction, for it was also present in control recordings As these recordings were obtained immediately before vagal traction, manipulation of the viscera during the transthoracic gastrectomy may have been largely responsible

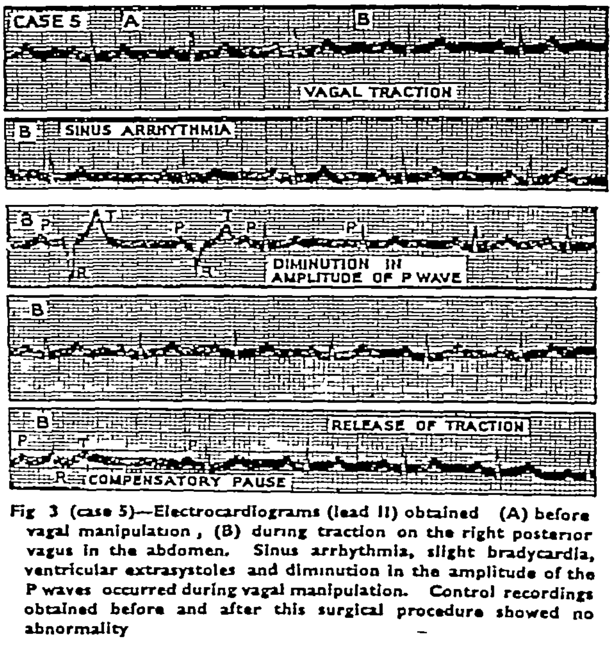


Fig 3 (case 5)—Electrocardiograms (lead II) obtained (A) before vagal manipulation , (B) during traction on the right posterior vagus in the abdomen. Sinus arrhythmia, slight bradycardia, ventricular extrasystoles and diminution in the amplitude of the P waves occurred during vagal manipulation. Control recordings obtained before and after this surgical procedure showed no abnormality

(1938) noted that "traction reflexes" were definitely diminished when regional anæsthesia and inhalation narcosis were used together However, many of these writers have attributed the cardiac irregularities to the anæsthetic agents or to oxygen lack

Manipulation of the Œsophagus

The electrocardiographic findings during manipulation of the œsophagus appear, in the main, to be identical with those described above However, Ressinger has reported auricular flutter occurring when an œsophageal carcinoma was explored, and bradycardia, hypotension, and progressive cyanosis have been noted when traction was applied to an œsophageal diverticulum (Barbour and Tovell 1948)

Of the 4 cases studied in my investigation, 1 showed auriculoventricular dissociation with idioventricular rhythm and premature beats (fig 1)

Case 25 —In a man, aged 68, with an œsophageal carcinoma, thoracotomy was performed under cyclopropane Cardiograms could not be obtained before the induction, but the pulse rate was regular at 80 per min , and the blood pressure was 140/100 The growth extended from $^{1}/_{2}$ inch above the diaphragm to the aortic arch, and since it was fixed no attempt was made to resect it During manipulation of the growth, irregularity in the pulse was noted by the anæsthetist, and the first cardiograms were then obtained In an attempt to stop this arrhythmia, intravenous procaine (2 ml of a 1% solution) was administered, but the irregularity persisted The patient died as soon as the wound was closed No appreciable blood-loss occurred during operation At necropsy no coronary disease or valvular heart disease was found The cause of death was not ascertained

In this patient all electrocardiograms taken during operation showed a regular auricular rate of 75 per minute, whilst the ventricular rate was consistently more rapid though less regular (80–100) According to Lewis (1925b) the rate of the escaping ventricles rarely rises above that of the auricles , in such cases the ventricles and auricles beat for the most part independently Yet in this case (and also in case 23) the idioventricular rate was greater than the auricular rate, indicating depression of the sino auricular node

As control recordings before operation were not obtained, the cause of this arrhythmia remains uncertain The necropsy findings suggest that the auriculo ventricular (A V) dissociation was not due to narrowing or occlusion of the larger coronary arteries, or to macroscopic changes in the heart muscle However, persistent heart block of a high grade often occurs in the absence of gross pathological changes Microscopic lesions, such as inflammation, degeneration, or fibrosis affecting the auriculo-ventricular tract may then be found (Lewis 1925a), but in the above case, examination of the junctional tissues was not performed Transient or functional A V block may be due to such diverse causes as asphyxia, uræmia, infectious diseases, or certain drugs (White *1947*), but there is no evidence of these in this case

The arrhythmia recorded during this operation may have been due to the anæsthetic or to the operative procedure, or both It is known that A V dissociation occurs spontaneously during cyclopropane anæsthesia , and it may also follow manipulation of the vagus The surgeon reduced manipulation of the mediastinum to a minimum, but he thinks that the vagus nerves were undoubtedly implicated in the growth, and traction on this may have led to the adverse result described Doubilet et al (1948) have demonstrated that the main vagal trunks lie in intimate relationship with the œsophageal musculature , so traction on the œsophagus must cause some disturbance of the vagus

Cyclopropane Anæsthesia —The arrhythmias seen during administration of cyclopropane can often be postponed or aborted by adequate premedication, or by intravenous injection of atropine sulphate (Seevers et al 1934, Meek et al 1937, Rovenstine and Hershenson 1938, Rovenstine and Martin 1941, Allen et al 1942) Some of these writers have suggested that the irregularities are caused by cyclopropane stimulating the parasympathetic, thus producing vagal effects on the heart Further, Adriani et al (1940) have shown that cyclopropane, like acetylcholine, will produce chromodacryorrhœa (red tears) in rats under the effect of eserine These workers conclude that acetylcholine is liberated during cyclopropane anæsthesia, which accords with the conception of cyclopropane as a parasympatheticomimetic agent Moreover, conduction defects, indicated by prolongation of the P–R interval and other severe forms of A V block, do not occur in dogs during cyclopropane anæsthesia if the cardiac vagus nerves have previously been divided (Robbins and Baxter 1937) , so vagal stimulation may be expected to increase the incidence of conduction defects

Vagal Manipulation —Auriculoventricular dissociation has been noted in animals after electrical or mechanical stimulation of the cervical and supracardiac portion of the vagus (Einthoven 1908, Cohn 1912, Robinson 1913, Cohn and Lewis 1913, Lewis 1914, Mautner and Luisada 1941) Various anæsthetics were employed, and it may be argued that the abnormalities were due to the action of these agents on the heart or medullary centres, rather than due to actual mechanical stimulation of the vagus nerve However, Iglaver et al (1941) showed that the electrocardiograms obtained when stimulating the parasympathetic nervous system by chemical methods (intravenous mecholyl) in unanæsthetised dogs were almost identical with the recordings produced by the earlier investigators during electrical stimulation of the vagus in the neck in anæsthetised animals

In man, A.V dissociation has followed mechanical manipulation of the carotid sinus in unanæsthetised subjects (Robinson and Draper 1912, Wilson and Arbor 1915, *Ferris et al* 1935) Weiss et al *(1934)* have described a case in which cardiographic evidence of complete A V dissocation followed distension of a traction diverticulum of the œsophagus Release of pressure in the diverticulum brought a return to normal sinus rhythm, and the administration of atropine, or the *infiltration* of

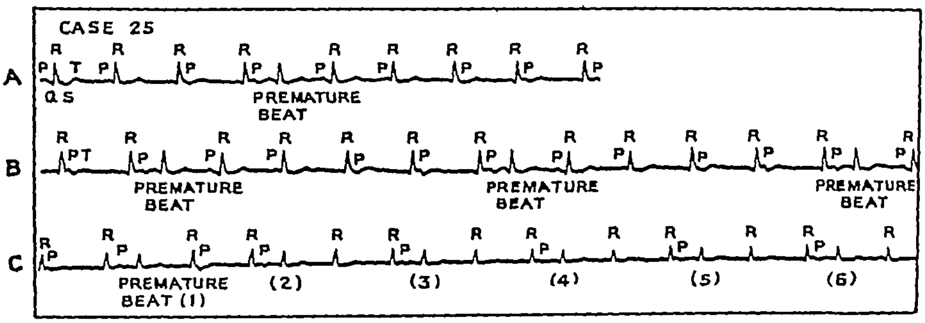


Fig 1 (case 25)—Electrocardiograms (lead II) obtained : (A) during slight traction on an œsophageal carcinoma (B) 5 minutes later after administration of intravenous procaine ; and (C) 8 minutes after B, and 10 minutes before death

The P waves were upright and normal in appearance , the auricular rate was regular at 75 per min. In A and B premature beats occurred every 6th beat , in C they occurred every 3rd beat In B, the typical sequence of the R–R intervals was *0 36*, 0 66, 0 70, 0 70, 0 74, 0 76, *0 36* sec , in C the sequence was *0 36*, 0 60, 0 66, *0 36* sec The idioventricular rate was quicker than the auricular rate in all recordings, the maximal rate being found in C The ventricular pacemaker may be near, or just below, the A V node, since all complexes, including the premature ones, appear normal

Conclusion : auriculoventricular dissociation with a fast idioventricular rhythm and premature beats noted in all recordings

CYANOSIS IN INFANCY FROM NITRATES IN DRINKING-WATER

MARY C EWING
M.B Edin
HOUSE PHYSICIAN, WEST SUFFOLK GENERAL HOSPITAL

R M MAYON-WHITE
M.D , Ph D Lond , M R C P , D C.H
CONSULTING PÆDIATRICIAN, IPSWICH AREA

METHÆMOGLOBINÆMIA as a cause of cyanosis in infancy has lately received a considerable amount of attention (see *Lancet* 1948) It is now recognised that a frequent cause is nitrate contamination of water used in making up artificial feeds for a baby In the bowel the nitrate is converted to nitrite, which, when absorbed, oxidises hæmoglobin to methæmoglobin The contaminated water has usually come from a shallow well Boiling such water is no safeguard Most of the cases reported have occurred in the country districts of the central States of the U S.A , where the syndrome is common and farmers speak of the cases as " blue water babies " (Donahoe 1949)

No cases have hitherto been published in the British Isles, but during the summer of 1950 2 cases have come to our notice in the Suffolk countryside

CASE RECORDS

Case 1 —A boy was born in hospital and discharged to his home in a village near Ipswich on the tenth day of life, April 23, 1950 Though breast feeding was not fully established at the time of discharge, the child was regarded as healthy At home full artificial feeding with a powdered milk was introduced and for a fortnight good progress was made At the age of 4 weeks the child s general health deteriorated , there were diarrhœa and vomiting, and the child s complexion was slate blue Feeding was stopped, and boiled water was substituted Next day the child was deeply cyanosed and very weak, and died in an ambulance on the way to the East Suffolk and Ipswich Hospital

Necropsy (Dr Trevor Shaw) —Apart from slight inhalation pneumonia no obvious cause of death was found in particular the cardiovascular system was normal Brown discoloration of all the solid viscera was noted, and spectroscopy of the blood showed methæmoglobin in high concentration. There was no evidence of hæmolysis No medicines had been given.

One of us (R M. M W) was consulted about other possible causes of methæmoglobinæmia in a child of this age The suggestion that the drinking water be examined for nitrates was followed up and proved fruitful. Water for the infant's milk mixture had been obtained from a shallow well and had been boiled before use Specimens of this water were found to be heavily polluted and unfit for drinking , in particular, nitrates were present at a concentration of 200 parts per million. A trace of nitrite was also present

The death of this infant was considered to be due to methæmoglobinæmia from the absorption of nitrites produced by the action of intestinal organisms on the nitrates in the water used to make up the milk mixture

Case 2 —A boy, aged 6 weeks, was admitted to the West Suffolk General Hospital, Bury St Edmunds on the evening of July 31, 1950, with deep cyanosis His mother had first noticed a bluish colour of his skin on the morning of the previous day Until then he had been healthy, feeding well and gaining weight He had vomited once, on the evening of admission. His mother stated that the blue colour had not changed since first seen, and was not altered by the effort of feeding or by crying The patient was the fifth child in the family, a normal delivery at term There was no history of cyanosis at birth or of subsequent " blue attacks " Breast feeding had been abandoned at ten days , thereafter he had been fed on a proprietary dried milk

On admission he was weak, limp, and intensely cyanosed Respirations were shallow, and the rate increased, but there were no abnormal physical signs in the heart or lungs There was no improvement of his colour or of his general condition after half an hour in an oxygen box Methæmoglobinæmia was suspected Blood drawn from a vein was deep chocolate-brown , spectroscopy confirmed the presence of methæmoglobin in considerable concentration. There was no evidence of intravascular hæmolysis

Treatment —An exchange transfusion was given. The catheter was introduced through a cut-down incision over the saphenous opening (Arnold and Alford 1948) A recent bottle of compatible blood from the hospital bank was prepared as a partly concentrated cell suspension by pouring off the supernatant plasma The exchange was given in 10 ml stages, and successive samples of the blood returned from the infant were analysed (see table) The volumes of the exchange were adjusted to leave a " credit balance " in favour of the infant to correct a pre existing anæmia (350 ml given, 270 ml withdrawn)

Progress —During the transfusion the child's condition steadily improved, the cyanosis giving place to a pink complexion. The colour of blood withdrawn from the baby became progressively less brown and more nearly that of normal venous blood By the end of the transfusion the infant was crying lustily He was offered and took a full feed , thereafter he behaved like a normal healthy child. The wound healed by first intention Though fit to be discharged, the boy was kept in hospital till the tenth day after admission, when we had a satisfactory report on his home water supply

METHÆMOGLOBIN LEVELS (CASE 2)

When estimated	(1) Total methæmo globin (g per 100 ml)	(2) Total hæmo globin (g per 100 ml)	(1) as percentage of (2)
Before transfusion (2 hours after admission)	4	9	45 %
During exchange			
After 100 ml withdrawn	3	10	30 %
After 200 ml.	2	12	15 %
After 250 ml	<1 5	12	<15 %
After transfusion (270 ml withdrawn)	<1 5	12	<15 %

The method used for estimating methæmoglobin was an adaptation of the method for carboxyhæmoglobin described by Harrison (1947) The samples for estimating methæmoglobin were compared in a Hartridge reversion spectroscope against serial dilutions of the same blood in which all the hæmoglobin had been converted to methæmoglobin by the addition of a crystal of potassium ferricyanide Total hæmoglobin was estimated by the Sahli acid hæmatin method

The methæmoglobin figures are approximate and illustrative only The quantitative analysis could not be made until three days after collection. It was determined that, under the conditions of storage, the methæmoglobin content of all samples diminished so quickly that no sample contained a detectable amount ten days after collection The figures in column (1) above, are therefore likely to be an under-estimate of the actual concentration of methæmoglobin present

---

DR FREEMAN REFERENCES—*continued*

Moses R (1947) *Ibid* 237 603
Noble, A B (1947) *Canad med Ass J* 56 490
Ressinger H (1927) quoted by Owen S E (1932) *Amer Heart J* 8 496
Robbins B H Baxter J H (1937) *J Pharmacol* 61 162
Robinson G C (1913) *J exp Med* 17 429
— Draper G (1912) *Ibid* 15 14
Rovenstine E A., Hershenson B B (1938) *Canad med Ass J* 39 538
— Martin S J (1941) *J Indiana med Ass* 34 201
Seevers M H Meek W J Rovenstine E A., Stiles, J A. (1934) *J Pharmacol* 51 1
Tanner N C (1948) *Proc R Soc. Med.* 41 652
Warren R. (1947) *Surgery* 22 246
Weeks C Ryan, B J Van Hoy, J M. (1946) *J Amer med Ass* 132 988
Weiss S Baker J P (1933) *Medicine* 12 297
— Ferris E B , Capps R C (1934) *Trans Ass Amer Phys* 49 177
White P D (1947) Heart Disease 3rd ed New York p 929
Widenhorn H L Voloni, I F , McLaughlin R. F (1938) *Anesth & Analges* 17 93
Wilson F N , Arbor, A (1915) *Arch intern Med* 16 989

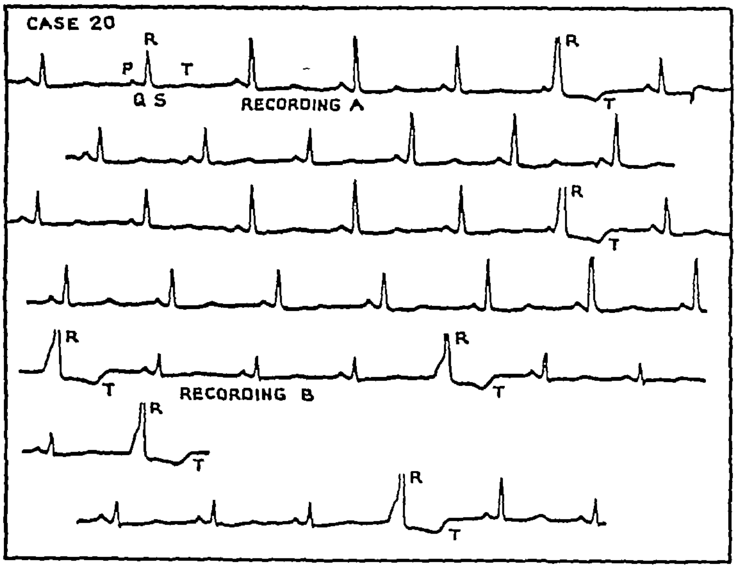


Fig 4 (case 20)—Electrocardiograms (lead II) obtained during œsophagectomy (A) Occasional ventricular extrasystoles present in continuous recordings 1–4. (B) One minute later, after division of the anterior and posterior trunks of the vagus over the lower third of the œsophagus, ventricular extrasystoles appeared regularly every 4th beat (continuous recordings 5–7)

for the cardiographic changes, but more probably these were due to cyclopropane anæsthesia

However, in 3 cases vagal manipulation seems to have been a definite factor in the production of a temporary cardiovascular disturbance Traction on the right posterior vagus nerve in the abdomen was associated with hypotension in case 26, and with bradycardia, ventricular extrasystoles, and diminution in the amplitude of the P waves in case 5 (fig 3) In case 20, control electrocardiograms during an œsophagectomy showed isolated ventricular extrasystoles, but after manipulation and subsequent division of the anterior and posterior trunks of the vagus nerve, over the lower third of the œsophagus, they appeared regularly every 4th beat (fig 4) In this case preliminary injection of procaine into the vagus failed to prevent the arrhythmia All 3 patients had had adequate premedication with morphine and atropine, or their derivatives

Manipulation or resection of the œsophageal or gastric branches of the vagus produced hypotension or definite electrocardiographic changes in 3 of the 13 patients receiving cyclopropane Auriculoventricular dissociation with idioventricular rhythm and premature beats was noted in 2 others (cases 23 and 25) during operation under cyclopropane Electrocardiographic changes did not follow vagal manipulation in the 9 cases where cyclopropane was not used (including 5 in which a regional block with local anæsthesia was given)

SUMMARY AND CONCLUSIONS

Profound disorders of heart rate, rhythm, and conduction may follow stimulation or division of the vagus nerve in its cervical or supracardiac course Significant changes rarely follow manipulation or resection of the nerve in the region of the diaphragm

Although cardiac arrhythmias have seldom been recognised clinically during vagotomy, it was thought probable that minor and transient irregularities might have remained undetected Accordingly, electrocardiograms were obtained during operative manipulation of the œsophageal and gastric branches of the vagus

Hypotension or significant electrocardiographic changes were noted in 3 of 13 patients in whom the œsophageal or gastric branches of the vagus were manipulated or divided under cyclopropane anæsthesia Auriculoventricular dissociation with idioventricular rhythm and premature beats was observed in 2 further patients under cyclopropane These 5 cases had had premedication with morphine and atropine or their derivatives Electrocardiographic changes did not follow vagal manipulation in the 9 cases where cyclopropane was not used

Cyclopropane stimulates the parasympathetic, and a summation of effects might be expected from vagal manipulation during cyclopropane anæsthesia The findings of this limited investigation suggest that when cyclopropane is used, manipulation of the œsophageal and gastric branches of the vagus should be avoided as much as possible

This work could not have been undertaken without the full coöperation of the surgical teams at Bristol Royal Infirmary I am especially grateful to Mr D C Bodenham, Mr T J Butler, Mr W M Capper, Mr H J Croot, and Prof R. Milnes Walker, for permission to investigate cases during operation, and for assistance readily given. I would like further to express my thanks to Prof C Bruce Perry for his encouragement and criticism, to Dr J H Challenger for the loan of the electrocardiograph, to Dr J A. Cosh for his help in the interpretation of the electrocardiograms, and to Dr F G Bolton for his constant interest and advice

Mr A H. Williams of the department of medicine, Cardiff Royal Infirmary, and Mr F A. Godman of the department of photography, University of Bristol, kindly photographed the continuous electrocardiographic recordings.

REFERENCES

Adriani J , Martin, S J Rovenstine, E A. (1940) *Proc. Soc. exp Biol , N Y* 45, 785
Allen, A W (1947) *Ann R Coll Surg* 1, 236
Allen C R , Stutzman J W , Foregger, R , Meek, W J (1942) *Anesthesiology* 3, 530
Barbour C M., Tovell, R M (1948) *Ibid*, 9, 514
Beck C S , Mantz, F R (1937) *Ann. Surg* 106, 625
Bittrich N M , Powers W F (1948) *Anesth. & Analges* 27, 131
Burstein, C L (1946) *Ibid*, 7 113
— (1949) *Anæsthesiology* 10 133
— Alexander, F A D (1947) *Ibid*, 8, 36
— Martin, S J ,Rovenstine, E A (1944) *J thorac. Surg* 13, 49
— Piazza T L , Kapp, L A , Rovenstine E A (1949) *Surgery*, 25 30
Cohn A E (1912) *J exp Med* 15 49
— Lewis, T (1913) *Ibid* 18, 739
Cole, W H , Reynolds, W Reynolds J (1947) cited in *J Amer med Ass* (1948) 136 801
Colp R , Klingenstein P , Druckerman, L J , Weinstein, V A. (1948) *Ann. Surg* 128 470
Cullen S C , Rovenstine E A (1938) *Anesth & Analges* 17, 13.
Dennis C Eddy, F D Frykman H M., McCarthy, A M., Westover, D (1948) *Ann Surg* 128, 479
Doubilet, H Shariroff B G P , Mulholland, J H (1948) *Ibid*, 127, 128
Dragstedt, L R , Owens, F M. (1943) *Proc Soc. exp Biol., N Y* 53, 152
— Woodward, E R , Harper P V Storer, E H (1948) *Gastroenterology* 10, 200
Dunlop, J G (1939) *Anesth & Analges* 18 301
Einthoven W (1908) quoted by Iglaver et al (1941)
Ferris E B Capps R B Weiss, S (1935) *Medicine* 14 377
Gullickson, M J , McRae, J H , Campbell, D A (1949) *Surg Gynec Obstet.* 89, 153
Hill, I G W (1932) *Edinb med J* 39 533
— (1933) *Quart J exp Physiol* 22 79
Hodge, G B , Messer, A. L (1948) *Surg Gynec Obstet.* 86, 617
Iglaver A. Davis D Altschule, M D (1941) *Amer Heart J* 22, 47
Lahey F H (1947) *Lahey Clin Bull* 5, 66
Lancet editorial (1947) ii, 95
Leigh, M D Bolton M K (1946) *Anesthesiology* 7 611
Lennox W G Graves R. C , Levine, S A (1922) *Arch. intern Med* 30 57
Lewis T (1914) *Heart* 5 347
— (1925a) The Mechanism and Graphic Registrations of the Heart Beat 3rd ed London , p 183
— (1925b) *Ibid*, p 200
Maher C C , Crittenden P J , Shapiro, P F (1934) *Amer Heart J* 9, 664
Martin S. J , Burstein C L , Rovenstine E A (1942) *Arch. Surg* 44, 943
— Miscall L Rovenstine E A (1944) *Amer J Surg* 63 240
Marvin, H M. Pastor, R B (1925) *Arch intern. Med* 35 768
— — Carmichael M (1925) *Ibid* p 782
Mautner, H Luisada A (1941) *J Pharmacol* 72 386
Meek W J Hathaway H R. Orth O S (1937) *Ibid* 61 340
Moore, F D , Chapman W P Schulz, M D Jones C M (1946) *New Engl. J Med* 234, 241

Continued at foot of next column

paid to its efficacy and speed of action On clinical grounds treatment was thought to be urgently necessary in our case 2 Exchange blood transfusion was used because we preferred the use of a familiar technique which offered logical treatment to experimenting on a critically ill child with a drug with which neither of us was familiar and which one of us knew to have been the subject of controversy in the treatment of the somewhat similar condition of carboxyhæmoglobinæmia We dismissed methylene-blue too lightly The experiments of Wendel (1939) and Hartmann et al. (1938) have since come to our notice Wendel showed that in high concentration methylene blue oxydised hæmoglobin to methæmoglobin, but in lower concentration (1 or 2 mg per kg of body weight) rapidly reduced methæmoglobin to hæmoglobin Many of the abovementioned reports of well water cyanosis mention disappearance of cyanosis within 30–60 minutes of the intravenous injection of methylene blue

Ascorbic acid is of value (Deeny et al 1943) in the treatment of chronic idiopathic methæmoglobinæmia but seems too slow in its action to have a place in the therapy of the condition under discussion here

Though treatment with methylene blue is rapidly effective, the child should not be discharged until a safe supply of water has been assured at its home Relapses are not unknown Ferrant (1946) reported 2 cases from Louvain in Belgium , the second child was readmitted, again with intense methæmoglobinæmia, five days after discharge from hospital and died before treatment could be given

DISCUSSION

So far as we know, no cases of well water cyanosis have been reported in adults, but in view of the hereditary nature of achlorhydria one wonders if a similar mechanism may not operate in some cases of “ familial idiopathic methæmoglobinæmia ” Most of the few cases reported seem to have been investigated in hospital, and the home background is usually not described Some of the patients have continued cyanosed in hospital and therefore seem unlikely to belong to the syndrome under discussion here The largest group of patients studied in one family “ lived on a farm in a remote and mountainous part of Ireland ” , they refused admission to hospital and were investigated in their own home (Gibson and Harrison 1947)

In the past nitrates and nitrites have been considered harmless in themselves, but they are held to be an important indication that the water is contaminated with sewage Ammonia and other nitrogenous compounds of manure are oxidised to nitrates by soil bacteria Thus the presence of nitrates or nitrites in a sample of drinking water suggests contamination by organic matter Theoretically it is possible for coliform organisms to be held back by the soil as water percolates through it, yet for nitrates in solution to pass into a well , in practice this rarely seems to happen coliform organisms being usually demonstrable in well waters containing nitrates

All the cases of “ well water cyanosis ” of which we have read have been in artificially fed young infants living in country districts , the water supply in each case has been a shallow well Surface and subsurface contamination of shallow wells is notoriously easy, particularly in summers like that of 1950 in England, when a heavy rainfall followed twelve months' exceptional drought Probably most of the shallow wells used for drinking in this country are in private ownership This is important from a public health point of view, for the local authority has powers to test such a supply only after receipt of a specific complaint about the water To the general public the greater palatability of cold water from a well makes it more acceptable in summer than lukewarm water from the above ground storage tanks of many village supplies

Popular belief that boiling the water makes it safe is misplaced in the case of nitrate contamination, for the nitrate concentration remains unchanged Case 1 illustrates another facet of the danger When the child first became ill with diarrhœa and vomiting, a neighbour recommended that feeding should be stopped temporarily and boiled water substituted This advice, though generally unexceptionable in gastro enteritis, can only make matters worse in methæmoglobinæmia of the type under discussion here

From our experience of these two cases and from our study of accounts of similar cases we endorse the recommendation given by Taylor (1949) that nitrates should be regarded as a potentially dangerous contaminant of drinking water, and that 20 parts per million should be regarded as the highest acceptable figure in water used for preparing an infant's milk mixture Some such standard figure seems desirable, if only as a guide, for the report of clinical cases of a public health hazard is likely to be followed by requests for analysis of samples from suspected sources Thus, since “ blue water babies ” have become recognised, surveys of water supplies have been carried out in the Middle West of America (Johnson et al 1946, Weart 1948) In one county in Illinois more than 25% of waters from rural wells contained more than 100 parts per million of nitrate nitrogen (Weart 1948) Such a state of affairs constitutes a real threat to the infant population of the neighbourhood

SUMMARY

Two cases are reported of cyanosis from methæmoglobinæmia in infancy Both children were reared in Suffolk villages, both were artificially fed, and in each case the water used to prepare the milk mixture was obtained from a shallow well In each case the well water was contaminated with coliform organisms and nitrates One child died before admission to hospital, but the other was treated by exchange blood transfusion and recovered

The cases are reported because they are believed to be the first examples in Great Britain of a syndrome which has recently become widely recognised in country districts of North America and the Netherlands The literature is briefly reviewed It seems to be acceptably established that young infants may have coliform organisms in the upper part of the intestinal tract , in such infants nitrates contaminating the drinking water may, on ingestion, be reduced by the organism to nitrites sufficiently high in the small intestine for the nitrites to be absorbed and methæmoglobinæmia to be produced

If suspected the condition is easily diagnosed The recognised treatment is the intravenous injection of methylene blue 1 or 2 mg per kg of body weight

The danger of nitrates in water fed to babies merits wider recognition Boiling such water does not render it safe It has been authoritatively recommended that 20 parts per million of nitrates should be regarded as the highest acceptable figure in water used for preparing an infant's milk mixture We endorse that recommendation

We are indebted to Dr Trevor Shaw and to Mr C T Dawson, Ipswich Borough Coroner, for permission to cite details of case 1, to Dr R H Clayton, M O H , Bury St Edmunds, for investigating the water supply in case 2 , to Dr Eric Wood and Dr S Greenburgh, public analysts of Norwich and of Cambridge, for their reports on the water supplies of cases 1 and 2 respectively Dr Wood has given us much information on matters that lie in his field rather than ours Mr S T Ryder, F I M L T, estimated the methæmoglobin in case 2

Since this paper was written, a third case, from another part of Suffolk, has been admitted under *one of us* This

Follow up—The child has been seen in the follow up clinic since discharge, he is healthy, without cyanosis, and without detectable methæmoglobinæmia

The suspicion that this was a case of "well water cyanosis" was entertained but could not be confirmed until after the transfusion treatment was completed Next day the mother was questioned She explained that the baby's feeds were made up by boiling water obtained by a bucket from a shallow well in the yard of a public house opposite her cottage Analysis of this water showed it to be "heavily contaminated with coliform organisms" (probable number of *Bact coli* in excess of 180 per 100 ml) and to contain 95 parts per million of nitrates Nitrites were absent The source was a simple dug well 42 ft deep containing 20 ft of water at the time of analysis Also available to this group of cottages (but not used by most of the inhabitants for drinking) was water from a deep bore supply to a storage tank. This water (considered unfit for drinking by the analyst as a result of his findings) did not contain nitrates though contaminated, but to a less degree, with coliform organisms

HISTORICAL REVIEW

Though enterogenous cyanosis holds its place in the classification of causes of cyanosis, methæmoglobinæmia sufficient to discolour the skin seems to be rare nowadays in intestinal disorders Henstall and Dameshek (1936) reported 1 case and collected 36 others previously published The early sulphonamide preparations provided a new example of cyanosis of this type Bismuth subnitrate, formerly used in the treatment of infantile gastro enteritis, has been given up because of this danger (Roe 1933)

Methæmoglobinæmia may follow the absorption of many chemicals besides sulphonamides and bismuth subnitrate, such as aniline and its derivatives acetanilid and phenacetin, nitrophenol, potassium chlorate, and various nitrites Occasional cases of methæmoglobinæmia in infants have been reported in which none of these chemicals was incriminated Such cases have been described as "idiopathic" methæmoglobinæmia (Schwartz and Rector 1940, Stahr 1941) Comly (1947) reported two such cases, but he recognised that nitrates contaminating the well-water used to make up the feeds were the cause of his two cases and suspected the same ætiology in several other cyanosed infants whose colour improved as soon as the water supply was changed Diarrhœa was a feature of Comly's cases, the conversion of ingested nitrates to nitrites he attributed to organisms present in the bowel during gastro intestinal disturbances He recognised that nitrites, but not nitrates, oxidised hæmoglobin to methæmoglobin Only young babies seemed to be affected Comly thought that the immunity of adults and older children drinking the same water was due to the relatively greater water intake in infancy

Cornblath and Hartmann (1948) investigated the mechanism of the enteric nitrate nitrite conversion by a series of in-vivo experiments on infants They emphasise the point that "well-water cyanosis" is limited to the first few weeks of life, when physiological gastric hypochlorhydria is greatest They showed that in such infants lower bowel organisms (*Bact ærogenes, Bact freundii*, and *Bact coli*) which have the property of reducing nitrates to nitrites are to be found in the upper intestine and may be grown even from saliva and stomach washings They found that the growth of these organisms was inhibited at a pH of 4 or less They showed that oral ingestion of water containing nitrate would only produce methæmoglobinæmia in infants who had a gastric juice of pH greater than 4 and nitrate reducing bacteria in the upper gastro intestinal tract Cornblath and Hartmann assume that, where gastric acidity inhibited the growth of colon organisms in the upper intestine, any ingested nitrate is absorbed harmlessly before conversion to nitrite can take place A baby aged 3 months with a transverse colostomy gave them the opportunity to demonstrate the point nicely In this child 200 mg of nitrate ion fed by mouth produced cyanosis and converted 25% of the hæmoglobin to methæmoglobin, 600 mg of nitrate ion injected into the colostomy for two days did not cause cyanosis and converted only 4% of the hæmoglobin to methæmoglobin

Methæmoglobin is a true oxide of hæmoglobin, the iron of the molecule being oxidised to the ferric form, it is only slowly broken down in the body and is too stable to be of use to the body for transport of oxygen The cellular anoxia caused by methæmoglobinæmia depends on this, but another factor operates in the same direction Like carboxyhæmoglobin, methæmoglobin shifts to the left the oxygen dissociation curve of a specimen of blood containing it (Darling and Roughton 1942) Thus, blood containing a proportion of methæmoglobin not only has its oxygen carrying power reduced by that amount but also such oxygen as is carried by the remaining hæmoglobin is less readily ceded to the tissues.

DIAGNOSIS

The diagnosis is not difficult The onset of cyanosis in a bottle fed baby should lead to suspicion of this condition if no gross abnormality can be found on examination of the cardiovascular and respiratory systems The suspicion warrants examination of the blood A specimen of venous blood containing an appreciable quantity of methæmoglobin is chocolate brown, clearly recognisable as abnormal to the naked eye by daylight or electric light, the presence of methæmoglobin is readily confirmed spectroscopically If methæmoglobin is found, inquiry should be made about recent medicines and the water supply If the water supply is suspected, the case should be notified to the Medical Officer of Health with a request for an analysis of the drinking water In all cases to date the nitrate polluted water has been drawn from a shallow well on a farm or in a small country village

Diarrhœa and vomiting are not essential features of the syndrome, but vomiting, presumably often from cerebral anoxia, is usual Inhalation pneumonia may complicate the condition Methæmoglobin is so easily detected that, if doubt exists, its presence should be excluded before it is assumed that the cyanosis is due to pneumonia

On a priori grounds it seems that the more water that is used in preparing the feeds the more likely is methæmoglobinæmia to be produced Thus, if the water supply is contaminated by nitrates, methæmoglobinæmia is most likely in those infants fed on mixtures made up from powdered milk (because the greatest amount of water is used), evaporated milk would occupy an intermediate position, and modified cow's milk mixtures should be the safest of artificial foods Donahoe (1949) suggests that both cows and women when drinking nitrate contaminated water may secrete the nitrate ion in their milk

TREATMENT

The history of our two cases illustrates the fact that nitrate methæmoglobinæmia is a cumulative poisoning, taking some days or a week or two to develop Once the ingestion of nitrates has been stopped, the disease is self limiting The necessary change to purer water can most easily be made by admitting the infant to hospital On admission many such infants are critically ill, and urgent treatment is called for because of the danger of continued tissue anoxia Oxygen cannot reduce the amount of methæmoglobin, the hæmoglobin may be presumed to be almost completely oxygenated Therefore the administration of oxygen should be regarded as no more than a temporary expedient while preparations are being made for specific therapy

The intravenous injection of methylene blue in doses of 1 or 2 mg per kg of body weight is the treatment of choice In the American published reports tribute is paid to its efficacy and speed of action On clinical grounds treatment was thought to be urgently necessary in our case 2 Exchange blood transfusion was used because we preferred the use of a familiar technique which offered logical treatment to experimenting on a critically ill child with a drug with which neither of us was familiar and which one of us knew to have been the subject of controversy in the treatment of the somewhat similar condition of carboxyhæmoglobinæmia We dismissed methylene blue too lightly The experiments of Wendel (1939) and Hartmann et al (1938) have since come to our notice Wendel showed that in high concentration methylene blue oxydised hæmoglobin to methæmoglobin, but in lower concentration (1 or 2 mg per kg of body-weight) rapidly reduced methæmoglobin to hæmoglobin Many of the above mentioned reports of well water cyanosis mention disappearance of cyanosis within 30–60 minutes of the intravenous injection of methylene blue

Ascorbic acid is of value (Deeny et al 1943) in the treatment of chronic idiopathic methæmoglobinæmia but seems too slow in its action to have a place in the therapy of the condition under discussion here

Though treatment with methylene blue is rapidly effective, the child should not be discharged until a safe supply of water has been assured at its home Relapses are not unknown Ferrant (1946) reported 2 cases from Louvain in Belgium, the second child was readmitted, again with intense methæmoglobinæmia, five days after discharge from hospital and died before treatment could be given

DISCUSSION

So far as we know, no cases of well water cyanosis have been reported in adults, but in view of the hereditary nature of achlorhydria one wonders if a similar mechanism may not operate in some cases of "familial idiopathic methæmoglobinæmia" Most of the few cases reported seem to have been investigated in hospital, and the home background is usually not described Some of the patients have continued cyanosed in hospital and therefore seem unlikely to belong to the syndrome under discussion here The largest group of patients studied in one family "lived on a farm in a remote and mountainous part of Ireland", they refused admission to hospital and were investigated in their own home (Gibson and Harrison 1947)

In the past nitrates and nitrites have been considered harmless in themselves, but they are held to be an important indication that the water is contaminated with sewage Ammonia and other nitrogenous compounds of manure are oxidised to nitrates by soil bacteria Thus the presence of nitrates or nitrites in a sample of drinking-water suggests contamination by organic matter Theoretically it is possible for coliform organisms to be held back by the soil as water percolates through it, yet for nitrates in solution to pass into a well, in practice this rarely seems to happen coliform organisms being usually demonstrable in well waters containing nitrates

All the cases of "well water cyanosis" of which we have read have been in artificially fed young infants living in country districts, the water supply in each case has been a shallow well. Surface and subsurface contamination of shallow wells is notoriously easy, particularly in summers like that of 1950 in England, when a heavy rainfall followed twelve months' exceptional drought Probably most of the shallow wells used for drinking in this country are in private ownership This is important from a public health point of view, for the local authority has powers to test such a supply only after receipt of a specific complaint about the water To the general public the greater palatability of cold water from a well makes it more acceptable in summer than lukewarm water from the above ground storage tanks of many village supplies

Popular belief that boiling the water makes it safe is misplaced in the case of nitrate contamination, for the nitrate concentration remains unchanged Case 1 illustrates another facet of the danger When the child first became ill with diarrhœa and vomiting, a neighbour recommended that feeding should be stopped temporarily and boiled water substituted This advice, though generally unexceptionable in gastro enteritis, can only make matters worse in methæmoglobinæmia of the type under discussion here

From our experience of these two cases and from our study of accounts of similar cases we endorse the recommendation given by Taylor (1949) that nitrates should be regarded as a potentially dangerous contaminant of drinking water, and that 20 parts per million should be regarded as the highest acceptable figure in water used for preparing an infant's milk mixture Some such standard figure seems desirable, if only as a guide, for the report of clinical cases of a public health hazard is likely to be followed by requests for analysis of samples from suspected sources Thus, since "blue water babies" have become recognised, surveys of water supplies have been carried out in the Middle West of America (Johnson et al 1946, Weart 1948) In one county in Illinois more than 25% of waters from rural wells contained more than 100 parts per million of nitrate nitrogen (Weart 1948) Such a state of affairs constitutes a real threat to the infant population of the neighbourhood

SUMMARY

Two cases are reported of cyanosis from methæmoglobinæmia in infancy Both children were reared in Suffolk villages, both were artificially fed, and in each case the water used to prepare the milk mixture was obtained from a shallow well In each case the well water was contaminated with coliform organisms and nitrates One child died before admission to hospital, but the other was treated by exchange blood transfusion and recovered

The cases are reported because they are believed to be the first examples in Great Britain of a syndrome which has recently become widely recognised in country districts of North America and the Netherlands The literature is briefly reviewed It seems to be acceptably established that young infants may have coliform organisms in the upper part of the intestinal tract, in such infants nitrates contaminating the drinking water may, on ingestion, be reduced by the organism to nitrites sufficiently high in the small intestine for the nitrites to be absorbed and methæmoglobinæmia to be produced

If suspected the condition is easily diagnosed The recognised treatment is the intravenous injection of methylene blue 1 or 2 *mg per kg of body weight*

The danger of nitrates in water fed to babies merits wider recognition Boiling such water does not render it safe It has been authoritatively recommended that 20 parts per million of nitrates should be regarded as the highest acceptable figure in water used for preparing an infant's milk mixture We endorse that recommendation

We are indebted to Dr Trevor Shaw and to Mr C T Dawson, Ipswich Borough Coroner, for permission to cite details of case 1, to Dr R H. Clayton, M.O.H., Bury St Edmunds, for investigating the water supply in case 2, to Dr Eric Wood and Dr S Greenburgh, public analysts of Norwich and of Cambridge, for their reports on the water supplies of cases 1 and 2 respectively Dr Wood has given us much information on matters that lie in his field rather than ours Mr S T Ryder, F.I.M.L.T., estimated the methæmoglobin in case 2

Since this paper was written, a third case, from another part of Suffolk, has been admitted under one of us This

Follow up —The child has been seen in the follow up clinic since discharge, he is healthy, without cyanosis, and without detectable methæmoglobinæmia

The suspicion that this was a case of "well water cyanosis" was entertained but could not be confirmed until after the transfusion treatment was completed Next day the mother was questioned She explained that the baby's feeds were made up by boiling water obtained by a bucket from a shallow well in the yard of a public house opposite her cottage Analysis of this water showed it to be "heavily contaminated with coliform organisms" (probable number of *Bact coli* in excess of 180 per 100 ml) and to contain 95 parts per million of nitrates Nitrites were absent The source was a simple dug well 42 ft deep containing 20 ft of water at the time of analysis Also available to this group of cottages (but not used by most of the inhabitants for drinking) was water from a deep bore supply to a storage tank. This water (considered unfit for drinking by the analyst as a result of his findings) did not contain nitrates though contaminated, but to a less degree, with coliform organisms

HISTORICAL REVIEW

Though enterogenous cyanosis holds its place in the classification of causes of cyanosis, methæmoglobinæmia sufficient to discolour the skin seems to be rare nowadays in intestinal disorders Henstall and Dameshek (1936) reported 1 case and collected 36 others previously published The early sulphonamide preparations provided a new example of cyanosis of this type Bismuth subnitrate, formerly used in the treatment of infantile gastro enteritis, has been given up because of this danger (Roe 1933)

Methæmoglobinæmia may follow the absorption of many chemicals besides sulphonamides and bismuth subnitrate, such as aniline and its derivatives acetanilid and phenacetin, nitrophenol, potassium chlorate, and various nitrites Occasional cases of methæmoglobinæmia in infants have been reported in which none of these chemicals was incriminated Such cases have been described as "idiopathic" methæmoglobinæmia (Schwartz and Rector 1940, Stahr 1941) Comly (1947) reported two such cases, but he recognised that nitrates contaminating the well-water used to make up the feeds were the cause of his two cases and suspected the same ætiology in several other cyanosed infants whose colour improved as soon as the water supply was changed Diarrhœa was a feature of Comly's cases, the conversion of ingested nitrates to nitrites he attributed to organisms present in the bowel during gastro intestinal disturbances He recognised that nitrites, but not nitrates, oxidised hæmoglobin to methæmoglobin Only young babies seemed to be affected Comly thought that the immunity of adults and older children drinking the same water was due to the relatively greater water intake in infancy

Cornblath and Hartmann (1948) investigated the mechanism of the enteric nitrate nitrite conversion by a series of in vivo experiments on infants They emphasise the point that "well water cyanosis" is limited to the first few weeks of life, when physiological gastric hypochlorhydria is greatest They showed that in such infants lower bowel organisms (*Bact ærogenes*, *Bact freundii*, and *Bact coli*) which have the property of reducing nitrates to nitrites are to be found in the upper intestine and may be grown even from saliva and stomach washings They found that the growth of these organisms was inhibited at a pH of 4 or less They showed that oral ingestion of water containing nitrate would only produce methæmoglobinæmia in infants who had a gastric juice of pH greater than 4 and nitrate reducing bacteria in the upper gastro intestinal tract Cornblath and Hartmann assume that, where gastric acidity inhibited the growth of colon organisms in the upper intestine, any ingested nitrate is absorbed harmlessly before conversion to nitrite can take place A baby aged 3 months with a transverse colostomy gave them the opportunity to demonstrate the point nicely In this child 200 mg of nitrate ion fed by mouth produced cyanosis and converted 25% of the hæmoglobin to methæmoglobin, 600 mg of nitrate ion injected into the colostomy for two days did not cause cyanosis and converted only 4% of the hæmoglobin to methæmoglobin

Methæmoglobin is a true oxide of hæmoglobin, the iron of the molecule being oxidised to the ferric form, it is only slowly broken down in the body and is too stable to be of use to the body for transport of oxygen. The cellular anoxia caused by methæmoglobinæmia depends on this, but another factor operates in the same direction Like carboxyhæmoglobin, methæmoglobin shifts to the left the oxygen dissociation curve of a specimen of blood containing it (Darling and Roughton 1942) Thus, blood containing a proportion of methæmoglobin not only has its oxygen carrying power reduced by that amount but also such oxygen as is carried by the remaining hæmoglobin is less readily ceded to the tissues.

DIAGNOSIS

The diagnosis is not difficult The onset of cyanosis in a bottle fed baby should lead to suspicion of this condition if no gross abnormality can be found on examination of the cardiovascular and respiratory systems The suspicion warrants examination of the blood A specimen of venous blood containing an appreciable quantity of methæmoglobin is chocolate brown, clearly recognisable as abnormal to the naked eye by daylight or electric light, the presence of methæmoglobin is readily confirmed spectroscopically If methæmoglobin is found, inquiry should be made about recent medicines and the water supply If the water supply is suspected, the case should be notified to the Medical Officer of Health with a request for an analysis of the drinking water In all cases to date the nitrate polluted water has been drawn from a shallow well on a farm or in a small country village

Diarrhœa and vomiting are not essential features of the syndrome, but vomiting, presumably often from cerebral anoxia, is usual Inhalation pneumonia may complicate the condition Methæmoglobin is so easily detected that, if doubt exists, its presence should be excluded before it is assumed that the cyanosis is due to pneumonia

On a priori grounds it seems that the more water that is used in preparing the feeds the more likely is methæmoglobinæmia to be produced Thus, if the water supply is contaminated by nitrates, methæmoglobinæmia is most likely in those infants fed on mixtures made up from powdered milk (because the greatest amount of water is used), evaporated milk would occupy an intermediate position, and modified cow's milk mixtures should be the safest of artificial foods Donahoe (1949) suggests that both cows and women when drinking nitrate contaminated water may secrete the nitrate ion in their milk

TREATMENT

The history of our two cases illustrates the fact that nitrate methæmoglobinæmia is a cumulative poisoning, taking some days or a week or two to develop Once the ingestion of nitrates has been stopped, the disease is self limiting The necessary change to purer water can most easily be made by admitting the infant to hospital. On admission many such infants are critically ill, and urgent treatment is called for because of the danger of continued tissue anoxia Oxygen cannot reduce the amount of methæmoglobin, the hæmoglobin may be presumed to be almost completely oxygenated. Therefore the administration of oxygen should be regarded as no more than a temporary expedient while preparations are being made for specific therapy

The intravenous injection of methylene blue in doses of 1 or 2 mg per kg of body weight is the treatment of choice In the American published reports tribute is

Full term babies in the main nurseries were discharged home as usual after an interval of 48 hours from the outbreak, but, in view of the possibility of sequelæ, they were seen every week for a month, with the exception of 2 babies who lived too far away and 2 who had been only slightly affected None of the full term babies developed any abnormal symptom, but some of the more severely affected ones had a raised reticulocyte count, particularly a fortnight after the outbreak, with normal hæmoglobin and red cell counts, which suggests that they had a compensated anæmia A typical example is a baby whose reticulocyte counts one, two, and three weeks after the outbreak were 2 1%, 3 2%, and 2 2%

Premature Babies—Two of these, each weighing 5 lb, were ready for discharge at the time of the outbreak, they were discharged and progressed normally at home Most of the other premature babies showed a reticulocytosis earlier, and to a higher level, than the full term babies, a week after the outbreak one premature baby had a reticulocyte count of 14 6%, and the smallest baby's count was 19 2%, although it had received a blood transfusion The degree of anæmia caused by the poisoning is difficult to assess in these premature infants, because they were all over a month old and already had some anæmia of prematurity, one of them had already been transfused for this before the outbreak But the fall in hæmoglobin seemed to be unexpectedly rapid, and ultimately 4 of these babies needed transfusion, the smallest baby twice The smaller premature babies concerned are still seen regularly and all but one have made uninterrupted progress, the exception being a baby who died two months after the outbreak and was found at necropsy to have ulcerative enteritis, thrombophlebitis of the superior mesenteric and portal veins, and splenomegaly with fibrosis of the Banti type

DISCUSSION

Several reports have been published of methæmoglobinæmia in the nursery from marking ink on diapers The first report was that of Rayner (1886) Kagan et al (1949) reviewed 73 cases in eight outbreaks and added 9 cases of their own

In a major outbreak in 1944 (Graubarth et al 1945), when 17 babies were affected in a nursery containing 32, certain symptoms were described which were not observed in any of our cases, including reduction in intensity of the cry, accelerated or difficult respiration, vomiting, abdominal distension, relaxed stools, jaundice, and hæmaturia There were 4 deaths, 3 being in premature babies, and 3 of the babies that died had bronchopneumonia Methylene blue was not thought to accelerate the rate of recovery

In another reported outbreak (Scott et al 1946), involving 32 babies, one premature infant died The same report describes further cases due to newly marked cloths used in washing the excoriated buttocks of 3 infants with relaxed stools, the first case to present in our outbreak was the only baby in the premature ward with sore buttocks Scott et al describe a case treated with methylene blue which completely recovered from the cyanosis within an hour

The outbreak described by Kagan et al (1949) was in a premature baby unit, 9 babies were affected, some of them considerably younger than ours, and apathy, vomiting, and anorexia were the main symptoms They suggest that the babies having ascorbic acid as a routine may have been protected from the toxic effects of the dye Bronchopneumonia followed in 5 of their 9 cases, at intervals of two to four weeks from the methæmoglobinæmia, whereas none of the unaffected babies in the ward had pneumonia in the same period.

CONCLUSIONS

The risk of absorption of marking ink should be more widely known and more readily considered in cases of cyanosis in infants We were fortunate to discover the toxic factor so soon, and, in view of the number of premature infants involved, we were lucky to have so few complications

To prevent similar outbreaks the makers of the marking ink now print a warning on their bottles that marked articles, particularly infants' clothing, must be laundered before use

SUMMARY

An outbreak of methæmoglobinæmia is described, involving a premature baby unit and the nurseries of a maternity hospital

The cause was the absorption of aniline dye from marking ink on newly marked napkins which had not been laundered

I am indebted to Dr V Mary Crosse for permission to publish this paper and for help in its preparation, and to Dr H Baar and Miss A Gillanders for pathological investigations

REFERENCES

Graubarth J, Bloom C J Coleman F O, Solomon, H N (1945) *J Amer med Ass* 128 1155

Kagan B M Mirman B, Calvin J, Lundeen E (1949) *J Pediat* 34 574

Rayner, W (1886) *Brit med. J* 1 294

Scott E P Prince G E, Rotondo, C C (1946) *J Pediat* 28, 713

FAMILIAL IDIOPATHIC METHÆMOGLOBINÆMIA

VIOLET K St G BREAKEY
M D Dubl, F R C P.I.
ASSISTANT PHYSICIAN,
ROYAL BELFAST HOSPITAL
FOR SICK CHILDREN

QUENTIN H GIBSON
M.D, Ph D Belf
SENIOR LECTURER IN
PHYSIOLOGY IN THE
UNIVERSITY OF SHEFFIELD

DOUGLAS C HARRISON
D Sc Lond, Ph D Camb
PROFESSOR OF BIOCHEMISTRY IN THE QUEEN'S UNIVERSITY
OF BELFAST

ALTHOUGH familial idiopathic methæmoglobinæmia is regarded as very rare, we have been able to report seven cases in two families (Barcroft et al. 1945, Gibson and Harrison 1947) and have described their treatment with ascorbic acid Later Gibson (1948) concluded that a deficiency of diaphorase I (co enzyme factor I) in the erythrocytes was responsible for the symptoms Evidence was presented that diaphorase I is an essential link in the chain of oxidation enzymes which maintains the hæmoglobin in normal persons in a functional state These conclusions were necessarily based on the study of cases from only two families Two further cases have now come to our notice, and we have made tests on them which extend the experimental basis for the hypothesis already put forward The results of these investigations, together with the successful treatment of the patients, are reported here

A further reason for publishing details of these cases of methæmoglobinæmia is the current interest in cyanotic children We have now investigated nine cases from the north of Ireland, and it seems possible that familial methæmoglobinæmia is not so exceedingly rare as is generally believed. The differential diagnosis (by clinical and spectroscopic methods) between this condition and congenital cyanotic cardiac disease may thus be of more than academic importance

TWO CASES

Case 1—A boy, aged 6 years, was brought to the cardiac department of the Royal Belfast Hospital for Sick Children on Feb 14, 1950 with a request from his mother for "the blue baby operation" He had been blue since birth, and case illustrated the therapeutic efficacy of intravenous methylene blue

REFERENCES

Arnold D P, Alford K M (1948) *J Pediat* **32** 113
Comly H H (1947) *J Amer med Ass* **129** 112
Cornblath M., Hartmann, A F (1948) *J Pediat* **33** 421
Darling, R C Roughton F J W (1942) *Amer J Physiol* **137** 56
Deeny J Murdock E T Rogan, J J (1943) *Brit med J* i, 721
Donahoo, W E (1949) *Pediatrics* **3** 308
Ferrant M. (1946) *J Pediat* **29** 585
Gibson, Q H, Harrison D C (1947) *Lancet* ii 911
Harrison G A (1947) Chemical Methods in Clinical Practice London
Hartmann A F, Perley, A M, Barnett, H L (1938) *J clin Invest*, **17** 699
Henstall H H Dameshek W (1936) *Ibid*, **15**, 464
Johnson G Kurz A Cerny, J Anderson, A, Matlock, G (1946) *J Iowa St med Soc* **36**, 4
Lancet (1948) i 956
Roe H E (1933) *J Amer med Ass* **101** 352
Schwartz A S, Rector, E J (1940) *Amer J Dis Child* **60**, 652
Stahr R (1941) cited by Comly (1947)
Taylor, E W (1949) The Examination of Water and Water Supplies London
Woart J G (1948) *Illinois med J* **93** 131
Wendel W B (1939) *J clin Invest* **18** 179

EPIDEMIC OF ANILINE METHÆMOGLOBINÆMIA IN NEWBORN BABIES

BETTY E HOWARTH
M B Lond, M R C P, D C H
PÆDIATRIC REGISTRAR, SORRENTO MATERNITY HOSPITAL AND PREMATURE BABY UNIT, BIRMINGHAM

ON Easter Tuesday, 1950, one of the babies in the Sorrento Premature Baby Unit was reported to be having a cyanotic attack after her 10 P M feed This baby, who was 7 weeks old and weighed $4^1/_2$ lb (birth weight 2 lb 15 oz), was accustomed to take her feeds well and was not subject to cyanotic attacks She was afebrile, her stools were normal, and there was no evidence of infection or other abnormal physical sign apart from the cyanosis She was treated as a case of vomit inhalation—by posture, aspiration, oxygen, and prophylactic penicillin

Two hours later another premature baby was found to be cyanosed after the midnight feed This baby, who weighed 2 lb 13 oz at 4 weeks (birth weight 2 lb 3 oz), still required some tube feeds and was liable to have cyanotic attacks after them, so she was treated in the usual way It was noted that the first baby, after two hours in an oxygen tent, had not recovered from her cyanosis but seemed in no way distressed

Daylight next morning revealed several more blue babies in the Premature Unit, 3 were mildly affected, 4 more severely, and the 2 who had been in oxygen tents all night were now deeply cyanosed In the severe cases the babies were a slaty grey blue colour, they were restless and looked rather anxious but cried lustily on examination and took their feeds as readily as usual There was no evidence of infection in any case, and respiration rates and temperatures were normal

The blue babies were segregated from the rest and specimens of blood were sent for spectroscopic examination to find out whether the cyanosis was caused by methæmoglobin or sulphæmoglobin

At this point reports of other cyanosed babies began to come in from the nurseries of the main hospital By midday 23 cases had appeared in the whole hospital 9 in the premature unit, 4 on each floor of the main block, and 6 in a separate ward There remained two wards in which there were no cases, one being the isolation ward and the other a separate block well away from the main hospital All the affected babies seemed well, apart from their colour, and were feeding normally

Various precautionary measures were taken, no mothers and babies were discharged from the hospital, no cases were admitted from the labour ward to an affected ward, and all the babies attending the premature baby follow up clinic were seen in the antenatal clinic and not allowed into the premature block

In the early afternoon a discussion of the possible toxic factors was held

Water was unlikely because, though all the wards had the same water supply, two had no cases of cyanosis

Feeds were excluded because most of the full term babies were fully breast-fed and the affected premature babies were taking several different feeds

Drugs There had been no recent new issue of any of the vitamin preparations which were the only drugs in common use in all the wards

Linen All the hospital linen is laundered together, so it could be a source of some common toxin

At this point the pædiatrician recalled a chance remark made to her earlier in the day—that newly marked linen might have been issued for use before being laundered This led at once to the discovery that, owing to a shortage of napkins when the laundry was closed for Easter, new unwashed napkins had been issued to the wards on Easter Tuesday, they had been marked during the previous week

Some of the affected babies were thereupon examined and found to be wearing brand new napkins marked "SORRENTO" with thick marking ink in letters often over an inch high The wards with no blue babies were the ones which had not run short of napkins over Easter and were still using an old issue All the new napkins were immediately collected and the mothers of the blue babies were told the full details of what had happened

A sample of the marking ink was sent to the city analyst, who reported that it contained aniline black, or a similar dye, dissolved in aniline

TREATMENT

The laboratory reported methæmoglobin absorption bands on spectroscopy of the blood from 4 of the most severe cases The babies were then divided into three groups, each containing premature and mature babies and, so far as possible, babies with different degrees of cyanosis

The *first group*, of 4 babies (3 premature and 1 full term), received a 1% solution of methylene-blue intravenously, the dose for the premature babies being 1 ml and for the mature baby 2 ml

The *second group*, of 9 babies (3 premature and 6 full term), were given 50 mg ascorbic acid by mouth before each feed (The hospital routine is to give to all premature babies 100 mg of ascorbic acid daily from the first week of life)

The *third group*, of 10 babies (3 premature and 7 full term), were left without treatment as controls

It had been intended to treat more babies with methylene blue, but by the time the later ones could be treated they had already improved so much after removal of the affected napkins that venepuncture was no longer justified, and they were therefore included in the control group

The smallest premature baby was given both methylene blue and ascorbic acid, because she was very severely affected and her weight (2 lb 13 oz) also made intensive treatment advisable

PROGRESS AFTER TREATMENT

The babies treated with methylene blue intravenously responded dramatically, improvement could be seen within a few minutes of the end of the injection, and the babies' appearance was completely normal within an hour The ascorbic acid and control groups recovered at about equal rates but more slowly than the methylene-blue group

Specimens of blood collected first thing next morning from babies in all three treatment groups showed no methæmoglobin band on spectroscopy Some specimens of urine collected twenty four hours after the outbreak contained *p* amidophenol, a breakdown product of aniline can be safely used in cases in which unmodified E C T would be contra-indicated. It has the advantage of not producing confusion

I am indebted to Dr Thomas Beaton, physician superintendent, St James Hospital, Portsmouth, for permission to carry out the original investigations and to Dr J Hamilton and Dr H. B C Sandiford, consultant anæsthetists, for technical advice and assistance

REFERENCES

Alexander L (1950) *Amer J Psychiat* 107 241
Gellhorn E (1950) *Proc R. Soc Med* 42 55
Heath, R G, Norman E C (1946) *Proc Soc exp Biol*, N Y 63 496
Leduc S (1902) *C.R. Acad. Sci Paris* 135 199
Liberson W T (1947) *Digest Neurol. Psychiat* 15 72
— Wilcox, P H (1945) *Ibid* 13 292
Milligan W L (1948) *Proc. R Soc. Med* 41 580
Paterson, A. S (1948) Lecture to Society of Psychiatry Brussels.
— Milligan W L (1947) *Lancet* ii 198
Rees, L (1949) *J ment Sci* 95, 162
Tietz, E B (1947) *J nerv ment. Dis* 106 150
— Thompson, G N van Harreveld A., Wiersma C A. G (1946) *Ibid* 103 144
van Harreveld, A. (1937) *Arch. Neerl. Physiol.* 22, 84
— Dandliker W B (1945) *Proc Soc exp Biol.*, N Y 60 391
— Frostig J P Resnick, S. Tyler D B, Wiersma, C A G (1944) *Arch. Neurol Psychiat* 51 232
— Kok D J (1934) *Arch. Neerl Physiol.* 19 24
Wilcox, P H (1946) *Dis Nerv Syst* 7 201
— (1948) Progress in Neurology and Psychiatry New York p 567

VITAMIN-B DEFICIENCIES AFTER GASTRIC OPERATIONS

Richard Welbourn
M.B Camb, F R C S
RESEARCH ASSISTANT, DEPARTMENT OF SURGERY, UNIVERSITY OF LIVERPOOL

Robert Hughes
M.D Lpool, M.R C.P
ASSISTANT PHYSICIAN, UNITED LIVERPOOL HOSPITALS

Charles Wells
M.B Lpool F.R C S
PROFESSOR OF SURGERY IN THE UNIVERSITY OF LIVERPOOL

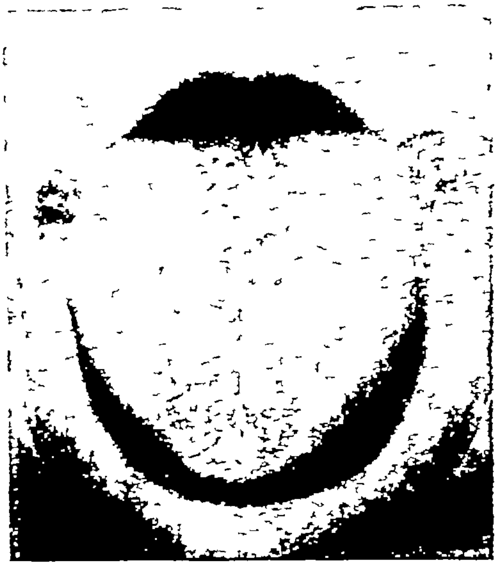
In our studies of the results of gastric operations (Welbourn 1950, Wells and Welbourn 1951) we have been impressed by the number of patients who developed symptoms and signs of vitamin-B deficiency In a few —e g, cases 3 and 8 below—the manifestations of deficiency appeared while the patient was on a peptic-ulcer diet, but in most patients they did not develop until a year or more after operation.

The possibility of vitamin B deficiencies as sequelæ is no contra indication to surgery in suitable cases, for as a rule the syndromes are easily recognised and readily corrected in their early stages Subtotal gastrectomy is one of the most satisfactory routine operations of general surgery (Wells and Brewer 1948), and besides relieving the primary condition it often greatly improves the patient's nutrition—for example, in one reported case, pellagra resulting from carcinoma of the stomach was cured by gastrectomy (Bean et al 1944) Nevertheless, unsuspected deficiencies of vitamin B are probably causing a great deal of unnecessary disability in patients whose gastrectomies would otherwise be wholly successful.

In the hope of drawing attention to the various forms that postoperative B complex deficiency may take, we are describing the manifestations we have encountered, with some illustrative cases The diagnoses have been established by the clinical features, the response to specific therapy, and the results of biochemical tests, the details of which will be published separately

RIBOFLAVINE DEFICIENCY

The syndrome we have seen most often is hyporiboflavinosis, either alone or associated with other deficiencies Browne and McHardy (1943) described 2 cases of this syndrome following gastrectomy, and 4 cases were reported by Adlersberg and Hammerschlag (1947) the superficial glossitis which Gordon Taylor et al. (1929) noted after gastrectomy was also probably caused by riboflavine deficiency The main lesions (see figure), which were described by Sebrell and Butler (1939) and by Kruse et al. (1940) are



Superficial glossitis and angular stomatitis typical of riboflavine deficiency, developing after subtotal gastrectomy

(1) Cheilosis (peeling of the lips)
(2) Angular stomatitis (transverse fissures at the corners of the mouth)
(3) Superficial glossitis

These are not necessarily all present at the same time Other features, such as dermatitis of the nasolabial folds and scrotal or vulval dermatitis, have not been prominent in the cases we have seen It has not been possible to have our patients examined routinely by slit lamp microscopy for corneal vascularisation, but this lesion was found in case 8

The following 2 cases are typical examples of riboflavine deficiency

Case 1 —A housewife, aged 50, had had dyspepsia due to a chronic duodenal ulcer for many years The ulcer remained active in spite of medical treatment Subtotal gastrectomy was performed in 1942 with an excellent result, except for occasional slight bilious vomiting but a year or so after the operation she began to have cracks at the corners of her lips and a sore tongue, which persisted.

On examination (Oct 2 1950) slight peeling of the lips and angular stomatitis were found The tip of the tongue was red. A blood film was normal, and Hb was 100% (14 8 g per 100 ml.)

Treatment was with riboflavine 3 mg by mouth t d.s.

Progress —The mouth lesions healed completely in two weeks and riboflavine was stopped after five weeks.

Follow-up —The mouth lesions remained healed on Feb 12 1951 (For further details see table)

Case 2 —A seaman, aged 42 had had a duodenal ulcer with dyspepsia intermittently since youth his occupation prevented him from following an ulcer régime Subtotal gastrectomy had been done in 1947 with an excellent result and he had returned to sea. At first his only symptoms were slight nausea and bilious regurgitation after a large meal, but for the past two months he had had a sore tongue ("feels as if surface has gone') and had been getting worse

On examination (June 2 1950) his tongue was smooth and red in the anterior two-thirds, with prominent fungiform papillæ A blood-count showed red cells 3,600,000 per c.mm Hb 58% (8 6 g per 100 ml), a film showed hypochromia.

Treatment was with riboflavine 3 mg daily by mouth.

Progress —The condition continued to deteriorate for about two weeks and angular fissures appeared it then suddenly started to improve On June 29 there was no soreness or other findings and agrees with the view generally held that familial methæmoglobinæmia is inherited as a recessive character

SUMMARY

Two cases of familial idiopathic methæmoglobinæmia are described

The erythrocytes showed an abnormally low capacity to reduce methæmoglobin in the presence of glucose or lactate

The hæmolysed cells were assayed for activity of diaphorase I (co enzyme factor I), and shown to be deficient as compared with normal controls

The patients were treated successfully with methylene blue and ascorbic acid

REFERENCES

Baltzan D M Sugarman, H (1950) *Canad med Ass J* **62**, 348
Barcroft H Gibson Q H Harrison, D C (1949) Hæmoglobin Barcroft Memorial Symposium London, p 223
— — — McMurray J (1945) *Clin Sci* **5** 145
Eder H A Finch C McKee R W (1949) *J clin Invest* **28**, 265
Evelyn K A Malloy H T (1938) *J biol Chem* **126** 655
Fishberg, E H (1948) *Ibid*, **172** 155
Gibson Q H (1948) *Biochem J* **42** 13
— Harrison D C (1945) *Ibid*, **39**, 490
— — (1947) *Lancet*, ii 941

NON-CONVULSIVE STIMULATION THERAPY

A NEW PSYCHIATRIC TREATMENT

W LIDDELL MILLIGAN
M D, B Sc Glasg
CONSULTANT PSYCHIATRIST, ST GEORGE'S HOSPITAL, MORPETH ; LATE DEPUTY PHYSICIAN SUPERINTENDENT, ST JAMES' HOSPITAL, PORTSMOUTH

SINCE the inception of electroconvulsive therapy (E C T), various attempts have been made to reduce the severity of the convulsion by using different types of current or by altering their wave form (Liberson 1947, Wilcox 1946, Liberson and Wilcox 1945)

Wilcox (1948) describes the Reiter apparatus which gives "modulated brief spiked impulses", but the technique is somewhat complicated, and, unless an initial convulsion is induced, is unpleasant to the patient (Alexander 1950)

Electronarcosis, first described by Leduc (1902) and developed by van Harreveld (1934, 1937, 1944, 1945), was finally proved clinically feasible by Tietz (1946) A modification in the onset of the convulsion was described by Tietz (1947) and a further advance was recorded by Paterson (1948) and Milligan (1948) This indicated that it was possible to produce a smooth convulsion in which the clonic stage is completely masked Some workers believe that electronarcosis could be produced without preliminary convulsion, and investigations are proceeding, but it seems likely that the apparatus will be elaborate

My own effort to devise a form of electrical treatment of a non convulsive type began in 1947 after Heath and Norman (1946), using 8 mm electrodes, had indicated the probability that a convulsion is not essential in order to gain benefit from electric therapy They attributed the benefit to hypothalamic stimulation, and this is supported by Gellhorn (1950)

To study the effects of a current of low milliamperage, a simple electrical device was constructed at St James Hospital, Portsmouth Using 50 cycle alternating current, this machine gave an output of 0–30 mA Applying an E C T headband to my head, I noted that at 1 mA a slight pricking sensation was felt below the electrodes As the current was increased, the sensation became more severe and seemed to extend in area until at 10 mA it became moderately painful A reddish flicker appeared before the eyes (consistent with 50 cycle frequency) and occasional blue radiating lines were observed After a few minutes, one could become quite used to the sensation and it was possible to read The current level could then be raised slightly, but the absolute maximum was 15 mA, when the burning sensation became almost unbearable It was therefore obvious that for clinical purposes 10 mA was the maximum

A series of depressed patients—mainly elderly—were treated by passing a current of 8–10 mA for one to two hours No striking results were anticipated with such a low current, but though really deep depressions remained unaltered, some of the more moderate types were relieved and several cases of senile anxiety and agitation were benefited These reactions gave rise to the hope that much more might be achieved if a higher level of current could be employed, but obviously this required a general anæsthetic Inspiratory stridor presented the main difficulty, and intravenous thiopentone and tubocurarine eventually proved to be the most successful combination, when the current did not exceed 90 mA, 10–15 mg of curare was sufficient, but above this level full curarisation and passage of an endotracheal tube was necessary

Using a standard time of fifteen minutes, the effect of varying milliamperage levels was tried on a series of patients in whom the main symptom was depression Thus, currents of 50, 70, 85, and 110 mA were employed, ten patients being treated in each case The most consistent results were obtained at 85 mA and this level was adopted for all subsequent treatments

Technique—The machine used is the Shotter Rich model described by Paterson and Milligan (1947), except that the electrodes are of special construction They consist of silver gauze circles, 2 in in diameter, mounted on 'Sorbo' rubber and incorporated in a rubber headband Electrocardiograph contact paste is used

The patient is given atropine gr $^{1}/_{75}$ by injection and 'Seconal' gr $1^{1}/_{2}$ by mouth, half an hour before treatment As no convulsion occurs, precautions are merely those advocated for general anæsthesia, except that it is advisable to remove metal objects from the hair The patient need not leave his own bed, and, as there is no sound save that of deepened respiration, the treatment can if necessary be carried out in a ward behind screens Thiopentone (0 6–0 8 g) and tubocurarine (10–15 mg) are injected intravenously, and, when the patient loses consciousness, the headband is applied The current is slowly raised to 85 mA (in two to three seconds) and if the correct amount of tubocurarine has been given the patient begins to breathe The only indication that the current is passing is a slight spasm of the facial muscles, the rest of the musculature being atonic In some cases it is helpful to stimulate respiration by increasing the current level to 110 mA and dropping it rapidly to 85 mA 'Carbogen' inhalation should be given, but this can be discontinued after a few minutes The current level is reduced to zero after fifteen minutes and the patient usually awakens about half an hour later Complaints of headache are uncommon' and patients who have experienced nausea and vomiting after E C T show no ill effects following treatment By connecting pairs of electrodes in series it is possible to treat two or even three patients simultaneously

Physiological Concomitants—The reactions are similar to those described by Rees (1949) in electronarcosis, except that the effect on the cardiovascular system is less The average increase in blood pressure is 20–30 mm Hg systolic and 10–15 mm Hg diastolic Lymphocytosis and rise in blood sugar are comparable to those following electronarcosis

Thirty patients suffering from depression have received this treatment, with improvement in each case An average of 10–12 treatments were required, the response on the whole being less rapid than with E C T On the other hand, agitation was usually relieved after one or two treatments and early relapse was observed less often than with E C T

Fifteen paraphrenics responded well, the most agitated and vehement becoming calmer and taking less interest in their delusions, in ten of these cases a complete remission followed Paranoid schizophrenia seemed to respond particularly well, good remissions resulting in eight out of ten patients treated An average of 15 treatments was required in the paraphrenic and schizophrenic groups

The method may seem cumbersome compared to E C T, but it is less likely to cause complications and can be safely used in cases in which unmodified E C T would be contra-indicated It has the advantage of not producing confusion

I am indebted to Dr Thomas Beaton, physician superintendent, St James Hospital, Portsmouth, for permission to carry out the original investigations, and to Dr J Hamilton and Dr H B C Sandiford, consultant anæsthetists, for technical advice and assistance

REFERENCES

Alexander L (1950) *Amer J Psychiat* 107 241
Gellhorn E (1950) *Proc. R. Soc Med* 43 55
Heath R G, Norman E C (1946) *Proc. Soc. exp Biol N Y* 63 496
Leduc S (1902) *C.R Acad. Sci Paris*, 135 199
Liberson, W T (1947) *Digest Neurol. Psychiat* 15, 72
— Wilcox, P H (1945) *Ibid* 13 292
Milligan W L (1948) *Proc R Soc Med* 41 580
Paterson A S (1948) Lecture to Society of Psychiatry Brussels.
— Milligan W L (1947) *Lancet* ii 198
Rees L (1949) *J ment Sci* 95, 162
Tietz E B (1947) *J nerv ment. Dis* 106, 150
— Thompson G N van Harreveld A., Wiersma C A. G (1946) *Ibid* 103 144
van Harreveld, A. (1937) *Arch. Neerl. Physiol* 22, 84
— Landliker W B (1945) *Proc Soc exp Biol N Y* 60 391
— Frostig J P Resnick S. Tyler D B Wiersma C A G (1944) *Arch Neurol Psychiat* 51 232
— Kok D J (1934) *Arch. Neerl Physiol* 19 24
Wilcox P H (1946) *Dis Nerv Syst* 7 201
— (1948) Progress in Neurology and Psychiatry New York p 567

VITAMIN-B-DEFICIENCIES AFTER GASTRIC OPERATIONS

RICHARD WELBOURN
M.B Camb, F.R C S
RESEARCH ASSISTANT, DEPARTMENT OF SURGERY, UNIVERSITY OF LIVERPOOL

ROBERT HUGHES
M D Lpool, M.R C.P
ASSISTANT PHYSICIAN, UNITED LIVERPOOL HOSPITALS

CHARLES WELLS
M.B Lpool F.R C S
PROFESSOR OF SURGERY IN THE UNIVERSITY OF LIVERPOOL

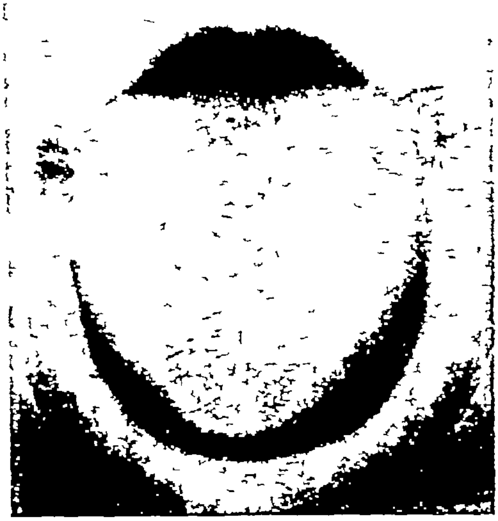
IN our studies of the results of gastric operations (Welbourn 1950, Wells and Welbourn 1951) we have been impressed by the number of patients who developed symptoms and signs of vitamin-B deficiency In a few —e.g, cases 3 and 8 below—the manifestations of deficiency appeared while the patient was on a peptic ulcer diet, but in most patients they did not develop until a year or more after operation.

The possibility of vitamin B deficiencies as sequelæ is no contra indication to surgery in suitable cases, for as a rule the syndromes are easily recognised and readily corrected in their early stages Subtotal gastrectomy is one of the most satisfactory routine operations of general surgery (Wells and Brewer 1948), and besides relieving the primary condition it often greatly improves the patient's nutrition—for example, in one reported case, pellagra resulting from carcinoma of the stomach was cured by gastrectomy (Bean et al. 1944) Nevertheless, unsuspected deficiencies of vitamin B are probably causing a great deal of unnecessary disability in patients whose gastrectomies would otherwise be wholly successful.

In the hope of drawing attention to the various forms that postoperative B complex deficiency may take, we are describing the manifestations we have encountered, with some illustrative cases. The diagnoses have been established by the clinical features, the response to specific therapy, and the results of biochemical tests, the details of which will be published separately

RIBOFLAVINE DEFICIENCY

The syndrome we have seen most often is hyporiboflavinosis, either alone or associated with other deficiencies Browne and McHardy (1943) described 2 cases of this syndrome following gastrectomy, and 4 cases were reported by Adlersberg and Hammerschlag (1947), the superficial glossitis which Gordon Taylor et al. (1929) noted after gastrectomy was also probably caused by riboflavine deficiency The main lesions (see figure), which were described by Sebrell and Butler (1939) and by Kruse et al. (1940) are



Superficial glossitis and angular stomatitis typical of riboflavine deficiency developing after subtotal gastrectomy

(1) Cheilosis (peeling of the lips)
(2) Angular stomatitis (transverse fissures at the corners of the mouth)
(3) Superficial glossitis

These are not necessarily all present at the same time. Other features, such as dermatitis of the nasolabial folds and scrotal or vulval dermatitis, have not been prominent in the cases we have seen It has not been possible to have our patients examined routinely by slit lamp microscopy for corneal vascularisation, but this lesion was found in case 8

The following 2 cases are typical examples of riboflavine deficiency

Case 1 —A housewife aged 50, had had dyspepsia due to a chronic duodenal ulcer for many years The ulcer remained active in spite of medical treatment Subtotal gastrectomy was performed in 1942 with an excellent result, except for occasional slight bilious vomiting, but a year or so after the operation she began to have cracks at the corners of her lips and a sore tongue, which persisted

On examination (Oct 2 1950) slight peeling of the lips and angular stomatitis were found The tip of the tongue was red. A blood film was normal and Hb was 100% (14 8 g per 100 ml)

Treatment was with riboflavine 3 mg by mouth t d.s.

Progress —The mouth lesions healed completely in two weeks and riboflavine was stopped after five weeks

Follow up —The mouth lesions remained healed on Feb 12, 1951 (For further details see table)

Case 2 —A seaman, aged 42, had had a duodenal ulcer with dyspepsia intermittently since youth his occupation prevented him from following an ulcer régime Subtotal gastrectomy had been done in 1947 with an excellent result and he had returned to sea. At first his only symptoms were slight nausea and bilious regurgitation after a large meal but for the past two months he had had a sore tongue ('feels as if surface has gone ') and had been getting worse

On examination (June 2 1950) his tongue was smooth and red in the anterior two thirds, with prominent fungiform papillæ A blood count showed red cells 3,600,000 per c.mm , Hb 58% (8 6 g per 100 ml), a film showed hypochromia

Treatment was with riboflavine 3 mg daily by mouth.

Progress —The condition continued to deteriorate for about two weeks, and angular fissures appeared, it then suddenly started to improve On June 29 there was no soreness or other symptom of hypovitaminosis The tongue was less smooth and less red Treatment with riboflavine was continued and ferrous sulphate gr 6 t d s by mouth started

Sept 5 improvement was maintained The tongue was normal, apart from considerable œdema of its margin Treatment with riboflavine and iron was continued

Sept 29 improvement was maintained The œdema of the tongue had nearly gone Hb was 101% (14 9 g per 100 ml) and a film was normal Treatment with riboflavine was continued, but the iron was stopped

Feb 5, 1951 the tongue was normal (for further details see table)

We have seen patients with apparently similar lesions who have not responded to riboflavine To many of them we have also given nicotinic acid, pyridoxine, pantothenic acid, iron, and 'Marmite' (Lindeboom 1950), but in case 8 only was there any improvement, and this seemed to be due to pyridoxine We have another patient—a man—who has developed glossitis, cheilosis, and dysphagia (a Plummer Vinson syndrome) since his gastrectomy He has no organic lesion in the throat, his peripheral blood is normal, and he has not responded to riboflavine, nicotinic acid, or 'Becosym' * by mouth The cause of the lesions in these patients remains obscure

ANEURINE (VITAMIN B_1) DEFICIENCY

We have seen several syndromes which we believe to be due to aneurine deficiency, but have seen no case of cardiac failure due to it

Established Peripheral Neuritis

Cases 6 and 8 (see below) had peripheral neuritis and other lesions In the following case peripheral neuritis had developed before any operation was done on the stomach, but it had progressed, and the nutritional state as a whole deteriorated, after gastrectomy Although megaloblastic pernicious anæmia ultimately developed, the neurological signs were more consistent with peripheral neuritis than with subacute combined degeneration of the cord

Case 3 —A housewife, aged 53, had been healthy in 1943, when she weighed *10* stone and was working actively At this time she had first noticed symptoms of duodenal ulceration with stenosis By 1946 she had atrophic gastritis and histamine fast achlorhydria, and had developed a deficiency state consisting of (1) severe iron deficiency anæmia (Hb 20% (3 g per 100 ml), red cells 1,500,000 per c mm , marrow probably hypoplastic) , (2) cheilosis, angular fissures, glossitis, and stomatitis , (3) pins and needles in the arms and legs , hyperæsthesiæ of the soles , ankle jerks sometimes present and sometimes absent , and impaired vibration sense in the legs , (4) œdema of the ankles (serum proteins 5 5 g per 100 ml) , and (5) loss of 4 stone in weight Iron, liver, and injections of unspecified vitamin had caused some improvement In October, 1947, when we first saw her, she had had an exploratory laparotomy, a gastro enterostomy and an entero anastomosis, but continued to have pain and vomiting, and was considered to have a stomal ulcer and a partial obstruction

Operations —Subtotal gastrectomy was done on Oct 24, 1947 The stoma was thickened, but no organic obstruction was found After operation the pain was relieved, but vomiting continued, and two further operations for chronic small bowel obstruction were done in the next three years

Progress and Treatment —There was no real improvement, and the intake of food became greatly reduced The deficiency state progressed steadily The anæmia became pernicious in type within a year of gastrectomy (Hb 76% (11 2 g per 100 ml) red cells 2,510,000 per c mm , colour index 1 51, marrow megaloblastic) and responded to liver injections The mouth lesions responded to treatment with vitamin B complex The nervous lesions progressed Pins and needles continued, but stopped temporarily after injections of aneurine Walking became very difficult, the ankle jerks and abdominal reflexes disappeared completely, the pupils became unequal, and gross Rombergism developed The œdema disappeared temporarily after aneurine injections The serum protein level was 5 9 g per 100 ml on one occasion when œdema was present. Another stone in weight was lost, and the patient became much emaciated Diarrhœa with steatorrhœa (70% absorption) developed

Follow up —In December, 1950, the patient was still alive but had moved to another district

Incipient Peripheral Neuritis

It has been observed (Spillane 1947) that, in countries in which beriberi is endemic, some people experience symptoms—e g , tingling in the extremities, muscle cramps, and a feeling of heaviness in the limbs—without developing any objective signs of neuritis These symptoms are also common in the earliest stages in those who develop frank beriberi (Smith 1946) Cases 3 and 8 had symptoms of this type for some years before more serious trouble developed We have seen several other patients who have developed these symptoms, and they have usually been relieved by aneurine In none of them have reflexes been lost or sensation diminished , but, if they had not been treated, we believe that they might well have developed frank peripheral neuritis Hyporiboflavinosis has been seen in some of these patients

Muir (1949) records a similar condition "It was found that many patients following gastrectomy suffered from painful legs and not a few of these showed œdema of the ankles " They were rapidly cured with aneurine *His cases differ from ours in that some of them* had areas of hyperæsthesia and diminished and unequal tendon jerks Further, his cases were seen within a year of operation, whereas few of ours developed symptoms until after this period

Cases 4 and 5 are typical of this group Note the time relations between the neuritic symptoms and the vitamin therapy It is clear that in both cases the symptoms were relieved when aneurine was given Other symptoms—e g , "dumping," bilious vomiting, and fatigue—were not influenced by vitamin therapy The patients were not told which symptoms were likely to improve

Case 4 —A *man*, aged 49, had had a duodenal ulcer for 29 years Subtotal gastrectomy had been done on Jan. 6, 1948, with a good result, apart from a mild "dumping syndrome " (fullness, fatigue, and nausea) and flatulence after large meals These had practically disappeared in 2½ years The patient had been hypertensive (190/100 mm Hg) for ten years, and thoracolumbar sympathectomy was done to relieve severe frontal headaches and giddiness The symptoms were relieved, but the blood pressure was not lowered, by the first stage of the operation

On examination on March 9, 1949, the patient complained of dead fingers and cramps in the legs He had cheilosis, slight angular fissures, and glossitis Nothing abnormal was detected in his nervous system

Treatment —On March 23, vitamin treatment was begun with '*Benerva Co*' † tab *3 t d s* by mouth

Progress —On April 28, 1949, the paræsthesiæ were less and the mouth lesions healed By May 23, 1949, the paræsthesiæ had gone, and the treatment was stopped

July 15, 1949 slight angular fissures were present, so the benerva was begun again

Sept 6, 1949 no symptoms or signs of hypovitaminosis were present and the benerva was stopped

March 10, 1950 the patient complained of pins and needles and numbness in hands and feet , muscle cramps in fingers and arms , intermittent peeling of lips, angular fissures, and sore tongue and lack of energy Nothing abnormal was detected in his nervous system A blood count showed red cells 4,600,000 per c mm , and Hb 96% (14 2 g per 100 ml) The serum protein level was 7 05 g per 100 ml A fat balance test showed 88 6% absorbed Radiography after a barium meal showed no significant abnormality A test meal showed achlorhydria E C G normal

Sympathectomy, on April 25, 1950, was followed by a stormy convalescence with chest complications Food intake was reduced and the patient was febrile

---

* 'Becosym' (Roche) contains aneurine 5 mg , riboflavine 2 mg , nicotinamide 20 mg pyridoxine 2 mg and calcium pantothenate 3 mg , per tablet We have usually given two tablets three times a day

† 'Benerva Co' (Roche) contains aneurine 1 mg , riboflavine 1 mg and nicotinamide 15 mg per tablet

May 18 the patient complained of very severe pins and needles, and muscle jerks at night prevented sleep, heaviness and weakness of hands Examination of his nervous system showed slight weakness of grip, but reflexes and sensation normal. Treatment was begun with intravenous aneurine 10 mg initially, followed by 3 mg daily by mouth.

May 22 slight but definite improvement

May 30 very great improvement

June 28 no symptoms of hypovitaminosis

July 6 no symptoms of hypovitaminosis. A blood count showed red cells 4,300,000 per c.mm., and Hb 89% (13 2 g per 100 ml) A blood film showed slight hypochromia and anisocytosis. The serum protein level was 5 85 g per 100 ml The treatment with aneurine 3 mg by mouth daily was continued and treatment with exsiccated ferrous sulphate gr 6 t d.s. by mouth begun.

Oct 5 no symptoms of hypovitaminosis and much more energy than previously Hb 96% (14 2 g per 100 ml.) Blood film normal. Serum protein 6 4 g per 100 ml. Treatment with aneurine was continued, but the iron was stopped. (For further details see table)

Case 5—A housewife, aged 61 had had a duodenal ulcer for eighteen years and cholelithiasis. Subtotal gastrectomy and cholecystectomy had been done on March 17 with a good result. She had a severe "dumping syndrome" (fullness and fatigue) after meals, and bilious vomiting, but felt very much better than before operation. For three years after the operation she had no teeth or dentures.

On examination on March 3, 1949, she complained of pins-and needles in her hands and feet, angular stomatitis, and glossitis. No abnormality was observed in her nervous system.

Treatment and Progress—On July 8, 1949, in addition to her other symptoms she complained of fatigue Her hæmoglobin was 80% (11 8 g per 100 ml) A blood film showed hypochromia

July 15, 1949 treatment was begun with benerva co tablets 2 t d s by mouth

Aug 18, 1949 the paræsthesiæ and mouth lesions improved, but fatigue persisted The treatment was continued

Sept 23, 1949 the mouth lesions had healed, but the paræsthesiæ and fatigue persisted Hb 88% (13 g per 100 ml) The treatment was continued.

Jan 20 1950 The condition remained stationary The treatment with benerva co was continued, together with aneurine 10 mg daily by mouth and 25 mg twice weekly by intramuscular injection.

March 24 the paræsthesiæ were much less, and fatigue less The treatment was continued

April 25 no paræsthesiæ or mouth lesions, but fatigue persisted Hb 80% (11 8 g per 100 ml) The benerva co was continued but the extra aneurine was stopped, and treatment with exsiccated ferrous sulphate gr 6 t d.s by mouth was started.

June 2 fatigue persisted Hb 84% (12 4 g per 100 ml) Serum protein 5·8 g per 100 ml. Treatment continued

Oct 10 fatigue very much improved while the patient was on holiday, but recurred when she returned home No paræsthesiæ or mouth lesions Hb 94% (13 9 g per 100 ml.) Blood film normal Treatment with iron was stopped, but benerva co continued (For further details see table)

The differential diagnosis of these cases may not be easy The symptoms must be analysed carefully and interpreted in the light of a thorough physical examination and investigations Similar symptoms have been found in some patients with osteo arthritis, cervical ribs, old osteomyelitis, Raynaud's phenomenon, and so on, and in them vitamin therapy has produced no improvement

NUTRITIONAL STATE OF PATIENTS AND FACTORS POSSIBLY AFFECTING IT VITAMIN REQUIREMENTS CALCULATED ON BASIS OF ANEURINE 0 6 MG PER 1000 NON-FAT CALORIES, RIBOFLAVINE, 0 6 MG PER 1000 TOTAL CALORIES AND NICOTINIC ACID 4 MG PER 1000 TOTAL CALORIES (B.M.A. 1950)

Case no	Nutritional data										Factors affecting nutrition												
	Sex and age (yr)	Weight (lb.)			Hæmoglobin % (Haldane)	Serum protein (g per 100 ml)	Vitamin B deficiencies				Operation done	Reasons for eating little	Daily food intake									Impaired digestion and absorption	Test-meal findings
													Calories		Aneurine (mg)		Riboflavine (mg)		Nicotinic acid (mg)			
		Before illness	Preoperative	Final postoperative			Aneurine	Riboflavine	Nicotinic acid	Other			Total	Non fat	Calculated requirement	Actual intake	Calculated requirement	Actual intake	Calculated requirement	Actual intake		
1	F 50	154	154	133	100	6 75	−	+	−	−	Subtotal gastrectomy	Bilious vomiting with big meals	1350	850	0 5	1 4	0 8	1·0	5	17		Achlorhydria
2	M 42	144	144	133	58	7 1	−	+	−	−	Subtotal gastrectomy	None	2600	1850	1 1	1·6	1 6	1 9	10	24		Achlorhydria
3	F 53	140	84	70	76 (PA)	5 5 to 5 9	+	+	−	−	Subtotal gastrectomy	Frequent vomiting	1250	750	0 4	0 7	0 7	1 0	5	7	Steatorrhœa	Achlorhydria
4	M 49	150	112	133	89	5 85 to 7 05	−	+	−	−	Subtotal gastrectomy	'Dumping' symptoms with big meals	2450	1550	0 9	1 5	1 5	1 5	10	15	Probable	Achlorhydria
5	F 61	132	84	112	67	5 8	+	+	−	−	Subtotal gastrectomy	Edentulous bilious vomiting and 'dumping' symptoms with big meals	2000	1000	0 6	0 8	1 2	1 5	8	3		Achlorhydria
6	F 60	?	?	Underweight	?	?	−	+	−	−	Partial gastrectomy	Occasional bilious vomiting	No details known								Probable	?
7	F 26	?	?		40	4 43	+	+	−	−	Vagotomy—gastroenterostomy	Very severe vomiting										?
8	F 60	168	73	105	76	5·65 to 6 81	−	+	−	? Pyridoxine	Subtotal gastrectomy	Frequent vomiting	950	600	0 4	0 5	0 6	0 6	4	2	Probable	Achlorhydria
9	M 48	?	?	Underweight	75	?	−	+	−	−	Gastroenterostomy	Poor appetite	No details known								?	Achlorhydria

Œdema

We have seen œdema of the ankles in some of our patients—e g , cases 3 and 8 All had normal exercise tolerance, heart size, and electrocardiograms, and in none of them was a serum protein level lower than 5 5 g per 100 ml found Œdema was present in some of Muir's (1949) cases after gastrectomy and it disappeared rapidly with aneurine therapy (see above)

Disturbances of Consciousness

Mental symptoms, disturbances of consciousness, and brain stem lesions may be caused by aneurine deficiency Wernicke's encephalopathy, with its classical triad of clouding of consciousness, ophthalmoplegia, and ataxia, is the best known example and it is often associated with various lesions of the stomach (Campbell and Russell 1941) The following 2 cases, occurring after gastrectomy and after vagotomy with gastro enterostomy respectively, belong, we believe, to this group Both also had the lesions of hyporiboflavinosis, and one had early peripheral neuritis Both responded rapidly to intensive therapy with vitamin B complex

Case 6 —A housewife, aged 60, had had a partial gastrectomy in 1944. The result had been good apart from occasional bilious vomiting and attacks of diarrhœa In November, 1947, she had become fretful and light-headed, and found difficulty in concentrating On Jan 8 or 9, 1948, she had suddenly lost consciousness, wandered about in a confused state, and been found lying on the floor next morning On Jan 25 there had been obvious mental disturbance, she had had grandiose ideas and been fretful and uninhibited, with faulty memory She had had a good appetite, but had continued to diet after her operation She had lost a little weight and could not walk

On examination there were slight bilateral papillœdema, slight tremor of the tongue, and hypotonia and incoördination of the limbs The knee jerks were greatly diminished and the ankle jerks absent There was slight loss of superficial sensation at the peripheries of the arms and legs The tongue was pale and smooth The blood pressure varied from 140/80 to 170/100 mm Hg The Wassermann reaction of the blood, the cerebrospinal fluid (C S F), radiography of the skull, and electrocardiograms were normal

Treatment and Progress —She was given intramuscular aneurine 5 mg a day and 'Marmite' and yeast tablets by mouth Her mental condition improved rapidly, the papillœdema disappeared, and the left knee jerk became brisk. She learnt to walk again, but with hesitancy and some ataxia She was discharged after only twelve days' treatment

Follow up —She was seen again five months later Mentally she was, if anything, rather depressed, and the reflexes and sensation in her limbs were normal

Case 7 —A woman, aged 26, had had an abdominal vagotomy in January, 1950, for a prepyloric ulcer After operation she had vomited for a week, after which she had been well for two months when she had started to vomit again

In June, 1950, she was readmitted to hospital and radiography after a barium meal suggested duodenal ileus rather than pylorospasm as the cause of the vomiting The clinical picture was complicated by an emotional upset A posterior gastro enterostomy was done on June 19

Treatment and Progress —The patient continued to vomit everything that she took by mouth, and two weeks later she became hallucinated and uncoöperative She had peripheral circulatory failure, early bilateral papillœdema, and paresis of both 3rd cranial nerves Intravenous fluids and gastric suction produced no improvement, and on July 3 she became comatose Angular fissures developed on the lips On July 4 she received aneurine 50 mg riboflavine 6 mg , and nicotinic acid 50 mg by injection, and next day her mental condition and ocular lesions were much improved Vitamin therapy was continued During the next few days, however, she developed extrarenal azotæmia and hypostatic pneumonia and became pyrexial The level of non protein nitrogen in her blood was 240 mg per 100 ml on July 10, and rose to 375 mg per 100 ml on July 12 At the same time her Hb decreased to 40% (5 9 g per 100 ml), and her serum protein level fell to 4 43 g per 100 ml. She became drowsy again but the ocular lesions did not recur She was treated with intravenous fluids, an intragastric drip of glucose and arachis oil, penicillin, and streptomycin, and transfusions of packed red cells She slowly improved, and by Aug 11 the level of non protein nitrogen in her blood was 30 mg per 100 ml and her Hb 72% (10 7 per 100 ml) Her mental condition improved considerably, and the angular fissures healed Convalescence was interrupted by an abscess in the buttock, but this was drained and was soundly healed by Oct 10, when she was discharged fit for work

PELLAGRA

Pellagra has been described in association with, and apparently secondary to, a great many pathological conditions, including peptic ulcer, carcinoma, and syphilis of the stomach The subject has been reviewed by Levy Simpson (1935) and by Bean et al (1944), who have collected from the literature and reported themselves more than 20 cases following operations of various types for peptic ulcer We have knowledge of several similar cases, but have had the opportunity of studying only two

Case 8 —A widow, aged 60, had developed ulcer dyspepsia in 1920, when she was aged 33 Previously she had been healthy, apart from a corneal ulcer, and weighed 12 stone She had had gall stones and gastric and duodenal ulcers, and undergone a cholecystectomy and four gastric operations, including a subtotal gastrectomy in 1946 About 1928 she had started to have pins and needles and cramps intermittently in the arms and legs, and constant fatigue In 1936 she had had a blow on the head, which had been followed by ? epileptic fits for some years At this time too she had developed headaches and started to have difficulty in remembering recent events Her diet had been fairly adequate up to 1946, when she had had a subtotal gastrectomy, but after this it had been greatly reduced and was deficient in nicotinic acid (see table) In addition she had vomited frequently

In June, 1947, she was thought to have a recurrent gastric ulcer, and underwent another operation No ulcer was found, but a small pyloric remnant was removed At this time she had glossitis and angular stomatitis, and her limbs were beginning to feel heavy and numb, but there were no objective signs of nerve involvement She had a mild iron-deficiency anæmia (Hb 78% (11 4 g per 100 ml)) By June, 1948, she had developed gross signs of deficiency The mouth lesions were more severe There was severe peripheral neuritis with stocking and glove anæsthesia to above the knees and elbows. Some reflexes were reduced but not absent, some were normal and others were exaggerated Position, vibration, and joint sense were reduced in the arms and absent in the legs There was gross Rombergism, and the patient could not walk. She had alternating constipation and diarrhœa and the typical skin lesions of pellagra on the arms and legs Her ankles were œdematous The anæmia had improved after treatment with iron by mouth Hb was 85% (12 6 g per 100 ml) Radiography after a barium meal showed the gastric stump to empty slowly, and a fractional test meal showed achlorhydria An electrocardiogram was normal, and the Wassermann reaction was negative

Treatment and Progress —The patient was given large amounts of aneurine, riboflavine, and nicotinic acid parenterally and marmite by mouth. During the next three months there was a gradual improvement The skin lesions disappeared, and the bowels became more normal The œdema disappeared and the areas of anæsthesia regressed slightly The paræsthesiæ stopped, and she learnt to walk and knit again Before her illness she had knitted without looking but she has never regained this ability The mouth lesions remained active

Follow up —She was not seen again until May, 1950 She had stopped taking vitamins, and her paræsthesiæ and cramps had returned She had constant fatigue and insomnia. The mouth lesions were as bad as ever and she again had alternating constipation and diarrhœa Her skin lesions were minimal, the nervous lesions were largely unchanged, and there was no œdema She had put on a little weight, but still weighed only 7½ stone Her Hb was 88% (13 g per 100 ml), serum protein level 5 65–6 81 g per 100 ml , and serum calcium level 10 15 g per 100 ml On two separate occasions a barium meal reached the cæcum in an hour but a fat balance test showed 95% absorption. There was evidence of corneal vascularisation in the eye which had *not* had a corneal ulcer ' There are vascular loops with secondary arcades at the margins of the cornea, more in the right (the side of the corneal ulcer) than in the left ' (Mr A. McKie Reid) The paræsthesiæ and cramps improved temporarily after aneurine by mouth, but later the peripheral neuritis and mouth lesions became active again in spite of aneurine, riboflavine, nicotinic acid, pyridoxine, pantothenic acid, and iron by mouth. In December, 1950, and January, 1951, she was given a course of becosym (2 ampoules daily) by injection, and 'Casydrol' by mouth. She put on a few pounds in weight, and her paræsthesiæ improved steadily. Her mouth lesions improved dramatically at first, but then relapsed again. Pyridoxine 20 mg. t.d.s. by mouth was given as well for three weeks, and the mouth lesions steadily improved, becoming better than they had been for four years. This improvement has been maintained on becosym by mouth alone. (For further details see table.)

The other patient was a man who developed alternating constipation and diarrhœa, and dark pigmentation of the skin of his forehead and the backs of his forearms and hands, two or three years after subtotal gastrectomy. Nicotinic acid 50 mg. t.d.s. by mouth restored his skin to a normal colour within a month but did not affect his bowels.

FATIGUE AND OTHER SYMPTOMS

The early symptoms of pellagra may resemble those of neurasthenia. There may be general fatigue, lassitude, anorexia, irritability, insomnia, depression, loss of weight, and so forth. Very similar symptoms may be caused by experimental aneurine deficiency in man (Williams and Mason 1941, Williams et al. 1939, 1940, 1943, Jolliffe et al. 1939). In this connection the following case is of interest.

Case 9.—A labourer, aged 48, had had a gastro-enterostomy for a duodenal ulcer in 1927. About 1944 his wife had noticed that he was becoming morose; in 1946 he had had several attacks of transient loss of consciousness resembling petit mal; and in 1947 he had become depressed and emotional. He had had double vision on one occasion, been troubled with insomnia, and had a poor appetite.

He was admitted to a mental hospital as a psychotic in March, 1947. He was confused, apathetic, depressed, somewhat disoriented in time, had difficulty in formulating his ideas, and could not find simple words. He had diarrhœa and became incontinent of urine and fæces. He had a bright pink smooth tongue. His gait was a little unsteady, and he had some incoördination in the limbs, but there were no other abnormal neurological signs. A blood-count showed 4,900,000 red cells per c.mm. Hb 75% (11.1 g. per 100 ml.), film normal. The Wassermann reaction of the blood was negative. The C.S.F. was normal.

Treatment and Progress.—Hypovitaminosis was suspected and the patient improved immediately when he was given nicotinic acid 50 mg. four times a day. Later this was increased to 100 mg. three times a day, and benerva co. tab. 2 three times a day was given as well. The patient was discharged cured two months later (report kindly sent by Dr. B. Finkleman).

A year later (August, 1948) he complained of extreme lack of energy and weakness, heaviness, and cramps in the legs. He was depressed and would not mix with the other patients in the ward. There was no diarrhœa or glossitis and there were no abnormal neurological signs. There was slight œdema of the ankles, and he was underweight. He had received 200 mg. of nicotinic acid intramuscularly daily and benerva co. tab. 2 t.d.s. by mouth for a week before admission without improvement. Examination of the blood showed red cells 4,200,000 per c.mm. and Hb 75% (11.1 g. per 100 ml.). A fractional test-meal showed achlorhydria. Radiography after a barium meal showed that the stomach emptied normally through the gastro-enterostomy stoma. The Wassermann reaction of the blood was negative and the C.S.F. was normal. The patient was given aneurine 20 mg. a day intramuscularly, marmite, and oral iron. His symptoms quickly improved and he became cheerful, energetic, friendly, and most helpful in the ward. He was discharged cured, seven weeks later.

Improvement in the mental condition was produced on the first occasion with nicotinic acid and on the second occasion with aneurine. It seems likely that two separate deficiency states were present on the two separate occasions.

Undue fatigue and lassitude are not uncommon after gastrectomy. They may be present all day or towards the end of the day, and not after meals only, like the symptoms of the efferent loop "dumping syndrome." In some cases—e.g., cases 4, 5, 8, and 9—they are associated with vitamin deficiencies, but even so they are not usually benefited by vitamin therapy. Sometimes they are due to anæmia, hypertension, or other organic causes, and disappear when the underlying condition is corrected. In some of the patients psychological and environmental factors seem to be responsible, but in others there is no obvious cause. The symptoms have been relieved, sometimes dramatically, in some of our patients by giving small doses of *d* amphetamine sulphate ('Dexedrine').

Loss of appetite, according to most workers, is almost constant in beriberi, pellagra, and experimental aneurine deficiency. It is rare after gastrectomy (although a few patients have *morning* anorexia), and only one of our patients with hypovitaminosis (case 9) complained of it. It is difficult to explain this, but at least one large series of cases of beriberi has been reported in which anorexia was almost unknown and constant hunger was the rule (Smith 1946). Loss of weight is common after gastrectomy, and is usually due to causes other than hypovitaminosis (Wells and Welbourn 1951).

DISCUSSION

We have seen and described vitamin B deficiencies after various types of gastric operation, but we have no information about the relative incidence of the deficiency syndromes after the different operations. We have studied in detail a continuous series of nearly 200 patients submitted to subtotal gastrectomy for peptic ulceration. The operation was of the anterior (or occasionally posterior) Polya type with a Hoffmeister-Finsterer Lake valve (Wells and Brewer 1948). In 100 consecutive cases reviewed 1–4 years after operation (including cases 2–5) we found the following conditions:

Conditions	*No. of cases*
Hyporiboflavinosis alone	4
Incipient peripheral neuritis alone	2
Hyporiboflavinosis + incipient peripheral neuritis	3
Hyporiboflavinosis + established peripheral neuritis	1
Total	10 (*10%*)

We have found a similar incidence in a rather smaller and less complete series of patients (including cases 1 and 8) who had the same operation 5–10 years ago. Some of the patients had iron deficiency anæmia as well, but hyporiboflavinosis and incipient peripheral neuritis were often encountered without any other signs of deficiency. Established peripheral neuritis and pellagra have, in our experience, been part of a more severe mixed deficiency syndrome. Our studies of blood pyruvic acid levels suggest that subclinical aneurine deficiency may be a good deal commoner than the established clinical syndromes (R. B. Welbourn and D. M. Chesterman, unpublished data).

A 10% incidence of cases of vitamin B deficiency after gastrectomy requires an explanation. It has been pointed out (Spies 1943, Riggs et al. 1944) that the usual ulcer régimes are deficient in several essential foods, including the vitamin-B complex. Other factors—e.g., vomiting, bleeding, and alkaline therapy—may further reduce the body's stores; and, although frank vitamin-B deficiency is rare in the course of peptic ulceration, many people may be potentially deficient by the time they come to operation. Thereafter several new factors are introduced, and we must consider in turn the possible mechanisms by which the deficiencies may develop.

Deficient Intake of Food

Postoperatively some patients (especially those subjected to gastrectomy) develop symptoms—e.g., bilious vomiting and the "dumping syndrome"—which seriously reduce the amount of food which they can eat

Four patients (cases 1 and 4–6) in the present series had these symptoms. On the other hand, other patients whom we saw with very severe symptoms had no signs of deficiency. Others vomit a proportion of the food which they eat, thus reducing their effective intake. This was an important factor in some of our most severe deficiencies (cases 3, 7, and 8).

One of the advantages of subtotal gastrectomy is that it allows patients to return to a normal mixed diet, and analysis of our patients' diets shows (see table) that, though some had a very low total calorie intake, the vitamin B content of their food was usually more than adequate. There is evidence that the requirement of aneurine is directly related to the intake of "non fat calories," and that the requirements of riboflavine and nicotinic acid are to some extent related to the total caloric intake (British Medical Association 1950). In the table we have shown the actual intake of vitamins compared with the requirements, calculated on this basis. In only two instances was there deficiency of nicotinic acid (cases 5 and 8), and in every case there was an adequate amount of aneurine and riboflavine. These cases are in every way typical; hence causes other than reduced intake of vitamins must be sought to explain the deficiencies.

Interference with Absorption of Vitamins

We discuss elsewhere (Wells and Welbourn 1951) the physiological effects of operations on the stomach, and emphasise the importance of the intestinal hurry which may result from gastrectomy. It is likely that by interfering with the digestion and absorption of food this contributes to the development of vitamin deficiencies (cases 3, 4, 6, and 8).

Another mechanism is suggested by the work of Petri and Wanscher (1937), Petri et al. (1937), and Sydenstricker et al. (1936), who have found that neutralised gastric juices, taken by mouth, will greatly improve pellagra in man. In experiments on dogs and pigs Petri (1936) and Petri et al. (1938a and b, 1940, 1943, 1944a, b, and c) have shown that "gastroprival" pellagra is caused constantly by total gastrectomy or by excision of the fundus (middle portion) of the stomach alone. This can be prevented by *neutralised* normal gastric juice in dogs (but not in pigs) and by pyridoxine (vitamin B_6) in both dogs and pigs. Nicotinic acid had no effect except in one pig which had had a pylorectomy only. These experiments suggest that the stomach plays some part in the absorption or utilisation of nicotinic acid and of pyridoxine. The fact that the gastric juice in these experiments was neutralised indicates that the effect was not due to its acidity.

Destruction of Vitamins

Both aneurine and riboflavine are stable in acid media only, and achlorhydria may allow appreciable quantities of the vitamins to be destroyed before they can be absorbed. The hydrochloric acid secreted by the stomach normally provides a strongly acid medium for the gastric phase of digestion, and the pH of the stomach contents is usually about 2. Chyme is rapidly diluted and neutralised in the duodenum, and finally passes through the jejunum and ileum at an approximately neutral reaction (pH 6–8). A subtotal gastrectomy usually produces complete achlorhydria (as in cases 1–5, 8, and 9), and food passes through the gastric stump and small intestine at this same neutral reaction (Wells and Welbourn 1951). Strongly alkaline reactions are not encountered.

In vitro experiments (Melnick et al. 1941) show that aneurine is stable in normal gastric juice at a pH of 1.5–8.0, but that up to 50% may be destroyed by incubation with bile or pancreatic juice at a pH of 8.0–8.5. At pH 4.5 no aneurine is destroyed. This suggests that there may be a stabilising factor in normal gastric juice. Riboflavine is also unstable in an alkaline medium, but its exact behaviour in the intestinal secretions has not, so far as we know, been worked out in the same detail as that of aneurine. Nicotinic acid is stable over a wide pH range. The significant facts about aneurine, and probably riboflavine also, are that in the normal alimentary tract they are kept at a stable acid reaction until they enter the small intestine, where they are rapidly absorbed. After gastrectomy the whole process of churning, liquefying, and diluting the food is done at the neutral reaction of the small intestine, and under these conditions appreciable quantities of the vitamins may be inactivated. We are trying the effect of hydrochloric acid alone on some patients, and have cured hyporiboflavinosis in one.

Diversion of Vitamins to Bacteria

Frazer (1949) has drawn attention to the fact that achlorhydria allows the colon organisms, which normally inhabit the colon and lower ileum only, to grow all the way up the small intestine. He believes that in the sprue syndrome vitamin deficiencies are caused largely by these bacteria diverting the B vitamins to their own use, thus depriving the host. It is possible that this is a contributory factor in the development of hypovitaminosis after gastrectomy. We have found that a free growth of *Bact. coli* and other common colon organisms can be obtained from the gastric contents in about half the patients who have undergone subtotal gastrectomy, but we have not found organisms constantly in the patients with vitamin deficiency. A free growth of *Bact. coli* was obtained from only one (case 4) of the cases described. It should be possible to test this hypothesis by giving intestinal antiseptics, but we have not yet done so.

Another way in which bacterial growth may contribute to hypovitaminosis is suggested by Brain (1950). He has found acute ulcerative stomatitis, apparently due to B complex deficiencies, in the early postoperative stage after total gastrectomies, and most of the cases have been in patients who had gross sepsis—e.g., empyema. He suggests that the bacteria in these lesions divert to their own use some of the B vitamins from the host, thereby producing a deficiency.

Prevention and Treatment of Deficiencies

It is important to encourage patients to eat meat, bacon, and other foods—e.g., eggs, fruit, green vegetables, and brown bread—which contain adequate quantities of vitamins and iron. It is wise to recommend marmite or some other source of the whole B complex regularly as a prophylactic against vitamin B deficiencies.

Patients with established deficiencies require specific therapy. For the purpose of investigation we have treated many of our cases with small doses of one specific factor at a time. But since several deficiencies may be present, and since administration of one member of the B complex may precipitate deficiency of another (Frazer 1949), it seems better to give routinely a vitamin B compound preparation. The dosage should be large, because of the possible destruction in the intestine. Individual vitamins may be given in addition when they are indicated. Most of the mild cases respond rapidly, but in resistant or acute cases the vitamins should be given parenterally.

SUMMARY

Vitamin-B deficiencies are relatively common after gastric operations and have been found in 10% of subtotal gastrectomies one or more years after operation.

Hyporiboflavinosis and incipient peripheral neuritis, due to aneurine deficiency, are the commonest syndromes. Less common conditions are established peripheral neuritis, Wernicke's encephalopathy and other disturbances of consciousness, and pellagra.

In most cases the diets contain sufficient vitamin B. Achlorhydria, which encourages destruction of aneurine and riboflavine and may allow diversion of vitamins to intestinal bacteria, is possibly the chief cause of the deficiencies. Vomiting and intestinal hurry may be contributory factors.

After gastric operations foods rich in vitamin B should be advised The deficiency states can be easily corrected in their early stages

We wish to thank Dr J F Wilkinson for information about case 3, Mr J Cosbie Ross and Mr James Gow for permission to report case 7, Dr B Finkleman for information about case 9, Mr W Lee, of the central photographic department in the University of Liverpool, for the photograph, Dr Fred Wrigley, of Roche Products Ltd, for helpful advice and criticism and for supplying vitamin preparations, and Miss E M Winstanley for her help with the diet analyses

REFERENCES

Adlersberg D, Hammerschlag E (1947) *Surgery*, **21** 720
Bean, W B Spies, T D Blankenhorn, M. A (1944) *Medicine, Baltimore*, **23** 1
Brain R H F (1950) Paper read at the Association of Thoracic Surgeons
British Medical Association (1950) Report of the Committee on Nutrition London
Browne D C, McHardy G (1943) *Sth med J* **36** 32
Campbell, A. C P Russell W R (1941) *Quart J Med* **10** 41
Frazer A C (1949) *Brit med J* ii 731
Gordon Taylor G Hudson R V, Dodds E C Warner J L Whitby L E H (1929) *Brit J Surg* **16**, 641
Jolliffe N Goodhart R Gennis J Cline J K (1939) *Amer J med Sci* **198** 198
Kruse H D Sydenstricker, V P Sebrell W H, Cleckley H M. (1940) *Publ. Hlth Rep Wash* **55** 157
Levy Simpson S (1935) *Quart J Med.* **4** 191
Lindeboom, G A (1950) *Gastroenterologia*, **75** 129
Melnick D Robinson W D Field H jun (1941) *J biol Chem* **138** 49
Muir A (1949) *Brit J Surg* **37**, 165.
Petri S (1936) *Acta path microbiol scand* **13** 350
— Bang O Kiaer W Kjerbye Nielsen A (1944a) *Acta med scand* **116** 273
— Norgaard F Bandier, E (1938a) *Ibid* **98** 117
— — — (1940) *Ibid* **104** 245
— — Bing J (1938b) *Amer J med Sci* **195** 717
— — Kiaer W (1944b) *Acta med scand* **119** 358
— — Trantner K Kiaer W (1943) *Ibid* **114** 184
— — — — (1944c) *Ibid*, **117** 90
— Wanscher O (1937) *Ibid*, **91**, 370
— — Stubbe Teglbjaerg E Stubbe Teglbjaerg H P (1937) *Ibid*, **93** 450
Riggs, H E Reinholt, J G Boles R S, Shore P S (1944) *J Amer med Ass* **124** 639
Sebrell W H Butler R. E (1939) *Publ. Hlth Rep Wash* **54** 2131
Smith D A (1946) M D thesis Cambridge
Spies T D (1943) *J Amer med Ass* **122** 497
Spillane J D (1947) Nutritional Disorders of the Nervous System Edinburgh
Sydenstricker V P Armstrong E S, Derrick C J Kemp P S (1936) *Amer J med Sci* **192** 1
Welbourn R B (1950) Paper read at the Association of Surgeons.
Wells C Brewer A C (1948) *Brit J Surg* **35** 364
— Welbourn R B (1951) *Brit med J* i 546
Williams R D Mason, H L (1941) *Proc Mayo Clin* **16** 433
— — Power M H. Wilder R M (1943) *Arch intern Med* **71** 38
— — Smith, B F (1939) *Proc. Mayo Clin* **14** 787
— — Wilder R M Smith B F (1940) *Arch intern Med* **66** 785

ACTINOMYCOSIS OF THE SPINE

M E WINSTON
M.B Edin F R C S.E
SENIOR ORTHOPÆDIC REGISTRAR, SOUTH MANCHESTER HOSPITAL GROUP

ACTINOMYCOSIS of the spine is a rare disease In a study of 678 cases of actinomycosis, Sanford (1923) reported only 4 involving the vertebræ and ribs

The diagnosis is not usually recognised until late, the great majority of cases being found at necropsy This is partly due to the fact that spinal symptoms are commonly absent, Parker (1923) reporting only 3 cases out of 8 with symptoms referable to the spine In a study by Meyer and Gall (1935) of 60 cases of mycosis of the spine, including 47 cases of actinomycosis, only 9 were correctly diagnosed during life, the usual diagnosis being tuberculosis, of the 60 patients, 54 died of the disease, giving a mortality of 90%

In view of the high mortality it seems worth while to publish a preliminary report on this case which has so far responded favourably to streptomycin

A woman, aged 35, was referred to medical outpatients on Dec. 20 1949, with seven months' history of pain in the back and right side, attacks of precordial pain, and loss of weight Her symptoms dated from the birth of her third child, before which she had been well In the puerperium she is reported to have had a pneumonitis In the subsequent seven months she had lost $1^1/_2$ stone in weight

Examination revealed a right sided pleural effusion, and a small collection of fluid at the left base Nothing abnormal was detected in the abdomen, cardiovascular system, or central nervous system. Radiography showed a small effusion at both lung bases and mottling of the spine involving the vertebræ and adjacent ribs posteriorly of segments T5–T9

On admission to hospital on Jan 11, 1950, the patient had over the affected vertebræ posteriorly a fluctuant swelling which started to discharge through a small sinus to the left of T3 and T4 The pus contained *Staph aureus* No tubercle bacilli were found in the sputum or the urine Red cell count was 2,300,000 and white cells 22,000 per c.mm, Hb 42% Erythrocyte sedimentation rate (Westergren) was 27 mm in 1 hr Temperature was 99–101°F, pulse rate 110, and respirations 20 per minute

Progress—The sinus discharged profusely, and a second swelling appeared over the lower dorsal vertebræ On Jan. 24, a diagnosis of actinomycosis was suggested, but three negative swabs were obtained before the streptothrix was demonstrated and cultured.

Penicillin 1,000,000 units four hourly, with potassium iodide gr 20 t d.s, effected no improvement. The abscesses recurred and discharged through several sinuses The pleural effusion at the right base reappeared, and on March 14, her general condition was poor On March 15, treatment was begun with streptomycin 1 g eight-hourly, and her spine was immobilised in a plaster anterior shell The effect was dramatic by April 4 the sinuses had healed completely, the pleural effusion had resolved, her general condition was good, and radiography showed improvement in the chest and spine. She was allowed to move freely in bed after a month, and on May 2 the streptomycin was reduced to 1 g b d Streptomycin was continued until June 13

The patient was allowed up, wearing a spinal support, on June 27, and subsequently attended as an outpatient She continued to make satisfactory progress, and the spinal support was discontinued in December 1950 At that time she was fit the sinuses had remained healed, and there was no recurrence of abscess formation X-ray examination showed that the spine had not yet regained normal density, and there was narrowing of the intervertebral space between T8 and T9, there was still some opacity at the base of the right lung

I am grateful to Mr E S Brentnall for permission to publish this case

REFERENCES

Meyer M Gall M. B (1935) *J Bone Jt Surg* **17** 857
Parker C A (1923) *Ibid*, 5 759
Sanford, A H (1923) *J Amer med. Ass* **81**, 655

Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

THE spring meeting was held in Cambridge on April 6 and 7, under the presidency of Mr S L HIGGS Among the subjects discussed were congenital dislocation of the hip, and the late results of disc operations

Congenital Dislocation of Hip

Mr H J SEDDON, opening a symposium on congenital dislocation of the hip, reviewed the results of treatment carried out at the Royal National Orthopædic Hospital during the first 40 years of this century Of 889 patients treated, 264 had been re examined recently by Mr G M Muller, in this series treatment had been begun 10–40 years previously Only half the patients were less than 3 years old when treatment was begun In three fifths of the cases treatment had been by manipulative reduction and immobilisation in plaster, and in half of these the results were still good In the remaining two fifths operation had been required at some stage Operative treatment had been undertaken (1) to reduce the dislocation when manipulative reduction was impossible, (2) to improve the acetabulum, (3) to correct anteversion, or (4) in cases of persistent dislocation to improve the function of the hip, usually by some form of osteotomy Open reduction had proved satisfactory in only 4 out of 20 cases Results of acetabulo plasty had been good in 22 out of 36 cases, rotation osteotomy had been satisfactory in only 3 out of 9 cases, and the results of palliative osteotomy were disappointing Any improvement on these results must be along the following lines (1) earlier treatment and improved methods of closed reduction, (2) earlier operation where conservative treatment was unsuccessful, and (3) improved methods for late or relapsed cases By the plan of treatment now pursued at the hospital, closed reduction was attempted by traction on an abduction frame, with cross traction medially through a strap round the upper thigh If reduction was not secured in four weeks open reduction was undertaken Acetabuloplasty was undertaken when the acetabulum failed to develop after closed reduction and, if thought necessary, at the time of open reduction Rotation osteotomy was advised if anteversion of the neck was deemed to impair stability

Reduction and Retention—Mr **DENIS BROWNE** thought that there were two elements in the production of congenital dislocation of the hip—namely, failure of development of the hip joint, and a mechanical thrust along the axis of the femur from intra uterine pressure This thrust, acting on the limb in the flexed intra uterine position of the fœtus, caused the hip to dislocate downwards and backwards, only after birth, when the hip was extended, did the femoral head become displaced upwards If this view was correct it was logical to reduce the dislocation by reversing the mechanism of its production His method was to place the limb in the "intra uterine" position with the child face downwards, then to push upon the upper end of the femur in the axis of the thigh, thereby he achieved successful reduction in 95% of cases After the primary reduction the hip was immobilised in plaster in the position of reduction for four weeks Subsequently the reduction was retained by means of the Denis Browne splint, which allowed a wide range of abduction movement at the hip, this favoured deep engagement of the femoral head in the acetabulum The splint was worn for up to nine months, and in about 100 cases he had not observed redislocation after it had been discarded

Trends in Operative Treatment—Mr **DAVID TREVOR** described the present practice at the Royal National Orthopædic Hospital with special reference to operative treatment, which was required in about two fifths of all cases Of 27 recent cases of open reduction that had been reviewed, 15 had been submitted to acetabuloplasty at the same time, and 7 had had a subsequent rotation osteotomy The oldest patient was aged 5 years 10 months The cases in which open reduction was necessary fell into two groups (1) those in which the femoral head was high with contracture of the soft tissues causing a narrow isthmus, and (2) those in which reduction was prevented by soft parts in and around the acetabulum The commonest obstruction was an infolded capsule, other causes were hour glass contraction of the capsule, an infolded limbus, resistant fibrous tissue within the acetabulum, and gross enlargement of the ligamentum teres In 5 cases redislocation had occurred after operative reduction Of 23 cases observed for more than a year 19 were satisfactory so far Full or nearly full movement was regained in most cases

Acetabuloplasty was often advisable at the time of operative reduction, especially if the acetabular roof sloped steeply An extracapsular technique, in which the acetabular roof was turned down and held by a wedge of iliac bone inserted into the site of osteotomy, was preferred Results so far were satisfactory in 14 cases observed for one year or more, and unsatisfactory in 2 If the opportunity for acetabuloplasty was missed the femoral head might become displaced high on the ilium, and acetabuloplasty by the ordinary "shelf" procedure became impracticable This was the type of case in which the Colonna operation was indicated. Rotation osteotomy was necessary when anteversion was sufficient to impair stability When it was found at the time of open reduction that anteversion was excessive, rotation osteotomy was undertaken about six weeks later

Arthroplasty for Persistent Dislocation in Adults—Prof R **MERLE D'AUBIGNÉ** (Paris) described his experience of arthroplasty for persistent dislocation of the hip in adults Operation should be undertaken only if the functional disability was severe Of 22 patients who had been operated on 8 had had bilateral operations, making 30 hips in all In 16 cases the interposed material had been a metal cup, in 13 an acrylic head, and in 1 the capsule To ensure stability it was necessary to bring the head well down, to deepen the acetabulum and enlarge its upper rim by means of a screwed on graft, and to displace the trochanter downwards After the operation the hip was immobilised in plaster in wide abduction for six weeks, after which active movements were begun, weight bearing was allowed after four months Results in the 14 cases observed for one year or more were excellent in 4, good in 7, and poor in 3, 11 were free from significant pain

DISCUSSION

Sir **HARRY PLATT** (Manchester) agreed with the plan of treatment adopted by the Royal National Orthopædic Hospital team His experience of 645 congenital dislocations showed that a good result could be achieved by closed reduction in two thirds of all cases He preferred reduction in one stage (by gentle manipulation) to prolonged traction on a frame In recent years he had undertaken open reduction more often than in the past In 88 open reductions the commonest obstacles to reduction had been abnormal attachment of the capsule, and broad ligamentum teres He thought that the so called capsular isthmus might sometimes be only an apparent narrowing of the capsule due to incomplete filling of the joint cavity by opaque fluid

Prof J **TRUETA** (Oxford) had found that the incidence of osteochondritis was 30% after reduction by traction on a frame, compared with 45% after manipulative reduction

Mr J C **SCOTT** (Oxford) emphasised that traction applied to the limb of the abduction frame should be light (not more than 2 lb in each line of pull) In his series of 116 cases reduction by traction failed in only 16%

Mr H A **BRITTAIN** (Norwich) preferred arthrodesis of the hip to arthroplasty in cases of persistent unilateral dislocation with arthritic symptoms in adults

Dr P G K **BENTZON** (Denmark) warned against twisting the hip capsule during attempted reduction. If the capsule was twisted, reduction was obstructed and the blood supply of the femoral head might be impaired

Mr W A **LAW** spoke of the need to excise the capsule completely in getting the femoral head down to the level of the acetabulum

Mr G C **GORDON** (Sheffield) thought that in the ætiology of congenital dislocation of the hip rhythmic contractions of the uterus during pregnancy might be a factor, though the pressure exerted was too slight to cause dislocation of a normal hip

Sir **REGINALD WATSON JONES** felt that assessment of results so early as one year after treatment was unsound Even intermediate results could not be assessed until the age of 17 or 18 years, when growth had ceased Anteversion was a problem that demanded careful study at all stages of treatment If allowed to persist, it led to faulty distribution of weight in the acetabulum and predisposed to redislocation

Late Results of Disc Operations

Mr A L **Eyre Brook** (Bristol) reported the results in 117 patients observed for one to six years after operation for sciatica diagnosed as being due to a disc lesion He had studied in particular the progress of patients in whom no causative pathology had been found at operation Unless he found a definite protrusion or indisputable adhesions he regarded the exploration as negative, he did not believe in "hidden" discs or disc scars Of the 117 operations, 11 gave negative findings, adhesions had been observed in 6, and in the remainder a definite protrusion was present Of patients in whom a definite lesion was found, 86% had no more than very minor residual complaints, and of the 21 men with disc lesions who were engaged in heavy work before operation, 18 were able to return to normal work On the other hand, all except 1 of the patients in whom no lesion was found had significant residual disability at the time of examination, in the 1 exception there was complete freedom from symptoms Of the 6 patients in whom nerve root adhesions were found, 4 had moderate relief and 2 had only slight relief

Mr **Trevor** thought that lumbar puncture and estimation of the protein level in the cerebrospinal fluid were advisable as a routine before exploration, and myelography should be done if lumbar puncture showed any abnormality If these precautions were neglected other lesions, such as tumour, might be missed

Professor **d'Aubigné** asked whether spinal fusion had been undertaken in any of the cases

Mr **John Charnley** (Manchester) felt that lesions of the intervertebral disc fell into the province of the orthopædic surgeon rather than the neurosurgeon Exploration had been negative in 16% of his patients In the earlier cases of his series he had sometimes failed to find lesions even when the straight leg raising test had been markedly positive, he considered that in such cases he had probably missed a disc protrusion at a different level. As his experience of the operation increased he found that negative explorations were less common and were usually in patients with only slight restriction of straight leg raising He held that the straight leg raising test was of the greatest value in diagnosis and assessment of the case for operation

Mr **Eyre Brook** felt that whereas lumbar puncture and myelography should be undertaken in problem cases, special investigations other than plain radiography were unnecessary in the straightforward case Exploration of a disc was almost devoid of risk, and in the exceptional case where the symptoms were found to be due to a tumour no great harm was done by the exploration He did not consider that spinal fusion should be undertaken at the time of a disc exploration If significant back pain arose afterwards, this should be assessed as a separate problem in the same way as back pain from other causes He agreed with Mr Charnley that the straight leg raising test was the most significant sign

MANCHESTER MEDICAL SOCIETY

Treatment of Perforated Peptic Ulcer

At a meeting of the section of surgery on March 13, Mr T **Heslop** expressed the opinion that the conservative method undoubtedly has a place in the treatment of perforated peptic ulcer the main difficulty was in formulating guiding principles on which to base personal judgment when deciding the merits of operative or conservative treatment Most of the series hitherto described were of selected cases For the past four years parallel series had been observed at two adjacent hospitals in Salford All the cases seen at Salford Royal Hospital were treated operatively, except a few in the days before this scheme had come into operation All cases admitted to Hope Hospital had been treated conservatively under the supervision of Mr A S Bullough

During the 5 year period 1946–50 Mr Heslop and Mr C Brun had observed at Salford Royal Hospital 124 cases of perforated peptic ulcer with 11 deaths (8 8%) irrespective of the method of treatment This series included a small group of 20 unselected cases which were treated conservatively, with a mortality of 10%, subphrenic abscess occurred once but resolved after drainage Of the 104 cases treated by emergency operation, 9 (8 6%) died The peak age incidence was at 30–39 years, the sex ratio being 1 female to 20 males

The salient points about operative treatment were adequate preoperative preparation, the minimum of interference inside the abdomen, with simple closure of the perforation and no exploration of the peritoneum, maintenance of gastric suction and controlled intravenous fluid administration for 24–48 hours, and prophylactic chemotherapy and early ambulation in the absence of complications

The prognosis and mortality depended on the time-interval from the onset of perforation, the age of the patient (mortality increasing greatly over 60 years), and the situation of the ulcer Perforated gastric ulcer (17 cases) carried a mortality of 30%, perforated duodenal ulcer (85 cases) only 5% Among the 9 fatal cases, only 5 patients died from general peritonitis within four days The preponderance of peritonitis as a cause of death was striking When this was established on admission it was questionable whether operation was of any benefit, when it developed after operation on early cases it could be traced to faulty operative technique or inadequate postoperative management, and these deaths should certainly be preventable

Mr A S **Bullough** reported his results with the conservative, or non operative, method of treatment in 102 consecutive cases of perforated peptic ulcer admitted since March, 1947, to Hope Hospital His reasons for adopting this method were the high mortality of operated cases, the occasional recovery of unoperated, desperate cases, the increasing conservatism of operative measures, the fact that at operation perforations were often found to be shut off, and the sterility of the fluid, which acted as a protective peritoneal reactive fluid

The method consisted in continuous gastric suction for several days, intravenous fluid therapy, and administration of antibiotics Patients were more comfortable than those operated on, and within a week were up and about and on light gastric diet Of the 4 females in the 102 cases, 1 died In the total series there were 8 deaths, 4 were of elderly persons admitted moribund, long perforated, and quite unfit for any operation, who died during the night following admission These cases would not have figured in the mortality statistics of any operative series The remaining 4 were late deaths (seventeen days to eight weeks), and all had unsealed perforations with fistulæ between stomach (2 cases) or duodenum (2 cases) and a cavity in the peritoneum containing gastric juice—not pus 3 of them had this cavity drained, and consequently developed an external fistula There were 93 duodenal perforations with 3 deaths, and 9 gastric perforations with 5 deaths There were 3 true subphrenic abscesses, with recovery in each after drainage

A possible criticism of the method was that it was impossible to be sure that all the cases were in fact perforations, but clinical experience, the subsequent course, X ray examination, and in some cases operation, all tended to show that they were. There was the risk of leaving unoperated some condition requiring operation 1 such case occurred On the other hand, a conservative method might conceivably preserve the lives of certain sufferers from coronary thrombosis, pneumonia, or acute pancreatitis, by avoiding a dangerous operation

Reviews of Books

The Principles of Pathology

R A WILLIS, M D, F R C P, professor of pathology in the University of Leeds London Butterworth 1950 Pp 667 50s

Professor Willis presents the subject of pathology in an unconventional way he will have none of the usual subdivision into general and special, but aims at a logical sequence, having in mind always the student who has just completed his studies in anatomy and physiology Pathology, he tells him, is extended anatomy and physiology it is the study of all that the body and its tissues can be and do under all possible abnormal conditions Therefore, he deals first with repair and regeneration, processes which the doctor will constantly observe throughout his professional career Then comes a series of chapters on inflammation and the sequelæ in particular sites, followed by chapters on bacteria, viruses, and parasites and the diseases which they produce, on immunity and diseases due to sensitisation, foreign bodies and poisons, and on disturbances of nutrition, metabolism, circulation, and hæmopoiesis A section on neoplasms, which is a summary of his *Pathology of Tumours,* is notably well presented, though not everyone will agree that myeloid and lymphoid leukæmias are best described under the heading of neoplasms of the hæmopoietic tissues Endocrine disturbances and obstruction and dilatation of hollow organs, so often produced by tumour growth, follow naturally, and the last chapter deals with the whole range of antenatal pathology

This is a pleasant alternative and an important supplement to the more conventional textbook of pathology Professor Willis's style is frank and critical and he has plenty of scope to expose misconceptions He makes full use of hand lens illustrations A glossary of Greek and Latin words, and good advice on the observing and recording of facts, and on the use and abuse of eponyms, are given in appendices A short account of the great pathologists supplements the historical details included in the text, some of which are refreshing and happily chosen

Vitamins and Hormones

Vol III Editors ROBERT S HARRIS, professor of biochemistry of nutrition, Massachusetts Institute of Technology, Cambridge, Mass, KENNETH V. THIMANN, professor of plant physiology, Harvard University, Cambridge, Mass New York Academic Press 1950 Pp 342 $6 80

THERE are eight reviews in this, our old friend of eight years' standing, and the publishers have managed to do the job at less than their price of two or three years ago—a most uncommon feat An article on the " animal protein factor " and B_{12} in nutrition, by L M and T F Zucker makes good reading, but our knowledge about B_{12} has been expanding so rapidly in the last few years that readers must be prepared to write the last few pages for themselves Henry Sherman, in a study of the relationship of pyridoxine to fat metabolism, raises a number of interesting questions without being able to give a final answer to any of them Those who are unhappy about the existence or physiological importance of the " antistiffness " factor for guineapigs, or about " relaxin " will find W J van Wagtendonk and R Wulzen, and F L Hisaw and M X Zarrow highly informative about these substances Both pairs of authors believe that pure chemical compounds are responsible for the effects which they themselves have done so much to describe, but neither the vitamin nor the hormone has yet been isolated in identifiable form Now that sugar cane juice has been found to be so rich in the " antistiffness " factor, however, there is every reason for hope that the biochemists will soon have this vitamin in the bag H K Mitchell contributes a paper on vitamins and metabolism in neurospora, and R Courrier, the French pathologist, writes on the interactions of œstrogens and progesterone, which he has been studying since 1926 R L Stehle has completed his review of the physiological actions of the posterior lobe of the pituitary Those who are anxious to know anything about the configuration
of the sterols may be recommended to read the last art
by C W Shoppee, now working at the Universit
Wales

Some of these reviews are, naturally, better t
others, but most of them begin at the beginning of t
subject, and outline its development, and this is inv
able for the outsider who wants to get a grasp of it
is seldom able to do as much from a volume review
recent works

The Life of Dr John Radcliffe, 1652-1714

CAMPBELL R HONE, Hon Fellow of Wadham Coll
Oxford London Faber & Faber 1950 Pp 149

THE Bishop of Wakefield has done the coming histo
service by writing this important biography Radc
was a Yorkshire man of middle class, fearless, ruthl
and shrewd, in admirable control of his temper, but us
language which bit hard when he was intolerably p
voked Common sense combined with fearlessness
dealing with patients of all kinds marked his long car
and his generosity—so conspicuous in the West Rid
of his county—was an instinct That impulse in mid
class folk which impels them to seek some gentle or e
noble forebear induced Radcliffe to claim Derwentwa
as his own, and this claim to the best blood in
Riding, which still flows in the Rudding Park fam
was seemingly tolerated For the medical reader t
volume deserves a niche near Paget's *Stephen and Bish
Paget* and Harvey Cushing's *Osler,* where they and it m
be read and re-read with profit and pleasure

General Clinical Counseling in Educational Institut

MILTON E. HAHN, professor of psychology, Universi
of California, Los Angeles, MALCOLM S MACLEA
professor of higher education at the university London
McGraw Hill 1950 Pp 375 30s

UNIVERSITY students sometimes seek, and often
need, guidance about their academic troubles an
decisions It is unlikely that any single person can gi
all such guidance as a student may require in the Unite
States, however, a profession has developed, and th
" counselor," is trained to help students in all the
educational and vocational difficulties " Clinical coun
seling " is defined by Professor Hahn and Professo
MacLean as " a process which takes place in a one to-on
relationship between an individual troubled by person
problems with which he has been unable to cope alon
and a professional personnel worker whose training an
experience have qualified him to aid others to reac
solutions to various types of personal difficulties "
must " be concerned with the total dynamic adaptatio
of the individual " These phrases have a familiar ring
" counseling " is the little sister of psychotherapy and i
this book she shows one of the family failings, for muc
flabby writing is required to express a commonplac
opinion The case for expanding advisory facilities fo
students, which has much to support it, is not helped b
this book

A Calendar of Country Receipts (*London* *Faber*
Faber Pp 192 16s)—Miss Nell Heaton not content wi
her victories in the realms of straight cooking, has invade
another that of the old time country lore of the still roo
and herb garden It is a fascinating place, a land of reveri
and nostalgia Miss Heaton, however, does not despi
modern short cuts to the results of our forebears In oth
words, the book is not only redolent of old housewifery a
medical lore, but practical And Leonard Huskinson
pictures add to its vivacity

Das Strichbild *Zum Form und Stoffproblem in d
Psychologie der Handschrift* (Stuttgart Thieme 195
Pp 60 DM 6 60)—Dr R Pophal, who is professor
graphology at the University of Hamburg, has been workin
at the criminological institute in that city on the analys
of strokes in handwriting as indices to personality Thoug
no doubt experienced and skilful in his interpretations, h
fails to give proof of the correctness of his apparently intuitiv
readings, and he makes the reader's task needlessly difficu
by his style The technical details he gives will be of interes
to graphologists, but the psychologists and physicians f
whom he has also intended the book are better served b
more humdrum studies

THE LANCET

LONDON SATURDAY, APRIL 28, 1951

Cortisone and Infection

How safe is treatment with 'Cortisone' or A C T.H ? dministration of these hormones is almost always tended by some signs of hyperadrenalism, and he danger of hyperadrenalism, as CUSHING [1] pointed ut, is increased susceptibility to infection In eating the pale rheumatic child with some disorder of is antibody responses, shall we gain only a fit-looking hild with no defences against infection, who makes is symptomless way to death from septicæmia ? his danger has been much in the minds of research-orkers, indeed, only two years after the discovery f the therapeutic action of cortisone, KASS and INLAND [2] can quote references to 123 reports dealing ith its influence on infection and immunity

Clearly these hormones may influence the body's eactions to infection at every stage from entry of the nvading organism to repair of the tissue damage he evidence is based mostly on experimental work with comparatively large doses, and there have been few satisfactory accounts of serious septic complications in man. Where A.C.T H has been used to treat bacterial pneumonias in man,[3] clinical remission has been prompt In one case, after 24 hours' treatment fever and pleural pain and physical signs disappeared, the patient felt well, and appetite returned, but at the same time both sputum and blood contained many type-8 pneumococci A.C T.H. was continued, and fever did not return, but not until the fourth day did the blood become sterile Nevertheless there seemed to be no interference with antibody response, specific antibodies appeared on the eighth day In general, the signs of illness in patients with pneumococcal pneumonia were suppressed by A C T.H., but it seemed that development of the infection was uninfluenced. With experimental pneumococcal infection, cortisone influences the outcome unfavourably, as Dr WHITE and Dr MARSHALL [4] showed in their report last week in these columns Similarly D'ARCY HART and REES [5] found that tuberculous infection of mice was enhanced by cortisone In man symptoms of tuberculosis are promptly alleviated although the disease itself is unaffected or aggravated, judging by radiographic and sputum examinations [6] This warns us of a possible future danger now that both B C G vaccination and cortisone therapy are becoming more common obviously cortisone should not be given to B C G-inoculated children until further work has shown that this is safe As regards group-A streptococcal infections, HAHN and his associates [7] have established that in man these are not benefited by cortisone in doses of 100 mg daily, in fact the duration of fever was increased, while other symptoms, such as malaise, sore throat, and headache, were found equally among treated and control groups Cortisone had an even more unfavourable effect on hæmolytic streptococcal infection in mice [8] and in rabbits [9] Likewise with malaria, in man administration of A.C T.H. has little adverse effect except to increase the peripheral blood parasite count, but in monkeys it may precipitate blackwater fever [10] In virus infections in man, such as poliomyelitis [11] and virus pneumonia,[3] the course of the disease is not shortened In mice and ferrets with virus-A influenza, A.C T H. increases the mortality-rate without affecting the lung changes or antibody responses [12] In some animal experiments the doses, weight for weight, exceed those given in man, and overdosage must account for some of the experimental findings

A similar conflict between experimental and clinical results has arisen in the investigation of wound healing Cortisone or A C T.H, in doses equivalent to 100–500 mg per day in man, delays or inhibits the healing of wounds in rabbits [13], but when patients with rheumatoid arthritis are maintained in clinical remission by small doses of cortisone, such as 100 mg or less per day, there may be no apparent interference with healing,[14] or healing may be speeded.[15] It all seems to be a matter of dosage, or rather of the degree of hyperadrenalism produced.[16] Most reports agree that mild hyperadrenalism is inevitable, but the relative absence of well documented descriptions of serious infection complicating treatment does not suggest that this is such a serious danger as animal experiments seem to indicate Certain precautions may help to avoid trouble Patients receiving these hormones should be repeatedly examined, and absence of symptoms should not be taken as proof of well-being, since an abscess may only declare itself as a painless lump It would be wise not to allow patients to give their own injections, unless their facilities for, and knowledge of, sterile precautions are good Patients on doses that produce well-marked hyperadrenalism should receive prophylactic injections of antibiotics, in any case we should not give such high doses for long, but should be content, as HENCH has observed, with the partial control of symptoms from smaller dosage Now that cortisone made up in tablets for oral administration has proved effective, there may be a greater danger of infections because of the greater ease of self-medication In those diseases, such as disseminated lupus erythematosus, Hodgkin's disease, and leukæmia, where granulopenia is known to occur, the total and differential white cell count must be investigated regularly, and blood cultures taken, if there is any reason to suspect bacteræmia The differential diagnosis between rheumatic fever and subacute bacterial endocarditis is sometimes difficult, and obviously the danger of wrongly treating the latter with cortisone must be borne in mind, particularly in older patients with established valvular lesions. A golden rule would be "wherever there is doubt, treat first with antibiotics." If the patient has rheumatic fever he will not respond, and cortisone can then be given; but if cortisone is given first he may respond, whatever the underlying cause, and much valuable time may be lost; or the patient may die from uncontrolled septicæmia if in fact he has bacterial endocarditis. Similarly the unwary may confuse pyogenic or tuberculous arthritis with gout or other non-infective arthritis; again, the rule must be to give antibiotics first wherever there is doubt. When antibiotics are given with cortisone, it would appear that large doses are necessary. With successful chemotherapy the reproduction rate of the invading organisms is reduced below the rate at which the natural defences of the body can deal with them; and cortisone impairs these defences, tipping the balance back in favour of the organism. Antibiotics may thus become relatively ineffective, and there is some evidence, both clinical[17] and experimental,[18] that this does take place.

---

[1] Cushing H *Bull. Johns Hopk Hosp* 1932 50, 137

[2] Kass, E. H Finland M. *New Engl J Med* 1951 224 464

[3] Finland M. Kass E H Ingbar S H Proceedings of the First Clinical A.C.T.H Conference Philadelphia and London 1950 p 529

[4] White R. G Marshall A H E *Lancet* April 21 1951 p 891

[5] Hart, P D A. Rees R J W *Ibid* 1950 ii 391

[6] See leading article *Ibid* p 632

[7] Hahn E O Houser, H R Rammelkamp C H Denny F W Wannermaker L W *J clin. Invest* 1951, 30 274

[8] Glaser B J Berry J W Loeb L H. Woods W B Doughaday W H *Proc. cent Soc. clin Res* 1950 23 38

[9] Mogabgab W I Thomas L *Ibid* p 75

[10] Kass E. H Gelman Q M. Ingbar S H Ley A B Harris, J W., Finland M. Proceedings of the Second Clinical A.C T.H Conference (in the press)

[11] Coriell, L E. Murphy L., Siegal A. C Stokes J jun Cook C D Proceedings of the First Clinical A C.T H Conference Philadelphia and London 1950 p 522

[12] Loosli C G Hall R B, Berlin B S. Alexander E R *J Lab clin. Med.* 1951, 37 464. Hall R B Loosli C G *Ibid*, p 603

[13] Ragan C Howes E C Plotz C M Meyer K., Blunt, J W, Cattes R. *Bull N Y Acad Med.* 1950 26 251

[14] Rosenberg E F Steinbrocker O See *Ann rheumat Dis* 1950 9 401

[15] Boland E W *Ibid*

[16] Creditor M. C Bevans M Mandy W L Ragan, C *Proc Soc exp Biol N Y* 1950 74 245

On the whole it would seem that uncontrolled infection is a complication of overdosage with cortisone; and that with common-sense rules about diagnosis, and vigorous chemotherapy where necessary, cortisone is safe enough and well worth what risk it entails.

Neurosurgery and Muscle Function

MOST of the operations performed by the neurosurgeon are undertaken to prevent, or to check, disorganisation of neural function produced by structures extraneous to the central nervous system itself—by tumour, abscess, foreign body, scar, or hæmatoma. In a proportion, however, the aim is to modify deranged neural function in such a way as to bring it nearer normal. Unfortunately, except in the restoration of continuity of peripheral nerves, no reconstruction of neural pathways is possible, and, to an already damaged nervous system, surgery can contribute only another lesion. None the less, such treatment has certain theoretical possibilities. If a pathological lesion at a certain "level" has released the activity of lower centres, it is clearly possible by suitable operative procedures to diminish, or even to abolish, the abnormal activity. Thus involuntary movements may be stilled, or rigidity replaced by flaccidity. Where abnormal activity is confined to certain muscle groups, the operation may be so designed that these alone are affected. Such surgery, however, does no more than relieve symptoms, and it may have undesirable consequences. For the normal performance of willed movement the mechanisms subserving involuntary activity must be normal; surgery, even if confined to these mechanisms, must therefore at the same time impair voluntary movement. In cases of infantile cerebral palsy surgery has an even more serious disadvantage in that it also impairs *potentiality* for voluntary movement. Further, apart from these motor effects, sensory and autonomic changes result from some of the procedures used. Hence, before deciding to operate, the harmful possibilities of the proposed operation must be weighed very carefully against the expected benefits.

In view of these facts, it was useful to hear the experiences contributed by neurosurgeons to a discussion by the neurological section of the Royal Society of Medicine on April 5. Dealing with spinal cord lesions, Mr HARVEY JACKSON pointed out that recovery of function is often substantial where interruption of the cord is incomplete; so in such cases resort to surgery is not considered. Where the patient is helpless, however, with a paraplegia in flexion and associated "mass reflexes" (paroxysmal sweating with flexion spasms of the affected parts, bladder contraction, involuntary defæcation, &c.), section of the anterior nerve roots from the 10th or 11th dorsal to the 1st sacral may be of great benefit. The spastic paralysis is replaced by flaccidity, and "mass reflexes" are abolished; the patient is made much more comfortable, nursing is facilitated, and, if the lesion is below the outflow to the arms, progression with the aid of suitable appliances may be rendered possible. Later in the meeting Dr L. GUTTMAN emphasised the necessity of severing the nerves to spastic abdominal muscles as well as to the legs if satisfactory results are to be obtained, though such an operation is a formidable undertaking in a patient in whom vasomotor control is poor. For complete transverse cord lesions he recommended the intrathecal injection of alcohol, despite the atony of the bladder induced thereby. This is a method by which flaccid paralysis may be produced when operation is contra-indicated by the presence of bedsores. Posterior root section was not recommended.

Several speakers referred to the treatment of spasmodic torticollis, but none claimed satisfactory results. Mr HARVEY JACKSON reminded his audience that the spasms may be abolished after prefrontal leucotomy, but held that the cost in personality change is too high to justify its adoption. He quoted JAMES COLLIER's view that spasms would continue in this condition even if, after operation, this was the only contractile structure left in the neck!

Turning to surgery in parkinsonism, Mr JACKSON thought that lateral cordotomy, by which the indirect pyramidal tract is severed for the relief of tremor, should be reserved for young patients in whom the tremor is strictly unilateral. The paralysis produced recedes after operation, but a certain amount of permanent spasticity remains. Tremor may return to some extent as voluntary power recovers. The incision he uses is similar to that originally advocated by PUTNAM.[1] Though results vary from patient to patient, the method has the advantage that the crossed spinothalamic tract is avoided, and it does not cause the permanent loss of pain and temperature sensation on the contralateral side of the body which is seen if the incision is carried further forwards. In the mind of the meeting there seemed to be little doubt that spinal cordotomy is the most satisfactory operation for the relief of parkinsonian tremor: ablation of areas of the cerebral cortex may be followed by epilepsy, and the operative mortality from interruption of the pyramidal fibres in the internal capsule is high. It is clear, therefore, that rgery has but a very limited place in the treatment parkinsonian tremor, and no satisfactory surgical ethod of reducing rigidity has so far been devised. t present, indeed, direct operative approach to oblems of abnormal neural function has only a nall, though useful, application. No doubt this will e extended.

---

[17] Dubois-Ferrière H *Pr méd* 1951 59 442

[18] Spain D M, Molomut, N *Amer Rev Tuberc* 1950 62 337

[1] Putnam T J *Arch Neurol Psychiat* 1940, 23 303

Anæmia in Pregnancy

EXPERIENCE in outpatient and antenatal clinics uggests that the incidence of anæmia in pregnancy s increasing. Today most women in this country ust continue their housework and shopping up o the latest possible moment, and anæmia, even if light, makes it more difficult for the woman to carry on, and also slows postpartum recovery. Yet this anæmia is always treatable, and is nearly always preventable; increased vigilance would obviate much unnecessary debility in pregnancy and the puerperium.

It is not easy to discover the incidence of anæmia in pregnancy. In 1944 FULLERTON and his colleagues[1] in Aberdeen put the figure at only 4%; at the other end of the scale, from the U.S.A. comes an estimate[2] that 54% of women attending an outpatient clinic in Michigan were anæmic; 27% had iron deficiency anæmia, 15% nutritional anæmia, and 12% both forms. In a more recent survey SCOTT and GOVAN[3] found that 4595 women in Glasgow had an incidence of 17.6% at their first attendance, and a further 2.5% became anæmic during the pregnancy. A serious difficulty in deciding whether anæmia is present is occasioned by the normal fall in the red cell count and the hæmoglobin level that begins after the first month of pregnancy and reaches a maximum at about the sixth month. The fall is caused by the increase in blood and plasma volume that takes place at this time; there is some increase in the red-cell mass—estimated by ROSCOE and DONALDSON[4] at 12%—but the increase in plasma-volume is of the order of 25%. It might be possible to estimate how far the red cell count and hæmoglobin level could be expected to fall, and low "normal" limits of about 4,000,000 red cells per c.mm. and 10.5 g. hæmoglobin per 100 ml. have been suggested, only patients with counts below these levels being counted as "anæmic." But TYSOE and LOWENSTEIN,[5] who have re-investigated this problem, found great variations from case to case, and they finally admitted the impossibility of predicting normal values for any given patient at any stage of pregnancy. They did, however notice that, whatever the hæmoglobin level, the concentration of hæmoglobin in the red cells remained normal: this concentration is conveniently measured by the ratio of the hæmoglobin to the packed cell volume (hæmatocrit), the resulting figure being the mean corpuscular hæmoglobin concentration (M.C.H.C.). In iron deficiency anæmia—the commonest anæmia of pregnancy in this country—the M.C.H.C. is significantly reduced, and therefore estimation of the ratio will discover this anæmia whatever the blood dilution. The M.C.H.C. will not detect the megaloblastic types of anæmia, but these are always severe enough to be obvious. Unfortunately no British survey has yet been reported on these lines.

In Britain iron-deficiency anæmia accounts for perhaps 95% of the cases of pregnancy anæmia; megaloblastic anæmia is relatively very rare; nutritional anæmia, though difficult to assess, probably arises only in combination with iron deficiency. The problem, therefore, is mainly to prevent, detect, and treat iron-deficiency anæmia.

During pregnancy the body's demands for iron are substantial: the fœtus is supposed to need 375 mg.; iron is needed, too, for the increase in the red cell mass and in other tissues, and to replace that lost in the blood at labour. There is, it is true, some saving from the absence of menstruation, but the iron needs of a normal pregnancy are reputed to exceed by 2–3 times the loss from menstruation over the nine months. MCCANCE and WIDDOWSON[6] state that the amount of iron needed by the pregnant woman is about 16–20 mg. daily. In 1947 BRANSBY and MAGEE[7] showed that the British diet then provided about 11 mg. of iron daily. Since 1947 the position, so far as iron-containing foods is concerned, has got worse. Meat is normally our richest source of iron; if the housewife lays out her money to best advantage she may get as much as 10 oz. of lean "stewing steak," but this will provide her with only about 15 mg. of iron for a week. Where she is to get her iron ration for the other six days is not very clear. Unrationed meats, some fish, peas and lentils, and wholemeal bread, all contain enough iron to contribute to the store; eggs would be useful, but in winter at any rate, these are too few to count. MCCANCE and WIDDOWSON's tables show that the only foods that approach meat in iron content are such things as sardines, the famous spinach, and some breakfast cereals (but not oatmeal porridge); boiled mussels contain three times as much iron as an equal weight of meat, and boiled winkles four times as much, but these can hardly become the daily portion for expectant mothers. SCOTT and GOVAN[3] estimated that the diet of their Glasgow mothers contained as much as 16.67 mg. of iron daily; but they did not give details, and in view of other estimates this seems exceptional. It is reasonably clear that in this country most expectant mothers can obtain at best only the bare minimum of food iron needed. Under these conditions, and under better conditions too, a woman depends on her iron stores to provide the iron required to meet the demands of pregnancy. These stores may be diminished by previous ill health (particularly gastro-intestinal disturbances), by previous poor diet, by pregnancies following too closely on one another, and by previous excessive menstruation. In other words, the incidence of anæmia in pregnancy depends as much on the mother's health and diet in the months preceding the pregnancy as on what happens during the pregnancy itself.

Prevention of anæmia therefore depends, partly at least, on an adequate diet before and during pregnancy. An American authority[2] puts it succinctly: if every woman could have 1 quart of milk, 4 oz. of meat, and 1 egg, and was given gr. 15 of ferrous sulphate daily during the pregnancy, most cases of anæmia—of all types—would be prevented He was surprised that even in a rich farming countryside many women failed to obtain this reasonable minimum In this country, under present conditions, the milk can be obtained , but not the rest—except for specially favoured people Ferrous sulphate is distributed in tablet form at many antenatal clinics, but this is not entirely successful for several reasons Firstly, the tablets often cause gastric disturbance, and less often diarrhœa , the women then accept but do not take the tablets This difficulty could be largely obviated by the routine use of enteric coated tablets, which are not expensive to prepare in bulk A second cause is more complicated We have learnt that the amount of iron that can get across the intestinal barrier in a given time is limited—doses in excess of gr 30 daily are excreted Hahn and his co-workers,[8] using radioactive iron as a tracer, have lately confirmed that in pregnant women the percentage absorption of iron from an oral dose of ferrous sulphate falls off with big doses The best proportional absorption is obtained with a dose as small as 9 mg Fe (about gr $^1/_2$ of desiccated ferrous sulphate) , increasing the dose to 120 mg Fe (gr 6 ferrous sulphate) only doubled the amount of iron actually absorbed They also found that absorption was maximal towards the end of pregnancy with a dose of 9 mg Fe only 10% was absorbed up to the fifteenth week , between the fifteenth and twenty-fifth weeks the figure rose to 35% , and after the thirtieth week to 40% They conclude that the indiscriminate distribution of iron tablets to pregnant women is of doubtful value The patients studied by Hahn and his colleagues were not, however, anæmic , in anæmic women the iron absorption can be expected to be much increased, roughly in proportion to the fall in hæmoglobin level But in anæmic women another difficulty arises if the iron stores are empty, such iron as is absorbed goes first to these stores, and only when a certain level is reached is the iron released to be combined into hæmoglobin Women whose iron stores are depleted, from any of the causes already named, will take the pills but may still become anæmic , and we have no way of detecting such cases

---

[1] Fullerton, H. W., Mair, M. I., Unsworth, P. *Brit. med. J.* 1944, ii, 373.
[2] See Sturgis, C. C. Hematology. Oxford, 1948.
[3] Scott, J. M., Govan, A. D. T. *Brit. med. J.* 1949, ii, 1083.
[4] Roscoe, M. H., Donaldson, G. M. M. *J. Obstet. Gynæc.* 1946, 53, 430.
[5] Tysoe, F. W., Lowenstein, L. *Amer. J. Obstet. Gynec.* 1950, 60, 1187.
[6] McCance, R. A., Widdowson, E. M. *Spec. Rep. Ser. med. Res. Coun. Lond.* no. 235. H.M. Stationery Office, 1946.
[7] Bransby, E. R., Magee, H. E. *Brit. med. J.* 1947, i, 525.

Iron deficiency anæmia is usually best treated by giving about gr 25 of ferrous sulphate daily by mouth, preferably in enteric coated tablets For those who do not respond to iron by mouth, or whose anæmia is detected only late in pregnancy, intravenous iron has proved a great success, and its use has almost completely removed the need for blood transfusion Scott and Govan[9] found that of their anæmic patients 22% were resistant to iron by mouth but responded well to intravenous administration of 100 mg of elemental iron daily They noted, however, that 34 5% of moderate and 40% of severe cases showed a delayed response to intravenous iron, which they attributed to lack of protein in the diet In the U S A Kartchner and Holmstrom[10] also report good results with intravenous iron in pregnancy anæmia, and emphasise its value when gastro intestinal upsets prevent effective oral administration. The megaloblastic, or "pernicious," anæmia of pregnancy presents as a severe anæmia with hæmoglobin commonly reduced below 7 g per 100 ml., the cause is unknown, but it does not seem to appear when nutrition is adequate Marrow-puncture reveals the diagnosis at once Treatment is by folic acid, parenterally if necessary at first in a dose of 100–150 mg , and then 20 mg daily by mouth Vitamin B_{12} is here of no value

Much more can be done to detect and treat pregnancy anæmia in the early stages It is not possible for every patient attending an antenatal clinic to have her hæmoglobin level and the M C H C estimated, this would put too great a strain on an already overburdened pathological service But if the obstetrician, and the midwife, could train themselves to look regularly at the conjunctivæ of their charges, they could select for investigation those that appeared unduly pale , and if anæmia were discovered, treatment should be started then and there The provision of proper nutrition in pregnancy is outside the doctor's control , but he can at least show how to make the best of what food there is

Annotations

VIOMYCIN

A NEW antibiotic which may prove useful in the treatment of tuberculosis was discovered last year in the U S.A , and was named 'Viomycin ' This is obtained from two strains of streptomyces—*S puniceus*, and *S floridæ* It is a strong organic base containing guanidine and a peptide linkage, and forms a sulphate which is stable in solutions of pH 5–6 at room temperature , little else is known about its chemistry It is bacteriostatic rather than bactericidal, and resembles streptomycin in that mycobacteria readily become resistant to it , tests show that the H37Rv strain of *Mycobacterium tuberculosis* becomes resistant to both drugs at about the same rate A strain of tubercle bacilli highly resistant to viomycin in vitro can be produced by serial transfer of the culture through eight solutions containing increasing concentrations of the drug Viomycin is, however, active against strains of tubercle bacilli which are resistant to streptomycin Unlike streptomycin it has relatively little activity against gram negative organisms in vitro though experimentally, it has proved more effective in vivo In vitro most strains of *Myco tuberculosis* are inhibited by concentrations of 1–5 μg per ml , and pneumococci, streptococci, and staphylococci are inhibited by concentrations of 40–100 μg per ml

Three different groups of workers[1] have shown that viomycin is as effective as streptomycin against tuberculosis in mice and guineapigs infected with the H37Rv strain of human tubercle bacillus , a daily dose of 0 5 mg significantly increases both the survival time and the survival rate of infected animals A daily intramuscular dose of viomycin 40 mg was as effective as streptomycin 100 mg These two antibiotics can be given together , they are not antagonistic but neither are they synergistic Viomycin is only slightly toxic to animals, and no ill effects were produced by giving rats subcutaneous injections of 50–100 mg per kg body weight daily for six weeks The same dosage was well tolerated by dogs for five months, but in cats it caused disturbances of posture and gait Viomycin can be given intramuscularly or intravenously without local irritation, and it can also be given by mouth In man, however, it seems to have more side effects than streptomycin Werner and his colleagues[2] gave daily intramuscular doses of 30–70 mg per kg body weight to 10 tuberculous patients The drug caused renal irritation in all, abnormalities of the serum electrolytes in 5, elevation of the blood urea in 4, impairment of vestibular function and partial deafness in 2, and hypersensitivity reactions in 3 The disturbances in the serum electrolytes included hypokalæmia, hypocalcæmia, hypochloræmia, and hypophosphatæmia, and an increase in the carbon dioxide combining power of the blood These changes were prevented or reversed by replacing the deficient ions In vitro the strains of *Myco tuberculosis* isolated from these patients before treatment were sensitive to viomycin 6 2–12 5 μg per ml., but after 60–70 days' treatment resistance increased 8–16 times, developing in the same way as resistance to streptomycin This investigation was made to test the toxicity of viomycin and its ability to produce drug resistance rather than to test its therapeutic value A favourable response was observed, however, in some of the patients, this may be of some significance because 8 of the 10 patients had failed to respond previously to streptomycin and para aminosalicylic acid (P A S) and were unsuitable for artificial pneumothorax or other surgical treatment Werner and his colleagues, though hesitating to make any therapeutic claim for viomycin at this stage, believe that the toxic effects are not serious enough to preclude its use in man, and that it could be used for treatment provided that more extensive trials show that it is as effective as streptomycin or P A S It has the advantage of being effective against strains which are resistant to streptomycin, and the development of resistance may be prevented by intermittent therapy, which has proved effective with streptomycin,[3] and with a combination of streptomycin and P A S[4] Conceivably combined intermittent treatment with viomycin, streptomycin, and P A S might prevent the appearance of resistance to any one of them

---

[8] Hahn P F Carothers E L , Darby W J Martin M Sheppard C W Cannon R O Beam A S Densen P M Peterson J C McClellan G S *Amer J Obstet Gynec* 1951 61 477

[9] Scott J M , Govan A D T *Lancet* Feb 17 1951, p 367

[10] Kartchner, F D , Holmstrom E G *Amer J Obstet Gynec* 1950, 60, 1288

[1] Hobby G L Lenert T F Donikian M Pikula D *Amer Rev Tuberc* 1951 63 17 Youmans G P Youmans A S *Ibid* p 25 Karlson A G Gainer J H , *Ibid* p 36 *Proc Mayo Clin* 1951 26 53

LIQUORICE IN ADDISON'S DISEASE

OUR readers will recall that last year Professor Borst and his colleagues[5] showed that liquorice extract taken by mouth had effects qualitatively similar to those of injected deoxycortone and of adrenocorticotropic hormone (A C T H), but that the similarity did not extend to the effect of A C T H on rheumatoid arthritis or of deoxycortone on Addison's disease These observations led Groen and his co-workers[6] to repeat Borst's observations in another case of Addison's disease Unlike Borst they found that liquorice was effective, after preliminary treatment with deoxycortone the disease was controlled by liquorice extract 15 g per day, and withholding the extract caused return of symptoms and the characteristic blood changes A further course of treatment with liquorice extract produced clinical remission and reversal of the blood changes, and the patient was finally stabilised on liquorice extract 20 g per day with a sodium chloride intake of 10 g per day These workers were unable to account for the failure in the case described by Borst, and Borst himself saw this second patient and was convinced of the benefit obtained Another patient with Addison's disease was treated by Groen et al with a crude preparation of one of the main ingredients of liquorice a daily dose by mouth of 3 3 g of ammonium glycyrrhizinate was given with success to this patient, who had previously been treated with deoxycortone 2 5 mg daily It is interesting to note that glycyrrhizonic acid contains glucuronic acid, and also glycyrrhetinic acid which has a formula closely resembling the group of steroid hormones to which deoxycortone belongs If in fact liquorice proves efficacious in some cases of Addison's disease the economic gain would be substantial, for deoxycortone costs 7*d* per mg, whereas powdered liquorice root costs 3*d* per oz

SOCIAL CASE-WORK

NEARLY three years since the coming into force of the National Health Service Act there are still doctors and others in the hospital services who cannot understand why almoners are necessary now that financial assessment of patients is not required An even larger number believe that an almoner's duties today should consist mainly in arranging for convalescence, for home helps, for splints or appliances—in fact for all those welfare services inside and outside the hospital that are so important for the patient's recovery Local health authorities certainly seem to hold this view, and arrangements and arguments about aftercare are apt to deal with the whole matter at a superficial level Actually medicosocial work, or social case work, in its application to medical problems goes deeper than this, and elsewhere in this issue Miss Margaret O'Farrell propounds a thesis that will come as a surprise to many She argues that instead of a medical or nursing training being an advantage for the medicosocial worker, it may even be a handicap, for it tends to induce an approach that prejudices the relationship of patient and almoner from the first

Miss O'Farrell says that in the early stages of the training of the almoner she should not be in a hospital, and this point of view goes some way to explain why the Institute of Almoners, whose latest report we reviewed on April 7, has not always been willing to accept for training those who have worked in hospitals as welfare clerks The recent announcement that the institute is opening its register to certain "unqualified" almoners is therefore all the more praiseworthy because it is accepting a risk that some thus recognised will never do more than welfare work at a superficial level. Of course such welfare work must be done, and it is better done by those trained in the understanding of human relationships, so the almoner's department of a hospital will remain, it is hoped, the spot where doctors and patients alike can take their troubles It is clear from articles and correspondence in the *Almoner* last year that the almoning profession is still working out a satisfactory compromise between the demands for such welfare work and the deeper need of patients to make the adjustments in their lives which their illnesses have made essential One immediate difficulty arises—namely, the shortage of almoners, to which the Cope Committee has again drawn attention, and the need to spread the supply over the whole country It is obvious that the welfare side of the work can be done more rapidly, with more "items of service" by each worker than is possible with the careful establishment, in a series of interviews, of a personal relationship that will enable the patient to face his or her situation and see clearly what action is involved Much of this work is psychological in character, and almoners are being criticised for attempting too much at this level, to the neglect of the superficial help over more material things on which the almoners' profession built up its reputation and which today is being to some extent relegated to untrained assistants

Inevitably the question is being asked "can we afford it ?" A possible answer is that hospital physician and surgeons who appreciate the social implications o disease are more and more demanding the type of case work that only the trained social worker can do. The question whether or not the health visitor can be regarded as a medical social worker in this respect is highly controversial. Recent correspondence in the *Times*, following the criticism that a nursing officer at the London County Council divisional health office might not necessarily be the best person for liaison between hospital almoners and the various agencies in the field of aftercare, showed an interesting difference of opinion. On the one hand representatives of the health visitors protested at what was regarded as a slur on public health nursing staff, and on the other hand supporters of the school care committee work claimed with some pride that the care committee organisers were trained social workers. There is some danger in recent developments well illustrated in *The Consul*—a modern Italian opera dealing with another set of human problems. The pathetic song in the consul's office, with the theme "My name is a number, my story a case," indicates what can happen when the personal relationship of social worker with patient is achieved only through a medium of files and correspondence. Social case work in a medical setting seeks to avoid this, and Miss O'Farrell's article is bound to set many thinking afresh.

---

[2] Werner, C A, Tompsett, R Muschenheim C McDermott W *Amer Rev Tuberc* 1951 63 49
[3] James L A, Sides, L J Dye W E Deyke V F *Ibid* p 275
[4] Temper C W Hughes F J jun Mardis R E Toubin M S Dye W E *Ibid* p 295
[5] Borst J G G Molhuysen J A Gerbrandy J de Vries L A de Jong J C Lenstra J B, Turner, K P *Lancet* 1950 ii 381
[6] Groen J Pelser H Willebrands A F Kamminga, C E *New Engl J Med* 1951 244 471

DIAGNOSTIC AIDS IN GENERAL PRACTICE

ON April 18 the general practice section of the Royal Society of Medicine heard an account of the diagnostic unit Dr John Hunt has established in his practice in London. On his return from the war Dr Hunt decided to see his patients in a building separate from his residence. Besides the rooms he needed for consulting rooms and waiting rooms, and a secretary's office, the house he chose contained a tiled basement room formerly used as a kitchen. This he adapted as a laboratory, which he put in charge of a full time technician recently demobilised from the R A F medical services. From the beginning he found this arrangement so satisfactory and so helpful that, when a chance came to secure adjacent mews premises, he took the further step of installing X ray and electrocardiographic apparatus under the care of a qualified radiographer. He has now had this combined diagnostic unit in full use for more than three years. The types of investigation undertaken include all the routine urine tests, blood counts, serum tests, and simple bacteriology; the more involved bacteriology, and all histology are sent elsewhere. In the same way, the X ray unit undertakes radiography of all bones and joints (including fractures), teeth and sinuses, and chests, but not such investigations as intravenous pyelography, or barium meals or enemas. The immediate interpretation of the findings in both laboratory and X ray room is made by Dr Hunt with the help of the technicians, but a consultant pathologist sees the report on each test, and a consultant radiologist sees each X ray film before any decision is deemed final.

In the past three years, Dr Hunt said, rather more than 5000 patients have passed through his hands—some for casual consultation, others with long illnesses. For these patients over 7000 laboratory tests have been made, and 1400 X ray examinations. Analysis of the cases shows that the range of work undertaken has not differed materially from that encountered in a typical general practice, but the proportion of tests is much higher than most general practitioners demand. Dr Hunt would be the first to admit that the results obtained often do no more than confirm a diagnosis already made, but he feels that the satisfaction of confirming the diagnosis, or occasionally of upsetting it, justifies the performance of these tests. His patients seem to share his views, for Dr Hunt is engaged solely in private practice, and each of the tests is paid for by his patients—and willingly paid for, we are informed—for the sake of a speedier and accurate diagnosis, and in preference to waiting for similar tests to be performed without charge through National Health Service arrangements. Dr Hunt realises that, because of their expense, facilities such as he enjoys could not be provided by doctors themselves for their N H S patients, but he believes there is scope for the public provision of units such as his to help groups of practitioners, or, failing this, for giving more practitioners direct access to the diagnostic departments of hospitals.

The discussion that followed showed what great importance the efficient modern practitioner attaches to obtaining proper pathological and radiological help, and showed also that under present conditions direct access by the practitioner to hospital departments is the means most favoured. Several speakers spoke of satisfactory arrangements in their own hospital areas, and none doubted that extension of this system of direct access is both desirable and practicable. Experience, it was said, has proved that practitioners do not abuse the right to go direct to the pathological and radiological departments and to use the specialists there as consultants. In the end, the load placed on the hospitals—both on the outpatient and the diagnostic departments—is less than if all patients have to be seen by a consultant physician or surgeon before tests are undertaken. Wherever possible, it was felt, the practitioner should make a habit of visiting the hospital and consulting with the radiologist or pathologist about their findings. Where this is regularly done, not only does he get the maximum help, but consultant practitioner relationships develop that are a source of mutual satisfaction.

PENICILLIN IN EMPYEMA THORACIS

PENICILLIN has revolutionised the treatment and prognosis of pulmonary suppuration. Combined with postural drainage, it has reduced to a rarity the operation of external drainage of lung abscess; for the few cases which do not respond the surgeon now prefers lobectomy. Penicillin is similarly useful in the management of suppurative bronchitis and bronchiectasis.

In empyema, however, the value of intrapleural penicillin is still disputed. The objections to this treatment centre on the mechanical complications of rigid pleura and fibrinous deposits which follow delay in the evacuation of pus, preventing complete re expansion of the lung once adequate drainage has been established. The early work by Roberts and others[1] showed the dangers of continuing too long with repeated aspiration and penicillin replacement, and Brock[2] has suggested that many of the cures so obtained are really cures of early pleural effusion. While in no way underrating this criticism of "conservative" treatment, Dr Asher and Dr Davies, whose article appears on an earlier page, have put this method of treatment once more to the test. They have obtained gratifying results in twelve consecutive cases of empyema treated by aspiration with replacement by 500,000 units of penicillin every 1–3 days, combined with systemic administration of the drug. Pus disappeared after an average of 40 days, and the average length of stay in hospital was $7^1/_2$ weeks. Full re expansion of the lung was achieved in all cases, and residual bronchiectasis was found in 1 only. Progress has been followed for 16–33 months.

Admittedly treatment by repeated aspiration takes time, but probably no longer than surgical drainage, and in skilled hands it is no more irksome to the patient. It can be regarded as a permissible method of treatment in the early stages of the disease and when the exudate is small, provided the physician is alive to the need for surgical intervention where fibrin forms quickly or the condition threatens to become chronic. Failures from this cause may become fewer as experience with fibrinolytic agents widens.

---

1 Roberts J E H Tubbs O S, Bates M *Lancet* 1945 i 39
2 Brock R C *Proc R Soc Med* 1947, 40, 645.

Special Articles

SOCIAL CASE-WORK IN A MEDICAL SETTING

MARGARET B. O'FARRELL
B.A. Oxfd, A.M.I.A
RESEARCH ASSISTANT, DEPARTMENT OF SOCIAL STUDIES
UNIVERSITY COLLEGE HULL

SOME years ago an almoner in an outpatient clinic at the end of the day found an elaborate drawing on the houseman's blotter. It was called These Also Came. In front was the patient and behind and above him were many lightly sketched figures—some with labels such as Wife, Foreman, Joe the Barman, Allotment Pal. Here was a ready made demonstration of that houseman's awareness, not only of the delicate variations in heart beats and breath sounds to which he had been listening, but also of the implications to his illness of the patient's home, family, job, and the whole complex of his interpersonal relationships beyond the walls of the hospital.

When a patient comes to a doctor he brings with him others who are a part of his situation or will help to get him out of it. The doctor asks himself, "What does this patient need? Is what he needs within his reach? If so, can he reach for it?" The patient is saying, "What is happening to me? What does this mean to me? What am I to expect?" Almost inevitably these other people from outside the hospital are mixed up in the answers, and it is where any of the answers seem to present obstacles to diagnosis or cure that the doctor may bring the social case-work service into play.

Few people distinguish between the individual approach of one human being to another and that of client and worker in the professional discipline called social case work. This is understandable because very little has been done in speech or writing in this country to explain, by describing the case work method, the difference between the two. Recently, in fact, a doctor who was trying to enlarge his understanding of its uses complained that, unlike medical men who explain an individual's disease in terms of the great physical systems of the body—circulatory, nervous, &c.—the social case worker never gave anything but examples, spoke in parables as it were, and left him to deduce the general principles.

It is a fair criticism that good intentions and a desire to help have in the past been accepted as a substitute for careful formulation of the principles involved in social case work. But at this stage, though we are by no means ready to set down definite general principles, we have enough experience to deduce with a fair amount of certainty a few basic working assumptions.

SOME BASIC PRINCIPLES

Doctors, like lawyers, have used the case method professionally for centuries to deal with an individual's problems in the light of his medical or legal situation. Clergymen, kind neighbours, and others also use the case method. How does social case work differ from these?

Social case work is primarily a service offered by a professional worker with a certain body of knowledge, a mind trained in orderly thinking, and a personality sensitive to human relationships. It is offered to an individual who is experiencing some breakdown, small or great, in his ability to deal with his own life, either because he is a victim of circumstances or because he makes his own trouble, or because of a combination of these factors.

The social case worker's body of knowledge should cover community resources and individual's rights in law, an understanding of human behaviour, of the social implications of disease, and of the factors and forces in society which help the individual to rise or which push him down.

The technique which the social case worker has to learn consists in being able to offer the service derived from this knowledge in such a way that the person to whom it is offered can take hold of it and use it. It is in the special nature of the relationship between the patient and the case worker that the value of the service lies.

Although any understanding of people which attempts to be orderly will be limited by the nature of the material—there can be few things on this earth presenting more variables than a human being—still it is possible at this stage to deduce from our social case work experience the following general concepts:

> It is a basic impulse in the normal man to want to manage his own affairs because there is no security to be had in being dependent on someone else.
>
> The individual grows through relationships with other people.
>
> Unless the damage is severe the growth process is strong so that temporary help will not produce dependency.

The aim of the social worker is to help the individual to regain as much independence as possible by:

> Giving him a special sort of understanding relationship in which he can practise, try things out as it were, in a protected environment.
>
> Giving help freely in ways which do not impede growth or increase dependency.

RÔLE OF THE CASE WORKER

There are two major ways in which help can be given to a person in need. One is by manipulating the environment; the other is by giving direct help in interviews when the patient is encouraged to adopt habits of mind which will make him able to solve his own problems as they arise. The degree to which one or other way is used depends both on the patient and his environment. It will be obvious that some people of extremely unstable character and some defectives have not the capacity to solve their own problems even with help. And there are others who are faced for a time at least with demands so impossible in relation to their strength that it becomes necessary that other people should direct their lives. For these the social case worker may have to help by providing, for instance, institutional care, a foster-home away from the neglectful parents, change of school away from the over ambitious teacher, or change of job away from the bad tempered foreman; or, more subtly, by drawing them into some situation which will give self-confidence a chance to grow, such as an invitation to join the patients' entertainment committee of a sanatorium, or by teaching a special skill to a disabled man who fears to leave the shelter of the hospital. All such action is based on an assumption that we know what is best for the patient.

But usually a patient in whom the doctor encounters obstacles to treatment or recovery can make some reasonable adjustment of his own life through working out in interviews with a case worker what it is he wants to do and what kind of help he needs in order to do it. This allows the patient to gain a new understanding of himself and the situation in the light of which he can take hold of the treatment offered him by the doctor and use it. The case worker, by accepting the patient as he is, by the words in which she shows understanding of his trouble, holds up, as it were, a mirror in which he can see himself and his situation more clearly and see how to act.

THE CASE-WORKER AND THE DOCTOR

It will be seen at once that this relationship is different from that of doctor with patient, and an understanding between the doctor and the social case worker of their different rôles is vital

Outside the hospital the individual who comes to an agency for help sees his problem as a social one, and that is why he brings it to a social worker In the medical social case work field the patient sees his problem as a medical one and he has therefore brought it to a doctor The doctor, who has become by tradition a symbolic figure with centuries of pain healing behind him, remains throughout the chief figure in this situation even if he only sees the patient once He automatically becomes the leader of whatever team is formed to deal with the patient's illness He is, in our culture, a symbolic figure of benevolent authority, and practically too he is the only one who can predict the stresses and strains involved in the illness It follows that where social case work is to be used in conjunction with medicine, then the responsibility of the doctor in enabling the patient to make use of the service, whether through general policies or personal introduction, cannot be too strongly emphasised Even where patients with social problems come to the case-worker by other routes in the hospital, this makes no difference—the action the case worker may take is supplementary, the relationship with the doctor is the basic one There is, in fact, no substitute for the doctor's genuine interest in the individual as a person and the patient's confidence in the doctor as someone who sincerely recognises his interests

Why, then, is not the medical social case worker's rôle an extension of the doctor's rôle—to do what the doctor would do if he had time? Years ago I was asked why medical social workers did not take the first part of a doctor's training before specialising, and recently it has been suggested that they should begin by taking part of the nurses' training

Possibly there is some confusion of thought in these points of view, springing from an incomplete understanding of the difference in the relationship of doctor with patient and of patient with social case worker The relationship of the doctor with patient—and incidentally of the nurse, and other specialists in the medical field, with the patient—is one of authority The doctor diagnoses, advises, orders, forbids, acts, treats, teaches, suggests, interprets, uses his personal influence and his symbolic aura to bring the patient to the goal which he, the doctor, has chosen The patient submits or rebels, accepts or refuses, is dependent or revolts from dependence on this authoritative figure With the medical social worker the relationship, to be successful, has to be entirely different The rôle of the case worker is to sit down with the patient and help him to work out his difficulty in his own way, not imposing her will or her goals on him, but looking at the whole situation from his angle and helping him to recognise and remove from his path those obstacles, personal or material, which impede his recovery and prevent his full cooperation with the doctor

To achieve this relationship the social case worker does not look at the patient's difficulties from any particular angle, such as law or medicine, but takes a general view The doctor, the lawyer, the clergyman, the industrialist each specialises in a particular service to the community The social case worker is a specialist too but of a different sort Her specialty is to attempt to understand the balance and interplay between all the services in the community and their relation to a particular patient who needs help

Thus, important as it is that the medical social case-worker should acquire knowledge of medicine later, it is even more important that she should spend the beginning of her training not in a hospital but in a position where she will receive the impact of all the great services and institutions equally

Public Health

LYMPHOCYTIC CHORIOMENINGITIS

REVIEW OF TEN CASES

P R DUNCAN
M B , B Sc Manc , M R C P
SENIOR MEDICAL REGISTRAR

A E THOMAS
M B , B Sc Manc , M R C P
MEDICAL REGISTRAR

MANCHESTER ROYAL INFIRMARY

J O'H TOBIN
B M Oxfd, Dip Bact Manc
LECTURER IN BACTERIOLOGY IN THE UNIVERSITY OF MANCHESTER

SINCE the virus of lymphocytic choriomeningitis (L C M) was first isolated by Armstrong in 1934 it has been shown in many countries to be the cause of one form of "aseptic meningitis" This syndrome consists of a short febrile illness of fairly sudden onset with meningeal irritation Complete recovery follows The cerebrospinal fluid (C S F) contains an excess of lymphocytes and is bacteriologically sterile The cause is often assumed, but rarely proved, to be the virus of L.C.M Infections due to this virus have been reviewed by Farmer and Janeway (1942)

MacCallum (1949) has reported five cases of aseptic meningitis from various parts of England which were caused by the virus of Armstrong One of these came from a Manchester house where mice carrying this virus were caught In 6 months we have seen ten cases of L C M in Manchester Serological methods have indicated the ætiology in all cases, and the virus was isolated from four of them Green et al (1949) have pointed out that the ætiological diagnosis in many published cases has been poorly substantiated, since it was based on clinical grounds only Other diseases—e g , glandular fever and mumps—may present a somewhat similar picture The clinical features of cases proved to be due to the virus of L C M are therefore described

CASE RECORDS

Case 1 —A married woman, aged 30, was admitted on Feb 25, 1950, to Manchester Royal Infirmary under the care of Dr C S D Don She complained of headache, vomiting, and cough She had collapsed at work twelve days before, feeling cold and shivery, with aching pains in the limbs After three days in bed a productive cough and left-sided pleuritic pain had developed These symptoms had persisted, and occipital headache and photophobia were also present on admission

On examination she looked thin, pale, and ill Her temperature was 101 8°F, pulse rate 120, and respirations 24 per min No other abnormality was found, apart from neck stiffness and absent abdominal reflexes Radiography of the chest showed miliary mottling in both lung fields

Progress —On Feb 27 the temperature was 101°F , headache was severe, neck stiffness more pronounced, and Kernig's sign positive The resting pressure of the C S.F was 70 mm , and the fluid was turbid, containing 2760 cells per c mm (all lymphocytes), and protein 180 mg , glucose 29 mg , and chlorides 680 mg , per 100 ml No tubercle bacilli or other organisms were seen on microscopy or cultured from this or later specimens of C S F

Treatment —Tuberculous meningitis was provisionally diagnosed on the clinical picture, the chest radiogram, and the low C S F glucose level Intrathecal and intramuscular streptomycin was given and continued for 3 days On March 1 the remarkable clinical improvement suggested the possibility of a virus meningitis , so a fresh specimen of C S F was taken, and the virus of L C M was isolated from it Serum obtained on Feb 27 did not fix complement when tested with L.C.M antigen, but serum obtained a month later was positive to a titre of 1 in 16

Other Investigations —On Feb 27 the erythrocyte sedimentation rate (E S R.) was 20 mm in 1 hr (Wintrobe) and a blood count showed red cells 4,760,000 per c mm , Hb 13 g per 100 ml , white cells 8700 per c mm (polymorphs 66%, lymphocytes 21%) On March 2 a Paul Bunnell test was negative, and the Wassermann reaction of the C.S.F negative On April 2 radiography of the chest showed that the lung fields were clear

Recovery continued uneventfully and the patient was sent to a convalescent home on March 13

Associated Illness—The patient said that 2 weeks before she became ill her son, aged 8 years, had developed anorexia and vomiting, with headache and neck stiffness She recalled particularly the striking degree of neck rigidity After a week in bed the boy had recovered On March 30, 8 weeks after the beginning of his illness, the boy's serum gave positive complement-fixation with L C M. antigen to a titre of 1 in 16

Mice—The virus of L.C M. was isolated from mice trapped at the house where the patient and her son lived

Case 2—A girl, aged 18, employed as a machinist, was admitted on May 19, 1950, to the Manchester Royal Infirmary under the care of Dr Don She had complained of influenza like symptoms for 2 weeks—headache, anorexia, and mild fever—and five days before admission the headache had increased and been accompanied by vomiting.

On admission she did not look ill, her temperature was 99 6°F, pulse rate 86, and respirations 18 per min The only abnormal physical sign was slight neck rigidity The resting pressure of the C S F was 150 mm The fluid was clear and colourless and contained 200 cells per c mm (all lymphocytes), and protein 180 mg, glucose 47 mg, and chlorides 740 mg, per 100 ml

Diagnosis—It was felt that lymphocytic choriomeningitis was a possible diagnosis, particularly as we knew the patient worked in a raincoat factory within 20 yards of the house from which infected mice had been trapped (case 1) From blood and throat washings taken at this time the virus was recovered later None was isolated from the C S F

Other Investigations—On May 20 the E S.R was 22 mm in 1 hr (Wintrobe), and a white-cell count 6300 per c.mm. (polymorphs 47%, lymphocytes 42%) Repeated total and differential white cell counts were normal—e.g, 6600 per c.mm. (polymorphs 62%, lymphocytes 29%) on June 26 On May 27 chest radiography was normal, and Wassermann reactions of the blood and of the C.S.F were negative On May 20 and June 1 Paul Bunnell tests were negative

Progress—After lumbar puncture the patient had no further headache She went home on June 2 and returned 6 days later to report that a painless swelling of the neck had appeared the previous day but was now subsiding This was a slight enlargement of cervical and axillary glands on both sides, but no abnormality was found in the fauces or elsewhere The white cell count was 8100 per c mm. (polymorphs 64%, lymphocytes 31% large mononuclears 5%) and a further Paul Bunnell test was negative

Serum obtained 14 days from the onset gave negative complement-fixation with L C M antigen. A second specimen 3 weeks later was positive to a titre of 1 in 8 No neutralising or complement fixing antibodies were present in sera obtained from the girl's parents

Mice.—Unsuccessful attempts were made to trap mice in the patient's home and the raincoat factory, but rodent destructors had visited the factory only a few days previously

Case 10—A woman technician, aged 23, employed in the laboratory of one of us (J O H T) had been in good health until early February, 1950, when she lost 7 lb in weight in 5 weeks During this time she had a poor appetite but no other symptoms and continued at work, subsequently regaining her normal weight

As she had been handling laboratory mice infected with the virus of L C.M during this period, serological tests were made The complement fixation test showed the following titres Feb 27, positive 1 in 2, April 13, positive 1 in 8, April 23, positive 1 in 8, Sept 21, positive 1 in 2 Neutralising antibodies against L.C.M. virus were demonstrated in the sera obtained on April 23 and Sept. 21

The clinical features of cases 1–9 are summarised in table I.

CLINICAL FEATURES

Three clinical syndromes in man have been attributed to the virus of L C M (1) meningitis, which has been most frequently described, (2) encephalomyelitis (Findlay et al 1936), and (3) an influenza like infection without apparent involvement of the nervous system (Armstrong 1940) In the present series all were cases of meningitis except case 10, the laboratory infection Symptoms suggesting a virus infection developed 7–21 days before the onset of meningitis in eight cases, in the ninth patient they lasted 3 days These premonitory symptoms included general malaise, pains in the back and limbs, shivering, sweating, and striking anorexia This characteristic onset was first described by Baird and Rivers (1938) Cough was a prominent premonitory symptom in three of our cases and chest pain in two Two patients described a temporary remission of their general symptoms for a day or two before the onset of headache and meningitis

In the meningeal stage severe headache and neck stiffness were usually accompanied by photophobia and vomiting, six patients looked really ill. On passive flexion of the neck, rigidity was observed in all, and Kernig's sign was positive in six of the nine cases No paralysis, cranial-nerve lesion, or other sign suggesting encephalitis was observed. Signs of meningism lasted longer than a week in only two cases The C S.F pressure was raised in one, and within normal limits in six, of the seven cases in which it was recorded Two patients were afebrile, and in the remainder temperatures ranged from 100° to 104°F In the three patients with greatest fever there was slight drowsiness Three of our patients had transient lymph gland enlargement In one this

TABLE I—SYNOPSIS OF CLINICAL FEATURES OF 9 PROVED CASES OF LYMPHOCYTIC CHORIOMENINGITIS

Case no	Date of admission	Sex	Age (yr)	Premeningitic symptoms for (days)	Severity of illness	Special features	Diagnosis proved by	Environment
1	Feb 25 1950	F	30	12	+++	Cough chest pain miliary mottling of lungs	C.S.F virus isolation C.F T	Mice carrying L.C.M virus. Son aged 8 C.F T +
2	May 19 1950	F	18	14	+	Lymphadenopathy (cervical and axillary)	Blood and throat virus isolation C.F T	Worked at mice-infested factory 20 yds. from case 1
3	Dec. 24 1949	M	28	21	++	Vomiting	C.F T, N T	Husband and wife No mice caught Son aged 3 C.F T −
4	May 10 1950	F	28	14	+++	Vomiting premeningitic remission	C.S F virus isolation C.F T	
5	Feb. 15 1950	F	33	21	+++	Vomiting cough temperature 104°F	C.S.F virus isolation C F T	Mice carrying L.C.M. virus
6	Dec 24 1949	F	21	3	++	Vomiting	C.F T	No mice caught
7	July 6 1950	M	28	14	+	Chest pain premeningitic remission lymphadenopathy (cervical axillary inguinal)	C F T N T	Mice carrying L.C M. virus Wife C.F T + N T + Sister C.F T + N T −
8	June 9 1950	M	35	11	++	Cough lymphadenopathy (cervical)	C F T N T	No mice caught Wife C.F T − N T +
9	March 27 1950	F	34	7	+	Nil	C F T N T	No mice caught

C.F T complement-fixation test with L.C.M. antigen. N T neutralisation test with L.C.M. virus.

between the doctor and the social case-worker of their different rôles is vital

Outside the hospital the individual who comes to an agency for help sees his problem as a social one, and that is why he brings it to a social worker In the medical social case work field the patient sees his problem as a medical one and he has therefore brought it to a doctor The doctor, who has become by tradition a symbolic figure with centuries of pain healing behind him, remains throughout the chief figure in this situation even if he only sees the patient once He automatically becomes the leader of whatever team is formed to deal with the patient's illness He is, in our culture, a symbolic figure of benevolent authority, and practically too he is the only one who can predict the stresses and strains involved in the illness It follows that where social case work is to be used in conjunction with medicine, then the responsibility of the doctor in enabling the patient to make use of the service, whether through general policies or personal introduction, cannot be too strongly emphasised Even where patients with social problems come to the case worker by other routes in the hospital, this makes no difference—the action the case worker may take is supplementary, the relationship with the doctor is the basic one There is, in fact, no substitute for the doctor's genuine interest in the individual as a person and the patient's confidence in the doctor as someone who sincerely recognises his interests

Why, then, is not the medical social case worker's rôle an extension of the doctor's rôle—to do what the doctor would do if he had time? Years ago I was asked why medical social workers did not take the first part of a doctor's training before specialising, and recently it has been suggested that they should begin by taking part of the nurses' training

Possibly there is some confusion of thought in these points of view, springing from an incomplete understanding of the difference in the relationship of doctor with patient and of patient with social case worker The relationship of the doctor with patient—and incidentally of the nurse, and other specialists in the medical field, with the patient—is one of authority The doctor diagnoses, advises, orders, forbids, acts, treats, teaches, suggests, interprets, uses his personal influence and his symbolic aura to bring the patient to the goal which he, the doctor, has chosen The patient submits or rebels, accepts or refuses, is dependent or revolts from dependence on this authoritative figure With the medical social worker the relationship, to be successful, has to be entirely different The rôle of the case-worker is to sit down with the patient and help him to work out his difficulty in his own way, not imposing her will or her goals on him, but looking at the whole situation from his angle and helping him to recognise and remove from his path those obstacles, personal or material, which impede his recovery and prevent his full cooperation with the doctor

To achieve this relationship the social case worker does not look at the patient's difficulties from any particular angle, such as law or medicine, but takes a general view The doctor, the lawyer, the clergyman, the industrialist each specialises in a particular service to the community The social case worker is a specialist too but of a different sort Her specialty is to attempt to understand the balance and interplay between all the services in the community and their relation to a particular patient who needs help

Thus, important as it is that the medical social caseworker should acquire knowledge of medicine later, it is even more important that she should spend the beginning of her training not in a hospital but in a position where she will receive the impact of all the great services and institutions equally

Public Health

LYMPHOCYTIC CHORIOMENINGITIS

REVIEW OF TEN CASES

P R DUNCAN
M B, B Sc Manc, M R C P
SENIOR MEDICAL REGISTRAR

A E THOMAS
M B, B Sc Manc, M.R.C.P
MEDICAL REGISTRAR

MANCHESTER ROYAL INFIRMARY

J O'H TOBIN
B M Oxfd, Dip Bact Manc
LECTURER IN BACTERIOLOGY IN THE UNIVERSITY OF MANCHESTER

SINCE the virus of lymphocytic choriomeningitis (L C M) was first isolated by Armstrong in 1934 it has been shown in many countries to be the cause of one form of "aseptic meningitis" This syndrome consists of a short febrile illness of fairly sudden onset with meningeal irritation Complete recovery follows. The cerebrospinal fluid (C.S F) contains an excess of lymphocytes and is bacteriologically sterile The cause is often assumed, but rarely proved, to be the virus of L.C.M. Infections due to this virus have been reviewed by Farmer and Janeway (1942)

MacCallum (1949) has reported five cases of aseptic meningitis from various parts of England which were caused by the virus of Armstrong One of these came from a Manchester house where mice carrying this virus were caught In 6 months we have seen ten cases of L C M in Manchester Serological methods have indicated the ætiology in all cases, and the virus was isolated from four of them Green et al (1949) have pointed out that the ætiological diagnosis in many published cases has been poorly substantiated, since it was based on clinical grounds only Other diseases—e g, glandular fever and mumps—may present a somewhat similar picture The clinical features of cases proved to be due to the virus of L C M are therefore described

CASE RECORDS

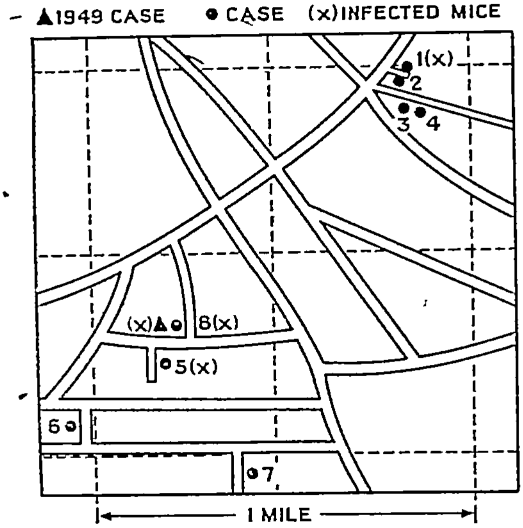
Case 1 —A married woman, aged 30, was admitted on Feb 25, 1950, to Manchester Royal Infirmary under the care of Dr C S D Don She complained of headache, vomiting and cough She had collapsed at work twelve days before, feeling cold and shivery, with aching pains in the limbs After three days in bed a productive cough and left sided pleuritic pain had developed These symptoms had persisted, and occipital headache and photophobia were also present on admission

On examination she looked thin, pale, and ill Her temperature was 101 8°F, pulse rate 120, and respirations 24 per min No other abnormality was found, apart from neck stiffness and absent abdominal reflexes Radiography of the chest showed miliary mottling in both lung fields

Progress —On Feb 27 the temperature was 101°F, headache was severe, neck stiffness more pronounced, and Kernig's sign positive The resting pressure of the C.S.F was 70 mm, and the fluid was turbid, containing 2760 cells per c mm (all lymphocytes), and protein 180 mg, glucose 29 mg, and chlorides 680 mg, per 100 ml No tubercle bacilli or other organisms were seen on microscopy or cultured from this or later specimens of C S F

Treatment —Tuberculous meningitis was provisionally diagnosed on the clinical picture, the chest radiogram, and the low C S F glucose level Intrathecal and intramuscular streptomycin was given and continued *for 3 days* On March 1 the remarkable clinical improvement *suggested the possibility* of a virus meningitis, so a fresh *specimen* of C S.F was taken, and the virus of L C M was isolated from it Serum obtained on Feb 27 did not fix complement when *tested* with L C.M antigen, but serum obtained a month later was positive to a titre of 1 in 16

Other Investigations —On Feb 27 the erythrocyte sedimentation rate (E S R) was 20 mm in 1 hr (Wintrobe) *and* a blood count showed red cells 4,760,000 per c mm, *Hb 13 g* per 100 ml, white cells 8700 per c mm *(polymorphs 66%,*



ıdence of human cases o lymphocytic choriomeningitis in relation to presence of infected mice.

jected both into guineapigs and into laboratory ice The guineapigs received 0 5 ml. of a 1 in 20 aulsion intraperitoneally, and the mice 0 03 ml. intra rebrally The virus was identified as described above Where there are no immediate facilities for isolating ie virus the brains of house mice can be sent by post a virus laboratory if they are freeze dried, for the rus is best preserved in this way

SEROLOGICAL DIAGNOSIS

An extract of spleen from infected guineapigs was used s antigen in the complement fixation test (Smadel et al. 939) All positive sera were tested with an extract f normal guineapig spleen to exclude non specific xation Complete fixation at a serum dilution of 2 strongly suggests the presence of specific antibodies, ut in all our cases complete fixation took place at a ilution of 1 8 or 1 16 in at least one sample of serum, ience the question of doubtful positive results did not rise in the final diagnosis Neutralisation tests were erformed in mice

Serological diagnosis is the routine method of choice, ecause the virus cannot be isolated unless there is a irus laboratory within easy reach Three specimens f serum should be collected the first as soon as the iagnosis is suspected, the second at 3–4 weeks, and he third at 4 months after the onset of the illness

EPIDEMIOLOGY

Armstrong (1940) has discussed the question of a reservoir of the virus of L C M in house mice Farmer and Janeway (1942), reviewing the close association between this virus reservoir in mice and human cases of the disease, have described a single focus of infection in Boston, Massachusetts The only four patients with L C M observed by them in the negro population in 8 years all lived, at the times of their illnesses, "within two city blocks of each other"

In the present series all the patients, except cases 9 and 10, have come from two localised areas of Manchester (see figure) * Cases 1–4 lived or worked within 200 yards of each other The others lived within a radius of 400 yards Infected mice were caught in the house of case 7, only 70 yards from the one where mice harbouring the virus had been found 18 months previously (MacCallum 1949) The virus could not be isolated from mice caught in five other areas of the city

TREATMENT

In view of the rapid spontaneous improvement in all the cases of our series on admission to hospital, it would have been difficult to assess the effect of any drug with anti-virus properties, had such been used Lumbar puncture was usually followed by rapid relief of the headache

SUMMARY AND CONCLUSIONS

The clinical features of nine cases of aseptic meningitis, proved to be due to the virus of lymphocytic chorio meningitis (L C M), are described Influenza like symptoms characteristically developed 1–3 weeks before the onset of the meningeal phase

The laboratory findings and methods used and differential diagnosis are discussed

The C S F glucose levels may be low in L C M

A positive diagnosis can be made by isolating the virus from blood, C S F, or throat washings, and by demonstrating complement fixing and virus neutralising antibodies in the serum

A case of laboratory infection without apparent involvement of the nervous system is described

A close association exists between human cases and house mice also infected with the virus of L C M

Our thanks are due to Prof Robert Platt, Dr C S D Don Dr R Ellis, Dr D C Liddle, and Dr A Morgan Jones for permission to publish details of the patients under their care to Dr L Stent for obtaining the specimens from cases 4 5, and 6, and to Dr F O MacCallum for supplying a strain of virus with which antigen and immune serum were prepared We are indebted to Dr C Metcalfe Brown, M O H of Manchester, for his department s help in obtaining mice for examination, and to Prof H. B Maitland for helpful criticism and advice

REFERENCES

Armstrong C (1940) *Harvey Lect*
Baird R D Rivers T M (1938) *Amer J Publ. Hlth* 28 47
Farmer T W Janeway C A (1942) *Medicine Baltimore* 21 1
Findlay G M Alcock, N S Stern R. O (1936) *Lancet* i 650
Green W R Sweet L K Pritchard R W (1949) *J Pediat* 35, 688
MacCallum F O (1949) *Mon Bull Min Hlth* 8 177
Rivers T M (1948) Virus and Rickettsial Infections of Man Philadelphia
Smadel J E Baird, R D Wall M J (1939) *J Exp Med* 70 53
Tidy H L (1946) *Lancet* ii 819
Van Rooyen C E Rhodes A J (1948) Virus Diseases of Man New York

Births and Deaths in War and Peace

The dramatic qualities of a national stocktaking by census should not be allowed to obscure the vital interest of the routine publications by the Registrar General As earnest of his wish to overhaul the way lost as a result of the war, he has put out both the medical statistical tables for 1949[1] and a review of the civil statistics for the period 1940–45[2] Taken together, they give an up to date picture of the trends in birth and death rates since the turn of the century and a preview of the net result which may appear in the tabulations of the latest census

While the 1949 death rate of 11 8 per 1000 was a little higher than in 1948, the consistent improvement in mortality experience in the under 35s continued—for children less than 5 years old the death rate was about an eighth of what it was a hundred years ago and just over half of its level in 1939 The infant mortality rate at 33 9 per 1000 approached the 1950 "all time low" of 29 8 per 1000 Among older men in particular, however, there appeared some disquieting features Real increase in the cancer death rate was indicated by an increase in the comparative mortality index, which takes account of the ageing of the population, a rise of some 6% since 1938 is largely due to the increase

---

* Since this paper was written we have seen a further four proved cases from these two Manchester foci of infection

[1] Registrar General s Statistical Review of England and Wales for the year 1949 Tables Part I Medical H M Stationery Office Pp 330 7s 6d

[2] Registrar General s Statistical Review of England and Wales for the six years 1940–45 Text Vol II Civil H M Stationery Office Pp 232 5s

TABLE II—C S F FINDINGS IN NINE CASES OF LYMPHOCYTIC CHORIOMENINGITIS

Case no	Highest cell count per c.mm	Lymphocytes (%)	Protein (mg per 100 ml)	Glucose (mg per 100 ml)*	Chlorides (mg per 100 ml)
1	2760	100	180	29	680
2	200	100	180	47	740
3	1000	75	50	+	700
4	4200	96	180	52	700
5	1040	100	80	32	680
6	1300	90	200	23	695
7	570	100	60	62	750
8	50	100	180	84	740
9	28	100	55	82	760

*Lower limit of normal = 45 mg per 100 ml

came on during the meningeal stage, and in the other two in early convalescence

LABORATORY FINDINGS

C.S.F—Results of C S.F examinations from nine cases are shown in table II The total cell count ranged from 28 to 4200 per c mm, and lymphocytes predominated, comprising 75–100% of the cells We found the glucose level to be lower than 45 mg per 100 ml in three of the eight cases in which quantitative estimations were made, although the glucose has usually been stated to be normal in this condition (Van Rooyen and Rhodes 1948, Rivers 1948) These findings, however, conform with those of Green et al (1949), who described low glucose levels in seven of their twenty-one cases

Blood—White cell counts were made in five of our cases and were in no way abnormal The Paul-Bunnell test was negative in all of eight cases in which it was done, these included the three with transient lymph gland enlargement In two of these, repeated Paul Bunnell tests were negative

DIFFERENTIAL DIAGNOSIS

A lymphocytic meningitis may also develop in poliomyelitis, virus encephalitis, mumps, Bornholm disease, herpes simplex, lymphogranuloma inguinale, syphilis, Weil's disease, canicola fever, torulosis, toxoplasmosis, mastoid disease, and cerebral abscess In our experience the two conditions which gave rise to difficulty in iagnosis were tuberculous meningitis and glandular ver

An insidious onset is common to tuberculous meningitis nd lymphocytic choriomeningitis Cough and vomiting may be present during the premeningeal stage of both diseases Low C S F glucose levels are found in tuberculous meningitis, but they are also found in some cases of lymphocytic choriomeningitis, adding to the difficulty of early diagnosis If tubercle bacilli are not identified in the C S F, the diagnosis is usually clear within a few days Recovery from lymphocytic choriomeningitis is rapid, and improvement in the patient's general condition is obvious within 48 hours

When neurological complications occur in glandular fever, lymph gland enlargement may be very slight (Tidy 1946) Negative Paul-Bunnell tests and the absence of the characteristic blood changes help to distinguish lymphocytic choriomeningitis from glandular fever

Premonitory symptoms resembling influenza, and a brief remission before the onset of meningism, support a diagnosis of lymphocytic choriomeningitis The presence of mice and the knowledge of other cases having occurred in the immediate neighbourhood may be of value

Final proof is given by isolating the virus of lymphocytic choriomeningitis from the C S.F, blood, or nasopharynx, and by demonstrating the presence of complement-fixing and virus neutralising antibodies in the patient's serum Complement fixing antibodies develop 2–3 weeks after the onset of the illness—i e, during or shortly after the meningeal phase—and persist for 6 months or longer Neutralising antibodies appear 2–3 months, or even later, after the onset and may remain for years

In our series the virus was isolated from the C S F in three cases and from the blood and throat washings in another Complement fixation tests were positive in all Neutralising antibodies were demonstrated in five of the six cases where this was attempted (table III)

ISOLATION OF VIRUS

From Human Sources

We were able to isolate the virus from the C S F when the cell count was greater than 500 per c mm, as were Green et al (1949) We therefore suggest that, if the cell count is above this level, the material of choice for the attempted isolation of the virus is the C S F, or, if the cell count is below this level, blood and throat washings should also be used. Guineapigs and mice, or sometimes guineapigs only, were inoculated within 10 minutes of obtaining the specimens from the patient Stocks of laboratory animals were free from L C M infection, a necessary precaution when dealing with this virus In no case in which both guineapigs and mice were used was virus isolated from one species and not from the other

Two guineapigs were injected intraperitoneally with up to 5 ml. of material, and five mice intracerebrally with 0 03 ml and intraperitoneally with amounts up to 1 ml One guineapig was killed on the 4th day after inoculation, and an emulsion of its spleen was injected intracerebrally into mice The other guineapig was kept and bled after 14 days or just before death if this occurred earlier Usually death took place between the 14th and 16th day when the guineapigs were infected with the Manchester strain. The guineapig serum was then tested for complement fixing antibodies The virus was further identified from the typical syndrome produced by intracerebral inoculation of mice, by neutralisation and cross protection tests, and by complement fixation of the infected guineapig spleen with immune serum

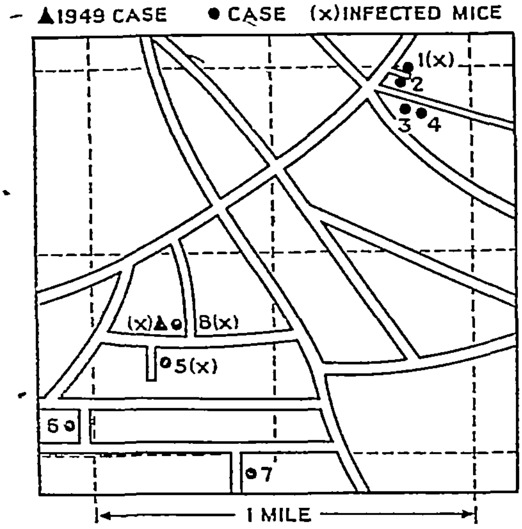
From House Mice

Virus was isolated from house mice as long as 36 hours after trapping The brains were removed and

TABLE III—SEROLOGY AND ISOLATION OF VIRUS IN 10 CASES OF LYMPHOCYTIC CHORIOMENINGITIS

Case no	Serology				Isolation of virus			
	Complement fixation test		Neutralisation test		From patient			From mice
	Titre*	Day after onset	Result	Day after onset	Result	Source	Day after onset	Result
1	— 1 16	14 42			+	C.S F (740 cells)	16	+
2	— 1 8	14 33			− + +	C.S F (200 cells) throat, blood	14	+
3	1 8 1 8	60 138	− +	60 138				
4	1 4 1 8	17 106	− −	17 106	+	C.S F (2200 cells)	16	
5	1 8	35			+	C.S F (500 cells)	23	+
6	1 4 1 16	18 67						
7	1 8 1 8 1 4	19 39 98	− +	39 98	−	C.S F (312 cells)	19	+
8	1 8 1 8	29 42	− +	29 12				
9	1 4 1 8	15 41	− +	41 108				
10	1 2 1 8 1 2	14 69 220	− + +	14 69 220				+

+ Positive result — Negative result
* Highest titre giving complete fixation



Incidence of human cases o lymphocytic choriomeningitis in relation to presence of infected mice.

injected both into guineapigs and into laboratory mice The guineapigs received 0 5 ml. of a 1 in 20 emulsion intraperitoneally, and the mice 0 03 ml. intracerebrally The virus was identified as described above

Where there are no immediate facilities for isolating the virus the brains of house mice can be sent by post to a virus laboratory if they are freeze dried, for the virus is best preserved in this way

SEROLOGICAL DIAGNOSIS

An extract of spleen from infected guineapigs was used as antigen in the complement fixation test (Smadel et al. 1939) All positive sera were tested with an extract of normal guineapig spleen to exclude non specific fixation Complete fixation at a serum dilution of 1 2 strongly suggests the presence of specific antibodies, but in all our cases complete fixation took place at a dilution of 1 8 or 1 16 in at least one sample of serum, hence the question of doubtful positive results did not arise in the final diagnosis Neutralisation tests were performed in mice

Serological diagnosis is the routine method of choice, because the virus cannot be isolated unless there is a virus laboratory within easy reach Three specimens of serum should be collected the first as soon as the diagnosis is suspected, the second at 3–4 weeks, and the third at 4 months after the onset of the illness

EPIDEMIOLOGY

Armstrong (1940) has discussed the question of a reservoir of the virus of L C M in house mice Farmer and Janeway (1942), reviewing the close association between this virus reservoir in mice and human cases of the disease, have described a single focus of infection in Boston, Massachusetts The only four patients with L C M observed by them in the negro population in 8 years all lived at the times of their illnesses, "within two city blocks of each other"

In the present series all the patients, except cases 9 and 10, have come from two localised areas of Manchester (see figure) * Cases 1–4 lived or worked within 200 yards of each other The others lived within a radius of 400 yards Infected mice were caught in the house of case 7, only 70 yards from the one where mice harbouring the virus had been found 18 months previously (MacCallum 1949) The virus could not be isolated from mice caught in five other areas of the city

TREATMENT

In view of the rapid spontaneous improvement in all the cases of our series on admission to hospital, it would have been difficult to assess the effect of any drug with anti-virus properties, had such been used Lumbar puncture was usually followed by rapid relief of the headache

SUMMARY AND CONCLUSIONS

The clinical features of nine cases of aseptic meningitis proved to be due to the virus of lymphocytic choriomeningitis (L C M), are described Influenza like symptoms characteristically developed 1–3 weeks before the onset of the meningeal phase

The laboratory findings and methods used and differential diagnosis are discussed

The C S F glucose levels may be low in L C M

A positive diagnosis can be made by isolating the virus from blood, C S F, or throat washings, and by demonstrating complement fixing and virus neutralising antibodies in the serum

A case of laboratory infection without apparent involvement of the nervous system is described

A close association exists between human cases and house mice also infected with the virus of L C M

Our thanks are due to Prof Robert Platt, Dr C S D Don Dr R Ellis, Dr D C Liddle, and Dr A Morgan Jones for permission to publish details of the patients under their care to Dr L Stent for obtaining the specimens from cases 4 5, and 6, and to Dr F O MacCallum for supplying a strain of virus with which antigen and immune serum were prepared We are indebted to Dr C Metcalfe Brown, M.O.H of Manchester for his department s help in obtaining mice for examination, and to Prof H. B Maitland for helpful criticism and advice

REFERENCES

Armstrong C (1940) *Harvey Lect*
Baird R D Rivers T M (1938) *Amer J Publ. Hlth* 28 47
Farmer T W Janeway C A (1942) *Medicine Baltimore* 21 1
Findlay G M Alcock N S Stern, R. O (1936) *Lancet*, i 650
Green W R Sweet L K, Pritchard R W (1949) *J Pediat* 35, 688
MacCallum F O (1949) *Mon Bull. Min Hlth* 8 177
Rivers T M (1948) Virus and Rickettsial Infections of Man Philadelphia
Smadel J E Baird R D Wall M. J (1939) *J Exp Med* 70 53
Tidy H L (1946) *Lancet* ii 819
Van Rooyen C E Rhodes A J (1948) Virus Diseases of Man New York

Births and Deaths in War and Peace

The dramatic qualities of a national stocktaking by census should not be allowed to obscure the vital interest of the routine publications by the Registrar General As earnest of his wish to overhaul the way lost as a result of the war, he has put out both the medical statistical tables for 1949 [1] and a review of the civil statistics for the period 1940–45 [2] Taken together, they give an up to date picture of the trends in birth and death rates since the turn of the century and a preview of the net result which may appear in the tabulations of the latest census

While the 1949 death rate of 11 8 per 1000 was a little higher than in 1948, the consistent improvement in mortality experience in the under 35s continued—for children less than 5 years old the death rate was about an eighth of what it was a hundred years ago and just over half of its level in 1939 The infant mortality rate at 33 9 per 1000 approached the 1950 "all time low" of 29 8 per 1000 Among older men in particular, however, there appeared some disquieting features Real increase in the cancer death rate was indicated by an increase in the comparative mortality index, which takes account of the ageing of the population, a rise of some 6% since 1938 is largely due to the increase

---

* Since this paper was written we have seen a further four proved cases from these two Manchester foci of infection

[1] Registrar General s Statistical Review of England and Wales for the year 1949 Tables Part I Medical H M. Stationery Office Pp 350 7s 6d

[2] Registrar-General s Statistical Review of England and Wales for the six years 1940–45 Text Vol. II Civil H M. Stationery Office Pp 232 5s

TABLE II—C S F FINDINGS IN NINE CASES OF LYMPHOCYTIC CHORIOMENINGITIS

Case no	Highest cell count per c mm	Lymphocytes (%)	Protein (mg per 100 ml)	Glucose (mg per 100 ml)*	Chlorides (mg per 100 ml)
1	2760	100	180	29	680
2	200	100	180	47	740
3	1000	75	50	+	760
4	4200	96	180	52	700
5	1040	100	80	32	680
6	1300	90	200	23	695
7	570	100	60	62	750
8	50	100	180	84	740
9	28	100	95	82	760

*Lower limit of normal = 45 mg per 100 ml

came on during the meningeal stage, and in the other two in early convalescence

LABORATORY FINDINGS

C S F—Results of C S.F examinations from nine cases are shown in table II The total cell count ranged from 28 to 4200 per c mm, and lymphocytes predominated, comprising 75–100% of the cells We found the glucose level to be lower than 45 mg per 100 ml in three of the eight cases in which quantitative estimations were made, although the glucose has usually been stated to be normal in this condition (Van Rooyen and Rhodes 1948, Rivers 1948) These findings, however, conform with those of Green et al (1949), who described low glucose levels in seven of their twenty one cases

Blood—White cell counts were made in five of our cases and were in no way abnormal The Paul-Bunnell test was negative in all of eight cases in which it was done, these included the three with transient lymph gland enlargement In two of these, repeated Paul Bunnell tests were negative

DIFFERENTIAL DIAGNOSIS

A lymphocytic meningitis may also develop in poliomyelitis, virus encephalitis, mumps, Bornholm disease, herpes simplex, lymphogranuloma inguinale, syphilis, Weil's disease, canicola fever, torulosis, toxoplasmosis, mastoid disease, and cerebral abscess In our experience the two conditions which gave rise to difficulty in diagnosis were tuberculous meningitis and glandular fever

An insidious onset is common to tuberculous meningitis and lymphocytic choriomeningitis Cough and vomiting may be present during the premeningeal stage of both diseases Low C S F glucose levels are found in tuberculous meningitis, but they are also found in some cases of lymphocytic choriomeningitis, adding to the difficulty of early diagnosis If tubercle bacilli are not identified in the C S.F, the diagnosis is usually clear within a few days Recovery from lymphocytic choriomeningitis is rapid, and improvement in the patient's general condition is obvious within 48 hours

When neurological complications occur in glandular fever, lymph gland enlargement may be very slight (Tidy 1946) Negative Paul Bunnell tests and the absence of the characteristic blood changes help to distinguish lymphocytic choriomeningitis from glandular fever

Premonitory symptoms resembling influenza, and a brief remission before the onset of meningism, support a diagnosis of lymphocytic choriomeningitis The presence of mice and the knowledge of other cases having occurred in the immediate neighbourhood may be of value

Final proof is given by isolating the virus of lymphocytic choriomeningitis from the C S F, blood, or nasopharynx, and by demonstrating the presence of complement fixing and virus neutralising antibodies in the patient's serum Complement fixing antibodies develop 2–3 weeks after the onset of the illness—i e, during or shortly after the meningeal phase—and persist for 6 months or longer Neutralising antibodies appear 2–3 months, or even later, after the onset and may remain for years

In our series the virus was isolated from the C S F in three cases and from the blood and throat washings in another Complement fixation tests were positive in all Neutralising antibodies were demonstrated in five of the six cases where this was attempted (table III)

ISOLATION OF VIRUS

From Human Sources

We were able to isolate the virus from the C S F when the cell count was greater than 500 per c mm, as were Green et al (1949) We therefore suggest that, if the cell count is above this level, the material of choice for the attempted isolation of the virus is the C S F, or, if the cell count is below this level, blood and throat washings should also be used. Guineapigs and mice, or sometimes guineapigs only, were inoculated within 10 minutes of obtaining the specimens from the patient Stocks of laboratory animals were free from L C M infection, a necessary precaution when dealing with this virus In no case in which both guineapigs and mice were used was virus isolated from one species and not from the other

Two guineapigs were injected intraperitoneally with up to 5 ml. of material, and five mice intracerebrally with 0 03 ml and intraperitoneally with amounts up to 1 ml One guineapig was killed on the 4th day after inoculation, and an emulsion of its spleen was injected intracerebrally into mice The other guineapig was kept and bled after 14 days or just before death if this occurred earlier Usually death took place between the 14th and 16th day when the guineapigs were infected with the Manchester strain. The guineapig serum was then tested for complement fixing antibodies The virus was further identified from the typical syndrome produced by intracerebral inoculation of mice, by neutralisation and cross protection tests, and by complement fixation of the infected guineapig spleen with immune serum

From House Mice

Virus was isolated from house mice as long as 36 hours after trapping The brains were removed and

TABLE III—SEROLOGY AND ISOLATION OF VIRUS IN 10 CASES OF LYMPHOCYTIC CHORIOMENINGITIS

Case no	Serology				Isolation of virus			
	Complement fixation test		Neutralisation test		From patient			From mice
	Titre*	Day after onset	Result	Day after onset	Result	Source	Day after onset	Result
1	—	14						
	1 16	42			+	C.S F (740 cells)	16	+
2	—	14			—	C.S F (200 cells)	14	+
	1 8	33			+	throat		
					+	blood		
3	1 8	60	—	60				
	1 8	138	+	138				
4	1 4	17	—	17		C S F (2200 cells)	16	
	1 8	106	—	106	+			
5	1 8	35			+	C S F (500 cells)	23	+
6	1 4	18						
	1 16	67						
7	1 8	10	—	39	—	C.S F (312 cells)	19	+
	1 8	39	+	98				
	1 4	98						
8	1 8	29	—	29				
	1 8	42	+	42				
9	1 4	15	—	41				
	1 8	41	+	108				
10	1 2	14	—	14				
	1 8	69	+	69				+
	1 2	220	+	220				

+ Positive result — Negative result

* Highest titre giving complete fixation

worst, it turned out to be genuine but so miserably lukewarm as to be hardly eatable.

If there is one thing one would expect to be first-class in an Indian hotel it is tea. But no—the beverage called tea was no more recognisable than the corresponding liquid of English station refreshment-rooms. (I once watched with relish a middle-aged woman customer and the two waitresses arguing over the nature of a cup supplied as coffee. The customer contended that it was tea and one waitress firmly agreed with her, while the other waitress was certain it was coffee. They sipped and argued in turn until the cup was empty, when the verdict had to be left as non-proven.) In complete contrast was the Ceylon tea, undoubtedly the best I ever tasted. I am told on good authority that there is nothing to choose between Indian and Ceylon teas as exported; but after this tour it will take a lot to convince me that Ceylon is not far the better of the two.

Returning to the monotony of the menus, hardly any hotels provided edible fruit. Here were we from the West with mouths watering from our visions of mangos and yams, built up from memories of the pictures in "Little Black Sambo" and "Little Black Quibba" (was he the one who cured his mother by providing a basket of mangos every day?), and all we got was stewed prunes or oranges.

Charges everywhere were high by English standards. But the most annoying feature was that the charge per day includes all meals; so however much one dines out the bill remains as high as ever.

* * *

Inspecting the fluid level in the battery of the modern car presents serious physical and optical difficulties. For a long time past I have thought about introducing a simple instrument for this purpose on the lines of a laryngoscope; but I have been disappointed to find that my garage man has beaten me to it by using a piece of broken mirror and a long arm. However, I am not unduly discouraged by the loss of priority because there still seems to be a big field for better diagnostic methods and manipulative technique in the automobile world. The sight of a mechanic trying to retrieve a small nut from an awkward corner makes me want to dash off for a suitable endoscopic instrument and a pair of crocodile forceps, if only to show him that we doctors are not such fools with our hands as he thinks. Consulting work in this specialty might be interesting, and there would be no complaints from patients or committees. Doubtless there would be hazards. Would the defence societies support me if I got into legal trouble for leaving a broken cystoscope bulb inside the cylinder head of somebody's ultravaluable post-war car?

* * *

The little boy was reading the label on a bottle in the family medicine-cupboard—from which he and his sister had often been dosed. "Up to six months half a teaspoonful," he read to himself, "six months to a year one teaspoonful; one to four years two teaspoonfuls." Then, turning to his mother, "Mummy, it must be dreadful to have a cough for four years."

* * *

Preserving cadavers for dissection in the Tropics is not so difficult as one might suppose. Evidently my African driver did not realise this fact, for when I caught him peering with disapproving eyes through the open door of the dissecting room, he asked me, "Why the bodies no rust, Sah?"

* * *

Some say you never see anything interesting in general practice; but I just met our local acromegaly chatting to our local syringomyelia in the middle of the village street. Is this a record?

* * *

PLURAL SHOCK

As I am walking on the links
I hear the hum of a Hillman Minx.
But stay—so loud the noise impinges,
Can it be several Hillmen Minges?

Letters to the Editor

MEDICAL RESEARCH IN REGIONAL HOSPITALS

SIR,—The National Health Service Act (1946) extended the power of the Minister for supporting medical research to regional hospital boards, boards of governors, and hospital management committees. The memorandum on this subject (R.H.B. [49]145) redefined the policy in relation to the Medical Research Council. The Ministry was to confine itself to promoting such investigation as can best be done within the framework of the health services for which it has immediate responsibility. The council was left with the wider, and particularly the long term, problems of medical research.

In a previous letter[1] I drew attention to the difficulty of financing research by hospital management committees as a result of the present system of budgeting. In your leading article[2] you underlined the danger of any hindrance to medical research. Since my last letter I have continued to make inquiries about the financing of research outside the teaching centres, and the picture I find is encouraging.

Six regional boards—Birmingham, Oxford, Newcastle, South western, South-west Metropolitan, and Sheffield—have recognised the need for stimulating medical research within their regions, and have appointed special research committees. These committees are backed either by Exchequer funds included in the regional-board budget or by endowment funds, and three research committees have substantial sums at their disposal. Other regions support certain specific research projects, or have available funds which could be used. There is no doubt that work involving appreciable sums of public money should have guidance from a research committee. Such guidance is, of course, available for those working under the Medical Research Council.

Simple clinical medical research in relation to the hospital service is an essential aspect, if only from the economic angle, in view of the high cost of inpatient treatment. Local interest in research should be stimulated by regional boards, but this need not prejudice alternative application for grants from the M.R.C. or other medical foundations. In my opinion, there is also scope for activity at the hospital-management-committee level so that small sums could be made available quickly for special apparatus or extra clerical assistance; but such moneys could come, not from Exchequer sources, but from the "free moneys" available to the hospital. Public interest could easily be stimulated in a local research fund, and the use of "free moneys" raises no difficulties in budgeting.

Fellowships related to the big medical foundations or academic centres are another valuable source of research expenditure. With the rising cost of living, however, some are no longer a reasonable financial proposition except for men with private means, and clearly reconsideration of them is needed.

I believe that with the development of regional research committees and with small sums readily available to hospital management committees, the whole attitude towards medical research in this country would undergo a radical change. It would no longer be considered a prerogative of the academic centres but part of the daily task at the regional hospital. Clinical research would become a life interest instead of being a means to an end—to get consultant status. The time is particularly opportune, for there are many younger consultants appointed to regional hospitals with recent experience of clinical or laboratory research, and, given suitable support, they could continue to make useful contributions to medical progress. The stimulation among men in the number of deaths from cancer of the lung, which rose from 3751 in 1939 to 9327 in 1949 Men, too, more commonly die by accidental violence and, even more significantly, by their own hand

---

[1] *Lancet*, 1951, i, 31.
[2] Leading article. *Ibid*, p. 19.

The importance of psychological factors thus implied is equally clear in the trends in marriage and birth rates Mating and reproduction are clearly affected by changes in the psychological climate which attend the fluctuations in our national fortune Although the birth rate had been falling continuously from its peak in the 1870s, the first world war produced a drastic ebb in the tide of births which did not expend itself until the rate reached its nadir of 14 4 in the depression year of 1933 The slight recovery to 15 1 achieved by 1938 was checked by the beginning of the second world war until, in 1941, when the national outlook seemed at its worst, the rate reached the lowest point in the history of registration in this country The turn in the tide of battle was accompanied by a dramatic reversal of this pessimistic trend, from 1944 onwards the rate soared up to a peak of 20 5 in 1947 Inevitably, perhaps, the reproductive stimulus of even militarily successful war had its less desirable side, while of the 94,381 extramaritally conceived births in 1938 some 70% were regularised by the later marriage of the parents, only 49% of the 516,355 such births in 1940–45 were thus regularised before the arrival of the child No doubt this was due to the separation which war movements enforced, but it is disappointing to find that even after the war many of the parents concerned took no advantage of the Legitimacy Act of 1926 Marriage rates are of course just as much influenced by variations in national morale, they followed the same trend of slump and boom as did the nation's economy and birth rate The loosening of moral standards reflected in illegitimacy is also seen in divorce, petitions rose in number from 10,304 in 1938 to 25,789 in 1945 But the perennial optimism of our race is seen in the fact that as many as three quarters of these divorcees remarried

With any luck, the surprising buoyancy of our national income may be mirrored in a continuation of the combined effect of the trends in births and deaths which produced between 1939 and 1945 a real acceleration in the rate of national increase

The First Quarter

The Registrar General[1] announces that provisional figures for England and Wales for the first quarter of this year show that the birth-rate has again fallen, while the stillbirth-rate has increased slightly compared with the first quarter of 1950 The death-rate was the highest for any March quarter since 1940

The birth rate was 16 3 per 1000 population, compared with 16 7 and 17 3 in the corresponding quarters of 1950 and 1949 The stillbirth-rate was 23 6 per 1000 total live and still births, compared with 22 9 in the first quarter of 1950 The death-rate was 19 0 per 1000 population, compared with 14 0 and 14 9 in the corresponding quarters of 1950 and 1949 The infant-mortality rate was 35 2 per 1000 related live births, compared with 36 8 and 40 4 in the same quarters of 1950 and 1949 In 1938 for the same period the rate was 69 3 per 1000 related live births

Immunisation in London

In a report on the London County area in the last quarter of 1950, the medical officer of health states that smallpox vaccinations fell slightly from 58% of births to 54%, but in the last quarter of 1949 the figure was 38% Diphtheria immunisations were maintained, the records indicate that nearly 62% of infants under 5 years of age have been immunised, and that the percentage is gradually rising Whooping cough and combined whooping-cough and diphtheria immunisations continue to decline steeply

In England Now

A Running Commentary by Peripatetic Correspondents

ONE disadvantage (the only one ?) of reading the weekly medical journals is the amount of half-baked information one acquires concerning the theory and treatment of obscure diseases outside one's own field When one gets ill these snippets keep returning to plague us Take my sciatica, for example During my first few days in bed, in the lucid intervals between doses of an analgesic which "leaves the mind clear," my thoughts ran mostly on the operations I had read about—what was it those chaps had said ? Not all cases needed an operation, certainly, but what cases, and why ? Fortunately my G P still believes sciatica has something to do with sitting on a cold bench, so he didn't even mention surgery,

In the second week, the risks of addiction to one or other (or both) of the drugs I was living on, began to loom up The neurologist who gave me "the works," complete with pin, cotton-wool, tuning fork, and hammer, and confidently confirmed the diagnosis, pooh poohed my fears and advised me to continue expectant treatment with a slightly different analgesic, he wouldn't hear of operation In the third week, bed sores became my chief preoccupation—if I got one would they try that treatment by excision there was an annotation about ? My physiotherapist colleague said certainly not but *he* seemed preoccupied with some new tricks of thumping, pressing, and twisting of the spine which left me all set for exacerbation of my acute symptoms. Apparently none of the gadgetry of physical medicine could be brought to my bedside except in a large lorry, and as I refused to sanction the building of a ramp on to my house, the only outcome of this visit was a cheery word and a good prognosis

By the fourth week I was eagerly searching the periodicals for articles, letters or even advertisements describing new treatments for my disease By now I was so well softened up that I would gladly accept any of them—even laminectomy seemed quite a simple and safe operation But when my orthopædic colleague arrived, after confirming the diagnosis (on the story alone) and giving me another reassuring prognosis over a cup of coffee, he only murmured "Plaster jacket tomorrow," adding just before the door closed behind him, "No question of operation," to my intense relief No operation ! How was it I hadn't realised before what a clever chap he was ?

So the plaster was applied, and the effect of my Diogenes like existence was magical The new encumbrance entirely occupied my mind, leaving no place for such trivialities as pain in my leg Before long, plaster-barrel and all, I could hobble back to work, with a chest like a pouter-pigeon's, back erect, sore groins, and an eternal longing to scratch where scratching was impossible, living only for the day when I could have a bath again

* * *

I agree with much of the criticism levelled at English hotels, but it is only fair to say that a 20,000 mile tour made this winter to India, Malaya, and East Africa (by air, of course) confirmed my impression that they are not unique in their imperfections And I saw few signs of improvement since my last trip three years ago

In India some of the discomforts arise from the chronic shortage of food, specially sugar and fats, and so are unavoidable The allowance of sugar for breakfast is one cube, and though a second helping is supplied on request it also will consist of a single cube The scarcity of fat shows itself particularly in the total lack of soap in hotel bedrooms, reminiscent of war time Britain My main objection, however, is to the catering Instead of concentrating on their own national dishes and showing us how they should be served, they give the visitor nothing but badly cooked versions of familiar Western dishes During my week in India curry appeared on the menu only once, but we had an inferior imitation of roast beef and yorkshire pudding nearly every day Then the food was seldom hot when it reached us In one famous Eastern hotel, for example, when I ordered the "Scotch pheasant" from the menu, expecting the pamphlets, and to organise social activities (e g, tennis tournaments, whist drives) in order to raise money to pay for the lectures, pamphlets, and other publications This last activity is very important because, even if the money was obtainable elsewhere, social activities are the best method of encouraging people to use the word "cancer" openly, and not to speak of it in whispers

---

[1] Registrar General s Return for the Week ended April 14 H M Stationery Office Pp 20 9*d*.

I understand that the Central Council for Health Education are interested in these suggestions In Durban I lately gave a talk on this subject to a mixed audience of medical, paramedical, and lay people, with the result that at the end of the meeting a Durban Cancer Education Committee was formed to carry out the duties mentioned above Surely the time is overdue for something to be done in this country to prevent thousands of unnecessary deaths and much untold suffering

London W 1 MALCOLM DONALDSON

SMOKING AND CANCER

SIR,—Dr Joules argues (April 7, p 797) that we should attempt to prevent carcinoma of the lung by publicising the close relation between this condition and smoking I do not wish to gainsay that this may be the best preventive measure, but before the argument can be regarded as watertight two assumptions must be made (1) that the reported increase in lung cancer is real, and (2) that the relation with smoking is causal.

For the moment let us pass by the first assumption but examine the second, because there seems to be a possible loophole so far unmentioned. Though smoking need not be the cause of lung cancer, it certainly seems reasonable to look for an environmental influence when incidence has apparently increased so greatly in recent years Concentration on environment may lead, however, to the constitutional aspect being ignored, and this aspect is not without interest Sheldon et al.[1] published two remarkable diagrams illustrating the tendency for carcinoma of the breast and carcinoma of the uterus to occur in association with one particular kind of physique, each series consisted of 100 consecutive cases It may be that carcinoma of the lung also occurs most frequently in individuals of certain build There is some evidence, too, that the habit of smoking is more prevalent in men of certain physique, and if this physique were the same as that of subjects disposed to cancer, then smoking could be closely associated with cancer without in fact causing it. The accompanying table gives the smoking habits of 308 undergraduates whose physique has been typed using Sheldon's metric technique

PERCENTAGE DISTRIBUTION OF NON-SMOKERS AND SMOKERS BY DOMINANCE OF SOMATOTYPE

Dominance	No	Non-smokers		Smokers	
		No	%	No	%
Endomorphs	56	29	51·8	27	48·2
Endomorph mesomorphs	31	17	55·0	14	45·0
Mesomorphs	118	69	58·5	49	41·5
Mesomorph-ectomorphs	17	10	59·0	7	41·0
Ectomorphs					
Mesomorphic	46	31	67·4	15	32·6
Endomorphic	40	30	75·0	10	25·0

Is it just coincidence that the highest prevalence of smoking in young men, and of breast and uterine cancer in women, occurs in those of similar body build? Or that tall thin people were most often non smokers and also comparatively free from cancer? Perhaps smoking acts as a trigger to a gun constitutionally loaded, and people of lanky build may smoke with relative impunity or merely smoke less because they more often dislike smoking

That smoking can be reduced is shown by a reduction since 1947 in the proportion of undergraduates smoking—a reduction usually attributed to increasing cost through taxation I do not wish to discuss either methods of reducing smoking or the thorny question of creating cancerphobia, but I would like to suggest the adoption, now that satisfactory techniques are available, of records of physical constitution in future research on cancer

R W PARNELL

Institute of Social Medicine, Oxford. Physician in charge, Student Health Service.

---

[1] Sheldon, W H, Hartl E M, McDermott E Varieties of Delinquent Youth New York 1949 p 754

GENERAL PRACTITIONER AND CONSULTANT

SIR,—I disagree entirely with Dr Robertson's suggestion (April 14) that there is a cleavage between the general practitioner and consultant I can only speak of my own town, Southampton, where, I strongly hold, there is a wonderful relationship between G.P.s and the consulting staffs of the hospitals

As chairman of the clinical meetings which are held once a month, I find that there is a considerable amount of exchange of opinion between G.P.s and consultants In many instances cases are shown by G.P.s, and, believe me, the standard of their presentation is very high

I regret this continual suggestion in print of the so called "gulf" or "cleavage" between G.P.s and consultants, which does not appear to exist in this town The medical ability of the G.P here is on a high level, and so why this suggestion of a falling standard? The position may be different in other parts of the country

HAROLD J BOWER

Southampton. Consulting Physician Royal South Hants and Southampton Hospital.

URETHRAL CARUNCLES

SIR,—Most gynæcologists will agree with Mr Campbell Begg (April 14) that partial prolapse of the female urethral mucosa is a common finding, and that true caruncle is relatively rare Many will also agree that the symptoms arising from such a caruncle often correspond with a trichomonas infection of the vagina Yet few, I hope, will sanction his provocative condemnation of the very existence of caruncles The adenomatous polyp of the meatus, and the exquisite tenderness of pedunculated fragments of granulation tissue, are lesions whose existence can hardly be doubted

Regarding terminology, the fact that the term has no pathological significance does not prevent its useful employment Does Mr Begg, I wonder, wage war against polyps, on the grounds that they are common to the surgery of the nose, bowel, and pelvis? Does he reject such a vintage term as epulis, which was employed before the microscope proved its protean nature? There may be no urethral caruncles in his Dominion, but there are still a few in the mother country

Birmingham W G MILLS

SIR,—Mr Campbell Begg rightly asserts that the majority of patients referred for opinion have in fact small areas of prolapsed urethral mucosa which cause no symptoms We observed this condition in 10 out of 58 normal menopausal women, and suggested that these "caruncular areas" were physiological.[1]

Mr Campbell Begg describes a type of caruncle which bled with friction. In our experience bleeding is not uncommon in a *true* caruncle which may also be tender and cause dysuria. The condition, however, can easily be differentiated from an asymptomatic prolapse of the urethral mucosa. Cautery usually cures a bleeding caruncle and relieves symptoms of dysuria and discomfort, the condition, however, may recur and once again give rise to symptoms of many small growing points of knowledge in this country could be achieved at a very small cost and might substantially raise the standard of hospital practice outside the teaching centres

---

[1] *J Obstet Gynæc* 1941 48 1

Department of Gastroenterology,
Central Middlesex Hospital
London, N W 10

F AVERY JONES

SALICYLATE, GENTISATE, AND CIRCULATING EOSINOPHILS

SIR,—The leading article and the paper by Dr Meade and Dr Smith in your issue of April 7 prompt us to make the following observations on salicylates and adrenocortical activity

We have shown in animals and in man that heavy doses of salicylates mobilise "anti-arthritic" adrenal hormones[1] Further, we have attempted to ascertain the nature of these hormones and the amount mobilised, but hitherto no definite conclusion has been possible It seems, however, reasonable to say that the therapeutic effect of salicylates can, at present anyhow, hardly be explained in this way

Dr Meade and Dr Smith, in contradicting our findings on circulating eosinophils, *mention only part of our results* We wrote[2]

> *Small* salicylate doses with serum levels at the 4th hour of 20–30 mg per cent and below (4–5 g of salicylate) did not produce any fall of the eosinophils (16 cases), while in the case of levels of 30–35 mg per cent (6 g single dose) the decrease is about 50 per cent of the original (8 cases) *Higher* levels (7–10 g within 4–5 hours) are accompanied with more pronounced diminution of the absolute eosinophil count (3 cases)

We confirmed these results in most of our subsequent cases The eosinophil count, however, is also regulated by unknown factors, other than the hypophyseo adrenal system, and it is thus not surprising that results differ

Dr Meade and Dr Smith, however, gave 5 1 g salicylate (gr 75) and determined the (expected maximal) serum level two hours after the dose was taken This does not seem adequate for checking our results from 6–10 g doses and estimating the salicylate level at the 4th hour Also our method of salicylate determination was different[3]

Finally, it should be noted that, as the Mayo Clinic group have repeatedly remarked,[4] 'Cortisone' does not regularly produce eosinopenia in man

University Medical School
Szeged Hungary

E KELEMEN
M MAJOROS

ANGOR ANIMI

SIR,—In your annotation last week you quote the late Professor Ryle as saying that he had never met this symptom in its major form as a symptom of psychological disease, and that it cannot be removed by reassurance or by any other psychotherapeutic measures

I recently saw what appeared to be a classical case, apparently fitting very closely Russell Brain's description of

> a sense of disordered action of the heart, such as slowing, irregularity or increased rapidity of the heart beats In some cases there is an intense feeling of impending death—angor animi the patient remains perfectly still the surroundings seem to the patient very distant the extremities cold but the patient experiencing a sense of chill'

It is of additional interest, in view of John Hunter's and Professor Ryle's experience that the breathing appeared to be arrested, that my patient said she could not work her chest

Physical examination, including electrocardiography and electro encephalography, was entirely negative Emotional factors were suspected, but could not be confirmed by an experienced psychiatrist A chance remark then induced the patient to send for the psychiatrist again, because she had told him "a pack of lies' It emerged—to quote the psychiatrist—that, as a result of emotional complications concerned with a favoured twin, she had, in early childhood, developed a vivid phantasy which occurred during the night but not actually when she was asleep. She would wake up and feel convinced that there was a dead body in bed with her, and would lie awake for hours sweating and trembling, afraid to move or even to turn her head to dispel her fears She recognised her symptoms in later life as of the same type as those associated with the childhood experiences, and they had a close relation to emotional disasters and strains in the Forces and family life

After a frank discussion of this history, she improved very greatly and the vasovagal attacks—as I feel they must be regarded—ceased to trouble her to any extent, and finally seemed to have disappeared

No doubt there is some organic basis, but in this case the actuating mechanism appears to have been emotional

Hove, Sussex

W A BOURNE

PUBLICITY IN CANCER

SIR,—I was interested by Professor Russ's stimulating letter of March 24 Education of the public concerning cancer is a subject that has interested me since about 1930, and I organised 1200 lectures to the public for the British Empire Cancer Campaign between 1936 and 1940, when war put an end to further efforts This is a very small number compared to the total adult population, but having given many of the lectures myself, I was confirmed in my views as to the great value of such education, and that it is the only way of reducing the mortality from this disease in the immediate future

All statistical tables tell the same story of delay in diagnosis, pointed out by Professor Russ, and the latest report on international statistics of carcinoma of the cervix, which deals with 41,046 cases from 37 radio therapeutic institutes in 11 different countries, gives 13 7% in the first stage The Americans have shown that it is possible to reduce this delay by public education In Massachusetts the delay between the date the patient first noticed a symptom and that on which medical advice was sought was reduced by education from 6 months to 3 months There is a general belief in this country that this was accomplished at the expense of producing mass cancerphobia A short visit to the U S.A last May makes me think that this idea is quite wrong, but I agree that much of the literature published would be unsuitable in this country and would do little to dispel fear, which is undoubtedly the greatest single cause for the delay on the part of the patient Such shock methods are quite unnecessary, and indeed risk defeating the end in view

There are two stock objections by those who regard cancer education as undesirable (1) that it will increase apprehension and fear, (2) that it will flood the surgeries of the G P s with people who have no symptoms I know from my experience of lecturing to the laity that Emerson was right when he said "Knowledge is the antidote to fear"

How then can cancer education be carried out? Under the 1946 Act the local authorities are responsible for health education, but I am convinced that cancer education is not possible without first rousing the enthusiasm of the public itself, and getting its cooperation The following steps for a cancer campaign are suggested (1) to get the good will of the local medical officer of health, the local authorities, the local branch of the British Medical Association, and the regional hospital board, (2) to persuade the mayor of the town to call a meeting of representatives of the local voluntary organisations—e g, Red Cross, W V S, women's institutes, town's women's guild, rotary, inner wheel—in order to form a local cancer education committee The duties of this committee would be to organise lectures, to distribute

---

1 Kelemen, E Majoros M Tanos B *Lancet* 1950 ii 457
2 Kelemen E Majoros M, Iványi, J, Kovács, K *Experientia*, 1950 6, 435
3 Loberg, K *Biochem Z* 1926, 170 173
4 Sprague R. G, Power M H Mason H L Albert A Mathieson, D R Hench P S, Kendall E C Sloocumb C H Polley H F *Arch intern Med* 1950 85 199

HEIGHTENED PERCEPTION AFTER E C T

SIR,—I have recently become interested in an unusual phenomenon following electroconvulsive therapy (E C T)

A man, admitted to hospital because of melancholia with suicidal tendencies, was given a short course of E C T in the hope of relieving his symptoms The convulsions were followed by a period of confusion which lasted about an hour This phase was constantly succeeded by a transient phase of increased awareness of the environment, lasting some six hours

He described his feelings during this time in the following words 'Everything becomes more vivid and seems to take on a bolder outline The sky buildings and even women appear more beautiful All colours are intensified, black objects increase in blackness, and red ones become more red I am conscious of a delight in life which I have not experienced for a long time Knowing that it is temporary, I can thoroughly enjoy this period One can go to the heights of Mont Blanc but one cannot remain there ! Soon I drift back to my usual state of mild depression."

Another patient, suffering from an anxiety state with depressive features, claimed that a remarkable improvement in his colour vision had followed a short course of E C T

The general increase in visual acuity is somewhat reminiscent of the effect produced by the sudden relief of cerebral anoxia It can be argued that removal of depression, with its inhibiting effects, explains the augmented perception However Lhermitte and Parcheminey [1] and others have described hallucinosis following electro shock, which suggests a positive increase in activity by the sensory cortex

Basingstoke Hants J TODD

ORGANIC HYPERINSULINISM TREATED WITH ALLOXAN

SIR,—The article of Feb 24 by Dr Gilchrist and Dr Lynch is worthy of note, because the level of the serum citric acid in the case described is the highest I have ever heard of—i e , about 20 times normal This is all the more remarkable in a patient with hypoglycæmia, because I can confirm Dr Weil Malherbe's observation that the serum citrate level decreases in artificial hypoglycæmia The urinary excretion of citric acid is said to be excessive, but it must be regarded as only moderately increased as compared with the serum citric acid I have observed greater urinary excretion of citric acid per 24 hours in Addison's disease

Unless the test was influenced by pathologically increased levels of other blood constituents, it would seem reasonable to suppose the high citric acid level to be primarily of interest in explaining the pathogenesis It cannot be proved with certainty that the condition was one of hyperinsulinism It would be very remarkable if two such rare diseases as hyperplasia of the islets of Langerhans and primary liver cell carcinoma were to occur simultaneously The picture resembles rather that described in spontaneous hypoglycæmia as due to hepatic disease, and in very rare cases to liver cancer, but without pancreatic involvement The decrease in the amount of liver tissue has not always been regarded as sufficient to explain hypoglycæmia or the consumption of the large quantity of glucose that had to be administered to keep the patient alive In such cases the condition has been explained as a secondary hyperfunction of the islets of Langerhans, this must, of course, be regarded as purely hypothetical The possibility of changed metabolism of the large tumour masses and consequent increased consumption of glucose, together with decreased storage capacity of the liver, has also been suggested In the case reported the markedly increased serum citric acid might indicate such abnormal carbohydrate metabolism Reports of the citric acid metabolism in similar cases would be of interest Such high figures as 53 3 mg per 100 ml have hitherto been recorded only in animal experiments I have measured such levels in rabbits after the administration of guanidine or 'Synthalin', and Peters et al have reported similar levels in rats, guineapigs, and pigeons medicated with fluoroacetate

Medical Clinic
University of Lund Sweden. J MÅRTENSSON

ORGANIC CHEMISTRY

SIR,—Your review last year [1] of my book [2] includes the comment "Scottish readers will be horrified to read that whisky is made from maize or rye, neither of which is used in the production of 'Scotch'" I should like to point out that in the U S.A whisky is made almostly exclusively from maize and rye and not, as in Scotland, from barley Your review also remarks on the neglect in my book of a description of the energetic aspects of alcoholic fermentation, including the rôle and production of A T P This problem which has long been under investigation, involves physiological chemistry, and discussion of it has no place in a textbook of organic chemistry

Chemical Institute
University of Zürich P KARRER

CATION-EXCHANGE RESINS

SIR,—We have read with interest Mr Morton's article of April 14

As far as is known, the ion exchanges of these resins are governed by the law of mass action According to Kressman and Kitchener [3] the exchange of sodium and hydrogen ions is governed by the relation

$$\frac{C_{H}}{C_{Na}} \quad \frac{C_{Na\ res}}{C_{H\ res}} = K_{H/Na}$$

where C_H and C_{Na} are the concentrations of hydrogen and sodium ions in the solution in m eq per litre, $C_{Na\ res}$ and $C_{H\ res}$ are the amounts (in m eq) of sodium and hydrogen ion per g of resin, and $K_{H/Na}$ is the exchange equilibrium constant The corresponding equation for calcium and hydrogen ions is

$$\frac{(C_H)^2}{C_{Ca}} \cdot \frac{C_{Ca\ res}}{(C_{H\ res})^2} = K_{H/Ca}$$

Mr Morton's results do not disagree with this view For instance, in the second experiment quoted in his article, 1 g quantities of 'Zeo Karb' were allowed to react with different volumes of the same solution of sodium chloride from the results given the value of $K_{H/Na}$ calculated for the first tube is 3 30 and for the sixth tube 3 37 The agreement is excellent

Our own preliminary investigations suggest that, employing the technique of Kressman and Kitchener, 1 g of zeo karb 225/H has a capacity of 5 0 m eq and that the exchange equilibrium constant with sodium ($K_{H/Na}$) is 1 8 These results are calculated for dry resin, but air dried resin was used in the experiments and its moisture content, determined by drying at 100–120°C for 5 hours, was found to be 31%

Mr Morton's deduction that 1 g of resin equilibrated with a solution containing 6 m eq of sodium ion would be saturated with sodium is probably wrong, on the basis of his own figures it seems likely that about 86% saturation would be achieved The relation between the initial amount of sodium ion in the solution and the percentage saturation with sodium of the resin at equilibrium is a parabola Similarly 1 g of resin in presence of 0 7 m eq of sodium would have a "percentage efficiency ratio" of about 91%, and not 100% as stated

---

[1] Lhermitte J Parcheminey *Rev Neurol* 1943, 75 37

[1] *Lancet* 1950 ii 375

[2] Organic Chemistry London 1950

[3] Kressman T R E Kitchener J A *J chem Soc* 1949, 1190 1201

Histologically many caruncles consist of masses of granulation tissue Such a lesion, though obviously not neoplastic, cannot be described as prolapsed mucosa We believe therefore that the clinical term "caruncle" is no more misleading than the term "polyp," which is used to describe a variety of pathological lesions

The important fact emphasised by Mr Campbell Begg is that the condition of *true* erosion, although by no means rare, is not a common lesion

Department of Obstetrics and Gynæcology
University of Birmingham

C W Taylor
H C McLaren

COMBINED ABDOMINO-VAGINAL HYSTERECTOMY

Sir,—Mr Howkins, in his article last week on the above operation, mentions that some surgeons believe it worth leaving some portion of the vagina This has obviously to be considered in operating on the younger age groups Further, the slow healing of the cavity left by removal of the vagina, with its inevitable infection and continuous discharge requiring constant attention for up to six months, must be distressing to the patient

Might not this unpleasant (though temporary) complication be avoided by combining the radical surgical removal described by Mr Howkins, with all its advantages, with the relatively simple reconstruction of the vagina popularised by Sir Archibald McIndoe ? This would add little, if any, time to the operation, since the vaginal dissection is completed before the abdominal closure starts, and the reconstruction is a short procedure It is quite possible to cut the Thiersch graft from the thigh, without removing the patient's legs from the Lloyd Davies supports The skin is then inserted into the cavity either on a preformed acrylic mould or on a gutta percha mould, which is easily made at the time of operation

If hæmostasis has been obtained, and the walls of the cavity are reasonably smooth, healing should be sound in 10–14 days If the grafting were not completely successful, then there would be delayed healing, which would not be comparable to that of a granulating cavity It should be noted that a Thiersch graft has a high resistance to infection

In selected cases the addition of the reconstruction is, I am sure, a refinement worth considering

Odstock Hospital Salisbury J Ellsworth Laing

TUBERCULIN SENSITIVITY IN HOSPITAL CHILDREN

Sir,—Dr Lunn's article of Feb 17 is a most valuable contribution to an important problem Only large scale investigations of this kind will provide a scientific basis for tuberculosis control programmes, with or without B C G In view of the importance of this investigation, however, I wish to submit that the percentages reported in table I and II are erroneous

The calculation of the percentage of positive reactors (1071) was based on the total admissions (7555) and reported as 14 7% This would only be true if all "results not available" were negative However, as "results not available" will probably show the same incidence of positive and negative reactors the total of "results not available" (1309) should be deducted from the total admissions (7555 − 1309 = 6246) , and the positives (1071) should be related to the corrected figure of admissions (6246) This will give 17 1% positive instead of 14 7% The same correction will have to apply to the other percentages listed in tables I and II

Almirante Panama Gustav Engler

*** We have shown this letter to Dr Lunn, who replies as follows

"The point made by Dr Engler is important, and was not overlooked. Of the children for whom results of Mantoux tests were not available 1074 (82%) were under one year of age, and indeed, as was mentioned in the paper, 890 (83%) of these were under three months The incidence rate of positive reactors from birth to one year is very low (2 3% in table II, or 3 4% using the correction suggested by Dr Engler) It seemed, therefore, more appropriate to use the total number of admissions rather than the total number of Mantoux tests done as the basis for the calculation of percentage sensitivity rates "

THE ECONOMIC VALUE OF THE DOCTOR

Sir,—The letter from Dr Hughes (April 14), in which I regret to note that he seems to belittle the value of "prevention" in a health service, confirms what has been apparent for many a day—namely, that the word "health" by itself fails to convey to the hearer all that it connotes For clarity and simplicity, and to avoid misunderstanding, two words seem to be needed when we discuss health matters, because health, as the word is used today, has two main and distinct aspects—a maintenance of health or prevention of disease side, and a healing side

"Hygiene" is sometimes used for the first of these aspects , but it is an unsatisfactory word, and the Army medical authorities, in their search for a better word, have recently substituted the term "Army health" for hygiene This is an improvement, certainly, but does not quite meet the difficulty so far as civil affairs are concerned

The average individual comes into the world healthy, and what the various public health and Army health and other "preventative" workers are trying to do is to keep him healthy It is the "maintenance of health" they are mostly concerned with , this seems a better term than "prevention of disease" Disease to the average healthy person is something that is unlikely, he hopes, to happen to him The maintenance of health, on the other hand, is a personal matter , it is something of which every healthy individual understands the value, and in which he is interested If therefore we want to have good cooperation from the public, let us talk in future not so much of the prevention of disease, but rather of the maintenance of health

The National Health Service is, I feel, misnamed. It should surely be called the "National Back to Health Service" ! Is that not what it principally is ? The doctor whom Dr Hughes has in mind is not primarily concerned with maintaining health, for he is seldom consulted by the healthy individual , his job is, in the main, to treat the sick person, and help him to regain that healthy level from which he has fallen

To differentiate between these two aspects, two new words are needed Any suggestions ?

Public Health Adviser s Office,
Bad Salzuflen Germany

W Strelley Martin

TRANSPARENT FILM ENVELOPES FOR A SYRINGE SERVICE

Sir,—I read with great interest the article by Dr McCartney (March 3) Before the article appeared we had been testing these envelopes with a view to using them in the syringe service of this hospital, to overcome the shortage of glass tubes

We found that after sterilisation the syringes were sometimes non sterile, and we were at a loss to understand this On minutely examining the envelopes we found that small cracks had appeared which were not readily discernible to the naked eye It was thus felt that this was not an ideal way of packing syringes for sterilisation since handling in the wards and departments might render them non sterile, even though the envelope appeared intact These minute cracks seem to be due to slight brittleness of the envelope after sterilisation, despite the fact that the envelopes were not touched for a few hours after being sterilised

Evelyn P Button
Chief Pharmacist.

Ancoats Hospital,
Manchester

It should be added, however, that nothing like chaos prevailed in the heads of these savants, but an ordered system in which scientific and non scientific ideas were well integrated As Charles Singer remarked, in the setting of time Harvey, like a Janus head, looks backward into the realm of ancient wisdom and forward into the dawn of modern science It is we who introduce contradiction and inconsistency into what was a unified personality as well as a unique figure

Department of
Morbid Anatomy and Histology
Central Middlesex Hospital
London N W 10

WALTER PAGEL

HYPERCALCÆMIC URÆMIA WITH NEPHROCALCINOSIS

SIR,—In their article last week Dr Fulton and Dr Paget reported a case of nephrocalcinosis and uræmia which they ascribe to hypercalcæmia resulting from carcinomatosis of bone As the patient had an alkalosis, which is known to cause uræmia and nephrocalcinosis, it seems unnecessary to bring in the carcinomatosis and hypercalcæmia except as secondary factors, and it may be presumed that their other patients with bone secondaries did not develop hypercalcæmia and nephrocalcinosis because they were not alkalotic

Dr Fulton and Dr Paget do not seem to have taken the alkalosis very seriously, for it actually became much worse while the patient was in hospital, and there is no mention of any attempt to correct it before the patient was submitted to operation It would be interesting to know why the alkalosis became worse, for the patient was apparently not vomiting, and in any case is said to have had an achlorhydria

Department of Pathology
Royal Infirmary Bristol

G K McGOWAN

THE "CITROVORUM FACTOR"

The American Cyanamid Company, referring to our leading article of March 17, inform us that the synthesis and isolation of a pure substance with the biological properties of the citrovorum factor were first described by research workers of the company's Lederle Laboratories and Calco Chemical divisions [1]

Parliament

Mr Bevan's Statement

IN making his statement, in the House of Commons on April 23 on his resignation from office as Minister of Labour, Mr ANEURIN BEVAN said that the charges on spectacles and dentures might be called a triviality, but a triviality had been known to start an avalanche The Chancellor of the Exchequer this year proposed to reduce health expenditure by £13 million out of the budget total of £4000 million "What would happen next year? Or are you next year," Mr Bevan asked, "going to take your stand on the upper denture? The lower half apparently does not matter, but the top half is sacrosanct" The Chancellor of the Exchequer, Mr Bevan continued, was putting a financial ceiling on the health service With rising prices the health service was squeezed between that artificial figure and rising prices What was to be squeezed out next year? Was it the upper half? When that had been squeezed out and the same principle held good, what did you squeeze out the year after? Prescriptions? Hospital charges? Where did you stop?

Mr Bevan said he had been accused of having agreed to a charge on prescriptions That showed the danger of compromise Because if it was pleaded against him that he agreed to the modification of the health service, then what would be pleaded against his right hon friends next year, and indeed what answer would they have if the vandals opposite came in? The health service would be like Lavinia—all the limbs cut off and eventually her tongue cut out, too After all, the service was something of which we were all very proud Even the Opposition were beginning to be proud of it It only had to last a few more years to become a part of our traditions, and then the traditionalists would claim the credit for all of it

Why had the cut been made? With an over-all surplus of over £220 million and a conventional surplus of £39 million the Chancellor could not plead that he had to have the £13 million. That was the arithmetic of bedlam Surely he could not say that his arithmetic was so precise that he must have £13 million, when last year the Treasury were £247 million out. Had the American Medical Association, Mr Bevan asked, succeeded in doing what the British Medical Association failed to do?

Mr Bevan said he had been accused of agreeing to the prescription charge, but he pointed out, he knew that charge would never be made, for it was impracticable And in fact it never was made A proposed reduction of 25,000 on the housing programme had also never been made At that time he had to use what everybody called bad tactics He had had to manœuvre, but he saved the 25 000 houses and the prescription charge We had gone a long way against great difficulties "Do not let us change direction now," Mr Bevan urged "Let us make it clear to the rest of the world that we stand where we stood, that we are not going to allow ourselves to be diverted from our path by the exigencies of the immediate situation We shall do what is necessary to defend ourselves—defend ourselves by arms, and not only with arms but with the spiritual resources of our people"

National Health Service Bill, 1951

This Bill, which was read in the House of Commons for the first time on April 17, authorises the charges for dentures and spectacles announced by the Chancellor in his budget speech The Bill, which applies to England, Wales, and Scotland, also empowers the Minister of Health and the Secretary of State for Scotland to send patients with respiratory tuberculosis abroad for treatment

The charges for false teeth and glasses will be made to patients who obtain these aids under the "family-practitioner service" and to hospital outpatients, but no charge will be made to hospital inpatients. People who cannot afford to pay the charges will be able to apply to the National Assistance Board for help even though they are in full employment No charge will be made for sight tests or for dental treatment The amounts of the charges are specified in the Bill but they may be varied by order in council, subject to an affirmative resolution of both Houses. The charges cover about half the cost to the Exchequer and are as follow

Dentures—Full upper and lower £4 5*s* Single dentures 1–3 teeth £2 4–8 teeth £2 5*s*, 9 teeth or over £2 10*s*

Spectacles—£1 a pair plus the cost of the frames, which ranges from 3*s* 4*d* to 15*s* 1*d* Children's glasses in the standard type of frame will still be free of charge

The charges will be paid direct by the patient to the dentist or optician under the family-practitioner services, or to the hospital authorities and the fees payable by the executive council to the dentist or optician will be correspondingly reduced

Mr HILARY MARQUAND Minister of Health, moving the second reading on Tuesday, said that charges for dentures and spectacles must not be regarded as permanent features of the N H S In the next few difficult years he hoped to expand hospital services, including the hospital treatment of tuberculosis "More money was needed than the Chancellor could see his way to provide, and the measures taken to get that money were not an attack on the service" Dr CHARLES HILL remarked that uncontrolled rise in expenditure on the N H S might spell ruin for other social services

The second reading was agreed to without a division

---

[1] Brockman, J A, jun Roth B Broquist H P Hultquist M E. Smith J M jun. Fahrenbach M J Cosulich D B Parker R P Stokstad E L R. Jukes T H *J Amer chem. Soc.* 1950 72 4325

In the second paragraph of the article the effect of ion concentration upon the displacement of calcium from the resin by sodium and upon the reverse process is described This effect can be deduced from the relations given above The word "affinity" is confusing, and data are best discussed in terms of the exchange equilibrium constant

Magnesium trisilicate is known to release magnesium ions in the presence of acid, and Mr Morton's finding of a reduction in the amount of sodium ion removed by the resin when magnesium trisilicate is added to the system is to be expected The therapeutic value of magnesium trisilicate would be doubtful, because the "acidosis" is due to loss of base into the resin rather than to the associated release of hydrogen ions

We agree that patients treated with ion exchange resins need to be very carefully controlled It is our experience that the serum sodium determination is important

IAIN MACINTYRE
Sheffield ARTHUR JORDAN

THEORY OF CEREBRAL LOCALISATION

SIR,—In the light of Dr Gooddy's retort (March 31), may I add a little to my letter of March 17 ?

It is probably true that of recent years some neurologists have been at times somewhat rigid in their exegesis of localisation But this inflexibility has been largely in the matter of patterns of representation within the motor strip alone, and not so much in that of cerebral functional topography as a whole Thus argument has centred predominantly on the problem of the cortical representation of movements or of muscles Whilst the American school of neurologists has claimed direct muscular representation, in this country the opposite opinion has been held, and the lately published researches of Liddell and Phillips,[1] which at last confirm from the laboratory the view of cortical thresholds of excitability so brilliantly deduced by Walshe [2] from clinical observation alone, provide further evidence in support of the traditional English view

However, it may be questioned at this point whether the argument between the two camps is not really an artificial one—whether, that is, the two hypotheses are truly alternative and incompatible with one another It may be held that they are not absolutely discordant, and that therefore both views may possibly be right For my own part, I do not see any valid a priori obstacle to making such an assumption, and hence to thinking that both movements and muscles are simultaneously represented in the cortex It may be objected by some that such an idea is counter to reason, but then Nature is not overindulgent in fitting her behaviour to accord with the principles of logic It is relevant to note that current physical thought has been compelled to accept two interpretations at once of the nature of light that it has a continuous wave form, and that it also and at the same time consists in discontinuous packets of energy—theories which, judged at face value, would appear mutually exclusive

Still, although discussion of the details of physiological organisation within the motor area has bulked large in neurological literature, it must not be taken to make up the whole body of ideas about cerebral localisation It should be remembered that for more than twenty years now, Lashley [3] has been insisting on the functional equipotentiality of nervous tissue and he has accumulated a formidable body of evidence in support of his view In essence his work is also an experimental validation of Hughlings Jackson's older and virtually identical conception, that every part of the body is represented everywhere in the nervous system In the last few years the discovery [4] of secondary, and even tertiary, loci of motor and sensory representation in the cerebral cortex, and of complicated cerebellar representations of the body (derived both from the cerebrum and from the spinal cord) and even of the viscera, have provided, from a different angle, implicit confirmation of the Jacksonian concept, though so far as I am aware no one has yet drawn specific attention to this fact

I submit once again that, in face of all the evidence, it is vain and nugatory to assert that theories of cerebral localisation need overhauling simply in the light of the results of human hemispherectomy Nevertheless, the results of hemispherectomy do suggest the need for critical reassessment of Jackson's notion that destructive lesions cause only negative symptoms This is doubtless true for the outcome of planned ablations of nervous substance, whether therapeutic or experimental It is evidently not necessarily true where the destruction results from natural causes As a speculation it may be suggested that it fails where the lesion is patchy, so that islands of more or less normal cells are left in action scattered amidst functionless wastes of tissue, but that it holds good where there is uniform dissolution throughout an area,

Birmingham MICHAEL JEFFERSON

THEN AND NOW

SIR,—Discoveries are often "in the air" before they are made Fertile ideas and fortunate speculation have, not infrequently, prepared the soil for them This topic is touched on in the most interesting paper (April 14) by Dr Keevil and Mr Payne, who describe what appears to be a speculative anticipation of the circulatory motion of the blood by Reyna in 1546

I have lately drawn attention to a similar instance—namely, the assertion by Giordano Bruno in 1591, on philosophical grounds, that the blood "moves continually and very rapidly in a circle" [5] This seems to support the view that Reyna, too, expressed a philosophical concept which, at his time as well as later on, was "in the air" I have tried to trace it to the revival of certain Aristotelian and Neo Platonic theories in the Renaissance [6]

How much attention should we pay to such a speculative vision which anticipated a scientific discovery ? Today scientists and doctors who look back on these speculative anticipations may feel that they have but little interest and value, and be interested only by scientific evidence based on observational material—in other words, the "Harveian method" [7] The historian, however, not content with the extraction of "relevant" data, will take a larger view Harvey was inclined to accept a "philosophy of circles," as initiated by Aristotle, to Harvey blood circulation was one instance of a general cosmic law of circles, periodical processes, and circular patterns with reversion to the point of departure [8], and in this light the "philosophy of circles" before Harvey's time is of great historical interest, however remote it may seem from his scientific (i e, quantitative) studies The speculations about circulation, by Reyna, Bruno, and probably others of their time, belong to the "Verities yet in their Chaos," [9] as Harvey's own speculations have been aptly designated

---

1 Liddell E G T Phillips C G *Brain* 1950 73 125
2 Walshe F M R *Ibid* 1943 66 104
3 Lashley, K S Brain Mechanisms and Intelligence Chicago 1929
4 Dow R S *J Neurophysiol* 1939, 2 543 *Ibid* 1942, 5 121 Adrian E D *Brain* 1943 66 89, *Ibid* p 289 Snider, R S Stowell, A *J Neurophysiol* 1944 7 331 Hampson J L *Ibid* 1949, 12 37 Penfield W Rasmussen T Cerebral Cortex of Man New York 1950
5 Pagel W *Brit med J* 1950 ii 621
6 Pagel W *Amer J Hist Med* 1951 6 116
7 See Cohen H *Brit med J* 1950 ii 1406
8 Pagel W *Bull Hist Med* 1950 24 70
9 McNeil, C *Brit med J* 1950 ii 961

Great Britain for the Colonial Medical Service, and how many scholarships for medical training had been awarded during the last three years by the governments of Kenya and Sierra Leone—Mr JAMES GRIFFITHS replied No hospitals or dispensaries have been closed in Kenya but I regret that in February, 1951, staff shortages made it necessary temporarily to close 2 hospitals in Sierra Leone. Posts in the Colonial Medical Service are widely advertised and African medical students are encouraged to apply for them. During the last three years, the Kenya government has awarded 17 scholarships for medical training and has also paid £21,000 to Makerere College for the training of African medical officers. The Sierra Leone government has made 7 awards and 2 awards have been made to Sierra Leone students from the central allocation of colonial development and welfare funds.

Obituary

FRIEDRICH KARL KLEINE

M.D Halle

Dr Friedrich Karl Kleine, who has died in Johannesburg at the age of 81, had won international renown for his work on tropical medicine, especially on the life-cycle of the trypanosome. His friends and collaborators also respected his integrity, his dogged character which overcame all difficulties, his loyalty, and his delightful puckish sense of humour.

Kleine studied medicine in Halle, till in 1900 he became assistant to Robert Koch, then at the height of his fame, at the Institute for Infectious Diseases in Berlin. In 1902 he accompanied his chief to Southern Rhodesia to investigate African coast fever of cattle. In these animals he found two species of parasite, the smaller of which, *Theileria kochi*, proved to be new to science. He also did useful work on the immunisation of horses and mules against horse-sickness. In 1906 he became interested in the piroplasma of dogs, and he was one of the first to elucidate its life-history. But soon his interest turned to trypanosomiasis of man and animals, a subject to which he devoted the rest of his life.

From [illegible]

Fired by the work of David Bruce, Dutton, and others he was the first in 1909 to work out the life-cycle of the trypanosome *T brucei* in the body of the tsetse fly and to show conclusively that the infective forms were injected by the insect with the salivary secretions, the whole cycle occupying some three weeks. These observations were the starting-point of much new work on the epidemiology of trypanosome diseases.

Early in 1914 Kleine was in the Cameroons investigating sleeping-sickness, and he was soon engulfed in the first world war as head of the German medical services there. Nevertheless he continued his researches and he was able to confirm Leiper's discovery (1913) of the life-history of *Loa loa* in chrysops. At the end of the war he returned to the Robert Koch Institute in Berlin, but he was soon off again to his beloved Africa where in 1921 he tested the properties of the new 'Bayer 205' (now known as suramin) as the most effective drug in human trypanosomiasis. On this expedition he was accompanied by Fräulein H Ockelmann, an assistant in the institute who later became his wife and who was his co-worker during the last 30 years of his life.

Returning to Berlin in 1923 he became interested in the health section of the League of Nations, and in 1926 he was appointed the German delegate. The same year he investigated in Uganda problems of human immunity against trypanosomes in natives living in a focus of sleeping sickness. He also devised experiments to differentiate *T gambiense* from *T rhodesiense*. After a short period of recuperation in Europe, in 1929, he investigated the virulence of *T rhodesiense* in Tanganyika. During this period he and his wife underwent very considerable hardships while exploring undeveloped country.

In 1933 he became president of the Robert Koch Institute in Berlin, but three years later he spent another fruitful year at the Veterinary Research Institute in Onderstepoort in Pretoria studying foot-and-mouth disease in cattle and big game. His last journey before the second world war took him in 1938 to Tabora, Tanganyika, where he investigated the rôle of cattle as reservoir hosts of *T rhodesiense*. He celebrated his 70th birthday on Fernando Po, drawing up a report on the island's campaign against trypanosomiasis.

During the late war Kleine suffered from privations and persecution. His home in Berlin was destroyed and his only son died of wounds. After the fall of Hitler and at his advanced age he undertook single-handed the task of reorganising the tropical section of the Robert Koch Institute, visiting the department daily. But the lure of Africa proved too strong for him, and at the age of 78 he and his wife travelled to Johannesburg where under the kindly care of old friends Kleine passed his last days.

P H. M-B

JOHN GAY FRENCH

M S Lond, F.R C.S

MR Gay French, consulting ear, nose, and throat surgeon to the Royal Free Hospital and formerly senior surgeon to the ear, nose, and throat department of the Royal Northern Hospital, died on April 13 at the age of 79.

He was born at Mymensing in Bengal, the youngest son of Lieut -Colonel J Gay French, F.R C S, I.M.S, and he was educated at Trinity College, Dublin, and the University of London. He obtained an open entrance scholarship to St Mary's Hospital, and after graduating M.B in 1902, he held house-appointments there, and at St Bartholomew's Hospital, Great Ormond Street Hospital, and the Golden Square Hospital for Diseases of the Throat and Ear. In 1906 he was appointed to the staff of the Royal Northern Hospital and in the same year he took his B.S with honours. The following year he became assistant surgeon at the Central London Throat and Ear Hospital and he also obtained his M.S degree and the F R C.S. He was thus firmly established in his specialty when he joined the staff of the Royal Free Hospital and became lecturer in diseases of the ear, nose and throat at the London School of Medicine for Women.

Mr Gay French was also for many years on the staff of the Royal Masonic Hospital and he was for some time consulting specialist to the War Office. His published work included papers on middle-ear deafness, and he contributed the chapter on diseases of the pharynx and larynx to the *Dictionary of Practical Medicine* (1923).

T J H writes "Those who knew him well appreciated his kindly nature, his ready sympathy and encouragement to his younger colleagues, and his absolute integrity. As chairman of the medical committee of the Royal Free Hospital he showed balanced judgment impartiality, and sincere regard for the best interests of the hospital. He had a fierce presence and a somewhat gruff manner, but he was beloved by colleagues, students, nursing staff, and patients, who were quick to discern the real man, which his rather austere bearing could not conceal. He was a good raconteur with a great sense of dry humour. He enjoyed life and even when family losses might have embittered a lesser man he kept a brave, cheerful front, which, if possible, increased the admiration and affection in which he was held."

He married Elinor May Pipe-Wolferstan in 1911. Their three sons predeceased their father.

Prof K D WILKINSON

T L H writes 'For thirty years the friendship of Kenneth Wilkinson has been for me an exhilarating and delightful experience. He was a man with an exuberant vitality and self assurance which at first contact were almost overwhelming. Life for him was an exciting adventure to be savoured fully and vigorously and he liked to share his experience with his friends. His sense of humour was of the keenest and as a raconteur he had few rivals, and he could talk fluently, accurately, and humorously in many dialects. No-one who heard it will forget his presidential address on this subject given some years ago to the Birmingham Graduates Club. 'The Wilk,' as he was affectionately called, was indeed a fellow of infinite jest and most excellent fancy.

The Care of Old People

In the House of Lords on April 18, Lord **SALTOUN** moved "That this House regards with sympathy and concern the difficulties of old people and calls upon the Government to secure the greatest measure of coordination between the health services and other social services with a view to ensuring that adequate personal service and attention are available to such old people" Under the new system, he said, these people were nobody's care In the past six months 17 cases had been reported in the press of old people who were found dead in varying conditions of horror He refused to accept these conditions as normal Despite the efforts of all concerned the machinery of the health and social services did not work well, and some reform seemed to be imperative Often there were reports of elderly patients being refused admission to hospital, and a system in which a conscientious public servant had to resort to the device of refusing to sign certificates if old people died, and threatening to cite hospital officials at a subsequent inquest, was in Lord Saltoun's view self condemned In six months he had collected 11 cases where hospitals had refused to admit elderly persons To remedy the situation Lord Saltoun suggested the appointment of a local officer at borough or district level with responsibility for knowing all the cases in his area and with power to arrange for treatment in private homes at rates not exceeding the cost of county homes He should act as a focal point between county, borough, hospital, and Assistance Board After all, Lord Saltoun pointed out, the sensitive part of an elephant's trunk is at the tip

Lord **KERSHAW**, Lord in Waiting, said that though the Government were prepared to accept the motion, they did not accept many of Lord Saltoun's conclusions National Assistance officers were in touch with far more people than the former relieving officers could be It was absurd to pretend that the change-over from poor relief to supplementary pensions was not welcomed by aged people Of the 1,000,000 old people who applied for supplementary pensions when the National Assistance Board began, 700,000 were people who had preferred to make do without that relief, although many of them must have been in great distress There were now 600 county and local welfare committees at work and more were being continuously formed Since the end of the war 300 local-authority homes accommodating old people had been opened in England and Wales, and another 300 were in course of preparation Hospital beds were a problem that nearly defied solution, and Lord Kershaw agreed that there was need for closer coöperation between the various agencies dealing with old people A special committee of the Central Health Services Council would shortly report on this matter

Lord **AMULREE** agreed that people were trying hard to make this new social plan a success, but he supported Lord Saltoun's suggestion that it would be an advantage if someone was officially charged with the duty of finding out the conditions among the sick and infirm poor Prompt admission to hospital would nearly always ensure prompt discharge, that was as true for old people as it was for the young A short spell in hospital at the right time might often lead to many years of comparative health at home Though it was impossible to provide any more hospital beds at present, he suggested that the number of beds now available was probably sufficient for the needs of the aged population if they were properly used In some of the hospitals where the old and chronic sick patient was properly treated it had been possible in the course of a few years to cut down the number of beds to a third or even a quarter of the previous total and yet deal with the same or a bigger population In five or ten years' time Lord Amulree thought it would be unnecessary to provide more beds even for a vastly older population But while beds were still in short supply it had been suggested that, subject to a medical certificate, there should be compulsory admission to a hospital for a short time Lord Amulree thought there was something to be said for the proposal, but there should also, he suggested, be compulsory admission to an institution or home We could not place the whole burden on the hospitals, or they would get clogged up There should also be means of compelling younger people to look after their parents after they left hospital

Dangerous Drugs Bill

In the House of Lords on April 17 the **LORD CHANCELLOR** introduced this Bill, which is a measure to consolidate the Dangerous Drugs Acts 1920 to 1950, and section 28 of the Pharmacy and Poisons Act 1933

QUESTION TIME

Hospital Accommodation for Chronic Sick

Miss **IRENE WARD** asked the Minister of Health whether, in view of the shortage of beds for the chronic sick in the country, he would consider making it a statutory obligation on the regional hospital boards to accept cases recommended by medical officers of health as in need of care and attention. —Mr H A **MARQUAND** replied No, Sir

Pulmonary Tuberculosis among Foreign Workers

Mr **WILLIAM TAYLOR** asked the Minister whether he was aware of the prevalence of pulmonary tuberculosis amongst foreign workers in Bradford, and whether he would now cause a much stricter medical examination to be made of foreign workers entering this country by the immigration authorities —Mr **MARQUAND** replied Notifications of respiratory tuberculosis among foreign workers in Bradford in the years 1947 to 1950 were respectively 0, 6, 15, and 26 The last three figures represented 2 9, 5 4, and 10 4% of the total notifications in that city Over half the cases were European volunteer workers, who are medically examined for tuberculosis before being brought to this country, and most of the others were ex prisoners of war or members of the Polish armed forces I am examining with other Ministers concerned whether anything more can be done to prevent immigration of foreign workers with tuberculosis.

Charges for N H S Dentures and Spectacles

Commander A H P **NOBLE** asked the Minister what would have been the total saving if charge for dentures and spectacles had been made from the start of the National Health Service—Mr **MARQUAND** replied An exact calculation cannot be made, but I estimate that the saving in England and Wales would have been of the order of £50 million.

Patients Discharged from Broadmoor

In answer to a question Mr **CHUTER EDE**, Home Secretary, stated that in the ten years up to the end of 1950 the number of patients discharged from Broadmoor Institution was 148 males and 61 females, giving a total of 209

Morphia for Railway Accidents

Commander J F W **MAITLAND** asked the Minister of Transport whether he would introduce legislation to enable a supply of morphia to be included among the drugs and appliances kept in railway trains for service in case of accident —Mr **ALFRED BARNES** replied I could not recommend such a step If supplies of this dangerous drug were kept in railway trains, the risks of its misuse would in my view outweigh any possible advantages Experience has shown that qualified medical staff, with supplies of the necessary drugs, are almost invariably on the scene of an accident quickly

Cope Reports

Mr **IAN MIKARDO** asked the Minister of Health if he would make a statement upon the reports of the committees which, under the chairmanship of Mr Zachary Cope, considered the supply, demand, training, and qualification of medical auxiliaries in the National Health Service —Mr **MARQUAND** replied The Secretary of State for Scotland and I have now been able to study the reports, and we should like to pay tribute to the thoroughness and value of the investigation made by Mr Cope and the members of the committee The recommendations of registration made in the majority reports, which would require legislation, will now be taken by us as the basis of discussions with the appropriate organisations Meanwhile, pending the establishment of official registration machinery, we propose to apply the recommended qualifications to new applicants for posts in the National Health Service

Medical Services in the Colonies

Mr **JAMES JOHNSON** asked the Secretary of State for the Colonies how many hospitals and dispensaries had been closed down in Kenya and Sierra Leone through shortage of doctors, what steps were being taken to recruit African doctors in

PROTECTION FROM NOISE

The excessive noise to which many industrial workers are exposed often reduces their efficiency and occasionally causes permanent deafness Plugging the ears with cotton wool does not reduce the noise effectively, while ear plugs commonly preclude conversation. New plastic ear plugs, the 'Sonex ear defenders,' are said by the makers to reduce noise to one thousandth of the original intensity while still allowing normal speech to be heard These ear plugs are manufactured by Amplivox Ltd , 2, Bentinck Street, London, W 1

University of London

Dr A Fessard, professor of neurophysiology at the Collège de France, Paris, will deliver three lectures at University College, Gower Street, W C 1, at 5 30 P M on May 16, 21, and 22 He will speak on Comparative Electrophysiology

On Friday, May 18, at 5 30 P.M , at University College, Gower Street, W C 1, Prof D Bovet, of the Instituto Superiore di Sanita, Rome, will give a lecture on Natural and Synthetic Sympatholytic Drugs and their Structural Relationship with Sympathomimetic Substances

University of Sydney

The university invites applications for a senior medical research fellowship (£A900–1250) and for a junior medical research fellowship (£A800–1000) Further particulars will be found in our advertisement columns

Gresham College

On Monday, April 30, at 5 30 P M , at the college, Basinghall Street, London, E C 2, Prof Hamilton Hartridge, F R S , will give the first of four lectures on the Circulation of the Blood Further particulars will be found in our advertisement columns

Institute of Dermatology

From May 1 to June 22 at this institute, St John s Hospital, Lisle Street, London, W C 2, there will be a course of lectures on general dermatology and of lecture demonstrations on pathology, including medical mycology Clinical demonstrations for postgraduates will also be held on Fridays at 5 P M

Scottish Pneumoconiosis Unit

On April 21 Miss Margaret Herbison, M.P , opened the first Scottish pneumoconiosis unit at Bangour Hospital, West Lothian

Royal Appointments

Brigadier W R. D Hamilton, late R A M C , has been appointed as honorary physician to the King in place of Major General John Bennet, who has retired, and Major-General R D Cameron, late R A M C , director of medical services, British Army of the Rhine, honorary surgeon in succession to Major General W E Tyndall, who has retired

A Tudor Physician

During the Festival of Britain the Arts Council are holding a series of concerts of music by English composers at the Wigmore Hall. The programme of the concert on the early Tudor period, on May 30, includes a motet, discovered this year in the library of the Royal College of Physicians of London, by Dr Robert Fayrfax. It is entitled *O Johannes Beatissimus*

Isle of Man Health Services

Resolutions approving expenditure in the current year of £557,000 on health services, and of £600,000 capital expenditure on improvements and extensions to hospitals, to be spread over three years, have been passed by Tynwald, the Isle of Man parliament Introducing the estimates, Mr T C Cowin chairman of the social services board, said £43 000 would be needed to meet specialists remuneration for the current year and to discharge liabilities for past services The amount saved in four months, the beginning of October to the end of January, by the prescription charge of 6*d* said Mr Cowin, was £2183, and on the charge for containers £275 The main saving was expected from the deterrent effect Exempted from payment were 7337 children, 1648 pensioners, and 463 persons incapacitated through illness making a total of 9448

Of the £600,000 voted to the board about £75 000 had not been spent This was largely because it was not possible to complete a scheme for the remuneration of doctors for travelling or to appoint specialists

Royal Society

Those lately elected foreign members of the society include

Prof H M Evans M D who holds chairs of anatomy and biology in the University of California, for his researches in anatomy, embryology and experimental endocrinology

Prof K S Lashley PH.D who holds the chair of neuropsychology at Harvard University for his studies of the neurological basis of animal behaviour and of the factors involved in learning

R W G Wyckoff of Bethesda, Maryland, for his contributions to the study of viruses

The society invites application for a Locke fellowship (£1250 per annum) for research in experimental physiology and pharmacology Applications are also invited for two Stothert fellowships for research in medicine Further particulars of these fellowships will be found in our advertisement columns

Chelsea Clinical Society

The annual dinner of this society will be held at the South Kensington Hotel, 41, Queens Gate Terrace, S W 7, on Tuesday, May 8, at 7 30 P M

Oliver Memorial Fund

A fourth award, of the value of £50, will shortly be made from this fund to a British subject for work or services in connection with blood transfusion. Applications or suggestions should be sent before June 30 to Mr F W Mills, hon. treasurer, c/o National Provincial Bank Ltd , Holborn Circus, London, E C 1

Potassium Bromide

Notice will shortly be received by all doctors and chemists who are contractors with executive councils, advising them that sodium bromide may be dispensed in place of the potassium salt where supplies of the latter are not available to meet orders on N H S prescriptions No special endorsement of prescriptions will be required This arrangement has been agreed as a temporary measure, and no exception has been taken to it by the National Formulary Committee

Thames Pollution

The Minister of Local Government and Planning has appointed a departmental committee to consider and report on " the effects of heated and other effluents and discharges on the condition of the tidal reaches of the River Thames, both as at present and as regards to any proposed new developments in the area " Prof A J S Pippard, head of the department of civil engineering at the Imperial College of Science and Technology, has been appointed chairman Pollution of the Thames was discussed in these columns last week (p 914)

International Student Course for Social Medicine

The International Student Movement for the United Nations is holding a seminar on social medicine from May 7 to 9 at Geneva during the meeting of the World Health Assembly The speakers will include Dr Brock Chisholm, the director general of W H O , heads of W H.O 's various departments, and several national delegates to the assembly Further particulars may be had from the secretariat of I S M U.N , Villa Rigot, 1 avenue de la Paix, Geneva, Switzerland

Price's Textbook of Medicine

On April 17, on the occasion of the publication of the 8th edition of *A Textbook of the Practice of Medicine*, a dinner was held at the Athenæum with Dr F W Price as the guest of honour Mr Geoffrey Cumberlege, publisher to the University of Oxford, who was the host, stated with regret that Dr Price was retiring from the editorship He recalled that the book was first published in 1922, and noted that the sales were now divided almost equally between Great Britain and overseas He concluded by presenting to Dr Price a specially bound copy of the last edition Dr Donald Hunter who is succeeding Dr Price as editor, summarised his predecessor's achievement and spoke of the requirements of books designed to encourage interest in clinical medicine He emphasised the need for approaching all the problems of medical education with a clear vision of the end to which medicine is directed Dr Price, in responding, spoke of his regret at relinquishing the burden of editorship which he had carried for so long and alluded to those of his associates who had died The proceedings terminated with a speech by Mr G T Hollis, editor of Oxford Medical Publications, who touched on some particular aspects of the textbook, with reference to the fulfilment of its original purpose and its prospects for the future

"But behind the scintillating façade, which he could throw off as readily as he could assume, and the shafts of wit which delighted and did not wound, was a heart as kind and generous as one could meet He was a fine physician of the older school with a special knowledge of cardiology, acquired only after a long apprenticeship in the field of general medicine His powers of observation were unusually acute and his approach to a problem a model of clinical medicine at its best He held his opinions strongly and expressed them in dogmatic and forthright assertion, and right or wrong, they were not lightly to be shaken

"He had many interests, but he perhaps preferred the arts and crafts of man to the works of nature A good piece of machinery, a yacht under sail, a camera, old books, and good pictures—all delighted him, and his enthusiasm was infectious Whatever he undertook, teaching, writing, playing golf, he took infinite pains A most genial host, when times were propitious he entertained his friends with generous hospitality, and on these occasions he liked to show his admirable ciné films of local events and accompany with inimitable running comment

"In his delightful family circle he was at his best, primus inter pares, and his two marriages and the children of those marriages brought him great and lasting happiness When adversity came in the form of serious illness he met it with unflinching courage He adjusted his life to meet his limitations and set to work on a task he had long had in mind, a life of William Withering and a history of the contemporary scene in Birmingham Writing did not come easily to him, but with the help of his devoted and able wife this work was published just over a year ago He worked almost to the last, teaching when he felt able, and attending and contributing to the weekly staff rounds to the great delight of his colleagues Kenneth Wilkinson was devoted to the Birmingham Medical School, and by the fine quality of his service he has earned his place as one of the greatest of her sons"

Births, Marriages, and Deaths

BIRTHS

ARONSON —On April 20, in London the wife of Dr R. P Aronson—a daughter

CLARKE —On April 13 the wife of Dr Owen Clarke—a daughter

DACIE —On April 18 in London the wife of Dr J V Dacie—a daughter

DAVIES —On April 14 at Chester, the wife of Dr J H Davies—a son

DICK —On April 20 at Cambridge, the wife of Dr Peter Dick—a son

DOVE —On April 18 at Liverpool the wife of Dr W L Dove—a son

GRIFFITHS —On April 19 at Liverpool the wife of Dr G I T Griffiths—a daughter

JAMES —On April 17 in Boston Mass U S A the wife of Dr A H James—twin sons

KAGAN —On April 18 in London the wife of Dr R S Kagan—a daughter

KAY —On April 18 in London the wife of Dr M S Kay—a daughter

MCILROY —On April 17, in London the wife of Dr Malcolm McIlroy—a son

MITCHELL —On April 15 at Bolton Lancs the wife of Dr R J Mitchell—a son

O MAHONY —On April 18 at Aldershot the wife of Captain Patrick Noel O Mahony R A M C —a son

PURSER.—On April 14 the wife of Dr D W Purser—a son

STEWART —On April 22 at Oldham Lancs, the wife of Dr J G Stewart—a son

VON BERGEN —On April 12 at Wentworth Surrey the wife of Dr Julian von Bergen—a son

WALSH —On April 22 in London the wife of Dr R C Walsh—a daughter

MARRIAGES

REECE—GIBSON —On April 14 at West Twyford, Michael Reece M.B, to Patricia Gibson

TAYLOR—ROBERTSON —On April 14 at Northwood Middlesex Charles Matheson Taylor M B to Joy Robertson

DEATHS

HOOD —On April 18 Martin Crichton Hood M A Camb, M R.C.S, D P M

KING —On April 17 at Stratton North Cornwall Thomas Arthur King M.R C.S aged 78

OLIVE —On April 14 at Leamington Spa Eustace John Parke Olive O B E M A M.D Camb, F R C S

PLAYFAIR —On April 16 at Fishbourne Isle of Wight Ernest Playfair M B Lond M R C P, aged 79

ROHAN —On April 18 in London James Virgil Reynolds Rohan L.R.C P E aged 69

Notes and News

NEW MOVE AGAINST VENEREAL DISEASE

To eradicate a contagious disease it is necessary to treat existing cases and to prevent new ones With venereal diseases the treatment of all cases is especially difficult, because reluctant patients must first be made aware of the dangers of such disease so that they will overcome their feeling of shame and fear of social disapprobation, and prevention is a complex matter which touches all aspects of community life

In this country, where these problems are shared between national and local authorities, much progress has already been made But, as Mr A J King pointed out in London last week, there is real need for a new organisation concerned with the social implications Mr King was speaking on April 17 at a meeting, convened by the Medical Society for the Study of Venereal Disease to discuss the formation of a new organisation for combating venereal disease, the meeting was attended by representatives of the Churches, the medical and nursing professions, the Armed Forces, and 28 organisations concerned with social welfare Sir Allen Daley, the chairman, paid tribute to Colonel L W Harrison as the main proponent of the proposed organisation, and remarked that venereal disease was still very much a national and international problem There were ebbs and flows of public interest, and at the moment the public did not seem greatly interested, though these diseases were a menace to the health of the country

It was finally decided that membership of the new organisation, provisionally named the British Federation Against Venereal Disease, should be open to all interested societies and people Its aims are (1) to study conditions that favour venereal infection and ways of combating these, (2) to assist bodies seeking to counter venereal disease, (3) to encourage the spread of knowledge of the facts about venereal disease, and (4) to collaborate with other national and international organisations having similar objects The secretary is Dr F R Curtis, secretary of the Medical Society for the Study of Venereal Disease

LONDON CHILDREN AT FRENCH SPA

IN 1949, and again last year, International Help for Children arranged for some London boys and girls to take a six weeks' cure at La Bourboule, in the Auvergne The 25 children were chosen by the London County Council and were all sufferers from asthma, one of the conditions in which La Bourboule specialises The possibility of sending them for a further month this summer is under consideration, and last week accounts of the scheme and of the spa were given at a reception in London Mr Michael Lubbock, chairman of International Help for Children, said that the care given to the London children at La Bourboule (which has hitherto included free accommodation as well as free treatment) was greatly appreciated he could not speak of their physical improvement but they were transformed in spirits, and revivified M Buronfosse described the arrangements, Dr Ferreyrolles, who has practised at La Bourboule for 37 years, spoke of the medical indications of the spa, and Dr Henri Olivier, the medical administrator, demonstrated charts showing that bronchial spasm induced by histamine is overcome by inhaling the mineral water vaporised as an aerosol A film was shown illustrating the life and work of La Bourboule As noted in these columns eighteen months ago,[1] the spa lies at 2765 ft and has arsenical water, hot (60°C) and exceptionally radioactive Its most characteristic feature is its use by children who come for the treatment of catarrh, bronchitis (non tuberculous), asthma, anæmia, skin disorders, and debility after illness "Children unaccompanied by their parents live in special pensions or hostels, and have a carefully regulated régime including rest periods and several hours each afternoon in a large children's park, which is at once a medical centre for physical culture and a place of happily unregulated amusement on swings and merry go rounds or playing around a stream"

Though La Bourboule will still provide free medical care for the London children, about £30 must now be found to pay the fares and accommodation of each The address of International Help for Children is 43, Parliament Street, London, S W 1

---

[1] *Lancet* 1949, ii 1187

DIAGNOSIS AND TREATMENT OF BULBAR POLIOMYELITIS*

W. HOWLETT KELLEHER
M.D. N.U.I., D.P.H.
PHYSICIAN SUPERINTENDENT, WESTERN HOSPITAL, LONDON

THE term "bulbar" is usually applied broadly to any clinical type of poliomyelitis resulting from lesions in any part of the brain stem, although strictly it is only applicable to poliomyelitis with a lesion in the much more limited area of the medulla oblongata.

It was pointed out many years ago that, histologically, every case of poliomyelitis will show lesions in the brain. Hence every case is strictly classifiable as polioencephalitis or polioencephalomyelitis. Fortunately in the majority of cases the lesions in the brain are so slight as not to produce clinical signs of encephalitis. In some epidemics, however, they are sufficiently common to give rise to clinical signs in from a quarter to more than a third of all cases of poliomyelitis. For example, reviewing the disease as seen in this hospital in 1947, I found that about a third of the cases had symptoms denoting a lesion of the brain stem, with or without spinal lesions.

In the cerebrum lesions are rarely demonstrable, except in the motor area of the cortex. In the cerebellum only a very limited area, encompassing the roof nuclei, may be attacked. The apparent immunity of these tissues seems to depend on resistance to infection and to the restriction of the advancing virus to well defined pathways.

The histopathologists emphasise the rarity of cerebral lesions and attribute the spasticity occasionally seen in encephalitic types not to cerebral cortical damage but rather to activity of the virus in the brain stem. Damage in the brain stem can also produce restlessness and occasional drowsiness and even coma. Some, however, attach considerable importance to the rôle of cerebral hypoxia in the production of such symptoms.

By and large, then, when we talk of polioencephalitis we mean the not inconsiderable group of cases with lesions of the brain stem, notably the medulla; and the present time seems appropriate for a review of our knowledge of the clinical pathology and classification of this too often distressing localisation of virus.

We owe a great debt to our American colleagues for the abundant literature on bulbar poliomyelitis, largely based on quite recent experience. Bower (1949), of Los Angeles, cites case records of 4774 patients treated in his hospital in 1946–48, and no less than 783 of these had bulbar lesions. During the same period, in Minneapolis, Brown (1949) and his colleagues saw 318 cases of bulbar type, which represented rather less than a third of all cases of poliomyelitis observed by them.

It would be misleading in any study of the attack of this virus on the brain stem to assess either the effects of the lesions or the result of treatment from a limited experience. There is general agreement that both the incidence and the severity of bulbar lesions can vary in different epidemics. In 1947, at the Western Hospital, although we were meeting with a higher proportion of bulbar cases, the severity of the cranial nerve lesions was much less than I had anticipated from impressions of the danger of these lesions gathered in the pre-war years. In 1949 we met with a disturbingly higher proportion of dangerous forms of bulbar attack. I am probably not alone in having such experience in this country during that year.

Not so long ago it was grudgingly accepted that patients with the more dangerous types of bulbar poliomyelitis would die, no matter what was done for them. (All agreed that patients with lesions of the upper group of cranial nerves rarely, if ever, gave rise to any anxiety and would more or less recover in due course.) In recent years, however, claims have been made for much more successful results in the treatment of those gravely ill with lesions of the brain stem, both through a better recognition of the factors producing symptoms and through a better application of the principles directed to their alleviation. There are few diseases in which such rapid fluctuations in severity take place and where spontaneous recovery is so common. The evaluation of such measures is very difficult, and there is no unanimity about the line to be taken.

CLASSIFICATION OF TYPES

The most generally acceptable grouping is that adopted by the Minnesota Poliomyelitis Research Commission (1947) as follow:

(1) The cranial nerve nuclei group.
(2) The respiratory centre group.
(3) The circulatory-centre group.
(4) The encephalitic group.

Combinations of any of these groups may be met with.

LESIONS OF CRANIAL NERVE NUCLEI

The Minnesota Commission propose, for the purposes of symptomatology and therapy, a division of the cranial-nerve nuclei group into upper and lower subgroups. In the upper subgroup are included the nuclei of the 3rd, 4th, 5th, 6th, 7th, and 8th cranial nerves. In the lower subgroup, although all the nuclei of the 9th, 10th, 11th, and 12th cranial nerves are important, it is damage to the nucleus of the 10th nerve that gives rise to the most dangerous symptoms.

Upper Subgroup

Lesions of the upper subgroup were, in my experience here, very common in the 1947 epidemic, and many of them were very slight. When they occurred without spinal lesions they did not give rise to anxiety, apart from ultimate prognosis. On the other hand, there were many cases with spinal lesions in which the disease was mild, with pareses rather than paralyses.

Apart from nystagmus, ocular signs and symptoms were uncommon, slight, and usually of brief duration. We met with one example of choked disc, in a patient treated in a respirator, giving rise to fears, later proved to be ill founded, of a space-occupying lesion. The Minneapolis Commission mention one similar case seen by them in recent years. Lesions confined strictly to oculomotor nuclei were comparatively rare, and their effects were usually brief.

Disturbances of the 5th nerve are common. When they are complete and bilateral the result can be striking, as in a young lawyer patient of ours whose masseter muscles were totally paralysed. One felt tempted to conjecture, in view of the suggested relationship with fatigue, to what extent his profession might have precipitated that localisation!

We saw many more 5th nerve lesions in 1947 than previously or since, about 10% of the earlier cases being affected. As is usual, asymmetry was a feature. Paresis can be missed very easily unless a systematic examination is made. Tests against resistance are indispensable.

Facial nerve paralysis is not uncommon, and where it is extreme it is not uncommonly associated with lesions of the lower cranial nerve subgroup and therefore in the more critically ill. Although it usually conforms

---

* Notes of a paper read at a meeting of the Fever Hospitals Group of the Society of Medical Officers of Health, May 20, 1950.

Central Index of Translations

To keep research workers informed of developments in foreign countries the Association of Special Libraries and Information Bureaux is preparing a central index of translations which will include scientific papers, reports, and articles from foreign journals It is intended that the index shall provide a guide to all translations held in this country and the Commonwealth, and all organisations holding translations and willing to take part in the scheme are invited to get in touch with ASLIB A limited number of translations has already been indexed Inquiries and offers of coöperation should be made to ASLIB, 4, Palace Gate, London, W 8

A Teaching Film

Nucleus Film Unit have made a 16 mm silent teaching film on *Taking a Swab* The production was supervised by Prof Robert Cruickshank, and the script was prepared with the help of Professor Cruickshank, Dr R C Mac Keith, and Dr R E O Williams The film was made at St Mary's Hospital It has been found that copies which are lent for hire deteriorate rapidly, and this film is available for sale only from the unit, 21, Soho Square, London, W 1, at £10 per copy Within the British Isles copies can be borrowed for a preview

Chemistry in the Service of Man

In connection with the Festival of Britain the Chemical Council are holding four popular lectures on this subject at the Royal Institution, 21, Albemarle Street, London, W 1 On Wednesday, May 16, at 3 P M , Prof R P Linstead, D SC , F R S , will speak on Chemistry and the Amenities of Life , on May 23, at 3 P M , Sir Jack Drummond, D SC , F R S , on Chemistry and the Food We Eat , on May 30, at 6 P M , Prof J W Cook, D SC , F R S , on Chemistry and the Conquest of Disease , and on June 6, at 6 P M , Sir Cyril Hinshelwood, SC D , F R S , on Chemistry and Modern Thought Admission is free, but by ticket, obtainable from the council, 9, Savile Row, W 1

Mr H J Seddon, director of studies at the Institute of Orthopædics, Royal National Orthopædic Hospital, London, will be giving lectures at the medical schools at Stockholm, Lund, Uppsala, and Oslo during May

An Annotated Bibliography of Cortisone, A C T H , and Related Substances, for the first quarter of 1951, has been compiled by the cortisone committee of the Empire Rheumatism Council Copies (5s each) may be had from the secretary of the council, Tavistock House North, Tavistock Square, London, W C 1

A pamphlet on the *Operation of a Central Syringe Service* has been published by the Ballbrook Surgical Instrument Company Ltd , 9, Blackfriars Street, Salford, 3 Copies may be had without charge

The Chemistry of Inositol is reviewed by Mr Edward R Weidlein, jun , in bulletin no 6 of the bibliographic series issued by the Mellon Institute of Industrial Research Copies may be had without charge on application to the institute, University of Pittsburgh, Pittsburgh 13, Pa , U S A

Appointments

AITKEN D T M B Glasg , D P M asst psychiatrist, Parkside Hospital, Macclesfield Cheshire

BINKS J B M B Birm surgical registrar Great Yarmouth and Gorleston Hospital Norfolk

CAROTHERS J C D M B Lond D P M asst psychiatrist, St James s Hospital Portsmouth

CURRAN J N , M B N U I , D P M asst psychiatrist Prestwich Hospital Lancs

FALK SAMUEL, M B Manc , D.P M asst psychiatrist, Prestwich Hospital Lancs

HODGES R J H L.M.S S A asst anæsthetist Portsmouth group of hospitals

McDONALD ROBERT M B Aberd D P.H D P M asst psychiatrist, St James Hospital Portsmouth

SAVORY MARY, M B Camb F R.C.S F R C S E , D O M.S ophthalmic surgeon Royal Eye Hospital London

SCHRAGER JAKOB M D Belf D C P consultant group pathologist Wigan and Leigh hospital group Lancs

SCOTT, R D M B Camb M R C P D P M asst psychiatrist, Warlingham Park Hospital Surrey

STOCK S D , M B Lond F R C.S E medical registrar United Norwich Hospitals

Diary of the Week

APRIL 29 TO MAY 5

Monday, 30th

ROYAL EYE HOSPITAL, St George's Circus Southwark, S E.1
5 P M Prof Arnold Sorsby Antibiotics
INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1
5 30 P M Dr H J A Dartnall Physicochemical Aspects of Vision
INSTITUTE OF PSYCHIATRY Maudsley Hospital, Denmark Hill, S.E.5
5 30 P M Dr E Stengel Lecture demonstration

Tuesday, 1st

ROYAL EYE HOSPITAL
5 P M Dr T H Whittington The Phorias—Introduction to Orthoptics
INSTITUTE OF DERMATOLOGY St John's Hospital, Lisle Street, W C.2
5 P M Dr F R Bettley Psoriasiform Eruptions
EDINBURGH POST GRADUATE BOARD FOR MEDICINE
5 P M (University New Buildings Edinburgh) Sir Charles Symonds Intracranial Thrombophlebitis

Wednesday, 2nd

NEWSHOLME LECTURE
5 30 P M (London School of Hygiene, Keppel Street, W C.1) Prof Dugald Baird Reduction of Maternal and Fœtal Mortality (First of three lectures)
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Dr L C Thomson Electrophysiology of the Retina.
MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons, 18, Nicolson Street.) Dr D M F Batty Mr W A D Adamson Gastric and Duodenal Hæmorrhage

Thursday, 3rd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C.2
5 30 P.M Sir Stanford Cade Malignant Disease of the Tongue and Buccal Cavity (Otolaryngology lecture)
ROYAL ARMY MEDICAL COLLEGE, Millbank, S W 1
5 P M Dr W R Bett Episodes from the History of Military Medicine
NEWSHOLME LECTURE
5 30 P M Professor Baird Environment and Child bearing (Second lecture)
ROYAL EYE HOSPITAL
5 P M Dr A M Rackow Interpretation of Skull and Orbital X ray Films
ST GEORGE S HOSPITAL MEDICAL SCHOOL Hyde Park Corner, S.W.1
4 30 P M Sir Paul Mallinson Psychiatry lecture-demonstration
UNIVERSITY COLLEGE, Gower Street W C 1
4 15 P M Prof H A Krebs F R.S Energy Transformations in Living Matter (Second of four lectures)
INSTITUTE OF DERMATOLOGY
5 P M Dr R T Brain Physio and Electro therapy
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place, Edinburgh) Dr J B King Muscular Tone of the Gastro intestinal Tract
UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small's Wynd, Dundee) Prof. J McMichael Pharmacology of Heart failure in Man.

Friday, 4th

ROYAL COLLEGE OF SURGEONS
5 P M Dr Howard Gray (Mayo Clinic) Clinical and Experimental Investigation of the Circulation of the Liver (Moynihan lecture)
NEWSHOLME LECTURE
5 30 P M Professor Baird The Rôle and Organisation of a Maternity Service (Last lecture)
MIDDLESEX HOSPITAL MEDICAL SCHOOL W 1
4 P.M Sir Edward Mellanby F R S Chemical Manipulation of Food (Sanderson Wells lecture)
ROYAL EYE HOSPITAL
4 30 P M Mr A J Cameron Theatre Preparation and Post operative Procedure
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mr F Ridley Contact Lenses

Saturday, 5th

BIOCHEMICAL SOCIETY
11 A M (Department of Biochemistry South Parks Road, Oxford) Scientific papers

---

CORRIGENDA *Calcium Metabolism in Hyperthyroidism*—In figs 1–4 of the paper by Dr J Green and Dr A Lyall (April 14, p 828) the values of nitrogen, phosphorus, and calcium charted are grammes *per day* and not g per 100 ml as shown Having inadvertently introduced this error, we much regret any confusion caused

Activity of Plasma Labile Factor in Disease—In Dr Mario Stefanini s article of March 17, the penultimate sentence of the left-hand column on p 607 contains the words: "*0 1 ml* of each dilution is added to 0 09 ml of stored plasma" &c. This should read "*0 01* ml of each dilution," &c.

the systolic pressure may be normal. Hyperpyrexia is common, but the skin is cold and clammy terminally, with a mottled cyanosis. The patient is usually alert but restless and confused.

ENCEPHALITIC GROUP

Symptoms of encephalitis are exceedingly common in poliomyelitis. What is not so certain, however, is their cause. They generally appear as apprehension, restlessness, irritability, twitching of facial muscles, and tremors. Insomnia is well marked, and this, in young patients and in the absence of pain, is remarkable. In other cases, and less often, there may be confusion, somnolence, and even coma. I observed one such case in 1947 (Kelleher et al. 1949) in which aphasia, tremors, severe nystagmus, and a form of generalised tonic decerebrate-like rigidity were noted, preceding final coma and death. Despite absence of signs of lower-motor-neurone lesions there was histological evidence of gross destruction of anterior-horn cells at all levels in the cord. There were foci of acute inflammation and degeneration of parenchyma, in places almost purulent, in the basal ganglia, mid-brain, pons, and medulla—most severe in the mid brain. The cerebral cortex showed only œdema and congestion.

There is strong belief, however, particularly expressed in the American reports, that the very commonly noted encephalitic signs in poliomyelitis are in many cases not necessarily evidence of damage by virus but are due to hypoxia, for it has been claimed that oxygenation often caused the signs of encephalitis to disappear.

Bulbar poliomyelitis seems to be intimately concerned with the reaction of nervous tissue, to hypoxia or repeated anoxia. Thorner and Lewy (1940) held that single periods of anoxia lasting sixty seconds might produce distinct morphological change in brain tissue. Since then it has been shown that brain cells may become necrosed after a few minutes' anoxia, and that repeated anoxia can produce widespread damage to the brain.

Apart from the general effects on brain cells, the more critical results of hypoxia on important areas, such as the respiratory and vasomotor centres, cannot be ignored.

If, as some believe, the permeability of the capillary vessels of the lung alveolar walls is affected, the production of lung œdema may be facilitated. Workers in recent years describe further studies on the long terms effects on patients who had been subjected to periods of anoxia, and some cite 100% permanent damage, with resulting changes in personality and behaviour. Very many reports indicate the effects of anoxia due to cardiac arrest on the operating table.

Galloway (1947) states that the symptoms of hypoxia may be difficult to interpret where a severe infection may coexist, but cites restlessness, disorientation, and uncoöperativeness as early symptoms. He also warns that a shock like pallor, rather than cyanosis, may be a feature in terminal stages. This seems to me to smack of the white asphyxia of the late stage of obstruction in laryngeal diphtheria, believed to indicate imminent cardiovascular failure. Though the ill effects of hypoxia on cardiovascular and respiratory centres and on medullary cortex may be accepted as occurring, I find it difficult to understand how the severe oxygen defect seen so often in laryngeal diphtheria does not cause more lasting damage. I cannot recollect any patient, however ill, who, having survived the first period of shock following laryngeal diphtheria and tracheotomy, or its later pulmonary complications, did not appear to make an apparently complete recovery without evidence of postanoxic cerebral damage.

The symptoms of hypoxia include restlessness, dyspnœa, sleeplessness, and anxiety in the earlier stages, progressing through increasing pulse rate and blood pressure, cyanosis, and increasing dyspnœa to the final stage, where gradually increasing cyanosis merges into grey pallor and diminishing consciousness. Facial muscle twitching may also be noted.

The causes of anoxia in bulbar poliomyelitis (quite apart from that resulting from lesions of the cervical cord producing paralysis of respiratory muscles, and from interference with the proper functioning of vital autonomic centres in the medulla) are entirely mechanical or local. The most important defect of all is the accumulation of secretions in the pharynx mainly from involvement of the 10th cranial nerve. Also important is laryngeal abductor paresis or paralysis. Reflex laryngeal spasm, through irritation by food or fluid particles where glottic protection is defective, may be more important than is generally appreciated. The not uncommon complication of pneumonia and, particularly, atelectasis, will add to, or produce, hypoxia. Finally there is the dreaded complication, pulmonary œdema.

The importance of recognising the serious effects of lesions of the respiratory and cardiovascular centres in bulbar poliomyelitis is undoubted, for in a small proportion of cases it may be possible to save the patient. Recognition of the more local and mechanical defects, leading to defective oxygenation in bulbar poliomyelitis is, because of the claimed results for therapy, of much greater importance.

TREATMENT

Drugs

No drug has so far been produced that will specifically attack the virus, although there is experimental evidence of the susceptibility of the virus to certain chemicals, notably benzidine dyes and nucleic acid derivatives.

Antiserum need only be mentioned to be dismissed, owing to its failure over the years. The antibody content of serum, though undeniable, is variable, and the antibody may be effective only against one specific strain.

None of the antibiotics has yet proved useful against the very small poliomyelitis virus, and any claims of their value must be examined with great caution.

Claims have been made for the efficacy of huge doses of ascorbic acid, given parenterally and orally. Klenner (1949) in particular claimed outstanding results in the prevention of paralysis by this vitamin, but apparently did not use controls.

Curare has been advocated for bulbar poliomyelitis, notably and originally by Ransohoff (1947). The rationale of this therapy is the relaxation of muscular spasm, whether of bulbar or spinal origin. Applied to the respiratory muscle defects and in the presence of effective antidote its use seems rational. In pharyngeal dysfunction, where the major factor is spasm, it also seems sensible. Advocates for the use of curare claim that tracheotomy may be necessary, even in the most severe cases, only when there is bilateral complete abductor paralysis of the vocal cords. It is also said to obviate the use of the respirator. Others argue that the curarised patient is in even greater danger of obstruction from the collapsed throat and that he needs even more help from the respirator.

Sedative drugs have their uses in the pure encephalitic types, but their use in cases with respiratory depression and in cases with lesions of the lower cranial nerves and accumulation of buccal secretions may be dangerous.

Other Treatment

Bower (1949) recommends hot compresses to alleviate the tight respiratory muscles (the "frozen" chest). We have tried hot compresses, but usually only in respirator assisted cases, and I cannot express any strong views on their value.

Both Bower and others have urged the necessity for maintaining the electrolyte and fluid balance, but they emphasise the danger of overhydration, particularly to a lesion of a lower motor neurone, on rare occasions it may be more diffuse

Involvement of the 8th nerve, giving rise to vertigo and vomiting, is often seen in poliomyelitis Deafness seems to be so rare as to be extraordinary

Lower Subgroup

When we talk of the dangers of bulbar poliomyelitis it is usually the lesions of the 9th, 10th, 11th, and 12th cranial nerves, particularly the 10th, that give rise to anxiety Although from time to time we may suspect complications arising from destructive lesions of vital autonomic centres, causing disturbances in respiratory and cardiovascular function, it is the effects of respiratory difficulty, initiated by damage to not only the nucleus of the 10th cranial nerve but also the nuclei of the 11th and 12th cranial nerves that many of us have had cause to fear, and with every reason

It is with the accumulation of secretions owing to nervous dysfunction of the pharyngo laryngeal area that we must be principally concerned Innervation of this area is through the 9th, 10th, 11th, and 12th cranial nerves, particularly the 10th

Brahdy and Lenarsky (1934) described four types of dysphagia occurring in poliomyelitis regurgitation through the nose, accumulation of food, fluid, or oro pharyngeal secretions in the pharynx, regurgitation of food from the œsophagus, and inability to shut off the larynx, leading to cough and distress

Although in most cases of pharyngeal paresis or paralysis the soft palate is more or less involved, it is when that organ is affected alone, leading to projection of food into the nose, that we should have least cause to worry A pharynx functioning sufficiently well to accentuate a palatal defect is one which should be able, with care, to handle secretions and food

Great danger arises when deglutition troubles become extreme owing to the tendency for accumulations in the pharynx to interfere with the airway, and we must be constantly on the watch for signs of defects Though a nasal voice alone is not necessarily of serious import, it should constantly alert one to the possibility of more extensive involvement The pharynx must be carefully and repeatedly examined for puddling of secretions No difficulty in determining the degree of danger will arise when large and obvious secretions are present, but not infrequently, in my experience, quite small accumulations, not easily seen on the postpharyngeal wall, or accumulating in the glottic area, may cause considerable distress, if not immediate danger The danger in the lesser collections can arise from aspiration of even very small quantities into the larynx, which may set up reflex spasm and dangerous collapse I have known of one such case where an adult patient, injudiciously given a teaspoonful of water, collapsed and died In addition these small collections are not easily dealt with by suction apparatus With the patient lying supine in a respirator they can be still more troublesome, and they can be extraordinarily exhausting to the patient The accumulations may be very extensive, because up to 1500 ml. of oropharyngeal secretions has to be dealt with in twenty four hours The threat to the patient's airway is constant or recurrent

Apart from reflex spasm of the glottis and the hazards of defect in glottic control, 10th nerve damage may be responsible for abductor paralysis of the vocal cords, leading to rapid asphyxia Fortunately, this has not happened here, although we have had moments of anxiety where partial abductor paralysis was causing distress

LESIONS OF RESPIRATORY CENTRE

Grave dangers are associated with lesions of the autonomic centre in the ventral reticular substance of the medulla oblongata Such lesions have often been demonstrated histologically Clinically demonstrable lesions seem to be comparatively rare, but I doubt whether the condition is really so infrequent, for in the absence of special experience diagnosis must be difficult The difficulties are increased where the lesion arises in a case already complicated by palsies of lower cranial nerves, with or without respiratory dysfunction of spinal origin

Symptoms resulting from this lesion are believed to develop more often some days after the appearance of signs of lesions of cranial nerves, which may be mild. The patient usually exhibits irregularities of depth and rhythm of respiration Breathing tends to be shallow, although occasionally deep amplitude gives that reassurance about the innervation of the diaphragm and intercostals which one may be anxiously seeking Periods of apnœa may occur before final collapse The patient may be apprehensive and restless Some of the symptoms have been ascribed to hypoxia A raised blood pressure has been found in some of these cases, and has been attributed to overaction of the pressor centre in the reticular substance of the medulla, where it lies close to the respiratory centre, particularly if the vasodepressor area has been damaged. At the same time it is agreed that anoxia and hypercapnia may also cause hypertension

The respiratory centre seemed to be depressed in the following illustrative cases

Case 1 —A boy, aged 14, was admitted to the Western Hospital on March 14, 1949, with bilateral asymmetrical palatal paresis He complained of difficulty in swallowing, but no accumulation of secretions could be seen. There had been regurgitation of fluids into the nose two days before admission Slight stridor noted at times, especially on deep inspiration, was due to laryngeal abductor paresis The diaphragm was partly defective, but intercostal action was good The occasional presence of mucus in the throat prompted caution in the use of a cabinet respirator When the patient was tried in the respirator there was failure of synchronisation and there seemed to be a greater tendency to inspiratory stridor The respirator was therefore discontinued

For six days he was treated by postural drainage for the somewhat increased pharyngeal weakness, although it was suspected that much of the trouble was due to defect in glottic control Respiratory power remained adequate On the sixth day after admission he complained that he could not breathe properly Although his airway was clear, and there was adequate respiratory amplitude and entry of air, the respirations had slowed to about 10 a minute, with brief periods of apnœa The depth of respiratory excursion also varied, being at times adequate, at others shallow The boy was fully conscious, with good colour, but extremely apprehensive He asked to be placed in the respirator, a step which had already been decided, and, to our relief, there was good synchronisation. After a stormy passage he made a full recovery It is possible that anoxic damage to the centre, and not necessarily virus attack, may have precipitated the disturbance

Case 2 —A boy, aged 6 years, had palsies of the 7th and 10th cranial nerves, with mucus in the pharynx, but a clear airway was maintained by postural drainage There were no spinal pareses and no paresis of respiratory muscles The depth and rhythm of respiration varied within wide limits—at times periods of apnœa, at others shallow breathing followed a series of very deep inspirations There was no cyanosis The pulse was rapid The boy was quiet but showed occasional apprehensiveness He died suddenly thirty six hours after admission, after vomiting dark bloodstained fluid For two hours before death his respirations were, with full amplitude, of Cheyne Stokes type

LESIONS OF CIRCULATORY CENTRE

This complication has not been seen in our cases It occurs occasionally in the absence of lesions of cranial nerves but more often with such lesions The mortality is 80–90%, despite treatment The principal clinical features are a florid dusky red colour, cherry red lips, and a very rapid pulse The blood pressure varies but is usually low, with a very low pulse pressure, although complications were kept at a minimum and the operation carried a risk of less than 1%.

These and other writers emphasise that the operations should be high—i.e., through the second and third tracheal rings—and that constant care will still be necessary to keep the trachea aspirated, and it may also be advisable to administer oxygen, humidified and under pressure, to prevent anoxia and lung œdema. Postural drainage must be maintained also. Prophylactic penicillin should be administered. A 3% solution of warmed sodium bicarbonate, followed by isotonic sodium chloride solution, is administered through the tube by a dropper and afterwards carefully aspirated through a bevelled rubber tube with the patient in the postural drainage position.

The high tracheotomy is planned in anticipation of the event, which is not rare, that the patient must later be nursed in a respirator. A device for holding down the rubber collar towards the sternal notch can readily be devised and should be kept ready for use.

The same workers also discuss tracheotomy in a patient already in a respirator and point out the awkwardness of the technique in this emergency. The respirator is open, and the patient is oxygenated through the endotracheal tube, through which oxygen can be administered under pressure.

Collarless respirators have obvious advantages in this contingency. The Swedish Stille comes to mind and for both immediate and post-operative care should be far preferable to the tank type of machine.

Peterson and Ward (1948), discussing the problems of technique and aftercare for tracheotomy cases in respirators, draw attention to the new type of Monaghan collarless (cuirasse type) respirator, for which they claim great advantages both before and during operation and in aftercare.

I mention here two cases met with last year.

Case 3.—A woman, aged 44, was admitted with bulbar poliomyelitis; she had facial and pharyngeal paralysis but no spinal defect. There was full respiratory power and no obvious lesion of the autonomic respiratory centre. Despite an adequate angle of postural drainage, pharyngeal secretions were accumulating, cyanosis rapidly developed, and all efforts at assistance seemed to be useless. We felt that a tracheotomy might help, and I called in a laryngologist for the orderly planned operation which is advocated. Finding the airway apparently clear, he thought tracheotomy inadvisable—at any rate until after a further examination next day. Unhappily, the patient died an hour later. At necropsy the trachea and bronchi were found filled with frothy mucus. There was much œdema of all lobes of the lungs.

Case 4.—A boy, aged 8 years, had pure bulbar poliomyelitis showing as complete pharyngeal paralysis. No degree of postural drainage or aspiration appeared to help. There was full respiratory power. Again we called in a laryngologist, who could find no sufficient reason for tracheotomy. With the boy almost in extremis, an anæsthetist put in an endotracheal tube. There was a dramatic improvement: tracheal râles disappeared, and the patient was quiet and now obviously well oxygenated. A few hours later he collapsed and died suddenly. The tracheal tube was removed and was followed by a large accumulation of mucus which was obviously blocking the distal end. At necropsy the trachea and main bronchi were found plugged with dense mucus. There was congestion and emphysema of the right lung and a wedge-shaped patch of collapse at the base of the left lung. The surface of both lungs showed petechiæ.

We are probably all aware of the dire results of the combination of bulbar (lower cranial nerve) and spinal (cervical cord) lesions, and in the absence of specific techniques a 100% mortality is not rare. The American workers claim that a clear airway, which is essential for patients when treated in respirators, can be achieved only by tracheotomy at an early stage, preferably before the patient is placed in the machine. Oxygen under pressure is advised if there is any suspicion of pulmonary œdema. Other measures adopted, or advised, are bronchoscopy, suction through the tracheotomy opening, and [illegible]. It is recommended that humidified oxygen under pressure is being used [illegible] positive pressure within the cuirass. Due to these measures the Minnesota workers [illegible] a 75% mortality for the mixed spinal and bulbar group.

These workers recognised about 20% of bulbar patients with involvement of the respiratory centre; but they were dealing with a particularly virulent virus. In such cases they emphasise the necessity for oxygen [illegible] 100%, particularly because atelectasis and lung congestion are likely to develop. They state that [illegible] is shown by [illegible] chest [illegible] (Minnesota Poliomyelitis Research Commission 1947).

A mortality of up to 100% was experienced when the respirator was used, and they explain that [illegible] respiration in the presence of any obstruction in the airway will produce pulmonary œdema. They think tracheotomy essential in such a contingency.

They also advise, for lesions of the respiratory centre, oxygen and, in the presence of obstruction, tracheotomy, but point out that the results are in any case extremely poor.

Use of Respirator in Bulbar Poliomyelitis

It seems to be generally agreed that the use of the respirator in bulbar poliomyelitis is contraindicated unless a clear airway is ensured—by postural drainage, aspiration, or particularly tracheotomy, or by a combination of these measures.

CONCLUSIONS

From our experience at the Western Hospital and from a study of the American literature I hold that we should seriously consider tracheotomy and other appropriate remedial measures for the not inconsiderable number of cases of poliomyelitis in which dangerous bulbar lesions interfere with free oxygenation.

The poliomyelitis team should include an anæsthetist and a laryngologist, who should be prepared to perform tracheotomy as a carefully planned measure of prevention rather than cure of the dangerous sequelæ of respiratory obstruction.

REFERENCES

Bower, A. G. (1949) *J. Amer. med. Ass.* 141, [illegible]
Brahdy, M. B., Lenarsky, M. (1934) *Ibid*, 103, [illegible]
Brown, J. R. (1949) *Ibid*, 141, [illegible]
Curtis, L. (1950) *Ibid*, 142, 109
Galloway, T. C. (1947) *Ann. Otol.*, etc., 40, 123.
— Seifert, M. H. (1949) *J. Amer. med. Ass.* 141, 1.
Kelleher, W. H., [illegible], McCallum, F. O. (1949) *Brit. med. J.* ii, 21.
Klemmer, F. R. (1949) [illegible] *Med. Surg.* 111, [illegible]
Minnesota Poliomyelitis Research Commission (1947) *J. Amer. med. Ass.* 135, 425.
Peterson, R. L., Ward, R. C. (1948) *Ann. Otol.*, etc., 48, 130
Ransohoff, N. S. (1947) *Bull. N.Y. Acad. Med.* 23, [illegible]
Thorner, M. W., Lewy, F. H. (1940) *J. Amer. med. Ass.* 115, 1595

---

approximately 140,000 persons suffering from active tuberculosis are at large among the population of England and Wales and this figure is rising. All of these persons are potential sources of danger and a menace to non-infected individuals, particularly infants and adolescents. To me the great danger that we are facing in tuberculosis is the creation of a non-infected younger generation amidst an infectious older one. We should be warned by the rise in the incidence of the disease in the older age groups, particularly in males, and the simultaneous increase in notification of primary infection in young adults, particularly females. I would not venture to suggest that the tuberculosis problem reduces itself to the control of old men and young maidens, but I do suggest that we should be sure that every means is used to build up the resistance of susceptible age groups, so that they will not develop active disease from their first infection with virulent tubercle bacilli.—Prof. F. R. G. Heaf, *Brit. J. Tuberc.* 1951, 45, 41.

the danger of cerebral œdema from excess of sodium Excess fluid may also precipitate œdema of the lungs Repeated intravenous injections of glucose are advocated with a view to cerebral decongestion

Whether or not to institute nasal feeding has always been debatable In the milder cases of pharyngeal dysfunction, particularly where there is no glottic leak, nasal feeds may be very useful, or even necessary, where dehydration may otherwise be expected The feed must in every case be given with the greatest caution and only by those whose technique is known to be above suspicion In the presence of inadequacy of glottic closure, or fear by the patient, and particularly when vomiting or nausea might be caused, nasal feeds are a very real danger I have seen many cases where sudden collapse has followed during or shortly after the feed that I fear them except in the most suitable type of case In postdiphtheritic paralysis nasal feeds are extremely useful and only rarely dangerous In bulbar poliomyelitis it is another matter, especially if the patient is being treated in a respirator Regurgitation of the feed from the œsophagus may be a factor in many of the cases where a sudden vomit is supposed to be the cause of collapse Such a possibility is, of course, accepted in the dysfunction due to a lesion of the 10th nerve

The prominence recently given to anoxia and its dangers has drawn attention to its correction The administration of oxygen has to be considered It is a rational procedure, particularly where it can be given without disturbing the patient Tents are often advocated, and we have found them of value in selected cases, but it must be borne in mind that extra oxygen is unlikely to help where the airway is obstructed or is not frequently cleared

We now reach the crux of the whole problem in the physical correction of the results of pharyngeal defects in bulbar poliomyelitis How is the airway to be kept clear ? There is hardly a medical problem today which is more debatable, at least as regards some aspects of its suggested correction However, certain remedial approaches are acceptable and necessary The first of these is postural drainage, by which fluid secretions must be kept away from the lower pharynx

Apart from the danger of asphyxia, or aspiration pneumonia and/or atelectasis, there is also a firmly held theory that œdema of the lungs may be precipitated by obstruction The mechanics of this complication are explained by the high negative intratracheal and intrabronchiolar pressure caused by obstruction in the face of strong inspiratory efforts As a result there is a cuffing effect on the pulmonary capillaries, with consequent transudation of fluid, plasma, and even red cells into the alveoli It is suggested, as a corrective, that 60% oxygen be given, preferably with a positive mask pressure of 2–6 cm of water (Minnesota Poliomyelitis Research Commission 1947) Obviously, prevention is better than cure of this complication, but unfortunately too many patients are admitted at a late stage with obstruction already established The frothy bloodstained fluid from the alveoli will then be added to the buccal secretions to be dealt with, and a vicious circle is established

Early postural drainage, assisted by aspiration, should be the aim Aspiration may be intermittent, from the pharynx, or continuous via a nasal catheter A warning must be uttered against indiscriminate interference with, or roughness in handling, the introduced suction cannula

Cardon (1950) believes in intermittent laryngeal aspiration through a urethral catheter passed through the nose and guided into the larynx during inspiration, when the vocal cords are separated

For postural drainage of the pharyngo laryngeal area to be effective in the supine position there should be a tilt of at least 20°, and preferably more, from the horizontal In the prone position it may be less. A lateral position may help by directing the accumulated secretions to an area inside the cheek where they are more readily accessible It is obvious from a study of the angle of the terminal bronchioles at the bases that an angle of tilt of 45° or more may be necessary in the supine patient to clear these tubes where secretions have caused atelectasis With the patient prone this angle may be much reduced

I must confess to being puzzled about the different clinical behaviour of the pharyngeal paralysis cases seen in poliomyelitis and that in postdiphtheritic paralysis In diphtheria, so long as the heart held out and respiratory paralyses did not supervene, I have been confident that, provided efficient postural drainage was maintained, the patient's recovery was reasonably certain The question of anoxia, hypoxia, and pulmonary œdema did not seem to arise, certainly it was never thought that tracheotomy might be necessary to clear the airway Even in the absence of defect of the respiratory muscles the poliomyelitis pharynx presents a very different picture to me Perhaps it lies in the mechanism of lung œdema, possibly activated by disturbances of the vasomotor pressor centre in the medulla, causing high blood pressure and associated with right-sided dilatation of the heart Hypopiesia is the invariable accompaniment of toxic diphtheria

Tracheotomy in Bulbar Poliomyelitis

This is a thorny subject, and I cannot speak from experience, for so far tracheotomy has not been done in bulbar poliomyelitis in this hospital Although there are strong and vociferous advocates for this measure in the U S.A, there are also the rebels there, who, though grudgingly admitting its use in certain selected cases, are cautious in expressing favour towards it

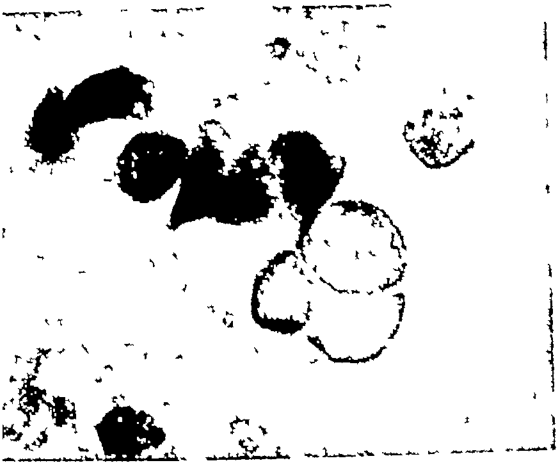
The advocates of tracheotomy press for its adoption at even a very early stage in bulbar poliomyelitis—i e, before hypoxia is present and certainly long before lung œdema is manifest Their views must be respected, for their experience is undoubtedly vast A claim for the recovery of at least 25% of patients who would otherwise have been lost is confidently made by them

Bower (1949) speaks of an experience of 233 tracheotomies in 284 bulbar cases since 1946, and claims increasingly good results where prevention rather than correction of anoxia was adopted

Galloway and Seifert (1949) are among the most enthusiastic advocates of tracheotomy They cite the following indications for operation

(1) Progressive anoxia, with secretions in the upper airway
(2) Unconsciousness or pronounced restlessness in a patient who does not respond to other treatment in a few minutes
(3) Pronounced restlessness or stupor in a patient in a respirator, even if the paralysis is apparently of a spinal type
(4) Accumulation of fluid, not otherwise certainly taken care of, in a patient who requires a respirator
(5) Bilateral spasm or paralysis of vocal cords
(6) Rapidly progressive bulbar symptoms
(7) Grave signs of vasomotor failure
(8) Untrained or inefficient attendants, inadequate equipment, or poor coöperation of the patient, with doubt that the airway will be constantly kept free from secretions

These workers emphasise that tracheotomy should be carefully planned and deliberate, rather than a rushed emergency, and that it should be performed preferably over a bronchoscope or endotracheal tube, the airway being kept clear thereby and pressures equalised It also kept the airway clear postoperatively In this way



(case 2)—Bone-marrow Group of large rounded cells largest in diameter and one of irregular shape with double nucleus

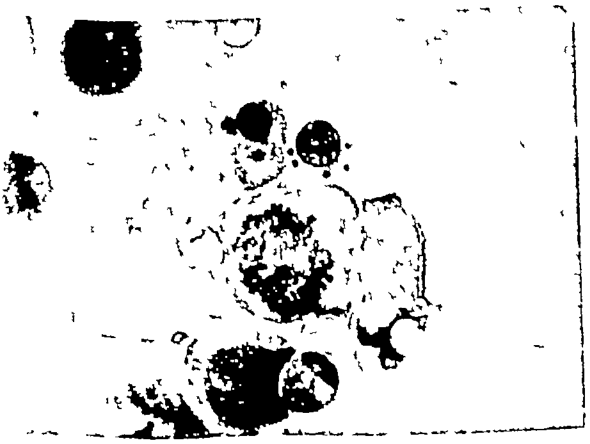
lood-count showed severe anæmia red cells 2,660 000 mm , Hb 6 2 g per 100 ml , white cells 6400 per c mm rential count normal)

ne *marrow biopsy* showed that nearly all the cells were primitive cells, with large fairly patterned nuclei and y dark blue or light-blue cytoplasm, often vacuolated 2) the cells were arranged in groups for the most part, a few were very large, with irregularly shaped nuclei r cells were few

ogress—The condition progressed only slowly at first weeks later a biopsy of the skull tumour showed a picture was thought to be neuroblastoma or reticulosarcoma iography at this time showed widespread lesions in the bones and the skull The case was regarded as unsuitable X ray therapy Blood transfusions were given, but the ent became steadily more anæmic Four days before h some of the primitive reticulum cells appeared in the d No necropsy was permitted

ase 3—A man, aged 41, was admitted to a medical ward ause he had had a severe epistaxis and was seriously mic. Increasing pallor had been present for four months, d for the past six weeks he had had an undiagnosed pyrexial ess

n admission his temperature was 100 2°F He was pale but icteric There were no skin lesions There was no enlarge nt of the liver spleen or lymph glands The urine was mal, and no abnormal signs were found elsewhere The cells were reduced to 1,340,000 per c mm and Hb to g per 100 ml , white cells were 3500 per c mm (differential nt normal), platelets were reduced to 10 000 per c mm



g 3 (case 3)—Bone-marrow Very large abnormal reticulum cell, 23 μ in diameter in mitosis ; below it a smaller cell of the same type above to the left a normal reticulum cell and to the right a normoblast.

The nose was plugged and blood transfusion given, but improvement was only temporary

The *sternal bone marrow* was very unusual (fig 3), it contained many very large cells, the smallest being about 15 μ in diameter, these cells had large rounded or oval nuclei filling most of the cell and having a finely stippled chromatin pattern the cytoplasm varied from moderately dark to deep blue and was vacuolated Many of these large cells were multinucleated, and some exceptionally large forms resembled a syncytium Mitotic figures were relatively common Reticulum and plasma cells of normal aspect were common Erythroblasts were relatively few and normoblastic in type, some of them showed nuclear abnormalities as well

Progress—No treatment had any effect, the hæmorrhages continued, and the anæmia worsened On the day before death a few cells like myeloblasts appeared in the peripheral blood The patient died eleven days after admission

Post-mortem Findings—Histological sections from necropsy material showed extensive infiltration of lymph glands and spleen with cells similar to those seen in the bone marrow, numerous giant cells were present In the liver there was a diffuse infiltration with little destruction of liver cells, giant cells were present here also

Case 4—A doctor, aged 45, had had pain in the chest, especially near the lower scapular region, for six months Radiography had shown no abnormality About two weeks before he was first seen he had noticed blurring of vision that soon progressed to diplopia He was examined by a neurosurgeon, who found a complete left sixth nerve palsy There was flattening above both scapular spines and tenderness over the right supraspinatus muscle, there was pain and tenderness in the fifth and sixth right intercostal spaces No obvious cause for this condition was found, and the patient was admitted to hospital fifteen days later In that time his general condition had deteriorated gravely

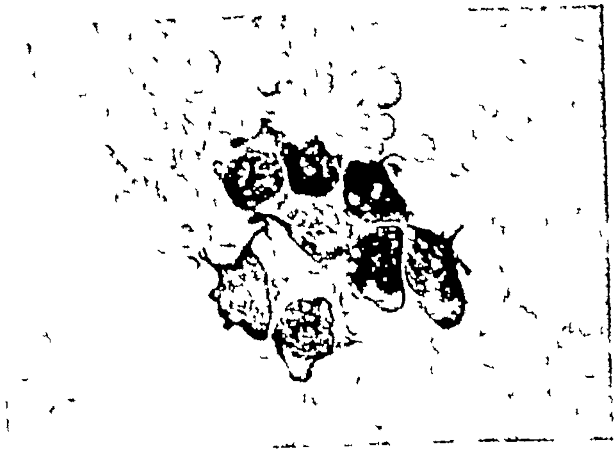


Fig 4 (case 4)—Bone-marrow Group of abnormal reticulum cells, some rounded and some irregular showing relatively coarse chromatin pattern of nucleus and very scanty cytoplasm ; largest cell in the group is 17 μ in diameter

On admission the right infraspinatus muscle was now grossly wasted and the left showed early wasting The sixth nerve palsy was unchanged The head and neck movements were stiff there were no other abnormal signs Radiography of the chest showed notably enlarged mediastinal lymph-glands and the appearance of three dorsal vertebræ suggested metastatic destruction of bone

A *blood count* showed red cells 4,870,000 per c mm, Hb 13 6 g per 100 ml, white cells 6900 per c mm (70% polymorphs and 1% classed as "abnormal reticulum cells")

Sternal marrow was packed with masses of large irregularly shaped cells with large nuclei occupying most of the cell and scanty dark blue cytoplasm that was sometimes vacuolated These cells were sometimes enormous, they occurred mostly in groups, and some of the groups looked more like syncytial masses than separate cells (fig 4) Mitotic figures were quite common Few normal granulocytes and erythroblasts remained The whole clinical and pathological picture suggested a rapidly extending reticulosarcoma

MYELOID RETICULOSIS

ITS DIAGNOSIS AND COURSE

M C G Israëls
M Sc , M D Manc , F R C P
LECTURER IN HÆMATOLOGY IN THE UNIVERSITY OF MANCHESTER

It has become common practice to classify as "acute reticuloses" those syndromes which run a relatively short course, have features resembling the leukæmias and Hodgkin's disease, but have neither the blood picture of the former nor the typical histological changes of the latter Other terms have been "reticulo endotheliosis," or "aleukæmic stem cell leukæmia," and it is quite likely that some of the cases in the Continental literature described as "paramyeloblastic leukæmia" were of this type In this confused field retrospective diagnosis is particularly unrewarding, and those interested in the historical arguments about these conditions will find them adequately set out by Downey (1938) It is not unfair to say that the diagnosis has most often been made after histological examination of post mortem material For instance, the acute histiocytic medullary reticulosis described by Bodley Scott and Robb Smith (1939) presented a recognisable clinical syndrome of pyrexia, splenomegaly, moderate enlargement of lymph glands and sometimes liver, anæmia, and leucopenia The bone marrow was not examined during life, but foci of histiocytic cells were reported in the sections of bone marrow obtained at necropsy, and the diagnosis was made by histological examination of tissues from the post mortem examination In Hodgkin's disease the bone marrow commonly shows a normal hyperplasia and it is extremely unusual to find Reed Sternberg cells either by the usual smear technique or by aspirating fragments and preparing sections (Limarzi and Paul 1949)

The cases described here were all diagnosed during life by the peculiar cells found in the bone marrow, and involvement of the bone marrow was the constant clinical finding The clinical picture varied but was fairly characteristic Very few such cases have been published Evans et al. (1949) described one in a girl, aged 14½, who developed firm tumour like nodules over the left scapula and in both breasts, she had anæmia but, at first, no hæmorrhagic symptoms In the bone marrow smears many odd looking very large cells with nuclei up to 50 μ in diameter were found, the cells had a light blue cytoplasm, the nuclei were delicately reticulated and vesiculated, only a few were seen in mitosis Sections from a biopsy of one of the nodes were reported as "reticulosarcoma" The patient was given X ray treatment, but it was ineffective, the anæmia increased, a hæmorrhagic syndrome with a low blood platelet count developed, and she died in a few weeks Necropsy showed infiltration of all lymph nodes and spleen, the pancreas was almost replaced by tumour tissue, only minute groups of cells were seen, however, in the liver and kidneys The final diagnosis was "possibly stem cell lymphosarcoma" Custer (1949) reproduces pictures from bone marrow biopsy smears and post mortem sections from a patient who presented with anæmia, leucopenia, and thrombocytopenia The marrow smear shows large cells with bizarre multiform nuclei, blue grey cytoplasm, and well defined borders, some cells appeared to form a syncytium, the marrow sections showed that the normal tissue was displaced by these polymorphic giant cells, and similar cells were found in the lymph nodes, liver, and spleen Orchard (1950) reports a case of Letterer Siwe's syndrome, in a child of 3½ years, in which abnormal cells that he calls "hæmohistiocytes" were found in the peripheral blood and the bone marrow biopsy smears

CASE RECORDS

Case 1 —A housewife, aged 51, was admitted to hospital with five weeks' history of chill, general malaise, aching pains, and loss of weight No hæmorrhages had occurred

On admission she looked ill and had pyrexia up to 102°F There were numerous soft palpable lymph glands, not much enlarged, at the base of the neck and in the axillæ The spleen was palpable and soft, the liver was not enlarged The cardiovascular, respiratory, and central nervous systems presented no exceptional features, the urine was normal

A *blood count* showed no anæmia red cells 4,660,000 per c mm , Hb 13 6 g per 100 ml , white cells 14,100 per c.mm. (polymorphs 53 5%, lymphocytes 27%, monocytes 1 5%, plasma cells 0 5%, and 27% were large cells of irregular, often elongated, shape, with large irregular nuclei occupying most of the cell)

A *sternal marrow smear* showed large numbers of these unusual cells, they varied in shape from an irregularly circular to an irregularly elongated outline, the cytoplasm was pale or moderately deep blue, and sometimes a few azure granules were seen, a typical cell is seen in fig 1 Some of the cells had a vacuolated cytoplasm, and some appeared to have phagocyted fat globules Mitoses were seen but were few Granulocytes appeared normal and there was an average number of normal erythroblasts present

Post mortem Findings —The patient's condition deteriorated rapidly, and she died seven days after admission At necropsy the abdominal lymph glands were notably enlarged and soft, the spleen weighed 1100 g and the liver 2050 g, the cut surface of the liver was mottled with small grey and hæmorrhagic areas Histological sections showed that the liver tissue was widely infiltrated with large round cells and large irregular cells resembling those seen in the marrow, in many areas the liver cells were entirely replaced by masses of these cells The spleen, lymph glands, and femoral bone marrow also showed extensive infiltration, like that seen in leukæmia

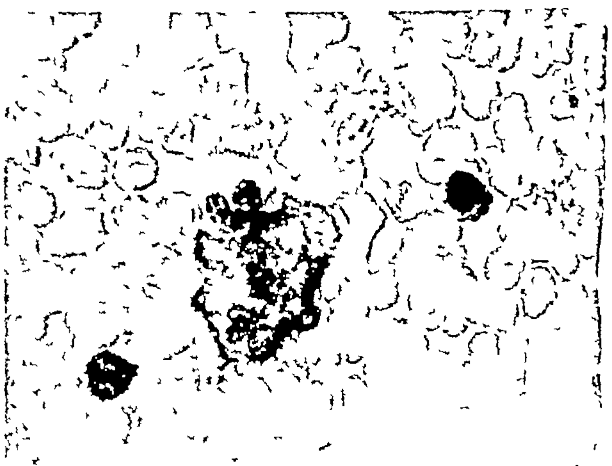


Fig 1 (case 1)—Bone-marrow smear Very large abnormal reticulum cell 30 μ × 22 μ with dark-staining irregular nucleus and dark vacuolated cytoplasm, polymorph next to it.
The smears shown in this and subsequent figures were all stained with Jenner-Giemsa and are reproduced at the same magnification (× 750)

Case 2 —A girl, aged 3 years 3 months, was admitted to hospital with the history that, six weeks before, she had fallen downstairs and bruised her eyes Three weeks later she had complained of headache, and proptosis was noted, her skull had been radiographed, but no fracture was found.

On admission both eyes were severely proptosed, the left more than the right, and there were subcutaneous hæmorrhages in the eyelids Firm tumours, about 2 cm across were present at the outer edge of the right supraorbital ridge and below the inner end of the left ridge The skull appeared widened between the parietal eminences, radiography showed widening of the sutures, and radiating spicules of bone in the supraorbital areas Lymph glands were slightly enlarged in the neck, but not elsewhere In the abdomen the liver was palpable 4 cm below the costal margin, the spleen was not palpable There was no rash and no hæmorrhage except in the eyelids odd cells were characteristically gathered into small s. Mitotic figures were seen in some of the large cells al granulocytes and erythroblasts were present but r

atment and Progress —Blood transfusion and nitrogen rd were given, but the effects were disappointing ne patient died four weeks after admission

t mortem Findings —The liver and spleen were enormous, larged lymph glands were found The microscopical es were most striking in the liver, which was grossly ated with large round cells and multinucleated giant imilar to those in the marrow smears, in the spleen the ghian bodies were no longer visible and the pulp was ellular, though giant cells were less prominent than in er

DISCUSSION

e clinical histories of these patients show a remark variety of syndromes, these syndromes resemble in those that have been recorded in leukæmias, but has always been some unusual feature that caused ation about the diagnosis The cases vary from to relatively chronic

e 1 presented as an acute leukæmia, but, although there ardly any anæmia, the patient was gravely ill and died six weeks after the onset, the necropsy showed wide l infiltration of abnormal cells like that seen in acute mia

e 2, when first seen, might have fitted the diagnosis of ma, anæmia was present from the beginning, but no mal cells were seen in the peripheral blood until just death, the course was about two months

e 3 presented the clinical picture usually associated with aplastic anæmia rather than acute leukæmia, there severe hæmorrhage and pyrexia, but no enlargement of spleen, or lymph glands, and, again, abnormal cells red in the blood only just before death, the course was eight weeks

case 4 the neurological signs drew attention to involve of the dorsal vertebræ and mediastinal glands, there was table anæmia, and there were few abnormal cells in the , the course was a little longer, being about three hs.

e 5 presented with thrombycytopenic purpura and gross omegaly, and the blood picture reflected only the loss of , the purpura was oddly distributed, being almost letely limited to the upper half of the body, again no rmal cells appeared in the peripheral blood until the last progress of the disease was much less rapid in this case, otal course being about six months

se 6 was almost chronic, the disease lasting some nine hs, and the presentation was that of a chronic leukæmia anæmia, and gross hepatomegaly and splenomegaly, iagnosis from chronic myeloid leukæmia was only made the bone marrow was examined.

e sole unifying feature in all these cases has been infiltration of the bone marrow with the grossly rmal cells, whose appearances in the biopsy smears lustrated in figs 1–6 A few workers have described ar cells in biopsy material Custer's (1949) case already been mentioned Tsevrenis (1947), in his iption of "leucoses with malignant cytology," shows with large atypical nuclei and vacuolated cytoplasm he names "leucoblastic cells of sarcomatous type" some less bizarre cells occurring in "reticulo sis" Moeschlin (1947) shows large cells of the type r discussion that he obtained from splenic puncture case of primary reticulosis of the liver and spleen, alls them "pathological reticulum cells" Bessis 3) describes these cells as cells of "histiosarcoma" reticulosarcoma" He describes the changes that can egarded as characteristic of sarcomatous change in cells These can be summarised as follows

The cells tend to be all similar in any one case

The cells are very variable in size, usually larger than al often enormous

The ratio of nucleus to cytoplasm is much larger than

4 The nucleus is very anomalous, often very large, with an inflated appearance, sometimes multiple, with more or less complete amitotic division, and vacuolar degeneration of the nucleus is common

5 The nucleoli are almost always abnormal—numerous, large, oddly shaped, and showing odd staining reactions

6 Abnormal mitosis is common.

7 The cytoplasm is often pale, almost always vacuolated

Bessis obtained these cells by puncture of an enlarged spleen or an actual tumour The bone marrow in his patients was normal, but there is little doubt that the description fits very well the cells found in the bone marrow of the patients described in this present paper

Whether or not we agree that the cells are in fact malignant, it is clear that the presence of such cells in the marrow indicates a disease that has usually a much more rapid course than the clinical state suggests, is notably resistant to any of the forms of treatment at present available, and has so far proved inevitably fatal The condition is here named "myeloid reticulosis" because this emphasises the one constant feature of the disease—involvement of the bone marrow—that can certainly be used for diagnosis during life The term reticulosis, rather than reticulosarcoma, is used because, although the cells fit the criteria given by Bessis (1948), histologically the changes are those that Robb Smith (1938) regards as characteristic of reticulosis—i e, there is proliferation of cells arising at many points, producing an apparent infiltration, but the destruction of stroma and the dissemination of cells by embolism that typify reticulosarcoma are not seen

If these patients present with a "blood" disease, the bone marrow biopsy that should be undertaken as part of the investigation will make the diagnosis clear But some of the patients do not present in this way at first, and the value of bone marrow biopsy in the investigation of obscure splenomegaly or infiltration of bones should be remembered

SUMMARY

Six cases are described characterised by infiltration of the bone marrow with abnormal types of reticulum cells

The clinical picture was variable, and the cases presented with an acute blood disease, an unexplained splenomegaly, or infiltration of bone marrow

The condition was often much more severe than the clinical state suggested, and the course was unexpectedly short

None of the cases responded to treatment, and all ended fatally

The condition has been named "myeloid reticulosis" because involvement of the bone marrow by abnormal reticulum cells was the only common feature

Case 2 was referred by Prof W F Gaisford and Dr H. B Marsden at the Royal Manchester Children's Hospital, case 3 by Dr J T Lewis, of Belfast City Hospital, and case 4 by Mr R A Bailey and Dr J Davson at Crumpsall Hospital, Manchester, to all those I am indebted for material and information. Cases 1, 5, and 6 were seen at Manchester Royal Infirmary under the care of Dr J F Wilkinson, director of the department of hæmatology

REFERENCES

Bessis M (1948) Cytologie sanguine normale et pathologique Paris p 75
Custer R P (1949) An Atlas of the Blood and Bone Marrow Philadelphia p 289
Downey H (1938) Handbook of Hematology New York vol II p 1275
Evans T S Cipriano A P, Ferrell E H jun (1940) *Conn St. med J* 13 1128
Limarzi L R Paul J T (1949) *Amer J clin Path* 19 929
Moeschlin S (1947) Die Milzpunktion Basle p 173
Orchard N P (1950) *Arch Dis Childh* 25 151
Robb Smith A H T (1938) *J Path Bact* 47 457
Scott R B Robb Smith A H T (1939) *Lancet* ii 194
Tsevrenis H (1947) Les leucoses à cytologie maligne Paris.

Progress —Radiotherapy was tried for relief of pain, but it had little effect on the general condition, and the patient died six weeks later

Case 5 —A girl, aged 14, had been vaguely unwell for about twelve months, and nothing definite had been found by her doctor A month before admission to hospital she had developed a pyrexial illness with stiffness of the neck and some temporary œdema of the neck, shortly afterwards a purpuric rash had appeared over the shoulders, upper arms, and breasts She had then been admitted to a local hospital, where she was found to have a very large spleen and some anæmia, with red cells 3,600,000 per c mm, Hb 11 8 g per 100 ml, and white cells 5200 per c mm (normal differential count), platelets were also normal—200,000 per c mm There was intermittent pyrexia up to 102°F, and radiography of lungs, bones, and abdomen showed no abnormality, sternal marrow showed erythroblastic hyperplasia but no abnormal cells In view of these indefinite findings, she was transferred to Manchester Royal Infirmary three weeks later

On admission the purpuric rash was present as before, the spleen reached to within 3 cm of the iliac crest, the liver was not enlarged, and no enlarged lymph glands were found No other hæmorrhages were present, her first menstrual period had occurred nine weeks before without incident She was somewhat more anæmic, Hb being now 8 8 g per 100 ml, and the platelet count had fallen to 145,000 per c mm Radiography still showed no abnormality No evidence of tuberculous infection was found Marrow from a vertebral spine showed erythroblastic hyperplasia, in addition there were numerous plasma and reticulum cells, mostly normal types, but some of the reticulum cells appeared to contain some lipid material, rather like Gaucher's cells It was considered that this might be a type of lipoidosis, and arrangements were made for splenectomy In the meantime the purpura had faded but the platelet count remained between 70,000 and 100,000 per c mm

Operation (Mr H T Simmons) —The spleen, though very large, was removed without difficulty, and several small splenculi also were removed, the liver appeared normal

Histological sections of the spleen showed none of the changes associated with lipoidoses, instead the pulp was infiltrated, not grossly, with curious and rather large cells with large vesicular nuclei and deeply staining cytoplasm, they were not myelocytes or lymphocytes and were unlike myeloblasts, there was some fibrosis of the spleen, and the malpighian bodies had pale hyperplastic centres The picture resembled Hodgkin's disease or some form of reticulosis more than anything else A section of the liver showed normal structure, but here and there were small collections of the curious cells seen in the spleen

Progress —The patient recovered well from the operation, and when she went home two weeks later she had no anæmia and the platelets were 623,000 per c mm She remained well for only four weeks Then the pyrexia recurred and the petechial rash appeared again She was readmitted to hospital two weeks later

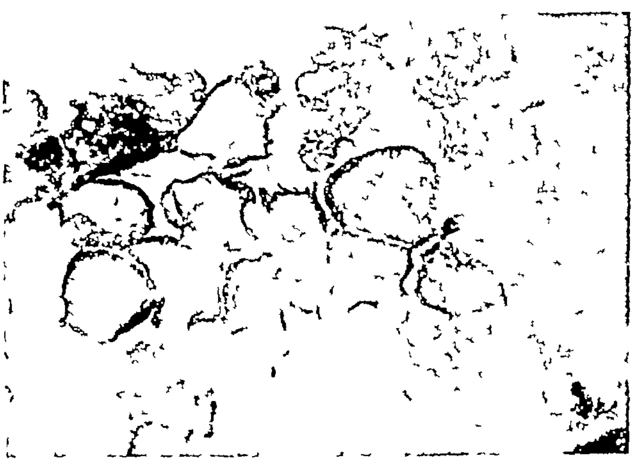


Fig 5 (case 5)—Bone-marrow Abnormal reticulum cells showing characteristic formation of groups or ‘ nests ’ of cells, the rounded irregular nuclei have a notably coarse chromatin pattern and the vacuolated cytoplasm is dark blue.

On readmission her temperature was 102°F, and she had an extensive petechial rash all over the trunk and breasts. The liver was now grossly enlarged to 10 cm below the costal margin Hb was 14 g per 100 ml, but leucocytes were now 27,400 per c mm (6% were immature granulocytes, 7% plasma cells, and 6% large unusual cells possibly monocytic, almost 50% of the nucleated cells counted were normoblasts), platelets were 115,000 per c mm In the bone marrow smears there were now many primitive reticulum cells arranged in clumps, most of the cells were about the size of the usual “ blast ” cell, but some were much larger (fig 5), normal granulocytes and erythroblasts were active as well The diagnosis was now clearly acute reticulosis

Treatment and Progress —Small doses of nitrogen mustard were given. The purpuric rash faded, but the liver remained enlarged, and the blood picture continued leuco-erythroblastic in type Later, primitive reticulum cells, like those in the marrow, appeared in the peripheral blood and accounted for 27 5% of the leucocytes present The patient was transfused and allowed to go home after three weeks Three weeks later she was much worse, with severe anæmia and extensive purpura, the liver was as large as before, lymph glands were not enlarged In spite of transfusion she died a week later No necropsy was allowed

Case 6 —A married woman, aged 56, was sent by her doctor to a local hospital because he had found an abdominal tumour The patient had noted gradually increasing abdominal distension for about nine months, and a month before had taken to her bed She had lost a lot of weight No hæmorrhages had occurred At the hospital the tumour was found to be an enlarged spleen, and, since the blood picture suggested a myeloid leukæmia, she was transferred to Manchester Royal Infirmary for treatment

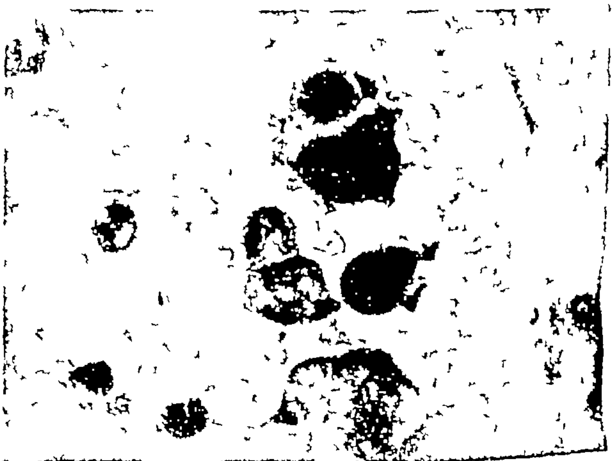


Fig 6 (case 6)—Bone-marrow Note syncytial type of cell with triple nucleus at top of field ; below there is a large irregular cell 22 μ in diameter, with much vacuolated cytoplasm , cytoplasm of cells is dark blue.

On admission she appeared thin and wasted There was no pyrexia No hæmorrhages were seen A few moderately enlarged lymph glands were present in the right axilla, but none elsewhere There were signs of pleural effusion at the base of the right lung The abdomen was greatly distended, the spleen was firm and enlarged, reaching almost to the pelvis, the liver was almost equally enlarged, no free peritoneal fluid was detected The urine was normal Radiography of the chest showed the right-sided pleural effusion but nothing else, and X ray films of long bones and the pelvis were normal

A *blood count* showed red cells 3,530,000 per c mm, Hb 7 6 g per 100 ml, white cells 13,200 per c mm (polymorphs 58%, lymphocytes 27%, monocytes 2%, eosinophils 8%, metamyelocytes 10%, ? myeloblasts 9 5%), normoblasts were 3 per 200 white cells, and platelets were 240,000 per c.mm

The *bone marrow* (fig 6) contained many bizarre cells, large cells with large finely patterned nuclei and well marked nulceoli and deep blue, often vacuolated, cytoplasm, many of these cells contained 2–4 nuclei and some very large forms with several nuclei appeared more like syncytial masses

TABLE II—COMPLICATIONS ENCOUNTERED IN EACH 24 HOUR PERIOD, AND OCCASIONS ON WHICH CASEIN HYDROLYSATE WAS GIVEN (IN PARENTHESES)

Result	Duration of infusion			
	0–24 hours	24–48 hours	48–72 hours	More than 72 hours
No complications	246 (7)	160 (57)	78 (34)	51 (21)
Local sepsis	20 (8)	25 (19)	22 (15)	16 (11)
Generalised septicæmia	0	4 (3)	3 (2)	1 (1)
Venous thrombosis	10 (2)	12 (4)	12 (9)	4 (1)
Total complications	30 (10)	41 (26)	37 (26)	21 (13)

any other solution In a $2^1/_2$% solution this was given during the course of 194 infusions, and complications—either thrombosis or infection—followed in 75 of these

Table II records the number of intravenous infusions given in each twenty four hour period, the complications encountered, and the number of occasions on which casein hydrolysate was given The numbers in some of these groups are small, but, when they are grouped together, it is seen that the percentage incidence of complications was definitely greater among those treated with casein hydrolysate

Duration of therapy	*0–24 hr*	*24–48 hr*	*48–72 hr*	*More than 72 hr*
Treated with casein hydrolysate	59	31	43	38
Not treated with casein hydrolysate	8	13	20	21

The values of χ^2 are 38, 9 3, 6 1, 1 8, and all of these on 1 degree of freedom are significant, except the last Thus the treated cases develop at least double the percentage of complications in each period

As regards duration of treatment, the percentage distribution of cases treated with casein hydrolysate and cases not receiving casein hydrolysate was as follows

Duration of therapy	*0–24 hr*	*24–48 hr*	*48–72 hr*	*More than 72 hr*
Treated with casein hydrolysate	9	43	31	18
Not treated with casein hydrolysate	55	25	12	8

Comparison of the distribution of these two groups of cases gives a very large value of χ^2, the cases given casein hydrolysate being associated with greater duration of therapy

In assessing these results account should be taken of at least two factors First, casein hydrolysate was given to patients in whom vomiting persisted, and who were considered to be more ill than those accepting oral feeds Secondly, in over 90% of the cases it was given after the first twenty-four hours, and it is reasonable to assume that the longer the duration of the intravenous infusion the more likely is the vein to become thrombosed

The *pH of the solutions* used was also investigated as a possible cause of thrombosis by damage to the endothelium of the vein, and on one occasion a considerable variation of the pH of the stock solutions (prepared in the hospital dispensary) was found The actual pH was as follows

Solution	*pH*
N/5 saline solution and 5% dextrose	4 67
Half-strength Hartmann's solution	5 86
Darrow's solution	9 37

Solutions with well marked acidity or alkalinity may well contribute to the onset of thrombosis Hence the pH of the solutions used for intravenous therapy should be estimated regularly

The *sterility* of the solutions used was investigated several times, but no evidence of bacterial contamination was found Casein hydrolysate is known to be an excellent medium for bacterial growth, and care is always taken to use it fresh from the container If only part of the solution is required, the remainder is discarded

2 *Method*

In most cases a Bateman needle or a Keith needle was used, but for a few patients 'Polythene' tubing was employed The Regional Blood Transfusion Service infusion sets were used, and the limb was kept in a suitable position with a padded wooden splint to which the limb was fixed by bandage or strapping Our impression was that the skill of the operator, particularly his ability to set up the intravenous infusion within a few minutes, had a considerable influence on the complication rate When the vein was exposed for long periods or was found with difficulty—circumstances likely to cause local trauma and venous spasm—the complication rate was increased Subsequent interference with the infusion apparatus, either by "milking" the tubing or by "adjusting" the needle in the vein, similarly predisposed to complications

3 *Introduction of Infection*

As stated above, the solutions used were sterile, and the apparatus used was likewise found to be free from infection A number of complications followed the setting up of infusions by a particular operator, from whose hands a profuse growth of pathogenic bacteria was cultured To eliminate local infection at the infusion site, the setting up of an intravenous infusion should be regarded as a surgical procedure requiring the same technique as that used in the operating theatre No one with local sepsis of the hands should be allowed to put up an intravenous infusion unless wearing rubber gloves, and masks should be worn to prevent the spread of infection from the nasopharynx Similarly, any adjustment of the needle that may be required should be undertaken only with full surgical aseptic technique

TABLE III—RELATIONSHIP OF SITE OF INTRAVENOUS INFUSION TO COMPLICATION

Site of intravenous infusion	No of infusions	Local infection	Generalised spread	Thrombosis of vein without infection
Right ankle	162	25	3	10
„ knee	2			
wrist	26	2		4
elbow	119	12	1	3
Left ankle	164	23	3	15
knee	2	1		
wrist	32	2		1
elbow	105	16	1	5
Jugular veins	9			
Tibia	3	2		
Site not stated	40			
Total	664	83	8	38

Some workers have suggested that infusion sites in the lower limbs are more liable to infection because of possible contamination with excreta Table III sets out the site of the intravenous infusion in relation to the complications encountered The frequencies in some of the classes being small, the data were condensed into table IV, where (in the 624 infusions in which the site was recorded) "lower body" includes ankle, knee, and tibia, and "upper" body includes wrist, elbow, and jugular vein The expected frequencies in each class, calculated on the assumption that the site of intravenous infusion has no effect on the type of infection, are shown in parentheses after the observed frequencies The value of χ^2 is 7 421 on 3 degrees of freedom, and the 5% level of χ^2 is 7 815 hence the observed result is below significance but sufficiently near to make a relation between site and infection fairly likely Examination of the data indicates that the infection rate was higher when the infusions

COMPLICATIONS OF INTRAVENOUS FLUID THERAPY IN CHILDREN

R McLaren Todd
M A , M D Camb , M R C P , D C.H
SENIOR LECTURER IN CHILD HEALTH, UNIVERSITY OF LIVERPOOL , PÆDIATRICIAN, ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL

The occurrence of fatal generalised septicæmia in three infants who had had intravenous infusions prompted this investigation, which covers all patients who received intravenous fluid replacement therapy at Alder Hey Children's Hospital, Liverpool, in 1949 Alder Hey is a general children's hospital to which children up to the age of fifteen with any type of medical or surgical condition, acute or chronic, are admitted During 1949 the average number of beds and cots occupied was 586, and 8160 patients were admitted Of the 332 (4%) children who received parenteral fluid therapy, 253 (76%) were infants in the first year of life There were 192 males, of whom 39 (20%) died, and 140 females, of whom 28 (20%) died The mortality rates of each age group were

Age		*No of cases*	*No of deaths*	*Age*		*No of cases*	*No of deaths*
Months	0–	44	14	Year	4–	2	1
,,	1–	39	10	,,	5–	7	3
,,	2–	34	7	,,	6–	7	2
,,	3–	23	2	,,	7–	1	—
,,	4–	23	4	,,	8–	4	—
,,	5–	18	4	,,	9–	4	—
,,	6–	13	1	,,	10–	7	1
,,	7–	25	5	,,	11–	5	1
,,	8–	13	1	,,	12–	4	—
,,	9–	11	1	,,	13–	4	—
,,	10–	4	—	,,	14–	1	—
,,	11–	6	2	,,	15–	2	—
Years	1–	13	2				
,,	2–	11	4		Total	332	67
,,	3–	4	2				

The conditions for which the children received intravenous therapy were diarrhœa and vomiting (211), pyloric stenosis (15), and miscellaneous medical (42) and surgical (64), most of the last-named being peritonitis resulting from appendicitis The age groups and diagnoses are listed in table I

METHOD

The total number of intravenous infusions given was 664, some patients receiving up to 7 infusions A standard régime of fluid replacement was followed in almost all the patients with diarrhœa and vomiting, and in a majority of patients with other conditions, but this plan of treatment was occasionally altered to meet particular problems The details of this basic régime are as follow

1 During the first six hours' treatment, shock and hæmoconcentration are relieved by giving 20 ml of plasma per lb of expected body weight, mixed with 20 ml of half strength Hartmann s solution per lb of expected body weight

2 During the following twelve hours Darrow's solution (40 ml per lb) is given, followed by

3 *N*/5 saline solution and 5% dextrose (20 ml per lb.) in the next six hours, making the total fluid intake in the first twenty four hours 100 ml per lb of expected body weight.

4 When vomiting persists or diarrhœa is severe and the child is very reluctant to take oral feeds, 75 ml of fluid per lb is given intravenously during the second twenty four hours. This fluid consists of $2^1/_2$% casein hydrolysate (60 ml per lb.) and *N*/5 saline solution with 5% dextrose (15 ml per lb) Alternatively, if the patient accepts fluids by mouth, no casein hydrolysate is given, but the intravenous infusion is continued so that the total fluid intake (oral and parenteral) is 75 ml per lb The fluid offered by mouth is *N*/5 saline solution and 5% glucose in amounts increasing at each feed by a seventh of the calculated daily fluid requirement, so that the volume of the seventh feed offered in the form of glucose saline is 75 ml per lb of expected body weight. When the full fluid requirement is being taken, a seventh of the calculated milk requirement is offered during the following twenty four hours, and this is increased by a seventh each day, so that the full calorie requirement (50 calories per lb.) is being offered on the seventh day

INCIDENCE OF COMPLICATIONS

The number of complications encountered in 664 infusions was 132

Complication	*No of cases*
Local infection at the infusion site	83
Generalised infection (septicæmia)	8
Venous thrombosis without infection	38
Hepatitis	1
Circulatory overloading	1
Wrist drop	1

"Local infection at the infusion site" connotes the presence of pus and does not include slight erythema of the wound "Venous thrombosis without infection" does not include minor degrees of œdema at the infusion site but implies more extensive œdema, often associated with a palpable thrombosed vein

THROMBOSIS AND INFECTION

The possible factors contributing to the onset of venous thrombosis and local or generalised infection can be considered under five main headings (1) the fluids used for intravenous therapy, (2) the method used, (3) the introduction of infection into the wound either during or after the infusion, (4) the nature and severity of the primary illness, and (5) the resistance of the infecting organisms to antibiotics

1 *Fluids Used*

The number of occasions on which the various fluids were used was

Plasma	211
Blood	90
Darrow s solution	304
N/5 saline solution and 5 % glucose	427
Casydrol ($2^1/_2$%)	104
Hartmann s solution (half strength)	295

The complications encountered are set out in table II

Our clinical impression was that complications were more often associated with casein hydrolysate than with

TABLE I—CONDITIONS FOR WHICH INTRAVENOUS THERAPY WAS GIVEN

Condition	Age																										
	Months												Years														
	0–	1–	2–	3–	4–	5–	6–	7–	8–	9–	10–	11–	1–	2–	3–	4–	5–	6–	7–	8–	9–	10–	11–	12–	13–	14–	15–
Diarrhœa and vomiting	21	17	20	16	16	13	10	15	12	8	4	3	5														
Diarrhœa and vomiting with parenteral infection	7	9	6	6	6	3	1	6	1	2		2	3														
Pyloric stenosis	4	8	2				1																				
Miscellaneous Surgical	5	2	1		1			1				1	4	6	3	1	6	4	3	3	3	6	5	3	4	1	1
Medical	7	3	5	1		2	1	3		1			2	5	1	1	1	3	1	1	1	1		1			1
Totals	44	30	34	23	23	18	13	25	13	11	4	6	13	11	4	2	7	7	4	4	4	7	5	4	4	1	2

given, the respirations became rapid and laboured, slight cyanosis was present, the heart-rate was rapid, there was œdema of the chest wall, and the liver was enlarged. The intravenous infusion was immediately discontinued, and within a few hours the symptoms disappeared

To avoid circulatory overloading it is our practice to record the volume of fluid given intravenously at hourly intervals, and in this case the hourly volume of fluid given was not in excess of the calculated amount A possible explanation is the big difference between the expected weight (9 lb) and the actual weight (6 lb 5 oz) and the calculation of the fluid requirement from the expected weight It seems reasonable, where the actual and expected weights differ widely, to calculate the fluid requirements on a figure between these two weights

WRIST DROP

Case 3 —A boy aged eight months was given intravenous fluids to combat dehydration due to diarrhœa and vomiting The intravenous infusion was set up at the right elbow, and thirty six hours later the flow became slow and œdema of the arm and hand was noted The infusion was therefore discontinued, although there was no evidence of venous thrombosis or sepsis, and there was no œdema elsewhere The œdema of the arm and hand persisted for ten days, wrist-drop was present, and early contraction of the fingers developed. Œdema of the muscles of the arm with pressure upon the radial nerve caused by tight bandaging of the limb during the intravenous infusion was considered the most probable explanation. No special treatment was given, the œdema gradually subsided, and full movements of the wrist and fingers returned within three weeks

CONCLUSIONS

After 664 intravenous infusions 132 complications were encountered. About 1 patient in 5 developed venous thrombosis or sepsis Though the mortality directly attributable to these complications was small, efforts should be made to avoid them either by improving technique or by using alternative procedures Some workers regard subcutaneous infusions as a satisfactory alternative to intravenous therapy, especially when given with hyaluronidase (Gaisford and Evans 1949) In our experience the rate of absorption of subcutaneous fluids, even with hyaluronidase, is too slow to restore the blood volume sufficiently rapidly in severely " shocked " infants In these patients intravenous therapy is essential, and the alternative procedure of giving fluids intravenously, whether into scalp veins, jugular veins, or peripheral limb veins, by needle and syringe during the initial period of " shock " is reasonable in practised hands Personally, I consider this technique far more difficult to acquire than that of setting up an infusion by the " cut down " method , and, unless all patients requiring intravenous therapy are treated in a special unit by expert operators, it is impracticable In the " cut down " technique fewer complications will arise if strict asepsis is practised.

Intramedullary tibial infusions are sometimes given to children, but in our experience they are dangerous and are apt to cause even more serious complications than intravenous infusions

In patients who refuse oral feeds for any length of time, particularly infants under the age of six months, it is essential to supply proteins in some form intravenously to prevent serious liver disease—a condition not encountered in this series Undoubtedly casein hydrolysate, even in a $2^1/_2\%$ solution, contributes materially to the onset of venous thrombosis, but if this substance prevents liver damage its use is nevertheless justified

Because infection of the intravenous infusion wounds is so prevalent, workers in some centres give penicillin as a routine to all patients receiving intravenous therapy Penicillin resistant organisms were present in most of our cases, and if any antibiotic is to be used as a routine it seems more reasonable to give streptomycin

I wish to thank Prof. Norman B Capon for his help and advice, Dr E G Hall, for the bacteriological reports, and Mr R L Plackett, M.A , of the department of applied mathematics in the University of Liverpool, for the statistical analyses

REFERENCES

Apley, J Wallis, H. R. E (1948) *Brit med. J* i, 197
Gaisford W , Evans D G (1949) *Lancet* ii 505
Lehane D Kwantes C M S Upward M. G , Thomson D R (1949) *Brit med J* ii 572

DIAPHRAGMATIC FLUTTER

C G Baker
O.B.E , M.D Lond , F R C P
ASSISTANT PHYSICIAN, AND ASSISTANT PHYSICIAN IN CARDIAC DEPARTMENT

A. Batty Shaw
M A , B M Oxfd M.R C.P
MEDICAL REGISTRAR

GUY'S HOSPITAL, LONDON

Irregular clonic spasm of the diaphragm, or hiccup, is a common disorder in health, and its significance in disease is well recognised Tonic spasm of the diaphragm is seen in chronic form in the emphysematous and occasionally in hysteria, and may occur in rabies, tetanus, and strychnine poisoning The abnormality of the diaphragm here described differs from hiccup and tonic spasm in that rapid and rhythmic contractions occur in attacks To describe the striking movements observed in our patient the term diaphragmatic flutter immediately seemed most apt, and it was interesting to find that the term had been similarly used by other workers That an uncommon or rarely recognised condition in medicine has few pseudonyms is a tribute to its characteristic appearance Diaphragmatic flutter is easy to recognise if the possibility is kept in mind, but otherwise it may be mistaken for paroxysmal tachycardia, valvular disease, or ischæmic heart disease The following case illustrates the main features of this uncommon and benign abnormality

CASE RECORD

A married woman, aged 42, was referred to Guy's Hospital in April, 1950, by Dr M. Cowan, of Catford, who had treated her over the previous nine months for attacks diagnosed as paroxysmal tachycardia There had been no improvement with sedatives and digitalis, either in the frequency or the severity of the attacks On examining her in one of her bouts of ' palpitation ' Dr Cowan heard a to and fro murmur over the heart and provisionally diagnosed aortic regurgitation In the absence of a history of rheumatic fever, Wassermann and Kahn tests were done but proved negative , it was at this stage that the patient came to Guy s and was seen by one of us (C G B) as an outpatient

The Attacks —She described her attacks clearly They started suddenly and occurred during the day or night, though they did not wake her She was aware when they ended, though the end was not so abrupt as the onset At first, nine months before, they lasted 2 or 3 minutes and happened about once a week, but recently she had been having five or six a day, each lasting up to 10 minutes Exertion or emotion might precipitate an attack, but not constantly The attacks were accompanied by shortness of breath, precordial discomfort and rapid palpitation in the chest She would sit down when at home, or stand still in the street, until the palpitation stopped

On the history alone it is difficult to see how a diagnosis of paroxysmal tachycardia could be avoided An attack occurred, however, at this first attendance It was then noticed that there was a rhythmic movement of the abdominal wall which was faster than the pulse rate, though this was about 120 per min. Synchronous with the abdominal movement but not with the pulse or apex beat, was a to and fro type of murmur heard all over the præcordium and lower chest, maximal in the mid axillary line on both sides The heart was

TABLE IV—PERCENTAGE FREQUENCIES OF COMPLICATIONS IN UPPER AND LOWER PARTS OF THE BODY

Type of infection	Site of drip		Total
	Lower body	Upper body	
Local infection	51 (44 29)	32 (38 71)	83
Generalised spread	6 (4 27)	2 (3 73)	8
Thrombosis of vein	25 (20 28)	13 (17 72)	38
No infection	251 (264 16)	244 (230 84)	495
Total	333	291	624

were administered in the lower body This conclusion, however, should be treated with reserve, for the cases treated were very heterogenous

4 *Severity of Illness*

253 (76%) of the patients were twelve months of age or less, and 204 (80%) of these 253 had diarrhœa and vomiting An attempt has been made to assess the severity of the illness in relation to the complication rate following intravenous therapy The difficulties to be met in doing this are well known, but it was felt that those cases requiring intravenous therapy within twelve hours of admission should be considered severe cases

The data, classified according to the complications encountered and whether the intravenous infusion was administered before or after twelve hours, appear in table v The expected frequencies, calculated on the assumption that the complication rate was not affected by the time of administration of the intravenous infusion, are shown in parentheses after the observed frequencies The value of χ^2 is 11 109 on 3 degrees of freedom, and the 5% level of χ^2 is 7 815 Examination of the data indicates that the infection rate in the under twelve hours group is lower than in the over twelve hours group because of the much lower local infection rate But the nature of the cases treated, and the other possible factors involved, make such conclusions very unreliable

5 *Resistance of Infecting Organisms*

The infecting organisms in the 83 cases of local infection of the infusion wound and in the 8 cases of generalised septicæmia were as follows

A Local Infection		
Staph. aureus coagulase positive		
Penicillin sensitive	16	30
Penicillin insensitive streptomycin sensitive	6	
Penicillin insensitive streptomycin insensitive	8	
Mixed *Staph aureus* infections:		
Staph aureus and *Strep fæcalis*	1	8
Staph aureus and *B proteus*	3	
Staph aureus and *Bact coli*	4	
Bact. coli		7
Bact coli and *B proteus*		1
B proteus		1
Ps pyocyanea		1
Strep fæcalis		1
Pus sterile on culture		24
No swab taken		10
Total		83
B Generalised Infection		
Staph aureus coagulase positive		
Penicillin sensitive	1	6
Penicillin insensitive, streptomycin sensitive	3	
Penicillin insensitive streptomycin insensitive	2	
Bact coli		2
Total		8

In the local infection group the pus was sterile in 24 cases and no swab was taken in 10 cases From the remaining 49 cases a pure growth of coagulase positive *Staphylococcus aureus* was obtained in 30, and in almost half of these the organisms were insensitive to penicillin though some were sensitive to streptomycin From the 8 cases of generalised infection coagulase positive *Staph aureus* was isolated in 6, and in 5 of these the organism was penicillin insensitive

HEPATITIS

Lehane et al (1949) found 1 case of homologous serum jaundice in a series of 214 patients under the age of ten years who had been given blood or plasma transfusions Apley and Wallis (1948) reported 2 fatal cases of homologous serum jaundice in infancy, and concluded from a study of the literature that in infancy this complication is extremely rare Only 1 case of hepatitis following a transfusion of plasma or of blood occurred in the present series of 332 cases The jaundice appeared seventy days after plasma had been given, there was no history of contact with a case of infective hepatitis, and necropsy did not reveal any other cause for the jaundice

Case 1 —A girl, born on Nov 13, 1948, was admitted to hospital on March 28, 1949, with four days' history of diarrhœa and vomiting She was much dehydrated on admission, and intravenous fluids were given. The routine régime of fluid replacement was used and consisted of 560 ml of half strength plasma and Hartmann's solution in the first six hours, 560 ml of Darrow's solution in the following twelve hours, and 280 ml of N/5 saline solution and 5% glucose in the following six hours Oral feeding was begun after the first twenty four hours, but dehydration recurred, and the same amount of plasma, Darrow's solution, and N/5 saline solution as before were given during the subsequent twenty four hours. Graduated feeding was then started again, and the child made an uninterrupted recovery She was discharged twenty-one days after admission

TABLE V—COMPLICATIONS ENCOUNTERED (EXPECTED FREQUENCIES IN PARENTHESES) IN PATIENTS RECEIVING INTRAVENOUS THERAPY WITHIN OR AFTER 12 HOURS OF ADMISSION

Type of infection	Intravenous therapy		Total
	Within 12 hours	After 12 hours	
Local infection	17 (28 98)	48 (36 02)	65
Generalised spread	4 (3 57)	4 (4 43)	8
Thrombosis of vein	17 (15 60)	18 (19·40)	35
No infection	110 (99 86)	114 (124 14)	224
Total	148	184	332

On June 6, 1949 (49 days after discharge) she was readmitted with two days' history of vomiting Jaundice was present, but no other abnormal physical signs were noted Within forty eight hours she became drowsy, and tonic convulsions supervened Death took place on June 8 At necropsy the liver was normal in size, its surface was speckled bright red and yellow, and its consistence was normal on section Throughout the liver the pattern showed peripheral fatty change, with bright red areas in the centres of the lobules On microscopical section there was zonal necrosis which had left only a few surviving cells at the periphery of the lobule there was marked fat infiltration of the outer half of the lobule, and periportal infiltration of polymorphs, plasma cells, and round cells

CIRCULATORY OVERLOADING

Case 2 —A boy, born on March 10, 1949, was admitted on May 14, 1949, with a history of bronchopneumonia two weeks previously which had responded to penicillin, and diarrhœa and vomiting starting twenty four hours before admission He was dehydrated, and an intravenous infusion was given for the initial forty eight hours His condition improved, but a relapse occurred on May 22, and further intravenous therapy was given The fluid requirements were based upon the expected weight, which for the birth weight of 4 lb 13 oz was 9 lb The actual weight was 6 lb 5 oz. The fluids ordered were 360 ml of plasma in six hours 360 ml of Darrow's solution in twelve hours, and 180 ml of N/5 saline solution and 5% glucose in the following six hours The full volumes of plasma and Darrow's solution were given, but because the infusion was running slowly, only 80 ml of N/5 saline solution and 5% glucose was given In the following twenty four hours 675 ml of N/5 saline solution and 5% glucose was prescribed, but, when about 600 ml had been as happened with the peripatetic flutterer in America (Porter 1936 and others) Awareness of the diaphragmatic movement is surprisingly rare, and palpitation as a presenting symptom has only been reported in one case (Dowman 1927) apart from the present patient

Signs

The common sign is epigastric pulsation at a rate of 70–200 a minute, either regular or with slight variations in rate and amplitude, in the unilateral movement with tetany one upper quadrant alone moves Thoracic expansion is diminished or absent, but it can be produced voluntarily without influencing the flutter, as in our patient The thorax may show pulsation, in the patient described by Handron (1941) the excursions of the diaphragm were 6 in and shook the whole body

Bruits may be heard on auscultation of the chest, particularly the lower part, due either to the diaphragmatic movement or, more probably, to secondary effects in the lungs. They may be mistaken for heart sounds with a tic tac rhythm or, when irregular, with auricular fibrillation (Cain and Ware 1946), for the to-and-fro murmur of aortic disease (Levine and Harvey 1949), or for a pericardial friction rub (Porter 1936, Goodman 1941) The description (Porter 1936) of the noise as "shuffling" was particularly apt in our case When the common symptoms of breathlessness and pain are present, it is easy to see how heart disease may be diagnosed, until the diaphragmatic origin of the sounds is recognised by their low site, their lack of timing with the pulse or heart sounds, or obvious abdominal pulsation. Fluoroscopy clinches the diagnosis. Though other workers had failed to show any abnormalities in the electrocardiogram during an attack, Söderström (1950) demonstrated small rapid oscillations on both standard and unipolar leads which he thought were due to the diaphragmatic movements. Similar waves were seen in our case but were shown to be due to changes in pressure of the electrode. The only abnormality found in many investigations of these cases is an occasional fall in the alkali reserve due to protracted hyperventilation (Gamble et al. 1925, Handron 1941)

TREATMENT

When due to tetany, diaphragmatic flutter will respond to treatment of that condition. When it is the result of encephalitis lethargica, treatment can only be symptomatic. When it is a nervous tic it may disappear spontaneously, or may respond to explanation, reassurance, and re-education in the use of the diaphragm Sedatives are clearly useful in such treatment Harris and Scherf (1945) used quinidine in their case in an attempt to prolong the refractory period of the diaphragmatic muscle with apparent effect. Gamble et al. (1925) found that freezing the exposed phrenic nerves with ethyl chloride temporarily arrested the flutter, and "cures" are reported (Dowman 1927, Speirs 1929, Skillern 1931 Greene 1932 Handron 1941) by phrenic avulsion or division, surprisingly little disability results even when this is done on both sides In the itinerant patient in America both phrenic nerves were crushed or divided on several occasions. A satisfactory paralysis was achieved on the left side, but the right half of the diaphragm could still flutter when the case was last recorded—by Senter et al. (1950), who therefore suggested that an accessory phrenic nerve was present In a condition which is essentially benign and which may be temporary, such radical treatment is only indicated when very severe symptoms have not responded to simpler measures after a period of observation It would then seem reasonable first to do a phrenic crush, which could later be followed by a division of the nerve if disabling attacks of flutter returned

References at foot of next column

PARALYTIC POLIOMYELITIS FOLLOWING INJURY

A Blair Harrington
M.D Aberd.

PRINCIPAL MEDICAL OFFICER, MINISTRY OF PENSIONS

In the last few years it has been established that in children recently submitted to tonsillectomy, poliomyelitis is especially likely to take the bulbar form, and it has been suggested that not only the site but also the incidence and severity of paralysis may be affected by prophylactic inoculations Geffen (1950) mentions a case in which appendicectomy was followed by abdominal paralysis

Horstmann (1950) states that, in her recent series, which included 248 cases of paralytic poliomyelitis, several of the patients had muscle weakness in limbs which had sustained trauma Otherwise, however, apart from the experimental work of Levinson et al. (1945), little has been written about the effect of direct local injury in poliomyelitis I have therefore taken an opportunity to review the records of 100 unselected cases of poliomyelitis acquired during service in the Armed Forces In 5 of these it was evident that trauma had preceded the paralysis The five case records are set out below

CASE RECORDS

Case 1 —On June 20, 1945, a soldier fell on his back while playing football. After a short rest he continued playing and finished the game His back was stiff and sore for a few days, but he did not go off duty On July 1 he had pains in the back, legs, and head. On July 3 he began to drag his left foot, and that evening his right leg felt weak.

When he was admitted to hospital on July 4 his neck was stiff, his left leg was tender and completely paralysed, and his right leg was very weak. He had retention of urine, which lasted ten days. Lumbar puncture produced cerebrospinal fluid (C.S.F.) under slightly increased pressure; clear, colourless, and containing 8 cells per c.mm. and 100 mg of protein per 100 ml. Culture proved sterile His temperature, which had risen to 101°F, reached normal on July 7 Radiography of the lumbosacral area and sacro-iliac joints on July 26 showed only a lumbosacral angle larger than normal.

Testing later confirmed the presence of slight weakness of the recti abdominis and erectores spinæ muscles. Paralysis of the obliqui externi abdominis muscles, however, remains The left leg too, is completely paralysed, but there has been a slight return of power in the right leg

DR. BAKER, DR. SHAW REFERENCES

Cain E. F Ware E. C (1946) *J Amer med. Ass.* 131, 1058
Dowman C E. (1927) *Ibid* 88 95
Fox, H (1898) *Brit. med. J* i 1134
Gamble C J Pepper O H. P Muller G P (1925) *J Amer med. Ass.* 85 1485
Goodman M. J (1941) *Ibid* 116 1635
Greene R. (1932) *Sth. med. J* 25 392.
Handron, C J (1941) *Ann intern. Med.* 14 1909
Harris R. Scherf D (1945) *Amer J med Sci.* 210 593
Karelitz, S (1932) Libman Anniversary Volumes. New York vol. ii p 633.
Kulenkamp G (1926) *Dtsch Z Nervenheilk.* 94 312
Leeuwenhoek, A. (1722) *Phil. Trans* 32 433
Levine S. A., Harvey W P (1949) Clinical Auscultation of the Heart. Philadelphia p 260
Marie P Binet L. Levy G (1922) *Bull. Soc méd. Hôp Paris,* 46 1075
Moore F H Schoff, C (1947) *Amer Heart J* 34 889
Porter W B (1936) *J Amer med. Ass* 106 992
Senter W J., Timberlake L F Nelson R (1950) *Ibid* 143 174.
Simonin Chevigny (1916) *Paris med.* 2 191
Skillern P G (1931) *J Amer med Ass* 96 2098
Smith H. (1932) *Amer J med. Sci* 183 837
Söderström N (1945) *Acta med scand.* 122 95
— (1950) *Ibid* 137 27
Speirs, G O (1929) *J nerv ment Dis.* 69 407
Whitehead, R. W Burnett C T Lagen J B (1939) *J Amer med. Ass.* 112 1237
Widström G (1944) *Nord. med.* 23 1368

not enlarged clinically, the sounds were normal, with no murmurs of intrinsic heart disease, and the blood pressure was 140/85 mm. Hg There were no signs of venous congestion, and the patient's distress was nervous rather than cardiac

Behind the X ray screen her heart was seen to be normal in shape and contour, but it was bouncing on the top of the diaphragm, both leaves of which were contracting rhythmically and violently at the rate of about 160 times a minute The term " flutter " seemed most apt to describe this odd behaviour of the diaphragm, and we found later that it had been thus described by others

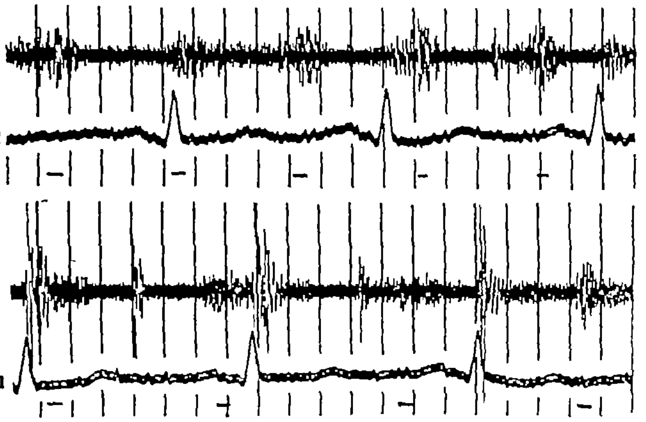
That this diaphragmatic flutter, and not heart-disease, was responsible for the patient's dramatic symptoms and signs was even more obvious on a second visit a few days later, when she was no longer nervous and her heart rate was only 70 per min In a further attack the dissociation between her pulse and her abdominal pulsation was very striking She was admitted for observation in July, 1950

Past History —The patient had had no serious illnesses, and she came of healthy stock She worked as a ward maid until her marriage at the age of 28 In 1942 she was " bombed out " three times, and she had been nervous ever since, she was easily upset and did not sleep well In 1946 she returned to part time work as a ward maid in addition to her own house work. She had no children There were no clear or unusual causes for worry or anxiety in her life

On examination no evidence of disease was found Her physique and weight were satisfactory She was slightly anæmic Hb 80%, red cells 4,200,000 and white cells 6500 per c mm (differential count normal) X ray examinations barium meal showed no diaphragmatic hernia or abnormality of stomach or duodenum, cholecystogram normal, lungs normal, no cardiac enlargement Serum calcium 10 8 mg and serum cholesterol 256 mg per 100 ml Alkali reserve 62 vols of CO_2 per 100 ml, with no reduction at the end of an attack

Electrocardiography showed a vertical heart with no abnormality in standard or unipolar leads During an attack an exploring electrode was placed in many positions, but abnormal tracings were obtained only at the mid point between the xiphisternum and umbilicus, this showed additional waves, irregular in shape and size, varying in rate from 190 to 320 per min similar waves could be produced by intermittent pressure on the electrode when the patient was not in an attack, showing that the abnormal waves did not result from the diaphragmatic flutter

When she was first in hospital, her attacks were as frequent as 6–8 a day but never occurred while she was asleep, they started insidiously or suddenly, and came on readily when she was examined During the attack she would lie flat on her back in bed and the pulsation of her abdominal wall could then be easily seen The rate of the pulsation in attacks was 160–240 per min, the rhythm was usually regular but occasional irregularities in rate and amplitude were seen (see figure) There was no thoracic movement, but she could take a deep breath or speak without altering the pulsation. There was no cyanosis during an attack but she was dyspnœic on walking or talking She felt some precordial discomfort, rather than pain, in the midline, but without the characteristic radiation of angina



Logarithmic sound tracings (Dr B G Wells): upper from right 5th interspace in mid-clavicular line lower from apex, both upper and lower with lead II of electrocardiograph Diaphragmatic flutter sounds are indicated by dashes and show alteration in rate 150 a minute in upper tracing with heart rate of 86 In tracing from apex the softer flutter sounds are overwhelmed by first and second heart sounds

The murmur could be heard all over her heart and lower thorax but was loudest in the mid axillary line, especially on the right, it had a to and fro rhythm, in time with the epigastric pulsation, it was medium pitched, roughish, and rustling, the term "shuffling" (Porter 1936) described it well. Dr B G Wells, who kindly came from St. Bartholomew's Hospital to take a phonocardiogram, demonstrated it graphically (see figure)

No trick movements would stop or abort the attacks, which lasted 4–10 minutes, and though they occasionally stopped suddenly they more often subsided gradually, particularly if the patient's attention was distracted by conversation or other interest

Progress —She was assured that she had no organic disease and was treated by simple explanation of the nervous mechanism, a routine sedative, and breathing exercises, with instruction in the full and proper use of her diaphragm On this regime her obvious nervousness decreased and the attacks diminished to about 3 short ones a day She has since attended as an outpatient, and though she still has attacks they bother her little, and she is leading a full and seemingly happy life

DISCUSSION

Flutter of the diaphragm is not a new observation, for it was described in 1722 by Leeuwenhoek Simonin and Chevigny (1916) give references in the French literature of the nineteenth century, when it was described as chorea of the diaphragm, Fox (1898) described the disorder in England, and since the first world war there have been scattered references to it on the Continent and in America

Ætiology

Diaphragmatic flutter has been reported equally in each sex and between the ages of 16 and 84 It may result from encephalitis lethargica (Gamble et al 1925, Kulenkamp 1926, Dowman 1927, Speirs 1929, Skillern 1931, Smith 1932) and is one of the central disorders of respiratory function reviewed by Marie et al. (1922) In 3 cases of tetany left sided contractions of the diaphragm synchronous with the heart-beat have been observed (Karelitz 1932, Widström 1944, Soderstrom 1945) during the actual disease, these were thought to result from irritability of the diaphragm Harris and Scherf (1945) noted similar movements of the diaphragm in operations on dogs, but they ceased when the left phrenic nerve was removed from contact with the heart or was severed Mr R C Brock tells us that he has not observed such movements during thoracic operations in man

The remaining cases reported, like our own, seem to be a form of tic Two cases have followed repeated abdominal operations, which are as likely to indicate an unstable personality of the patient as to support the suggestion that diaphragmatic adhesions are the cause of the flutter (Handron 1941, Smith 1932) Nervous and psychopathic features are common, and are well shown in an American patient who was the cause of no fewer than six separate reports (Porter 1936, Whitehead et al 1939, Goodman 1941, Cain and Ware 1946, Moore and Schoff 1947, Senter et al 1950)

Symptoms

Diaphragmatic flutter may be symptomless, particularly if it is one of several postencephalitic disturbances Breathlessness is the commonest complaint, occurring in attacks of sudden onset which may last from minutes to as long as seventeen days (Harris and Scherf 1945) Pain in the chest, felt at the site of diaphragmatic attachment of the ribs, in the epigastrium, or more often in the præcordium is common, it may radiate to the left shoulder or arm It is easy to see how this may give rise to a wrong diagnosis of myocardial ischæmia or infarction,

ENERALISED SCLERODERMA WITH INTESTINAL INVOLVEMENT

C Barrington Prowse
M.B Camb , M.R C.P
SICIAN, ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON

1945 Goetz, writing on the pathology of generalised oderma, concluded that "we are dealing with a emic disease neither solely nor primarily involving skin 'scleroderma' is only the obvious and striking ptom of a generalised disease and the most serious ptoms actually arise in the viscera." He suggested the term scleroderma should be abandoned "progressive systemic sclerosis" substituted it

here is ample justification for such a change, as a ly of the literature relating to the visceral lesions in roderma and acrosclerosis will show Various writers e dealt with the clinical, radiological, and pathological ects of its effects on the gastro intestinal tract, heart, gs, kidneys, bones, and muscles, and the vasomotor l endocrine systems Hitherto, however, these reports ve only attracted the attention of workers with a cial interest in such diseases, and too little importance s been attached to the responsibility of the general ysician for recognising their widespread nature Dysphagia, Raynaud's phenomenon, calcinosis, and erodactyly are familiar "complications," but the fact at scleroderma and acrosclerosis may cause fatal, lminating disease of the bowel, heart, or lungs is less ell known, and it is the purpose of this communication set on record a further case in which death was clearly ue to sclerodermatous infiltration of the gastro intestinal act

Only 2 cases of intestinal involvement were recorded efore 1942 (Kraus 1925, Rake 1931) Hale and Schatzki 1944) described the radiological appearances of the astro intestinal tract in 22 cases, in 4 of which the small ntestine was involved, and Goetz (1945) reported 6 cases in which an intestinal lesion was proved radiologically or pathologically, in 1 of which paralytic ileus developed. Pugh, Kvale, and Margulies (1945) recorded a case with involvement of the small intestine demonstrated by radiography, and Lushbaugh Rubin, and Rothman (1948) described another in which scleroderma of the intestine proved fatal by causing gangrene of a segment of the colon. Bevans (1945), in a full account of the histological appearances in 2 fatal cases, described diffuse lymphocytic infiltration in the jejunum there were dense collagen fibrils in the submucosa, and atrophy of both muscle layers with fibrous tissue replacement She also commented on the thickness and whiteness of both layers of the peritoneum, and the presence of numerous adhesions between the viscera She concluded that muscle atrophy throughout the gastro intestinal tract is an integral part of the disease and is responsible for some of the symptoms and signs observed in life.

Gastro-intestinal features were prominent in the case recorded here There was a complaint of dysphagia, achalasia of the cardia slight dilatation of the œsophagus, and distension with air (as noted by Bourne 1949) were demonstrated radiologically and at necropsy characteristic changes were found at the lower end of the œsophagus Paralytic ileus developed in the terminal stages, plastic peritonitis was demonstrated post mortem, and histological examination of the small intestine showed extensive round-cell infiltration of the submucosa, and atrophy of all layers with an increase in collagenous tissue

"Scleroderma heart disease" was described by Weiss et al. (1943) in a review of 9 cases, all had signs and symptoms of heart-disease, cardiac enlargement, and electrocardiographic abnormalities, and 6 died in congestive failure Heine (1926), Brock (1934), Mathisen and Palmer (1947), and East and Oram (1947) have each described 1 patient with scleroderma who died as the result of cardiac involvement In the present case, breathlessness was a prominent symptom, the heart was enlarged and the electrocardiogram abnormal, and, though these signs and symptoms could not be attributed solely to sclerodermatous infiltration of the heart muscle, there can be no doubt that it played a part

It is more difficult to attribute pulmonary fibrosis with certainty to a sclerodermatous process But fibrosis of the lower lobes was observed by Goetz (1945), who described specific histological changes in and around the alveoli and in the blood-vessels, Jackman (1943) mentioned basal pulmonary fibrosis in his account of the radiological features of scleroderma and acrosclerosis, and Murphy et al. (1941) described a young negress with similar radiographic pulmonary changes, and noted particularly that this patient had no previous history of chest disease More recently Lloyd and Tonkin (1948) reviewed the literature relating to pulmonary fibrosis in generalised scleroderma and reported 4 cases of their own; and Church and Ellis (1950) reported 2 cases with cystic pulmonary fibrosis, and referred to 3 others described by Dostrovsky (1947)

The case to be described here first came under medical care with a pulmonary illness, but though it is tempting, in the light of the subsequent course, to postulate that sclerodermatous fibrosis of the lungs predisposed to the acute infection, this cannot be proved. Signs and symptoms of pulmonary fibrosis were present when I examined the patient two years later, and an X-ray picture showed dense basal shadows on both sides Histological sections revealed changes similar to those described by Goetz (1945) and Bevans (1945)

Asthenia, pigmentation, progressive loss of weight, hypotension, and personality change were other features of the case, and when crises of vomiting occurred the clinical picture suggested Addison's disease Osler first discussed the differential diagnosis between scleroderma and Addison's disease, it would seem that Simmonds's disease might present the same clinical features However, biochemical tests showed no disturbance of sodium metabolism and the pathologist noted no abnormality of the endocrine glands apart from the very small size of the pituitary body

CASE RECORD

A man of 66 was referred to me on April 2, 1948, by his doctor, who had only recently taken charge of him. He complained of lassitude palpitations breathlessness, pains all over his body, and numbness of his fingers and of the left side of his face He stated that in May, 1946 he had a febrile illness, diagnosed as right-sided 'pneumonia and pleurisy,' which was treated for six weeks in a cottage hospital. Two weeks later he fell ill again and returned to hospital for another three weeks with left-sided 'pneumonia and pleurisy' X ray examination at that time revealed emphysema and chronic bronchitis, and later a small collection of fluid at the right base

After these episodes he failed to regain his normal health, and though never acutely ill he felt vaguely unwell. He noticed that his fingers tended to grow numb, and frequently turned bluish black for long periods, particularly during cold weather he also found that the skin over his hands was becoming tight Accordingly, in May 1947, he sought medical advice and was admitted to a 'clinic for investigation. It is not known what diagnosis was made, but colonic lavage and fasting were advised This treatment he refused at first, but submitted to in the following November while undergoing it he lost 2 st in weight but he recovered some of this after returning home The symptoms for which he had sought advice remained unchanged, and in addition he noticed increasing tightness of the skin of his face with impairment of sensation over the left cheek and gums.

The past, personal, and family histories were negative.

Case 2 —A lance bombardier injured the lower part of his spine on Aug 1, 1945, and developed very severe pain in the region of his coccyx He had several uncomfortable nights before it subsided On Aug 5 the pain returned and was worse in certain positions There was also a throbbing temporal headache Next day, while walking, he found that his left leg was weak and he could not control it On examination all the leg reflexes were absent, and the patient's temperature was 99 8°F Next day his temperature rose to 101 4°F, his neck was rigid, the lower part of his abdomen was weak, and both lower abdominal reflexes and knee jerks were absent There was no power in the left quadriceps, adductors, or hamstrings, and these muscles were also very weak on the right There was little power below the knee on either side No sensory loss was recorded Lumbar puncture on Aug 7 produced clear C S F not under increased pressure There were 30 cells per c mm , but there is no record of any test for protein Retention of urine began on Aug 10 and required catheterisation. Dysuria continued for the next ten days

Examination in 1947 showed a complete flaccid paralysis of the left leg, which was thin, cold, and blue There was some improvement in all muscle groups in the right leg, and the abdominal muscles had recovered

Case 3 —While playing hockey on Nov 5, 1943, an aircraft man collided with another player and fell on the right side of his head At the same moment he was struck a heavy blow on the right shoulder by his opponent s stick He felt slightly dazed for a moment but got up and remembers finishing the game

On the evening of Nov 7 he developed a severe headache, and next day he had sweating, malaise, anorexia, and constipation He vomited several times and had a temperature of 101 8°F and pulse rate 106 His neck was stiff and ached, and he then found that he could hardly move his right arm His left arm was slightly weaker than normal , next day the weakness had spread to his right leg Lumbar puncture on Nov 8 showed clear C S.F under normal pressure and containing an excess of small lymphocytes By Aug 19 the left arm and right leg had almost recovered, but flaccid palsy of the right arm persisted

Early the next year the arm showed only some power in the finger flexors and flexor carpi radialis and ulnaris muscles All other muscles tested, including those of the shoulder girdle, were paralysed The other limbs and trunk were normal

Case 4 —On July 26, 1943, an aircraftman jumped off a lorry and landed on his heels and his back He felt a sudden pain " stabbing upwards " in his thighs After a day in bed because of headache he felt quite well On July 31 he had an aching pain in the back and thighs, stiffness of the neck, and general malaise He thought he had a cold and stayed in bed for the day On Aug 2, on attempting to get up, he found there was no power in his legs

On examination two days later his lower limbs were flaccid and tender, and all tendon reflexes were absent There was no sensory loss He was constipated, and on Aug 5 he developed retention of urine and had to be catheterised until Aug 7 On Aug 9 the C S.F was clear and showed 8 cells per c mm and 30 mg of protein per 100 ml It was sterile on culture, and Lange's curve and the Wassermann reaction were negative Radiography of the dorsolumbar spine on that date showed no abnormality

He was febrile and developed oliguria between Aug 9 and 14 , this may have been related to his poor fluid intake, for urinary flow was established again by Aug 16 after a glucose saline drip had been set up Examination then showed that in addition he had weakness of the lower abdominal and lower intercostal muscles On further lumbar puncture on Aug 30 the C S.F contained 250 mg of protein per 100 ml and only 2 lymphocytes per c.mm

When examined in February, 1944, he had flaccid paralysis of the right rectus abdominis, lower intercostals, and lower fibres of the erectores spinæ muscles There was moderate weakness of these muscles on the left side but both legs were completely paralysed All tendon and shin reflexes were absent below the costal margins There was no sensory loss or difficulty of control of urine or fæces

Case 5 —A driver was admitted to hospital on Nov 7, 1944 He had a perianal abscess, and this was opened shortly after admission, but a sinus formed Smears and culture of the discharge showed *Staphylococcus albus* only (*Corynebacterium diphtheriæ* was never found by direct smears or on culture) Pains in the back appeared on Nov 11 when the abscess had been incised, and on Nov 13 weakness suddenly developed in the legs , the left rapidly became completely paralysed, and only flexion and extension at the right knee remained Lumbar puncture then showed 380 red cells and 10 lymphocytes per c mm , 35 mg of protein per 100 ml, 690 mg of chloride per 100 ml , and no growth on culture The temperature rose to 100°F next day

There has been slight improvement in his condition since When examined recently his left leg was paralysed except for weak flexion movements at his left knee and hip Knee and hip movements of the right leg were fairly strong, but there was complete flaccid palsy below the knee, with clawing of the toes Bladder control was normal At no time was there any sensory loss

DISCUSSION

Horstmann and Paul (1947) emphasise the variation in the interval between the apparent exposure to the virus and the onset of symptoms , they cite extremes of three days and five weeks Clearly there is a latent period after infection, and they mention a case in which polio myelitis virus was detected in the stools nineteen days before the patient developed paralysis

In 4 of the 5 cases described above, the disease appeared within five days of the injury Apparently trauma upsets the balance between the virus and the host and precipitates the disease The effect seems similar to that of fatigue, which, as Ritchie Russell (1947, 1949) has shown, provokes paralysis, which may select the muscles most used

Since neither the time nor the route of virus invasion of the central nervous system is yet properly known, attempts to explain the effect of local trauma can only be speculative There do, however, seem to be two chief possibilities either the local injury opens up some pathways of infection to the spinal cord, or else the effect of local trauma is to alter the spinal-cord cell physiology in such a way as to reduce resistance to the virus, which may be already established in the cord

SUMMARY

Of 100 unselected cases of paralytic poliomyelitis 5 had a history of trauma which preceded by a few days the appearance of paralytic poliomyelitis

In each of these cases paralysis appeared in muscles closely related to the site of the trauma

Possible factors in the production of this paralysis are briefly discussed

I should like to thank Dr W Ritchie Russell for his helpful criticism, and the Director General, Medical Services, Ministry of Pensions, for permission to publish.

REFERENCES

Geffen D H (1950) *Med. Offr* 83 137
Horstmann, D M. (1950) *J Amer med Ass* 142 230
— Paul, J R (1947) *Ibid*, 135, 11
Levinson, S O , Milzer A. Lewin P (1945) *Amer J Hyg* 42,204
Russell W R (1947) *Brit med J* ii, 1033
— (1949) *Ibid*, i 465

" we find ourselves forced to the conclusion that we must have better and more mature individuals filling the positions of responsibility in every country if our vaunted civilization is to advance and not be swamped by all the primitive urges of hate, aggression, domination and the other unlovely characteristics It is, therefore, a matter of great urgency that we should have everywhere, in local communities, on civic councils and in the various societies which affect us, men and women who are better balanced and more in tune with their fellows Every one of us has something to contribute, not merely to our immediate entourage, but through them to the wider councils of the community and ultimately to the affairs of state"—Dr J R Rees in his foreword to the *Health of the Mind* (3rd ed , London, 1951)

Some widening of the distal 4 in of the œsophagus and a white opacity of the mucosal lining in the distal half Plastic peritonitis, with coils of bowel adherent to one another and to parietal peritoneum by fine adhesions Lymphatics visible leaving the small intestine and entering the mesentery Liver not enlarged but excess fat present Adrenals normal, apart from post-mortem changes Pancreas, kidneys, gall bladder, bladder, prostate, and spleen normal

Microscopical Appearances

Skin —The epidermis is thinned The dermis consists of relatively acellular collagenous tissue, and there is a little round cell infiltration.

Lungs (fig 3) —The original pathology is obscured by bronchopneumonia, but there is marked interstitial fibrosis with thickening of the alveolar walls Some of the vessels show intimal thickening with diminution in the size of the lumen.

Intestine (fig 4) —The wall of the small intestine shows extensive round cell infiltration of the submucosa There is some atrophy of all the layers and an increase of collagenous tissue

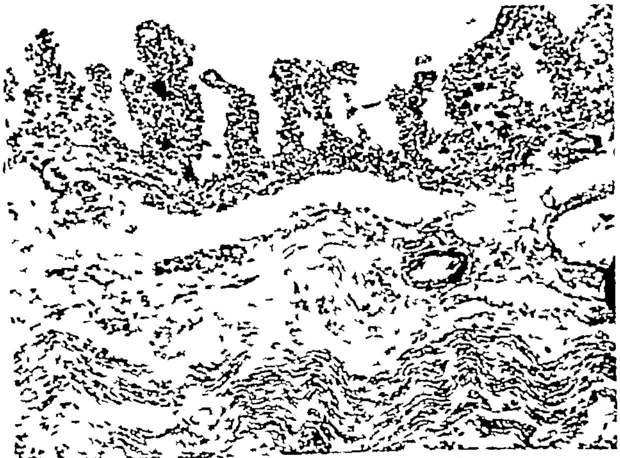


Fig 4—Section of intestine (× 85)

Heart —The pericardium is infiltrated with polymorphs and round cells The myocardium shows some perivascular fibrosis

SUMMARY

A case of scleroderma is described with widespread visceral lesions, all of which produced signs or symptoms and contributed to the fatal result Particular stress is laid on the intestinal features of the case—firstly because death eventually resulted from paralytic ileus, and secondly because the effects of scleroderma on the intestine have seldom been reported

My thanks are due to Dr L R Janes for the necropsy report, to Dr R W P Johnson for the histological notes, and to Dr S A Belshaw for his careful records of the case

REFERENCES

Bevans M (1945) *Amer J Path* 21 25
Bourne W A (1949) *Lancet* i 392
Brock W G (1934) *Arch Derm Syph Chicago* 30 227
Church R E Ellis A R P (1950) *Lancet* i 392
Dostrovsky A (1947) *Arch Derm Syph Chicago*, 55, 1
East T Oram S (1947) *Brit Heart J* 9 167
Goetz R H (1945) *Clin Proc* 4 337
Hale C H Schatzki R (1944) *Amer J Roentgenol* 51 407
Heine J (1926) *Virchows Arch* 262 351
Jackman J (1943) *Radiology* 40 163
Kraus A (1925) *Med Klin* 21 921
Lloyd W E Tonkin R D (1948) *Thorax* 3 241
Lushbaugh C C Rubin L Rothman S (1948) *Gastroenterology* 11 38
Mathisen A K Palmer J D (1947) *Amer Heart J* 33 366
Murphy J R Krainin P Gerson M J (1941) *J Amer med Ass* 116 499
Pugh D G Kvale W F Margulies H (1945) *Proc Mayo Clin* 20 110
Rake G (1931) *Johns Hopk Hosp Bull* 48 212
Weiss S Stead E A jun Warren J V Bailey O T (1943) *Arch intern Med* 71 749

EXPERIMENTS ON FAT ABSORPTION IN A CASE OF CHYLOTHORAX

W H R Auld
M B Aberd
ASSISTANT, DEPARTMENT OF CLINICAL CHEMISTRY, UNIVERSITY OF ABERDEEN

C D Needham
M D Lond , M R C P
ASSISTANT PHYSICIAN, ROYAL INFIRMARY, ABERDEEN

After about seventy years' intermittent research, the mechanism of the intestinal absorption of fat still remains unknown The work of Frazer (1943, 1946, 1947) and his colleagues has added considerable information, but their conclusions are not yet everywhere accepted They have studied fat absorption in all phases—intraluminar, intramural, and distributive (Frazer 1946)—in a large number of experiments and have advanced their partition hypothesis This postulates that not only fatty acids but also unhydrolysed triglyceride fat can be absorbed as such from the small intestine, and that they follow different paths, fatty acids being mainly absorbed into the portal circulation for transport to the liver, whereas neutral fat travels via the lacteals and thoracic duct to the systemic circulation and thence to the storage depots In support of this they have described experiments (Frazer 1943) in which they fed rats with fats stained with Sudan IV They found that in the animals consuming a neutral fat the dye accumulated in the fat storage depots throughout the body, whereas in those consuming the equivalent fat in the form of the products of hydrolysis—i e , fatty acid and glycerol—the dye was deposited mainly in the liver

Much of the work on this subject has been done on laboratory animals In man investigations have been confined mainly to fat-excretion and fat balance studies, to qualitative intraluminar changes while absorption is taking place, and to changes in the fat content of venous blood, usually systemic In the one case in which portal blood was examined (Sherlock and Walshe 1946) no increase in fat content could be demonstrated after feeding butter with and without added lipase, but their patient had hepatic cirrhosis, a fat balance test suggested that fat absorption was defective, and the systemic blood fat level did not rise

PRESENT STUDY

A male patient, aged 32, came under observation because of a non traumatic chylothorax of unknown origin There seemed to be a communication between a lymphatic channel and the left thoracic cavity, and chyle accumulated there at a constant rate of about 600 ml a day The clinical details and the management of the patient will be published elsewhere An opportunity was taken of using this case to test Frazer's hypothesis and to supplement his work with stained fats in a rather different fashion Although the ingestion of neutral fat stained with Sudan III has been used for many years as a diagnostic test to differentiate chylous effusions in the thorax or peritoneal cavity from pseudo chylous effusions where no communication exists with the lymphatic channels, we have not been able to find any report on the effect of giving split fat under the same conditions

The investigation lasted 14 days, during which we made three experiments In each the patient was fed a split or unsplit fat stained with a known quantity of Sudan III, and the dye recovered from the pleural cavity was estimated quantitatively Maximal recovery was achieved by paracentesis under fluoroscopic control to remove all but the last ounce of fluid During the investigation the patient received an ordinary ward

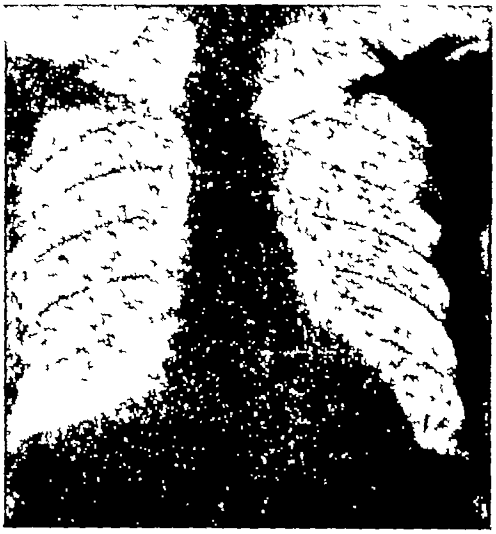


Fig 1 (March 19, 1948)—Heavy abnormal shadowing at both lung bases , right more than left. Slight general enlargement of left and right ventricles , aorta unfolded

His appearance was consistent with his stated age He was slightly built, and his thinness was accentuated by the tightness with which the shiny and pigmented skin was drawn over the malar bones, around the mouth, across the chest, and about the hands and forearms , he did not like smiling because it hurt him Second degree clubbing of the fingers and toes was present, and some fingers of each hand were white or blue Pulmonary ventilation was limited by emphysema and fixity of the thoracic cage, the skin, and the subcutaneous tissues , movement, air-entry, and resonance were impaired at the left base, and fine râles were heard in both lower lobes The heart was a little enlarged, its sounds were normal, and there were no murmurs, but extrasystoles were noted, the blood pressure was 112/80 mm Hg The tongue was furred but otherwise normal , there was no pigmentation of the buccal mucous membrane Abdominal examination was negative, and the testes normal

A provisional diagnosis of scleroderma was made, and this was later confirmed by skin biopsy Investigation showed

Blood-count —Red cells 5 000 000, Hb 86% colour index 0 86 white cells 12 500 polymorphs 68% eosinophils 1%, monocytes 2% lymphocytes 28%, basophils 1%

Erythrocyte sedimentation rate —27 mm in first hour

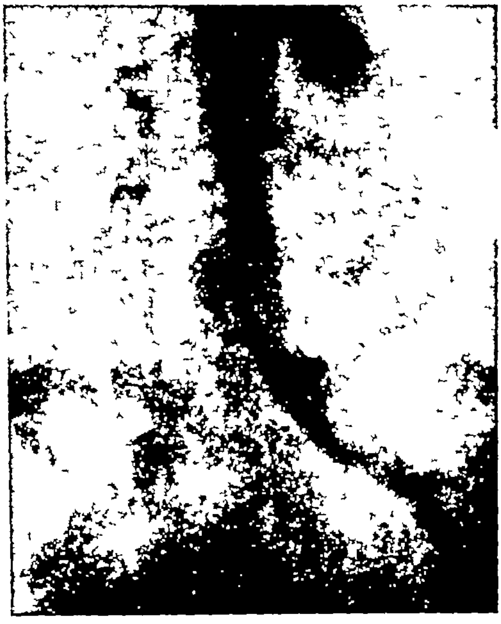


Fig 2 (April 9, 1948)—Barium swallow Achalasia of cardia. Slight general dilatation of œsophagus which is distended with air

Plasma proteins —Total 7 5 g per 100 ml Albumin 4 4 globulin 3 1 Albumin globulin ratio 1 4 1 0

Blood cholesterol —128 mg per 100 ml

Plasma chlorides —590 mg NaCl per 100 ml

Blood urea —26 mg per 100 ml

Radiography of the chest (fig 1) showed emphysema and chronic bronchitis with dense shadows at both bases, particularly the right Slight general enlargement of both ventricles was evident , the aorta was unfolded and atheromatous A barium swallow (fig 2) showed achalasia of the cardia and slight general enlargement of the œsophagus the appearances suggested chronic œsophagitis Radiography of the hands revealed nothing abnormal Electrocardiography showed sinus rhythm , rate 60 , ventricular extrasystoles , left axis deviation , and some splintering but no widening of initial deflections , with T waves flat in all leads, inverted in lead III

On April 11 the patient developed a mild pyrexia, and two days later he complained of cough and abdominal pain with vomiting signs of basal bronchitis appeared, but resolved on penicillin therapy He became better in himself during the next few days, but on April 23 vomiting recommenced, and was accompanied by abdominal distension and absolute constipation paralytic ileus was diagnosed A course of acetylcholine and enemata relieved the obstructive symptoms, and general improvement followed again For almost a month he remained fairly well, having a good appetite and normal bowel actions , the only untoward incidents were bouts of dyspnœa and palpitation, almost certainly of emotional origin, and a further fall in blood pressure to 80/60 During this month an attempt was made to treat the scleroderma by massage and local applications to the hands, forearms, and chest , and with thyroid extract, gr $^1/_3$ b d , and dihydrotachysterol min 5 t d s He noticed an improvement in the resilience of the skin over his forearms and hands, but no objective changes were observed Moreover, in spite of symptomatic improvement, he continued to lose weight , for this reason thyroid medication was discontinued after two weeks

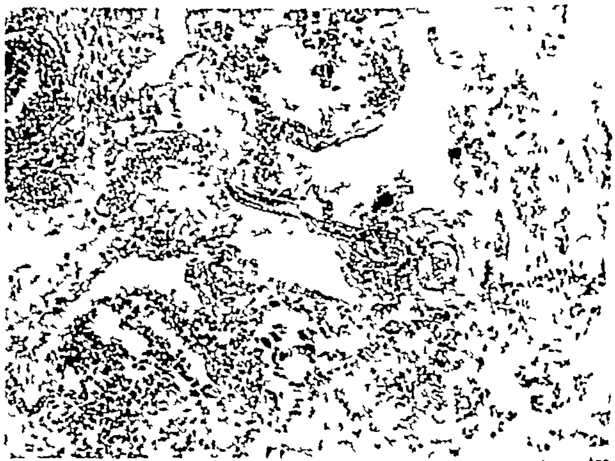


Fig 3—Section of lung (× 120) The vermiform object in the centre is a cotton fibre in the mounting medium

On June 27 the bowels again ceased to work, and two days later vomiting and hiccup with abdominal pain and distension returned Acetylcholine was given again but with little effect , he became progressively weaker, developed hypostatic pneumonia, and died on July 13

POST MORTEM FINDINGS

Macroscopic Appearances

Extreme emaciation Considerable pigmentation of skin Scleroderma of skin of fingers, hands, and lips Clubbing of toes and fingers

Brain normal Pituitary body very small Tongue, mouth, and neck normal Thyroid small but normal in appearance

Fine adhesions obliterated both pleural cavities Bilateral bronchiectasis of both lower lobes with confluent bronchopneumonia Heart weighed 9 oz Pericardial sac obliterated by fine adhesions Muscle wasted , yellowish in colour Valves normal save for some atheroma at base of mitral cusps, and small ulcerated areas on tricuspid valve Chordæ not thickened or shortened Aorta atheromatous, especially abdominal portion.

What factors determine the different courses taken are not clear The physical state of the material being absorbed may play a part, for, according to Frazer (1947), the neutral fat is absorbed in particulate form of 0 5 μ or less in diameter, whereas fatty acid is in the molecular state as a water soluble complex One might not be surprised that the neutral fat droplets should find their way into the readily permeable lymphatics, but it is difficult to see what prevents the appearance of the more freely diffusible fatty acids there Bloom et al. (1950) feeding C^{14} labelled fats to rats have recovered from thoracic duct fistulæ 58–85% of the isotope when given in neutral fat, and 70–92% when given in fatty acid. Further work is needed to clarify the relation of these findings to those of Frazer and to our observations

The Chylous Fluid

The fluid was odourless, milky white, and formed a delicate clot on standing A cream rose to the surface, especially in the specimens with a high content of fat Samples kept at room temperature without any preservatives showed no signs of bacterial growth even after several weeks The fluid contained polymorphs and lymphocytes but no red cells The total content of protein was 2 2–4 2 g per 100 ml , representing a loss of about 20 g a day from the body It is thus not surprising that signs of protein depletion with loss of weight and œdema sometimes appear as a result of chylothorax, especially if the leak is more complete than in the present case and if no steps are taken to supplement the diet

A chemical analysis of the lipid constituents of two specimens of fluid is given in the accompanying table

LIPID CONSTITUENTS OF CHYLE RECOVERED

Specimen	Free fatty acid titrated against standard alcoholic NaOH (factor 26 8) (mg per 100 ml)	Phospholipid (Hack 1947) (mg per 100 ml.)			Cholesterol (Bloor 1916) (mg per 100 ml)	Neutral fat (by difference) (g per 100 ml)	Total lipid (ether soluble fraction purified with petroleum ether) (g per 100 ml)
		Lecithins and cephalins	Sphingomyelin	Total			
1	214	233	32	265	120	2 12	2 72
2	100	206 5	35 5	242	155	1 35	1 85

The greater part of this is in the form of neutral fat and may vary within wide limits according to the consumption of fat by the individual On a greatly restricted intake of fat it may be reduced to 0 3 g % (Reiser 1937) Of interest is the unexpected concentration of fatty acid in the free titratable form Possibly this is an artefact derived from lipolysis of neutral fat on standing, although sampling and initial treatment took place in a very short time after the specimens were obtained An even higher concentration, 730 mg per 100 ml , has been found by other workers (Dittebrandt et al 1943) The remarkable resistance of chyle to infection is probably related to this high content of fatty acid The total amount of phospholipid falls within the normal concentration for plasma, as does the concentration of sphingomyelin Attempts to estimate the choline containing fraction by the reineckate method (Hack 1947) were abandoned owing to inconstant recoveries of choline reineckate from the same sample and from a standard solution of choline Although Swift and Neuhof (1946) have found the total cholesterol level low in comparison with normal plasma, this was no so in the specimens examined from this patient

SUMMARY

The effects of feeding fats stained with Sudan III were observed in a patient with non traumatic chylothorax

When stained neutral fat was given, a substantial amount of dye was recovered from the chylothorax, whereas, when the equivalent amounts of stained fatty acid and glycerol were given, no dye was recovered in one instance, and only a small amount in another

The findings support Frazer's hypothesis on the absorption of fat

An analysis of some of the lipid constituents of chyle was made

We wish to thank Dr John Green for his valuable assistance

REFERENCES

Bloom B Chaikoff I L Reinhardt, W O , Entenman, C , Dauben W G (1950) *J biol Chem* 184 1
Bloor W R (1916) *Ibid* 24 227
Dittebrandt, M. Todd W R West E S (1943) *Arch. Biochem* 2 429
Frazer A C (1943) *J Physiol.* 102 306
— (1946) *Physiol. Rev* 26 103
— (1947) *J Soc. chem Ind. Lond.* 66 379
Hack M H (1947) *J biol. Chem.* 169 137
Reiser J (1937) *Ibid* 120, 625
Sherlock, S , Walshe V (1946) *Clin. Sci* 6 113
Swift E A., Neuhof H (1946) *J thorac. Surg* 15 173
Yater W M (1935) *Ann. intern Med* 9 600

COLONIC REPLACEMENT OF THE STOMACH

JAMES MORONEY
M.B Lpool, F.R C.S
SURGEON BROADGREEN HOSPITAL LIVERPOOL, AND CLATTERBRIDGE GENERAL HOSPITAL, CHESHIRE

THIS is a preliminary account of a method of surgical treatment which I have devised for peptic ulcer and persistent post gastrectomy symptoms My objects in this paper are to set forth the principles on which it is based, and to give a short account of the evidence in support of the use of a tissue so far not employed in gastric surgery Of 22 patients (20 with peptic ulcer and 2 with post gastrectomy symptoms) submitted to operation, all have made satisfactory recoveries and all are very well The history of the treatment of peptic ulcer is strewn with similar accounts of such immediate success, and this optimism seems to be as characteristic as spontaneous remission of symptoms is characteristic of the disease For the final assessment of the value of treatment, careful follow up and the passage of time are necessary

EFFECTS OF SUBTOTAL GASTRECTOMY

Subtotal gastrectomy with removal of the pylorus is probably the most widely practised surgical measure for the relief of gastric and duodenal ulcer It gives the lowest proportion of recurrent or stomal ulceration, but this is none the less probably about 4% (*Lancet* 1950) Careful postoperative observation reveals such symptoms as failure to gain weight, fullness after a moderate sized meal and bilious vomiting, " dumping symptoms," and steatorrhœa, and various forms of malnutrition Post gastrectomy disabilities have been reported by Muir (1949) at some time in 75% of patients, and 34% were considerably handicapped Some patients (not many) are worse , others have exchanged ulcer symptoms for different symptoms Important, too, is the fact that after so radical an operation there can be no restoration of the *status quo ante*, and the field of surgical choice is limited, difficult, and uncertain

In addition to the secretion of an acid juice the stomach has other functions, among the most obvious of which are those of retaining a meal for some hours after eating, macerating it, and then passing it gradually to the duodenum After subtotal gastrectomy the gastric stump is usually anastomosed to the jejunum and the duodenal stump is closed The result is

1 The duodenum (10 in) and the greater portion of the first foot of jejunum are excluded from the food canal It is an established fact that there is a gradient of resistance in

diet except for the 14 hours before, and 24 hours after, the start of each test, when fat was withheld. Each experiment began in the morning 2 hours after a light fat-free breakfast. The pleural cavity was partially emptied before each experiment. A large collection might have exerted some back pressure on the ruptured vessel and reduced the flow of chyle, whereas complete evacuation would have rendered subsequent aspirations in the next few hours difficult. Each test dose was prepared by dissolving Sudan III 50 mg. in the fat and, after having made certain that no particles remained in suspension, administering this through a Ryle's tube.

Estimation of Sudan III

Solutions of 0.1, 0.2, 0.3, and 0.4 mg. per 100 ml. of Sudan III in chyle were prepared by adding 0.5, 1.0, 1.5, and 2.0 ml. of a 10 mg. per 100 ml. solution of Sudan III in ethyl alcohol to 50 ml. samples from a large collection of chyle removed before any dye had been given. These were evaporated to dryness at 60°C and the residues extracted for 6 hours in a Soxhlet apparatus with ether. The ether residues dissolved in 20 ml. of benzene served as standards.

Each collection of fluid was estimated separately for its dye content, a 50 ml. aliquot being taken within a short time of withdrawal, for, on standing, the stained fat separated to the top like cream, and after this had occurred it was difficult to re-establish a homogeneous mixture. After drying and ether extraction the ether residue was dissolved in 20 ml. of benzene and compared with the nearest standard in a visual colorimeter, an Ilford spectrum yellow-green (no. 605) filter being used.

EXPERIMENTS

Experiment 1. Oleic Acid and Glycerol

Specimens of chylous fluid were withdrawn from the thoracic cavity before, and 1, 2, 4, and 48 hours after, the administration of the mixture of 20 ml. of stained oleic acid (*B.P.*) and 5 ml. of glycerol. No staining took place in any of the specimens, so far as could be judged by direct inspection and by ether extraction, and it was concluded that little or no dye had reached the chylothorax.

Experiment 2. Neutral Fat

Immediately after the removal of the last unstained specimen in experiment 1, 20 ml. of stained olive oil was given. Staining of the chylous fluid was apparent 3 hours later, and 5 hours after the fat had been given 2.70 litres of pink chyle had been aspirated. After 3 days a further aspiration was done under fluoroscopic control to empty the pleural cavity completely of 3.54 litres of pink chyle. In all, 10.40 mg. of Sudan III was recovered.

Experiment 3. Oleic Acid and Glycerol (Repeat)

Experiment 1 was repeated in view of the persistent absence of dye from the chyle. This was done 6 days after the start of experiment 2. Since the original dose of fatty acid had produced some nausea, the 50 mg. of Sudan III was given dissolved in 10 ml. of oleic acid with 2.5 ml. of glycerol. On this occasion a preliminary specimen and specimens removed 2 and 4 hours afterwards were again unstained. At $6^{1}/_{3}$ hours the pleural cavity was emptied of 2.64 litres of unstained fluid under fluoroscopic control. At 8 hours the patient inadvertently received a quantity of neutral fat in the form of butter and an egg for his tea. Next morning only 390 ml. of fluid could be aspirated, but fluoroscopy was not used. The chyle was then definitely pink. After another 5 days the chest was emptied of a further 3 litres, which showed only the barest discernible trace of dye. The total amount of dye recovered during this period was 2.55 mg.

Any further experiment was rendered impossible by a change in the fluid. It had hitherto been typically chylous, but it had now become thin, slightly milky, and yellowish tinged with red owing to numerous red blood cells. A pleural reaction due to numerous paracenteses seemed to have developed. The fluid was, and remained, sterile on culture.

A week later thoracotomy was done, and a fatty fibrous layer covering the visceral and diaphragmatic pleural surfaces was removed. Subsequently the patient made a good recovery without any recurrence of chylothorax.

DISCUSSION

The hourly flow of lymph from the abdomen and lower extremities has been estimated at 60 to 100 ml. in man (Yater 1935), but there is no certainty that in any of the cases the total amount had been recovered. The volume collecting in our patient's pleural cavity averaged 600 ml. per 24 hours—i.e., considerably less than the smallest estimate for the total flow through the thoracic duct. It is well recognised that the thoracic duct passing upwards from the cisterna chyli may consist not of a single structure but of a ramification of several vessels which may, moreover, enter the venous system at different points. It seems likely that the anatomical arrangement was such in this case, and that the ruptured vessel transported only part of the chyle from the abdomen. If we take the recovery of dye in experiment 2 (21%) as an indication of the percentage of the neutral fat which passed through the affected vessel, the absorption and distribution of triglyceride fat seem mainly, though not necessarily wholly, to take place by the chylolymphatic route. Any not thus accounted for would, according to Frazer, constitute the hydrolysed fraction absorbed by the portal system.

Of greater significance perhaps are the results of the other two experiments. In experiment 1, when the patient received the approximate equivalent of the neutral fat given in experiment 2, in the form of the products of hydrolysis, no dye whatsoever reached the pleural cavity during the subsequent 48 hours, although chyle was accumulating there as usual. In experiment 3 a smaller dose of fatty acid was given. On this occasion a small quantity of Sudan III, considerably less than in experiment 2, was recovered from the chylothorax, but it arrived there later, somewhere between $6^{1}/_{3}$ and 24 hours after the ingestion of the stained fatty acid, whereas there was visible staining at 3 hours, and heavy staining at 5 hours in the experiment with neutral fat. Probably the neutral fat which the patient unfortunately ate for his tea 8 hours after the ingestion of the stained oleic acid dissolved some dye from the heavily stained oleic acid still remaining in the intestine, Sudan III being soluble in both types of fat. This would explain the presence of a small quantity of Sudan III in the effusion next morning, and the discrepancy between the first and the third experiments.

These findings could be criticised on the grounds that the leakage of chyle through the fistula may have been intermittent. However, during the 36 days' observation in hospital until the sudden change in type of effusion, aspirations were done on 18, and throughout this period the recovery remained constant at about 600 ml. a day. On no occasion was there a failure to obtain a substantial volume of fluid, such as might have been expected had the fistula been leaking intermittently.

If, as has for so long been generally accepted, complete hydrolysis were an essential preliminary to the absorption of any fat, one would expect about the same degree of staining of the chylous effusion to follow the ingestion of split as of unsplit fat. But the well-marked difference in staining of the chyle in the present experiments is in agreement with Frazer's work on feeding sudanised fats to rats, and supports his theory that the two kinds of fat are treated differently in the intestine and absorbed by different routes—the fatty acids via the portal circulation, and the neutral fat via the lymphatics.

ulcerative or inflammatory effects of gastric juice. Pfeiffer (1939) has shown that the diarrhœa in gastrojejunocolic fistula is due not to "gastric" irritation but to a small bowel enteritis from the passage of fæcal material into the jejunum.

Lastly, the pH of the colon is mildly to the acid side (6.5), suggesting that it might be more resistant than the jejunum.

There is very little experimental evidence of the effect of gastric juice on the colon, but what there is suggests that it is not unduly susceptible. In 1900 Reerink (Ivy et al. 1950) found that patch implants of the colon into the stomachs of dogs did not ulcerate. Dragstedt and Vaughan (1924) took a loop of a dog's colon (12 cm. long) with its blood supply intact, and opened it out as a flap. The flap was sewn into a large window in the stomach 1 in. from the pylorus. At the end of a year the colon was entirely normal macroscopically and microscopically.

MUCUS PROTECTION THEORY

One theory of the cause of peptic ulceration is that of diminished protection by mucus. Florey and Harding (1934) suggested as a result of experiments in five different species of animals that malfunctioning of Brunner's glands, which secrete mucus profusely in the duodenum, may be responsible for duodenal ulcer. They showed, too, that the duodenum is the most resistant portion of the small intestine because of the mucous secretion of Brunner's glands. The vagus is the secretory nerve to Brunner's glands as well as to the stomach, but nervous secretion is, of course, only one phase in their secretory activities.

Florey et al. (1941) state that the colonic mucosa can maintain a layer of mucus on its surface and can vary its thickness by secretion or reabsorption according to the needs of the moment. The alkali content of colonic secretion is considerable, and probably has the function of neutralising acids produced by bacterial action. Wright et al. (1938) have shown that the interior of fæcal masses from the cat's colon has a pH as low as 4.8, but at the surface the pH is 7.

Ivy et al. (1950), summarising the evidence of the protective action of mucus in the prevention of autodigestion of the stomach, state:

> "… the difference in resistance of the epithelium of the stomach to HCl-pepsin is undoubtedly chiefly due to the continuous layer of mucus-secreting epithelium possessed by the stomach and not by the duodenum and jejunum. The greater resistance of the duodenum compared to the jejunum is due to the scarcity of mucous glands in the latter."

OPERATIVE PROCEDURE

The following anatomical and physiological findings are relevant to the operation described below.

1. The pylorus admits the tip of the little finger, but beyond the pylorus the duodenum is the widest portion

TABLE I—RECORDS OF 20 CASES OF GASTRIC RECONSTRUCTION FOR PEPTIC ULCERATION

Case no.	Sex and age	Duration of symptoms (years)	Previous medical treatment	Complications of ulcer	Lesion at operation	Remarks
1	M 40	4	3 years	Nil	G.U.	Healed tuberculosis chest; right nephrectomy for tuberc. 4 years ago. Gained 1 st. in 2 mths; very well and gaining weight 3 mths later
2	M 49	10	Never strict	Nil	Anterior and posterior D.U.	5 lb. above preop. weight at 3 mths
3	M 63	4	Some	Nil	Two ulcers on lesser curvature	Preop. weight gained at 3 mths
4	F 51	20	Strict 2 years	Nil	Chronic posterior D.U. penetrating pancreas	Long loop. Stomach slow at first but much better at 2 mths. Gaining weight rapidly at 3 mths
5	M 54	8–10			Posterior D.U. penetrating pancreas	
6	M 45	15	10 years	Perforation 9 years ago; admitted with hæmatemesis	Chronic D.U.; pyloric stenosis	Long loop. Enormous appetite; rapid gain in weight
7	M 37	10	10 years	Ulcer leak	G.U.	Rapid gain in weight
8	M 40	22	For years		Anterior and posterior D.U. penetrating pancreas	
9	F 66	2	2 years	Hæmatemesis	G.U.	
10	M 52	30	Several years	Nil	Anterior D.U. penetrating liver	
11	M 24	13	5 years	Nil	Chronic D.U.	Orphan living in lodgings. Gross loss of weight preoperatively
12	M 50	30	9 years since gastrojejunostomy	Jejunal ulcer	Large jejunal ulcer; D.U.	
13	M 34	7	5 years		Chronic D.U. and G.U.	
14	M 48	2	Some months	Nil	Anterior and posterior D.U.	
15	F 64	2	Nil	Hæmatemesis	Anterior D.U. and posterior G.U.	Admitted with hæmatemesis
16	F 60	4	4 years	Hæmatemesis and melæna 2 years ago		Admitted with severe hæmatemesis
17	M 29	6	4 years	Perforation 3 years ago followed by subphrenic abscess	Anterior D.U. penetrating liver; posterior D.U. penetrating pancreas; pyloric stenosis	Gunshot wound of liver 1943; F.B. still present. Only single layer of sutures possible at colodnodenal anastomosis posteriorly. Gaining weight; condition excellent 6 weeks later
18	M 45	10–15	10 years	Perforated while under medical treatment immediately preoperatively	Prepyloric ulcer and D.U. penetrating pancreas	
19	M 39	6	Never kept to diet	Ulcer leak	Posterior D.U.	
20	M 52	11	4 years diet	Perforation 4 years ago	Large prepyloric ulcer	

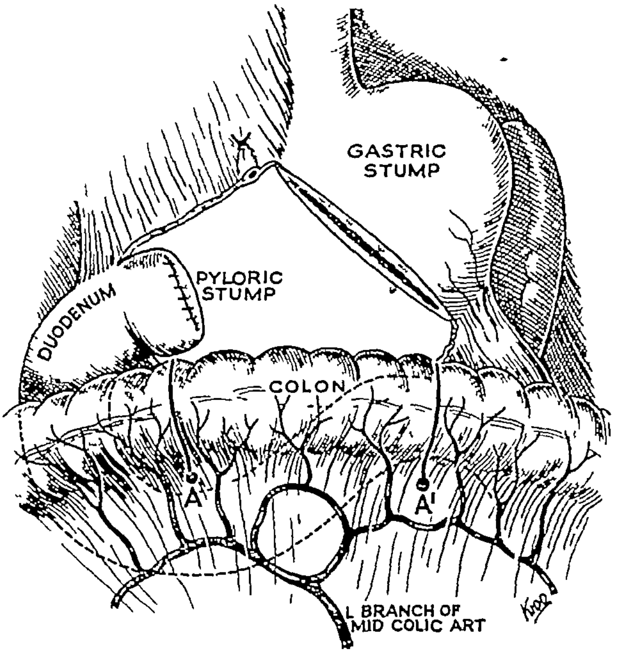


Fig 1—Extent of gastric resection The pylorus is removed separately after insertion of the posterior seromuscular coloduodenal suture A, A¹: sites of division of colon and transverse mesocolon

the small intestine to acid chyme, and that this is highest in the duodenum and lowest in the terminal ileum The upper jejunum is chosen as the point of anastomosis, not because it is the most resistant but because gastroduodenal anastomosis is usually not possible without (*a*) limiting the amount of stomach resected, (*b*) difficult and dangerous mobilisation of the duodenum

2 Masticated food untreated and unmixed with pancreatic juice, bile, and high intestinal juice, is passed directly into the second foot of the jejunum Rapid emptying of the small intestine is common after gastrectomy Iron is absorbed in the duodenum and higher jejunum, so it is not surprising that microcytic anæmia is not uncommon, particularly as rapid emptying of the stomach is almost the rule

3 Fatal leakage of the blind duodenal stump may occur in the immediate postoperative period if there is distension of the duodenum from obstruction at the anastomosis The most experienced gastrectomists confess to this mishap as an occasional cause of fatality

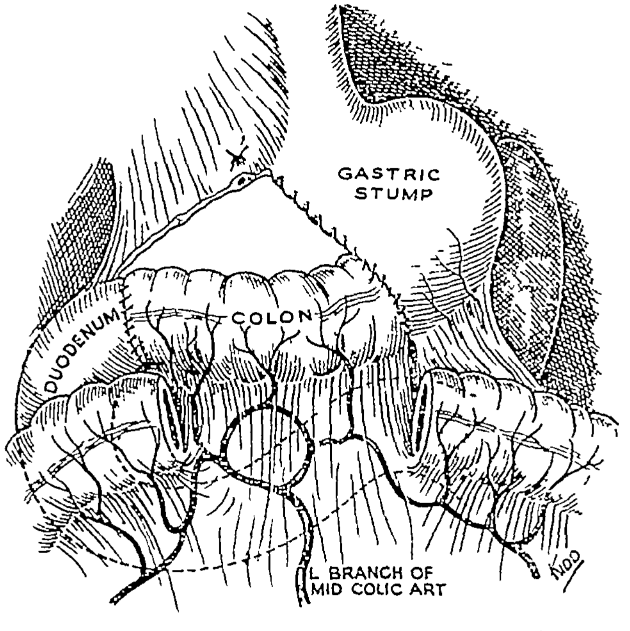


Fig 2—Gastrocolic and coloduodenal anastomoses completed

The perfect operation is one which reduces acidity sufficiently to prevent recurrent or stomal ulceration, and interferes little or not at all with the functions of the stomach and duodenum Subtotal gastrectomy satisfies the first of these criteria but ignores the latter

PROPERTIES OF COLONIC MUCOSA

For some years I have been interested in finding a method by which the acid reducing effect of subtotal gastrectomy could be achieved without unduly reducing the stomach's capacity, while retaining the normal process of the stomach emptying by the duodenum This is technically possible in some degree at least, if the colon is as resistant to gastric juice as I have reason to believe it is If it is only as resistant as the jejunum, the operation would still be justifiable having regard to other considerations

Nearly five years have passed since I operated on a man with a gastrojejunocolic fistula, too ill to be treated by any method but division of the transverse colon on either side of the fistula and invagination of the colonic ends into the stomach The continuity of the colon was restored by end to end suture (Moroney 1948)

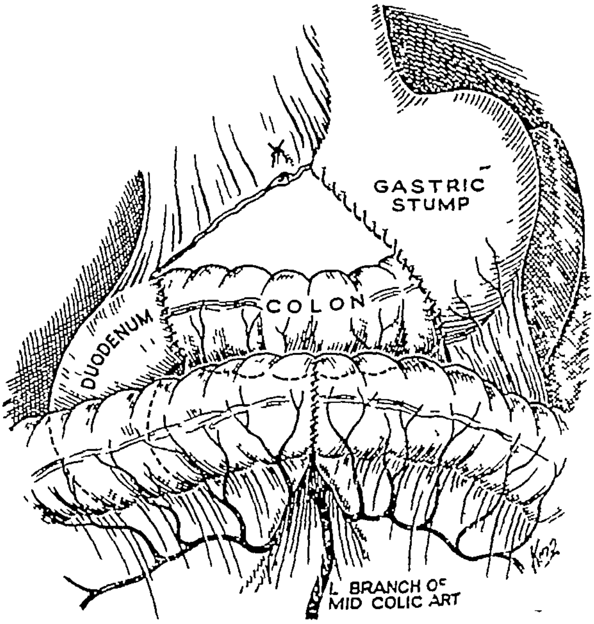


Fig 3—Operation completed

This patient has since remained well, and the two colonic loops in his stomach have not ulcerated, although they have been exposed to a juice which had "caused" a duodenal ulcer, and subsequently a jejunal ulcer sufficiently severe to perforate the colon The jejunal ulcer, too, has healed, and the original duodenal ulcer has not been reactivated It would appear that the colonic implants have had a beneficial effect, probably because of their profuse mucous secretion, which is an excellent buffer of acid

Wilkie (1934) first practised colonic exclusion in a case of gastrocolic fistula from a gastric ulcer At a second operation eleven weeks later he noted that the colonic loops in the stomach were practically empty and pale, they certainly were not inflamed or ulcerated. The only other case similar to my own was described by Eggers (1939) His patient remained quite well for some years, but had a recurrence at the site of his original lesion in the duodenum with acute perforation, later carcinoma of the ascending colon was successfully resected, and there were no further ulcer symptoms

I have previously observed—and have since confirmed this in 2 cases of gastrojejunocolic fistula—that the colonic mucosa in these patients is singularly free from ulcerative or inflammatory effects of gastric juice Pfeiffer (1939) has shown that the diarrhœa in gastro jejunocolic fistula is due not to "gastric" irritation but to a small bowel enteritis from the passage of fæcal material into the jejunum

Lastly, the pH of the colon is mildly to the acid side (6 5), suggesting that it might be more resistant than the jejunum

There is very little experimental evidence of the effect of gastric juice on the colon, but what there is suggests that it is not unduly susceptible In 1900 Reerink (Ivy et al 1950) found that patch implants of the colon into the stomachs of dogs did not ulcerate Dragstedt and Vaughan (1924) took a loop of a dog's colon (12 cm long) with its blood supply intact, and opened it out as a flap The flap was sewn into a large window in the stomach 1 in. from the pylorus At the end of a year the colon was entirely normal macroscopically and microscopically

MUCUS PROTECTION THEORY

One theory of the cause of peptic ulceration is that of diminished protection by mucus Florey and Harding (1934) suggested as a result of experiments in five different species of animals that malfunctioning of Brunner's glands, which secrete mucus profusely in the duodenum, may be responsible for duodenal ulcer They showed, too, that the duodenum is the most resistant portion of the small intestine because of the mucous secretion of Brunner's glands The vagus is the secretory nerve to Brunner's glands as well as to the stomach , but nervous secretion is, of course, only one phase in their secretory activities

Florey et al. (1941) state that the colonic mucosa can maintain a layer of mucus on its surface and can vary its thickness by secretion or reabsorption according to the needs of the moment The alkali content of colonic secretion is considerable, and probably has the function of neutralising acids produced by bacterial action Wright et al. (1938) have shown that the interior of fæcal masses from the cat's colon has a pH as low as 4 8, but at the surface the pH is 7

Ivy et al. (1950), summarising the evidence of the protective action of mucus in the prevention of auto digestion of the stomach, state

> "the difference in resistance of the epithelium of the stomach to HCl pepsin is undoubtedly chiefly due to the continuous layer of mucus secreting epithelium possessed by the stomach and not by the duodenum and jejunum The greater resistance of the duodenum compared to the jejunum is due to the scarcity of mucous glands in the latter "

OPERATIVE PROCEDURE

The following anatomical and physiological findings are relevant to the operation described below

1 The pylorus admits the tip of the little finger, but beyond the pylorus the duodenum is the widest portion

TABLE I—RECORDS OF 20 CASES OF GASTRIC RECONSTRUCTION FOR PEPTIC ULCERATION

Case no	Sex and age	Duration of symptoms (years)	Previous medical treatment	Complications of ulcer	Lesion at operation	Remarks
1	M 40	4	3 years	Nil	G U	Healed tuberculosis chest right nephrectomy for tuberc. 4 years ago Gained 1 st. in 2 mths very well and gaining weight 3 mths later
2	M 49	10	Never strict	Nil	Anterior and posterior D U	5 lb above preop weight at 3 mths
3	M 63	4	Some	Nil	Two ulcers on lesser curvature	Preop. weight gained at 3 mths
4	F 51	20	Strict 2 years	Nil	Chronic posterior D U penetrating pancreas	Long loop Stomach slow at first but much better at 2 mths Gaining weight rapidly at 3 mths
5	M 54	5–10			Posterior D U penetrating pancreas	
6	M 45	15	10 years	Perforation 9 years ago admitted with hæmatemesis	Chronic D U pyloric stenosis	Long loop Enormous appetite rapid gain in weight
7	M 37	10	10 years	Ulcer leak	G U	Rapid gain in weight
8	M 40	22	For years		Anterior and posterior D U penetrating pancreas	
9	F 66	2	2 years	Hæmatemesis	G U	
10	M 52	30	Several years	Nil	Anterior D U penetrating liver	
11	M 24	13	5 years	Nil	Chronic D U	Orphan living in lodgings Gross loss of weight preoperatively
12	M 50	30	9 years since gastrojejunostomy	Jejunal ulcer	Large jejunal ulcer D U	
13	M 34	7	5 years		Chronic D U and G U	
14	M 48	2	Some months	Nil	Anterior and posterior D U	
15	F 64	2	Nil	Hæmatemesis	Anterior D U and posterior G U	Admitted with hæmatemesis
16	F 60	4	4 years	Hæmatemesis and melæna 2 years ago		Admitted with severe hæmatemesis
17	M 23	6	4 years	Perforation 3 years ago followed by subphrenic abscess	Anterior D U penetrating liver posterior D U penetrating pancreas pyloric stenosis	Gunshot wound of liver 1943 F B still present Only single layer of sutures possible at coloduodenal anastomosis posteriorly Gaining weight condition excellent 6 weeks later
18	M 45	10–15	10 years	Perforated while under medical treatment immediately preoperatively	Prepyloric ulcer and D U penetrating pancreas	
19	M 39	6	Never kept to diet	Ulcer leak	Posterior D U	
20	M 52	11	4 years diet	Perforation 4 years ago	Large prepyloric ulcer	

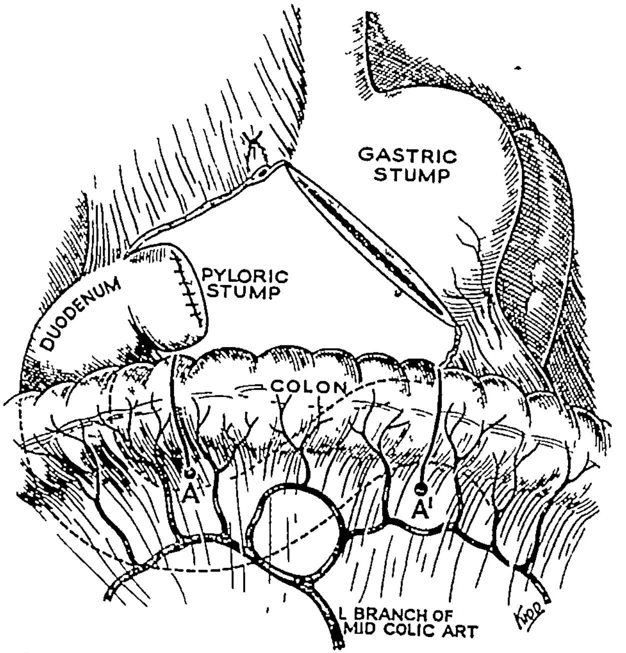


Fig 1—Extent of gastric resection The pylorus is removed separately after insertion of the posterior seromuscular coloduodenal suture A A^1: sites of division of colon and transverse mesocolon

the small intestine to acid chyme, and that this is highest in the duodenum and lowest in the terminal ileum The upper jejunum is chosen as the point of anastomosis, not because it is the most resistant but because gastroduodenal anastomosis is usually not possible without (*a*) limiting the amount of stomach resected, (*b*) difficult and dangerous mobilisation of the duodenum

2 Masticated food untreated and unmixed with pancreatic juice, bile, and high intestinal juice, is passed directly into the second foot of the jejunum Rapid emptying of the small intestine is common after gastrectomy Iron is absorbed in the duodenum and higher jejunum, so it is not surprising that microcytic anæmia is not uncommon, particularly as rapid emptying of the stomach is almost the rule

3 Fatal leakage of the blind duodenal stump may occur in the immediate postoperative period if there is distension of the duodenum from obstruction at the anastomosis The most experienced gastrectomists confess to this mishap as an occasional cause of fatality

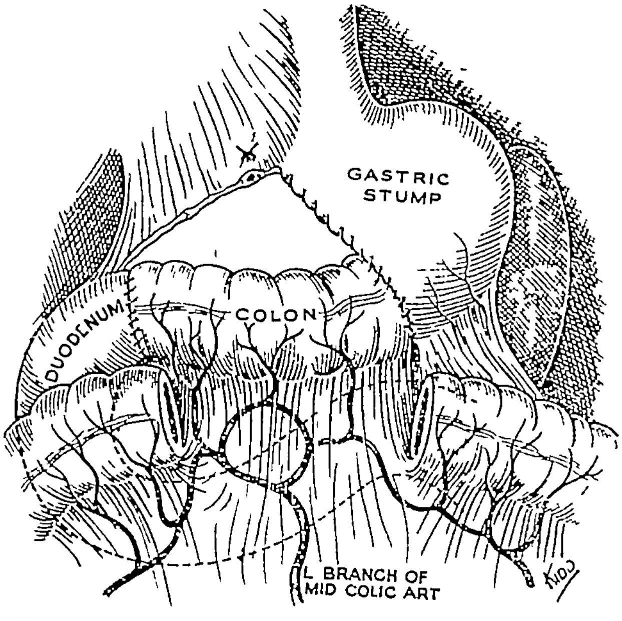


Fig 2—Gastrocolic and coloduodenal anastomoses completed

The perfect operation is one which reduces acidity sufficiently to prevent recurrent or stomal ulceration, and interferes little or not at all with the functions of the stomach and duodenum Subtotal gastrectomy satisfies the first of these criteria but ignores the latter

PROPERTIES OF COLONIC MUCOSA

For some years I have been interested in finding a method by which the acid reducing effect of subtotal gastrectomy could be achieved without unduly reducing the stomach's capacity, while retaining the normal process of the stomach emptying by the duodenum This is technically possible in some degree at least, if the colon is as resistant to gastric juice as I have reason to believe it is If it is only as resistant as the jejunum, the operation would still be justifiable having regard to other considerations

Nearly five years have passed since I operated on a man with a gastrojejunocolic fistula, too ill to be treated by any method but division of the transverse colon on either side of the fistula and invagination of the colonic ends into the stomach The continuity of the colon was restored by end to end suture (Moroney 1948)

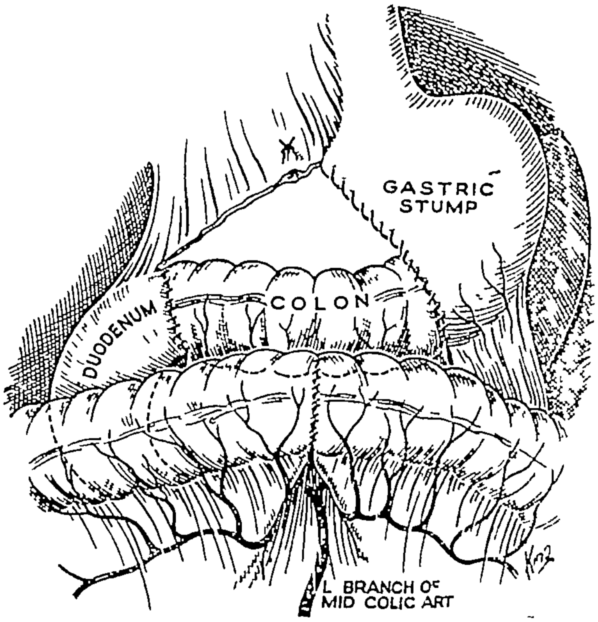


Fig 3—Operation completed

This patient has since remained well, and the two colonic loops in his stomach have not ulcerated, although they have been exposed to a juice which had "caused" a duodenal ulcer, and subsequently a jejunal ulcer sufficiently severe to perforate the colon The jejunal ulcer, too, has healed, and the original duodenal ulcer has not been reactivated It would appear that the colonic implants have had a beneficial effect, probably because of their profuse mucous secretion, which is an excellent buffer of acid

Wilkie (1934) first practised colonic exclusion in a case of gastrocolic fistula from a gastric ulcer At a second operation eleven weeks later he noted that the colonic loops in the stomach were practically empty and pale, they certainly were not inflamed or ulcerated. The only other case similar to my own was described by Eggers (1939) His patient remained quite well for some years, but had a recurrence at the site of his original lesion in the duodenum with acute perforation, later carcinoma of the ascending colon was successfully resected, and there were no further ulcer symptoms

I have previously observed—and have since confirmed—this in 2 cases of gastrojejunocolic fistula—that the colonic mucosa in these patients is singularly free from

THE NATURE OF AUTO-AGGLUTININS

G W G Bird
M.B Madras
LIEUT COLONEL, ARMY MEDICAL CORPS, OFFICER IN CHARGE, BLOOD TRANSFUSION DEPARTMENT, ARMED FORCES MEDICAL COLLEGE, POONA, INDIA

SERUM obtained from a woman with acquired hæmolytic anæmia of unknown ætiology, and belonging to group AB (as determined by testing fresh cells thoroughly washed with isotonic saline solution at 56°C) contained non specific "cold" agglutinins (Landsteiner and Levine 1926) active at room temperature against groups O, A, and B, and the patient's own cells

The patient had never been transfused but had been pregnant twice Her first child had died at the age of 5 days, no intelligent description of its illness could be obtained The second child (group AB) is now aged 9 months and has always been in good health The patient's husband is group B No Rh antibodies were present in her serum

The non specific agglutinins were completely absorbed by the patient's own cells and ceased to agglutinate O, A, and B cells as well

Another sample of the patient's serum was absorbed with O cells till they were no longer agglutinated Activity against A, B, and the patient's own cells persisted The serum was next absorbed with A cells till they were no longer agglutinated Activity against B and the patient's own cells persisted, Finally, the serum was absorbed with B cells till they were no longer agglutinated The activity against the patient's own cells persisted, though the reaction was weak

The "non specific" agglutinins present in the serum seem to be a combination of agglutinins consisting of anti O, anti A, anti B, and anti own cell components The patient's cell antigens therefore seem to consist of A, B (the patient was group AB), O, and at least a fourth component This would explain why all agglutinin components were absorbed by the patient's cells but were removed specifically by O, A, and B cells

The titre and thermal amplitude of the various antibody components detected are shown in the accompanying table

Antibody component	Titre at 4 C	Highest temperature at which active (up to 37 C)
Anti O	128	37 C
Anti A	128	37 C
Anti B	16	30 C
Anti-own cell	8	30 C

It was found that A and B group specific substance could also absorb the anti A and anti B components respectively

Attempts to split off the absorbed agglutinins by the method of Landsteiner, as described by Schiff and Boyd (1942), were unsuccessful However, Schiff and Boyd state that failure is common and should not be considered a contradiction of a successful absorption experiment

Owing to the lack of a sufficiently large panel of typed cells it was impossible to determine whether the anti O component of the serum was true anti O or the anti H of Morgan and Watkins (1948), or to identify the antibody remaining after absorption with O A, and B cells

Seven sera of group AB containing auto agglutinins acting only in the cold were examined Absorptions were done in the cold, and the separation of serum effected with a refrigerated centrifuge In all seven sera anti O, anti A and anti B components were detected, though the anti own cell component was not demonstrable

DISCUSSION

The suggestion of Dockeray and Sachs (1941) that an anti O agglutinin present in certain sera may be responsible for auto agglutination seems to be correct, though not wholly so

Stratton (1943) could attribute auto agglutination to anti O activity in three cases but not in two others in one of the latter all cells were agglutinated with almost equal intensity, whereas the other showed slightly greater activity against O cells Multiple specific antibodies may explain his findings

Possibly the non specific and specific cold agglutinins encountered together in two sera by Boorman et al (1946) and in a case previously examined by me represent incompletely investigated examples of similar cases

The thermal amplitude of an auto agglutinin in respect of O cells, "compatible" A or B cells from the iso-agglutinin point of view, and the individual's own cells, has been observed often to be different in each case Multiple specific antibodies would explain this fact The suggestion of Bialosuknia and Hirszfeld (1923), that different cold agglutinins come into action, at different temperatures, seems to be justified However, these workers have not defined the exact nature of these agglutinins

Auto agglutinins belong to the γ globulin fraction of the serum (Stats et al 1943), a different fraction from that to which the iso agglutinins belong (Cohn 1947) They are probably of immune origin, their production being stimulated by the broken down stromata of red cells, or by various diseases—e g, virus pneumonia

The fact that auto agglutinins may have specific action against ABO antigens is possibly definite proof that there are two types of ABO antibodies Two types of Rh antibodies are known to exist (Wiener 1948), but the possible presence of two kinds of ABO antibodies has so far only been inferred or demonstrated indirectly (Wiener et al 1949)

I am grateful to Dr A E Mourant for his perusal of the original draft and for many helpful suggestions, to Mr K K Gopal Pillai for technical assistance, to the National Chemical Laboratory, Poona, for use of their refrigerated centrifuge, and to the Director General, Armed Forces Medical Services, India, for permission to publish

REFERENCES

Bialosuknia W Hirszfeld L (1923) cited by Riddel V (1939) Blood Transfusion London
Boorman K E Dodd, B E Loutit J F Mollison, P L (1946) *Brit med J* 1, 751
Cohn E J (1947) *Ann intern Med* **26**, 341
Dockeray G C Sachs H (1941) *J Path Bact* **52** 203
Landsteiner K, Levine P (1926) *J Immunol* **12** 441
Morgan, W T J, Watkins W M (1948) *Brit J exp Path* **29** 159
Schiff F Boyd W C (1942) Blood Grouping Technic New York
Stats, D Perlman E Bullowa J G M Goodkind R (1943) *Proc Soc exp Biol N Y* **53** 188
Stratton F (1943) *Lancet* i 613
Wiener A S (1948) *Ann Allergy* **6** 293
— Wexler I B Hurst J G (1949) *Blood* **4** 1014

BACILLÆMIA DUE TO SHIGELLA SONNEI

REPORT OF A CASE

P Tatham
M.B Lond
HOUSE PHYSICIAN

T Pearse Williams
M D Lond, F.R C P
PHYSICIAN

G T Stewart
M D Glasg
PATHOLOGIST

PADDINGTON GREEN CHILDREN'S HOSPITAL, LONDON

BACILLÆMIA due to *Shigella shigæ* or to *Sh flexneri* is well recognised though rare, but we have been unable to find any record of bacillæmia due to *Sh sonnei* since 1914, when this organism was first isolated

Felsen (1945) reviewing published reports from 1900, found 34 cases of bacillæmia in Shigella infections, but not one of them was due to *Sh sonnei*

High fever is unusual in Sonne dysentery, and the clinical state of the patient seldom indicates any need for of the small intestine. The diameter is in most cases equal to that of the transverse colon.

2. Movements in the transverse colon are almost negligible apart from "mass movement," so that if it is utilised in a way that seems to be anatomically antiperistaltic this is not a serious matter, within limits; and this is proved by satisfactory emptying in my cases.

3. That the colon is very distensible is well known, but so is the duodenum. I operated on a man three years ago who had had a peculiarly low gastrectomy performed two months earlier; the duodenum was closed and an anastomosis with a very long loop to the jejunum had been made. Three hours after a high intestinal obstruction from volvulus of the stomal loops, he had a mass in the right hypochondrium almost the size of a fœtal head; and this, I confirmed at operation, was the distended duodenum.

4. A free loop of transverse colon can be cut without endangering its blood supply.

A preliminary course of medical treatment makes resection easier and safer. The colon is treated with succinylsulphathiazole, and the final colonic washout two hours before operation ensures an empty colon. A slow blood transfusion, begun at the start of the operation, prevents shock, and the patient returns to bed with a pulse of good volume and a rate of about 80–90 per min. A Ryle's tube is passed preoperatively.

A midline incision is usually satisfactory, but for reconstruction of a previous gastrectomy a double Kocher is the incision of choice. The stomach and pylorus are widely resected with excision of the ulcer. The insertion of the posterior coloduodenal seromuscular suture is easier if the stomach is divided to the left of the pylorus and closed as shown in fig. 1. After the insertion of this suture the pylorus and pyloric antrum are resected. A free loop of transverse colon with its blood supply intact is taken. One end is sutured to the duodenum with two layers of catgut, the other to the gastric stump (fig. 2). The optimum amount of colon to use, and the best method of anastomosis to the gastric stump, are still uncertain; in end-to-end anastomosis I have used between $2^1/_2$ in. and 5 in. In 4 cases a lateral anastomosis of the colon to the stomach was made and 7 in. was used.

The colonic continuity is restored by end-to-end anastomosis (fig. 3), and in the majority of cases no clamps are used on the colon or duodenum. It is usually unnecessary to tie any vessels in the transverse mesocolon. The abdomen is closed with a small corrugated rubber drain in the right hypochondrium, and 1 g. of streptomycin is injected down the Ryle's tube before the patient returns to bed.

Penicillin and streptomycin parenterally are begun on the day of operation and continued for five days. In only 3 out of 22 cases was the wound infected, and the infection was slight.

In all cases there is still the opportunity of excising the loop and performing a gastrojejunal anastomosis, or of making a short circuit from the "stomach mechanism" to the jejunum, should time show this to be necessary or desirable.

The records of 20 cases submitted to this operation are summarised in table I. A further 2 cases were operated on by this technique because of post-gastrectomy bilious vomiting.

Case 21.—Woman aged 48. Indigestion, 30 years. Subtotal gastrectomy for gastric ulcer 18 months ago, followed almost at once by bilious vomiting and loss of weight; 6 months later jejunal loops reversed with no improvement. Weight loss in 18 months, 3 st. Bilious vomiting, eating only bread and butter. Persistent hypochromic anæmia.

Colonic restoration of stomach. At 6 weeks able to eat anything for the first time in 30 years. Gaining weight. No vomiting.

Case 22.—Woman, aged 64. Perforation 4 years ago. Gastrectomy for duodenal ulcer 1 year ago; jaundice 6 months later. Weight loss in 1 year, 3 st. Bilious vomiting.

Colonic restoration of stomach; gall-bladder normal. Very comfortable at 1 month. Able to eat anything. Gaining weight. No vomiting.

Data on the 3 cases in which gastric reconstruction was not undertaken are given in table II.

TABLE II—DATA ON CASES IN WHICH GASTRIC RECONSTRUCTION WAS NOT UNDERTAKEN

Case no.	Age (yr.)	Lesion	Contra-indication	Operation
1	52	Duodenal ulcer	Diverticulitis of pelvic colon	Gastrectomy with gastrojejunal anastomosis
2	17	Acute hæmatemesis; gastric ulcer	Colon not prepared	As in case 1
3	65	Pyloric stenosis; cholelithiasis; myocarditis	Unnecessary	Gastrojejunostomy; cholecystectomy

All patients have had radiological examination with barium meals a month after operation, and some at three months. In the majority the "stomach mechanism" empties in 1–5 hours, though with longer loops emptying is slower; in some emptying is more rapid, but at three months the rate seems to be settling down to about $2^1/_2$–4 hours. The anastomoses are completely healed, and the mucosal pattern of the small intestine is "feathery"; emptying of the small bowel is not unduly quick. In 4 cases I have seen the colonic loop fill with barium, the loop contract with refilling of the stomach, and at the same time a trickle down the duodenum. This suggests that some maceration of food takes place as in the normal stomach.

Fractional test-meal (more likely to be of value in this type of anastomosis than others) shows complete achlorhydria, or very little acid, and excess of mucus. The glucose-tolerance curves are normal, and there is no evidence of steatorrhœa.

Clinically all patients have had complete relief of symptoms, and can eat larger meals than those who have had subtotal gastrectomy. The gain in weight has been steady. The earliest case is only in the fifth postoperative month.

CONCLUSION

This procedure is surgically a little more extensive, but physiologically much less destructive, than subtotal gastrectomy. It shows early promise that the function of the normal stomach may be largely preserved with consequently little or no interference with the function of the small intestine. At this early stage the value of this function cannot be assessed.

SUMMARY

After gastric resection there are advantages in restoring the food canal in continuity, and in providing a "stomach storage" mechanism.

A method of achieving this in man, using a free loop of transverse colon, is described. The colon is comparatively resistant to gastric juice.

Of 22 patients submitted to this operation all have survived. 20 were operated on because of peptic ulcer, and 2 because of post-gastrectomy bilious vomiting.

The longest postoperative follow-up is 5 months. Longer observation and further research are necessary for the evaluation of this technique.

REFERENCES

Dragstedt, L. R., Vaughan, A. M. (1924) *Arch. Surg.* 8, 791.
Eggers, C. (1939) *Ann. Surg.* 110, 667.
Florey, H. W., Harding, H. E. (1934) *J. Path. Bact.* 39, 255.
— Wright, R. D., Jennings, M. A. (1941) *Physiol. Rev.* 21, 10.
Ivy, A. C., Grossman, M. I., Bachrach, W. H. (1950) Peptic Ulcer. Philadelphia. pp. 98–105.
Lancet (1950) ii, 373.
Moroney, J. (1948) *Brit. J. Surg.* 35, 171.
Muir, A. (1949) *Ibid*, 37, 165.
Pfeiffer, D. B. (1939) *Ann. Surg.* 110, 659.
Wilkie, D. P. D. (1934) *Ibid*, 99, 401.
Wright, R. D., Florey, H. W., Jennings, M. A. (1938) *Quart. J. exp. Physiol.* 28, 207.

THE NATURE OF AUTO-AGGLUTININS

G W G Bird
M.B Madras
LIEUT COLONEL, ARMY MEDICAL CORPS, OFFICER IN CHARGE, BLOOD TRANSFUSION DEPARTMENT, ARMED FORCES MEDICAL COLLEGE, POONA, INDIA

Serum obtained from a woman with acquired hæmolytic anæmia of unknown ætiology, and belonging to group AB (as determined by testing fresh cells thoroughly washed with isotonic saline solution at 56°C) contained non specific "cold" agglutinins (Landsteiner and Levine 1926) active at room temperature against groups O, A, and B, and the patient's own cells

The patient had never been transfused but had been pregnant twice Her first child had died at the age of 5 days, no intelligent description of its illness could be obtained The second child (group AB) is now aged 9 months and has always been in good health The patient's husband is group B No Rh antibodies were present in her serum

The non specific agglutinins were completely absorbed by the patient's own cells and ceased to agglutinate O, A, and B cells as well

Another sample of the patient's serum was absorbed with O cells till they were no longer agglutinated Activity against A, B, and the patient's own cells persisted The serum was next absorbed with A cells till they were no longer agglutinated Activity against B and the patient's own cells persisted, Finally, the serum was absorbed with B cells till they were no longer agglutinated The activity against the patient's own cells persisted, though the reaction was weak

The "non specific" agglutinins present in the serum seem to be a combination of agglutinins consisting of anti O, anti A, anti-B, and anti own cell components The patient's cell antigens therefore seem to consist of A, B (the patient was group AB), O, and at least a fourth component This would explain why all agglutinin components were absorbed by the patient's cells but were removed specifically by O, A, and B cells

The titre and thermal amplitude of the various antibody components detected are shown in the accompanying table

Antibody component	Titre at 4 C	Highest temperature at which active (up to 37 C)
Anti O	128	37 C
Anti A	128	37 C
Anti B	16	30°C
Anti-own cell	8	30°C

It was found that A and B group specific substance could also absorb the anti A and anti B components respectively

Attempts to split off the absorbed agglutinins by the method of Landsteiner, as described by Schiff and Boyd (1942), were unsuccessful However, Schiff and Boyd state that failure is common and should not be considered a contradiction of a successful absorption experiment

Owing to the lack of a sufficiently large panel of typed cells it was impossible to determine whether the anti O component of the serum was true anti O or the anti H of Morgan and Watkins (1948), or to identify the antibody remaining after absorption with O, A, and B cells

Seven sera of group AB containing auto agglutinins acting only in the cold were examined Absorptions were done in the cold, and the separation of serum effected with a refrigerated centrifuge In all seven sera anti O, anti A and anti B components were detected, though the anti own cell component was not demonstrable

DISCUSSION

The suggestion of Dockeray and Sachs (1941) that an anti O agglutinin present in certain sera may be responsible for auto agglutination seems to be correct, though not wholly so

Stratton (1943) could attribute auto-agglutination to anti O activity in three cases but not in two others in one of the latter all cells were agglutinated with almost equal intensity, whereas the other showed slightly greater activity against O cells Multiple specific antibodies may explain his findings

Possibly the non specific and specific cold agglutinins encountered together in two sera by Boorman et al (1946) and in a case previously examined by me represent incompletely investigated examples of similar cases

The thermal amplitude of an auto agglutinin in respect of O cells, "compatible" A or B cells from the iso agglutinin point of view, and the individual's own cells, has been observed often to be different in each case Multiple specific antibodies would explain this fact The suggestion of Bialosuknia and Hirszfeld (1923), that different cold agglutinins come into action, at different temperatures, seems to be justified However, these workers have not defined the exact nature of these agglutinins

Auto agglutinins belong to the γ globulin fraction of the serum (Stats et al 1943), a different fraction from that to which the iso agglutinins belong (Cohn 1947) They are probably of immune origin, their production being stimulated by the broken down stromata of red cells, or by various diseases—e g, virus pneumonia

The fact that auto agglutinins may have specific action against ABO antigens is possibly definite proof that there are two types of ABO antibodies Two types of Rh antibodies are known to exist (Wiener 1948), but the possible presence of two kinds of ABO antibodies has so far only been inferred or demonstrated indirectly (Wiener et al 1949)

I am grateful to Dr A E Mourant for his perusal of the original draft and for many helpful suggestions, to Mr K K Gopal Pillai for technical assistance, to the National Chemical Laboratory, Poona, for use of their refrigerated centrifuge, and to the Director General, Armed Forces Medical Services, India, for permission to publish.

REFERENCES

Bialosuknia W Hirszfeld L (1923) cited by Riddel V (1939) Blood Transfusion London
Boorman K. E, Dodd, B E Loutit J F Mollison, P L (1946) *Brit med J* i 751
Cohn E J (1947) *Ann intern Med* 26 341
Dockeray G C, Sachs H (1941) *J Path Bact* 52 203
Landsteiner K Levine P (1926) *J Immunol* 12 441
Morgan W T J Watkins, W M (1948) *Brit. J exp Path* 29 159
Schiff F Boyd W C (1942) Blood Grouping Technic. New York
Stats D Perlman E Bullowa J G M Goodkind R (1943) *Proc Soc exp Biol N Y* 53 188
Stratton F (1943) *Lancet* i 613
Wiener A. S (1948) *Ann Allergy* 6 293
— Wexler I B Hurst J G (1949) *Blood* 4 1014

BACILLÆMIA DUE TO SHIGELLA SONNEI

REPORT OF A CASE

P Tatham
M.B Lond
HOUSE PHYSICIAN

T Pearse Williams
M.D Lond, F.R C.P
PHYSICIAN

G T Stewart
M.D Glasg
PATHOLOGIST

PADDINGTON GREEN CHILDREN'S HOSPITAL, LONDON

Bacillæmia due to *Shigella shigæ* or to *Sh flexneri* is well recognised though rare, but we have been unable to find any record of bacillæmia due to *Sh sonnei* since 1914, when this organism was first isolated

Felsen (1945), reviewing published reports from 1900, found 34 cases of bacillæmia in Shigella infections, but not one of them was due to *Sh sonnei*

High fever is unusual in Sonne dysentery, and the clinical state of the patient seldom indicates any need for blood culture in diagnosis. We have made blood cultures from seven children with Sonne dysentery and have had one positive result. In four of these cases the temperature was 102–104°F.

CASE RECORD

A boy, aged 2 years, was admitted on Dec. 17, 1950. Unwell during that morning, he had had a rigor in the afternoon and passed four unformed yellow stools. He was then admitted to hospital and shortly after passed an unformed stool, lost consciousness, and became cyanosed, rallying after a short interval. His temperature was 104°F and pulse-rate 140. He was not obviously dehydrated. A subcuticular whitlow was present on the right index finger. There were no other abnormal findings. Septicæmia was provisionally diagnosed and a blood culture made. During the next twenty-four hours the boy passed seven stools, each containing blood and mucopus. Thereafter he had one bowel movement daily. His temperature fell to normal next day, and his general condition improved gradually. No other member of the family of six was similarly ill.

Treatment.—The patient was given phthalyl sulphathiazole followed by chloramphenicol. The stools remained positive for *Sh. sonnei*. Succinyl sulphathiazole was then given, after which a negative rectal swab was obtained.

Investigations.—A non-motile gram-negative organism was isolated from the blood, fæces, and urine. This organism produced acid without gas in glucose and mannite with weak acidity in lactose and saccharose after forty-eight hours. No indole was produced. Saline suspensions of living and of heat-killed organisms from each of the three sources were agglutinated in a few hours at 55°C to a titre of 1:250 by standard *Sh. sonnei* antiserum. The patient's serum, a week after onset of the illness, agglutinated suspensions of standard *Sh. sonnei* and his own strain of the organism to titres of 1:250 and 1:200 respectively. Two successive periods of an hour's incubation at 37°C of mixed standard *Sh. sonnei* suspension (concentrated) and the patient's serum removed the agglutinins from the latter for the patient's organism. Reciprocal absorption (patient's organism with standard antiserum) removed the agglutinins against the standard suspension.

There can be little doubt that infection with *Sh. sonnei* produced in this child an unusually severe though brief illness due to invasion of the blood by the organism at the onset.

We are grateful to Mr. E. McHenry for technical assistance.

REFERENCE

Felsen, J. (1945) Bacillary Dysentery, Colitis and Enteritis. New York.

Medical Societies

RENAL ASSOCIATION

THIS association met in London on April 26, under the chairmanship of Dr. A. A. OSMAN.

KIDNEY AND CIRCULATORY SYSTEM

Prof. K. J. FRANKLIN suggested that, although he was confining his remarks to the blood circulatory system, the large size of the renal lymphatics should stimulate research workers to investigate more fully the physiological significance of these structures. He pointed out that the circulatory system and kidney function are closely inter-related. The kidney requires a sufficient and normally distributed blood-supply in order to function efficiently, while the circulatory system is profoundly influenced by renin and "vaso-excitor material" (V.E.M.), which are produced by ischæmic renal cortical tissue. We are ignorant, he said, of the possible effects of the modern so-called "hypotensive anæsthesia" on renal function during and after operation.

Turning to the influence of nervous impulses on the kidney, Professor Franklin said that until the work carried out at the Nuffield Institute for Medical Research during the period 1945–47 there was no indication that nervous impulses reaching the kidney did other than produce a generalised vasoconstriction throughout the kidney, although the morbid anatomical findings in symmetrical renal cortical necrosis, and Claude Bernard's mention of arterial streamlines in the renal veins, might have given an earlier clue to the true state of affairs.

Direct visual observation of events within the mammalian kidney is not possible. Hence indirect methods must be used. The inherent limitations of such techniques must be realised, and a rigorous appraisal made of the effect of operative procedures and of the validity of assumptions and mathematical calculations. Renal vasoconstriction in response to acute hypoxia is nervously mediated, and in Professor Franklin's view the interlobular arteries and their offshoots can constrict completely in response to stimulation which results in only partial occlusion of the main renal artery. Cineradiographic, radiological, and histological evidence supports the view that renal ischæmia involves the progressive occlusion of the interlobular arteries and their glomerular branches. The evidence suggests that this vasoconstriction affects the most peripherally situated vessels first and spreads through the renal cortex concentrically, from without inwards, as far as the basal glomeruli. During renal cortical ischæmia blood is diverted through the juxtamedullary (or "basal") glomeruli and the vasa recta system. Whether the medulla is congested or not depends on the balance between reduction in total renal inflow and reduction in cortical flow, and perhaps also on renal venous constriction.

Professor Franklin held that such terms as "greater circulation" and "lesser circulation" in connection with the renal vascular system are best avoided. He strongly deprecated the use of the terms "renal shunt" and "Oxford shunt" unless these are precisely defined.

In conclusion, he reviewed some experimental and clinical evidence suggesting that a diversion of blood from the renal cortex, similar to that observed experimentally, takes place in man under certain conditions—with exercise or dioxan poisoning, and as the ætiological factor in the symmetrical renal cortical necrosis associated with concealed accidental hæmorrhage.

RENAL CHANGES IN OBSTETRIC SHOCK

Dr. A. TELFORD GOVAN, who discussed renal changes in obstetric shock, divided his cases into four groups: (1) non-toxæmic cases with shock caused by such conditions as postpartum hæmorrhage, placenta prævia, or uterine rupture; (2) toxæmic cases, mostly with accidental hæmorrhage; (3) 10 cases of symmetrical cortical necrosis; and (4) 10 cases of "lower nephron nephrosis." From a study of the renal pathology in 120 fatal cases in the first group, he has found that where death takes place within the first two hours both cortex and medulla are pale and the vessels spastic; between two and three hours there is relative congestion of the medulla and deep glomeruli, and the cortical veins are full of blood; thereafter the cortical vessels appear to reopen patchily, polymorphs are numerous, and intertubular œdema sometimes develops. In 1 case with well-marked necrosis of the proximal convoluted tubule posterior pituitary extract was given repeatedly during the stage of shock.

In the second group the early renal changes are identical, but all stages are prolonged. After about ten hours vascular dilatation occurs, and this persists for up to forty hours. The cortex is swollen and the glomeruli grossly congested, their capsules being ballooned out by plasma. Some glomerular degeneration may take place. After twenty-four hours tubular necrosis is well marked, blood or hæmoglobin casts are common, and thrombi are found in the small arteries and glomeruli These changes indicate that damage may be caused by the vascular dilatation as well as the preceding spasm

With "lower nephron nephrosis" the early changes are similar After four days casts may be found in almost every tubule, but their number then diminishes, and the tubules show evidence of rapid repair Ballooning of the glomerular capsule is pronounced, and there are varying degrees of glomerular thrombosis and damage These lesions differ only in degree from those found in cortical necrosis, and Dr Govan feels that both syndromes have the same ætiology In addition, the earlier phases of both "lower nephron nephrosis" and symmetrical cortical necrosis can be seen in toxæmic cases of shock

Dr Ian MacGillivray spoke on the clinical aspects of renal dysfunction in obstetric shock In all cases of shock there is an immediate rise of blood urea Where this is not great there is usually only transient renal dysfunction, but the group in which there is a greater rise and a persistently low urine urea are almost all cases with a combination of concealed accidental hæmorrhage and toxæmia, and the shock lasts longer and oliguria persists even after recovery from the shocked state. Oliguria of more than three days' duration is of grave prognosis

Dr MacGillivray went on to discuss the clinical aspects of Dr Govan's cases of "lower nephron nephrosis" and cortical necrosis He suggested that the stimuli conducive to renal cortical necrosis in pregnancy are pre eclamptic toxæmia or sepsis, associated with shock The same factors occurred in the cases of "lower nephron nephrosis", but toxæmia alone can induce this condition, and those cases in which toxæmia and shock were present did not have both factors to a severe extent Of 4 non toxæmic cases with "lower nephron nephrosis," 3 had sepsis and shock, and the 4th had had an intra uterine injection of posterior-pituitary extract while in the shocked state All the cases of cortical necrosis had a well marked rise of temperature on the second or third day, unassociated with sepsis This fever was not present in the "lower nephron nephrosis" cases, except for 1 in which some degree of thrombosis of the renal cortical arterioles was found post mortem Dr MacGillivray suggested that the rise of temperature may be associated with massive thrombosis in the renal cortex He did not think hæmaturia reliable as a diagnostic criterion of cortical necrosis, because this was present also in his cases of "lower nephron nephrosis" He advised four hourly temperature charting, since the fever of cortical necrosis may be transient

Any shocked patient, especially with associated pre eclampsia, may develop a severe renal lesion and the blood urea is a better prognostic guide than the amount of urine passed Fatal renal lesions may be avoided by preventing shock, or treating it early, and oliguria persisting for more than three days is probably best treated with limitation of fluids and a protein free diet

SPINAL ANÆSTHESIA AND THE KIDNEY

Dr A H Galley recalled that chloroform lowers the systemic blood pressure and reduces the glomerular filtration rate, and that ether stimulates the neuro hypophysis Soda lime, as used in closed circuit anæsthesia, is not a completely efficient carbon dioxide absorbent In the presence of reduced pulmonary ventilation during closed circuit anæsthesia, enough carbon dioxide might accumulate to cause diversion of blood from the periphery of the renal cortex This danger can be overcome by intermittently squeezing the anæsthetic bag

In view of some recent work by Professor Franklin and his colleagues Dr Galley felt that spinal anæsthesia might influence renal function by abolishing the effects of stimulation of the chemoreceptor centres in the spinal cord which are responsible for the renal circulatory responses to hypoxia and hypercapnia In addition, the hypotension and hypoventilation which result from spinal anæsthesia are disadvantageous from the point of view of their possibly adverse effects on renal function

Therapeutically, spinal analgesia is a supplementary measure in the treatment of a number of conditions, including hypertensive encephalopathy in pregnancy Dr Galley concluded with a plea for its application as soon as possible after the decision has been made to enlist the help of the anæsthetist

---

Reviews of Books

Insects and Hygiene

James R Busvine, ph.d, d sc, Department of Entomology, London School of Hygiene and Tropical Medicine London Methuen 1951 Pp 482 30s

Insects do not play the overwhelming part in public health in this country which they do in tropical lands, nor is the visible destruction in the home as spectacular as that achieved by termites, for instance, in warmer climates But the fact remains that we have a very large number of insect pests of greater or less importance to medicine, commerce, and domestic life At one time or another they force themselves upon the notice of the medical officer of health, the sanitary inspector, and every applied entomologist who has to do with warehouses or private homes or the many trade processes vulnerable to insects Dr Busvine sets out to provide a complete compendium of the information required to cope with these pests, starting with a straightforward account of the structure and classification of insects, their anatomy and physiology, and the general principles of their ecology Chapters follow dealing with the general principles of insect control and its organisation, and the theory and uses of insecticides The insects themselves are dealt with on a practical ecological basis houseflies and blowflies, the blood-sucking flies, the arthropod parasites of the human body, pests of foodstuffs, refuse and sewage, clothes moths and carpet beetles, wood-boring beetles, stinging and biting insects, and various nuisances Technical appendices include keys to most of the insects, and information about the more important insecticides, and references and a good index complete a book that is both comprehensive and practical

James Lind Founder of Nautical Medicine

Louis H Roddis, captain, Medical Corps, U S Navy New York. Henry Schuman. 1950 Pp 177 $3

The reading of biographies of certain naval heroes —admirals all—tends to become a weariness of the flesh It is a pleasant change, therefore, to turn to the biography of a naval surgeon and to find there a better balanced picture of old-time sea life, where battles were only occasional and sickness unfortunately occurred every day of the week. The battle against disease at sea in the 18th century was particularly hard, and since people are always ready to read of a good fight, Captain Roddis has told again the story of James Lind, M D, of Edinburgh, who took such a prominent part in it

Lind went to sea in 1739, remaining there until 1748 when he returned to Edinburgh In 1753 he published his *Treatise on the Scurvy* and four years afterwards *An Essay on Preserving the Health of Seamen in the Royal Navy* These two books helped him to the appointment of physician in charge of the new Royal Naval Hospital Haslar in 1758 Here he wrote his third book, *Essay on Diseases Incidental to Europeans in Hot Climates* His *Treatise on the Scurvy* added to the long record of the experiences of seamen and earlier surgeons a note of his experiments in the *Salisbury* 50 guns in 1748, which led him to conclude that lemon or orange juice was a rapid, sure and simple cure for the disease and a preventive Captain Cook, as we all know put Lind's ideas into practice with splendid results

It is perhaps worth noting that though Henry VIII did much for the Navy, he did not build its first ship in 1488 (his acces sion was in 1509), and that though Charles I built some fine ships, he was absent minded about their crews more than half starved, they mostly died of scurvy The book is a graceful tribute by a naval surgeon of today to a naval surgeon of long ago who was always honest both with himself and others

The Order of the Court

J DUDLEY PANK London Hodder & Stoughton 1951 Pp 191 8s 6d

Mr Pank has a long experience of approved schools, and his thesis is that the delinquent boys in such schools "could be the salt of the earth if the iron hand were substituted for the kid glove" In spite of this rather forbidding manifesto, the author appears as a likeable and sensible person, whom the psychologist would be very willing to admit as a good influence in his own right and regardless of his theoretical approach Mr Pank's contact with his charges seems on his own showing to have been intuitively sound, and it is unfortunate that he seems to limit his theoretical deductions to his own experience, and even there to document them thinly in demanding the restoration of the birch he adduces no evidence whatever to rebut the very large body of contrary evidence, while his call to the "cranks who are in favour of abolishing punishment" to "themselves try to control over a hundred youths such as ours with no other methods than persuasion" could be met very fully from the records of work such as the Hawkspur Experiment alone It is unfortunate to see a born teacher with an obvious sympathy and understanding for his charges so poorly informed of the work and methods which others advocate, and of the successes they have obtained

Steroid Hormones and Tumors

A LIPSCHUTZ, M D, director of the department of experimental medicine, National Health Service of Chile Baltimore Williams & Wilkins London Baillière, Tindall, & Cox 1950 Pp 309 46s 6d

THIS monograph presents in condensed form and logical sequence the results of 15 years of experimental work by the author and his numerous associates Much of the work is already well known from previous publications on the subject of tumorigenesis and antitumorigenesis with steroid hormones It deals with the induction of those curious fibromatous and fibromyomatous tumours of the abdominal cavity of the domestic guineapig by continuous dosage with œstrogens, their prevention by combined dosage with luteinising hormone, and their disappearance on withdrawal of the originating stimulus Some unpublished data are included The quantitative, timing aspects, and general implications of the experiments are discussed as also are the precise origin and classification of these atypical yet reversible growths The latter discussion is highly valuable

Experimental work dealing with the induction of tumours directly or indirectly by œstrogenic hormone both in his own and in other laboratories is described with a full bibliography The author is always careful to make a distinction between evidence that provides proof of autonomous growth (metastasis, transplantability) and that which does not, at the same time stressing the gradations in response from reversible hyperplasia to full autonomy Contributions and opinions of others are accorded impartial consideration and there is a list of 900 references The whole monograph is illustrated lavishly and well

The Esophagus and Pharynx in Action

A Study of Structure in Relation to Function WILLIAM LERCHE, M D, F A C S, Associate Professor of Surgery, University of Minnesota, Minneapolis, Minnesota Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 229 40s

SURGICAL literature badly needs a book about the œsophagus and pharynx in action As soon as surgical technique loses touch with the knowledge of function and the causes of dysfunction patients suffer in vain It therefore seems a pity that a book with so attractive a title should consist of anatomical description of the not only dead but embalmed œsophagus served up with much conjecture

Under the title "rumination" Dr Lerche will a detailed dissection of an œsophagus, and then say "Since no clinical history was available my belief that the condition was due to rumination could not be confirmed" He seems to have lost sight of the normal action of the œsophagus in passing food down to the stomach, and he concentrates on how it behaves with fluid and wind coming upwards From the arrangement of a few muscle fibres examined months after death, he deduces that the body was in the process of belching as the spirit fled, he can even assert that half the belch reached the lower segment of the œsophagus while some of the wind frittered away in the upper segments

The author may have spent much time in microscopic dissection of muscle bundles, but, if so, it is all the more disappointing that he has obscured his anatomical work by untenable hypotheses, poor illustrations, and a somewhat misleading title

---

Poisons Guide Volume I (London *Chemist and Druggist* 1951 Pp 89 20s)—This work, the previous edition of which appeared in 1944, has been revised by Mr W A Whatmough in the light of changes in the poisons regulations, and is now set out in a more easily read form Together with volume II which is being prepared the book is claimed to form an "encyclopædia of poisons law"

Zoogeography of the Land and Inland Waters (London Sidgwick & Jackson 1951 Pp 208 30s)—The world is divided into eight natural geographical regions, and the fauna of each is described here both as it is now and as it was previously according to the geological record Prof L F de Beaufort has successfully compressed his vast material into a small book with a good bibliography and index The account is clear and concise, and the tracking of the fauna that colonised the British Isles is as enthralling as a good detective story

Dible and Davie's Pathology (3rd ed London J & A Churchill 1950 Pp 963 54s)—Dible and Davie's *Pathology* first appeared in 1939 and proved its worth as a standard textbook This edition is brought up to date by Prof J Henry Dible, the senior author, whose wide experience and outlook, both in pathology and bacteriology, have allowed him to introduce much recent work without asking too much of his readers Indeed, the book is a pleasure to read from the introductory homily to the final page The more important and dramatic historical facts are well presented, and the whole subject of pathology is made lucid and stimulating

Emergencies of Childhood (London James Nisbet 1950 Pp 64 6s)—This good short book on first aid, by Dr R Gamlin, is marred by inflated language "Synopsis of general procedure in hæmorrhage control" is not a better, but a much worse, way of saying "what to do for bleeding The advice is in the main sound, but though it is true that the burned child should be conveyed to hospital as rapidly as possible," it is a pity that Dr Gamlin recommends his readers to apply 'strips of gauze soaked in sodium bicarbonate' It is now generally agreed that only a clean towel or dry dressing should be put on burns Moreover it would be wise to mention that tannic acid or gentian violet should never be applied to burns or scalds which entirely or partly encircle the finger The illustrations are helpful, and it was a good idea to include Dr Breen s pictures of fever rashes

Freud Dictionary of Psychoanalysis (New York Philosophical Library 1950 Pp 208 $3 7)—This is a glossary, edited by Nandor Fodor and Frank Gaynor, of the more important psycho analytical terms, arranged in alphabetical order, illustrated by brief extracts from the writings of Sigmund Freud himself Reference is made, alongside each extract to the work in which it occurs, and there is a key at the beginning of the book to the various writings A chapter and page reference might usefully have been included with each extract for those interested in tracing each definition to its source and studying it in its relevant context There are some surprising omissions, such as the terms abreaction, anaclitic, economic, metapsychology, omnipotence, organ pleasure and reaction formation, space for which might well be found in a further edition by pruning some of the terms which Freud does not use in any but the ordinarily accepted sense—such as beauty phantasy, and intoxication

THE LANCET

LONDON SATURDAY, MAY 5, 1951

Priorities

Parliament is likely, it seems, to agree to the proposed charge on dentures and spectacles though not without misgivings, for this departure from the cherished principle of a comprehensive health service open to all, without individual payment, may open the way to further and more hurtful impositions Last week, when the Bill empowering the Minister to make these charges came before the House of Commons for its second reading, the Minister of Health was at least able to dispel concern that this move had been dictated by the Treasury The Chancellor, he said, had raised by £7 million last year's ceiling for expenditure on the National Health Service, but the Minister and the Secretary of State for Scotland had found that, even with the new aggregate allotment of £400 million from the taxpayer, they would still have a deficit of £23 million This they reduced to £13 million by curtailing the original hospital estimates, and the remainder was to come from the new charges, which this year would yield the necessary £13 million but in a full year would yield £25 million Mr Marquand declared that in deciding on these charges he had had four aims in mind (1) to maintain the essential parts of the service, (2) to spare the seriously ill, (3) to avoid a high cost of collection, and (4) to deter abuse The prescription charge, previously proposed but never enforced, satisfied the fourth criterion, but none of the others, and he had decided against a "hotel" charge in hospitals because most patients had lost their wages and received only sickness benefit, which anyhow was reduced after eight weeks' stay But what if a further retrenchment proves necessary in the future ? Each year since the service started its cost has risen, with the upward adjustment of salaries and wages and inflationary pressure, and the extra £12 million from dentures and spectacles in a full year will not go far to meet rising prices, let alone finance new developments No such moderately acceptable solution as has been found this year is likely to come to hand again

Saving on one or other part of the service—either by cutting expenditure or imposing charges—may be sought for one of two reasons first to curb extravagance, or secondly to maintain the essentials of the service as the value of the pound falls, by diverting expenditure from one heading to another It is well to distinguish between these two grounds even though they both happen to underlie the proposals now before Parliament At the start of the National Health Service—as at the inception of most large ventures—there was a good deal of needless spending, but gradually the loose ends were trimmed, and the trimming process has been hastened in the last twelve months since Sir Stafford Cripps explained that no further large increase could be countenanced. Undoubtedly some further saving is still possible without detriment to the public or any part of the service, and in last week's debate Dr Jeger suggested that alternative means of economy might be found in encouraging opticians to use the patient's old spectacle frames instead of always supplying new ones, in asking the patient to provide his own containers for medicines, in obtaining dental supplies at a lower cost, and in modifying dental and other fees But such extravagance as remains is now mainly in the wasteful use of expensive supplies rather than in the scope of their provision, and the effort will have to be directed towards showing those engaged in the service how waste can still be avoided.

The other type of saving—whether it is exercised by reducing expenditure or by introducing a charge—involves altering the balance of the service, because it will reduce either certain facilities or the demand for them Here improvisation is out of place, and in the debate Dr Charles Hill complained with some reason that when charges are imposed, "they should not be slapped on" as these ones were Who then is to make sure that the service is not thrown out of balance ? Perhaps the Minister But the Ministry is the apex of a tripartite service, and individual experts who might be the Minister's most helpful advisers would be more than human if they did not favour the division they serve Like health itself, a health service is really indivisible, and the thoughts of many are turning towards better integration both centrally and peripherally Why, it is asked, should we not have regional councils who would receive block grants enabling them to secure a balanced service for each area ? Objections are that no one has yet devised a method by which such councils could be kept within reasonable size while representing every aspect of the service, and that the upheaval would arrest the development of the service at a moment when it is just beginning to take root Fortunately there already exists another means of achieving the same end In the Central Health Services Council the Minister has an expert body which is in a position to review the whole service, indeed in the Commons debate the Minister quoted to good effect a committee of the council in support of the charge on dentures The council's first task would be to examine the apportionment of resources between each of the three branches (the need for such a review declared itself as soon as the Chancellor insisted last year that the service must operate within a more or less fixed upper limit), and its second task would be to list priorities in economy and development Such a survey should be continuous, and the findings should be published In this way those who work in the service would have some assurance—which they are now denied—that the balance is sound, and the public would be better able to judge the fairness of any future step to dock expenditure One factor that may yet bedevil the health service is uninformed public opinion This danger is described by Professor McKeown[1] when he says

> Medical services developed entirely or mainly in response to popular pressure are likely to prove very unsatisfactory Popular opinion will certainly urge a proliferation of the curative services ’

In the final count the major decisions on health-service finance must be political, just as decisions on pensions or sickness benefits or education are political, but public—and thus political—opinion can properly be shaped by expert and impartial advice Last week's debate underlined the need

---

[1] McKeown T *Almoner* 1950 3, 2

Absorption and Distribution of Fat

AFTER seventy years' research physiologists are still not quite certain how fat is absorbed FRAZER,[1] of Birmingham, has lately brought forward evidence suggesting that both free fatty acids and unhydrolysed fat (i e, "split" and "unsplit" fat) can be absorbed as such from the small intestine, though by different pathways According to FRAZER, free fatty acids are absorbed mainly into the portal circulation and are transported to the liver, while neutral unhydrolysed fat is absorbed by the lacteals and travels via the thoracic duct into the venous system and finally to the storage depots of the body These views are based on observations on rats fed with fats stained with Sudan III When stained neutral fat was fed the dye accumulated in the fat storage depots, whereas when stained fatty acid and glycerol (hydrolysed fat) were given the dye was found mainly in the liver

Clinical investigations have hitherto been confined largely to studies on the excretion of fat and on fat balance SHERLOCK and WALSHE[2] found that in the portal blood of a patient the fat content was not increased after a meal containing butter, but this patient had hepatic cirrhosis, and a fat balance test suggested that fat absorption was abnormal FRAZER's results are reinforced by the clinical observations of Dr AULD and Dr NEEDHAM, reported on p 991 of this issue They administered fats stained with a known quantity of Sudan III to a patient with non traumatic chylothorax and estimated quantitatively the dye in the fat recovered from the chyle in the pleural cavity Each test was made two hours after a light fat free breakfast and after emptying the pleural cavity of most of the chyle When stained neutral fat was administered about 21% of the Sudan III was recovered from the chylothorax, whereas when the equivalent amounts of stained fatty acid and glycerol were given no dye was recovered in one instance and only a small quantity in another This last result was attributed to the patient inadvertently receiving some neutral fat in the form of butter and an egg It would thus seem that neutral fat was absorbed and distributed, although not wholly, via the chylolymphatic route and that hydrolysed fat travelled in some other manner, since no Sudan III reached the pleural cavity although chyle accumulated as well These observations support FRAZER's view that the two kinds of fat, neutral and hydrolysed, are absorbed by different routes—neutral fat via the lymphatics and fatty acids via the portal system Why two different routes should exist is not quite clear The division may depend on particle size, fatty acids and their salts being of molecular size, and neutral fat particles 0 5 μ or less in diameter

Emulsified fat can be absorbed direct from the blood stream SHAFIROFF and MULHOLLAND,[3] of the New York College of Medicine, and STARE and his co-workers,[4] at Harvard, have shown that fat emulsions can be given intravenously to ill and emaciated patients with perfect safety, and that such fat can be utilised just as easily as fat taken by mouth The New York workers obtained the best results with a preparation containing a 10% protein hydrolysate, 6% gelatin, and 50% glucose, and provided enough was infused a positive nitrogen balance was maintained Administration of the preparation over long periods produced pyrexial reactions in some patients, but no other untoward effects Liver and kidney function were not impaired, lipoid pneumonitis was not observed, and liver biopsy on some of the patients showed the presence of stored fat, but no infiltrative or parenchymal degenerative lesion The oxygen uptake rose just after the infusion, indicating that the fat was being oxidised, but a mild acetonuria and transient ketonæmia showed that oxidation was incomplete The Harvard workers report similar results, and they have traced the pyrexial reactions to the presence of pyrogens in the commercial oils Using tracer elements, SHAFIROFF et al[5] have shown that a considerable amount of the infused fat is utilised They followed the fate of the fat by infusing an emulsion of linoleic acid hydrogenated with deuterium, an isotope of hydrogen The oxygen uptake rose sharply after the infusion, and some 50% of the fat was excreted within twenty four hours via the lungs as water vapour and carbon dioxide Similar tests by others on animals have shown that the remainder of the fat is converted into phospholipids and deposited in the fat depots[6]

Further observations with tracer elements incorporated in fat molecules may soon complete our knowledge of fat absorption

Modifications in Gastrectomy

THERE are healthy signs that surgeons do not regard with unqualified satisfaction the results of the popular Billroth II type of gastrectomy It is surprising that an operation which converts the duodenum into a diverticulum and re establishes the continuity of the food channel by joining a loop of jejunum to the stump of stomach should work satisfactorily in three quarters of the cases such extensive modifications of normal physiology seldom turn out so well But in 25% of patients the operation substitutes new symptoms for old, and it is this which has set surgeons looking for modifications of old procedures, or new operations, to alleviate peptic ulcers The cardinal difficulty in dealing surgically with peptic ulcers is that the most reliable way of decreasing the flow of gastric juice (which is the immediate cause of the ulcers) is to ablate the cells which produce it The ablation creates two new problems The first is the shortage or absence of gastric juice in the digestive processes, which may lead to nutritional deficiencies[7] The second is mechanical The gastric reservoir after operation, unguarded by an exit sphincter, is so decreased in size that food, prepared only by the teeth and the saliva, is tipped in considerable quantity straight into the jejunum The small intestine, which is particularly trouble-free if treated properly, may "kick" when given jobs for which it was not designed, and "dumping" symptoms are the result

---

[1] Frazer A C J *Physiol* 1943 **102** 306 *Physiol Rev* 1946, 26 103 *J Soc chem Ind Lond* 1947 66 379

[2] Sherlock S Walshe V *Clin Sci* 1946 6 113

[3] Shafiroff B G P Mulholland J H *Ann Surg* 1951 133 145

[4] Neptune E M. Geyer R P Saslaw I M Stare F J *Surg Gynec Obstet* 1951 92 365

[5] Shafiroff B G P Mulholland J H Baker J *Exp Med Surg* 1951 9 155

[6] Lerner S R Chaikoff I L Entenman C Dauben W G *Proc Soc exp Biol N Y* 1949, 70 384

[7] Welbourn R Hughes, R Wells, C *Lancet*, April 28 1951 p 939 Wells C Welbourn R *Brit med J* March 17 1951 p 516

Nutritional deficiencies are probably inherent in any effective operation for peptic ulcer, but these can be remedied by appropriate therapy Mechanical troubles cannot be so easily overcome, and the search for more satisfactory alternative techniques has been very active in the past few years Vagus resection was one attempt to surmount the disadvantage of extensive gastric resection In its pure form it has been found wanting, and judgment must be reserved on its merits when it is added to other modifications of the stomach, such as pyloroplasty it was years before plain gastro enterostomy was discovered to be unsatisfactory A return to the Billroth I operation, in which the stump of the stomach is anastomosed to the duodenum, has been made in some clinics The operation is more difficult to do than the Billroth II procedure, and it may be impossible if the duodenum is extensively scarred by ulceration, but the results are claimed by those experienced in the technique to be excellent and to show a very low incidence of dumping Time and further results will show whether the Billroth I operation is staging a serious "come back", but, though it preserves duodenal function, it must still suffer from the disadvantage of leaving a small stomach which lacks a pyloric sphincter Aylett[8] has recently described an operation in which the pylorus is transected and the duodenal end closed The jejunum is divided a few inches below the duodenojejunal flexure and its distal end anastomosed to the pylorus, its proximal end is then put end to side into the body of the stomach, and bile and pancreatic juice thus run directly into a normal sized stomach and neutralise its acidity

The latest attempt to decrease the peptic activity of the stomach while retaining its function as a reservoir is described in this issue by Mr Moroney He has made use of a segment of transverse colon, isolated except for its mesentery and blood supply, and has swung it upwards to bridge the gap between the stomach and duodenum which is left by an ordinary gastric resection The size of the "stomach" is thus preserved, it has motility, and most of its new lining secretes quantities of protective mucus but no peptic juice The function of the duodenum is preserved, and restoration of the continuity of the colon presents no difficulty The 22 cases which Moroney reports, though all the patients are well, are too slender a basis for a considered judgment of the operation s merits, but the idea is interesting and the early results seem exceedingly satisfactory The idea of colon replacement of the stomach has also been put forward by Lee[9] (whose report reached this country after we had accepted Mr Moroney's article) Lee, impressed by the deplorable nutritional state of some patients after total gastrectomy for carcinoma, has proposed using the ascending colon to replace the stomach His technique is to divide the ileum just proximal to the ileocæcal valve and the colon in the region of the hepatic flexure, and to swing the isolated right colon into the place left by a total gastrectomy The stump of ileum is anastomosed to the œsophagus, and the colon end of the isolated loop to the duodenum, and continuity of bowel is restored by an ileo-transverse colon anastomosis This operation has been done 3 times by Lee without mortality, but it is clearly much more formidable than Moroney's technique, and thus it could never be more than occasionally suitable in cases of peptic ulcer

Meanwhile a Billroth II type of operation must remain the standard treatment for peptic ulcers requiring surgery It is known to give a high proportion of satisfactory results and to carry a low mortality Progress is only possible if new ideas and operations are tried, but the essentials in such trials are that they should be made only by highly competent people, well versed in accepted techniques and assisted by proper follow up facilities The gastro intestinal tract in man is unfortunately very different from that of animals, and the results of a new operation for gastric disease cannot be predicted from operations on dogs As, however, it is necessary to make the final experiment on man, let the experimenters make sure that no lesson escapes them, and let the rest of us wait till the results of the experiments are known before repeating them ourselves

---

Annotations

HYALURONIDASE IN LOCAL ANALGESIA

For nearly twenty years[1] it has been known that certain tissue extracts and bacterial products contain a mucolytic enzyme, now known as hyaluronidase, which causes the rapid spreading and disappearance of fluids injected into the subcutaneous tissues Hyaluronidase hydrolyses hyaluronic acid, a viscous polysaccharide present in the interstitial spaces making it less viscous so that aqueous solutions penetrate the tissues more easily The effect of the enzyme lasts for about 24 hours after injection

At the moment hyaluronidase is of most clinical value when used for subcutaneous infusions in infants,[2] and it is widely employed for this purpose However, the first clinical report on hyaluronidase[3] dealt with its use as an aid to local analgesia, and two years ago Kirby et al.[4] reported that by mixing hyaluronidase with a local analgesic it was possible to anæsthetise a larger area of skin Then last year Moore[5] studied the effect of injecting hyaluronidase and amethocaine in a series of over 500 nerve blocks, and found that the mixture had a more rapid analgesic effect than amethocaine alone but that the effect lasted for a shorter time unless vasoconstrictors were used as well Hyaluronidase enabled fluids to pass through areolar tissue but not through fascial barriers The method was most successful when used for nerve blocks for hernia operations, and in splanchnic block A disadvantage was that the rapid absorption of the analgesic made toxic reactions more likely Thorpe[6] has lately described how he manipulated a fracture painlessly after the surrounding hæmatoma had been injected with a mixture of procaine and hyaluronidase Analgesia was rapid and complete, and the effect lasted for more than an hour It is always difficult to insert the needle accurately when injecting deeply placed nerves, as in splanchnic and paravertebral blocks, and also where bony landmarks are indistinct, as in inguinal hernia blocks In such cases hyaluronidase is likely to be of special value, since the spreading of the solution will make a successful block more certain

---

[8] Aylett S O *Brit med J* March 3 1951 p 454

[9] Lee C M *Surg Gynec Obstet* 1951 92 456

[1] *Science* 1934 79 61

[2] Hechter O Dopheen S K. Yudell M. H *J Pediat* 1947 30 645

[3] Cosentino C *Pathologica*, 1940 32 26

[4] Kirby C K Eckenhoff J E Looby, J P *Surgery*, 1949 25 101

[5] Moore D C *Anesthesiology* 1950 11 470

[6] Thorpe J N *Lancet* Jan 27, 1951 p 210

THE PROPER USE OF PUNISHMENT

THE practice of ignoring inconvenient evidence, though a common enough human failing, sits uneasily on members of the legal profession Lord Goddard's conviction, quoted by Dr F R C Casson in our correspondence columns, that young offenders need more punishment and less psychiatry is shared by many a simple business man and surburban housewife—people who have not encountered evidence to the contrary, or learnt to weigh opinion against fact Yet, as we point out in a review of Mr Dudley Pank's book, evidence has been steadily accumulating for many years now that the best results with young offenders are not to be obtained by "more punishment" The reason, as Dr Casson points out, is that no one "learns" from the severity of those whom he regards as oppressors The attitude of the young delinquent to punishment, he says, can only be understood "in terms of a prisoner of war resisting and resenting the stern measures of his captors" His loyalties are elsewhere, and until they can be won to the service of society he will remain a rebel Mr C A Joyce's[1] methods at the Cotswold School are a living reminder that violence is seldom a useful form of punishment, and that penalties, to be constructive, must appear to the delinquent not as examples of adult despotism but as something he brings down on himself by his own free choice Possibly this is the use of punishment which Lord Goddard had in mind

CUTANEOUS ANTHRAX

FORMERLY cutaneous anthrax was fatal in about a fifth of untreated cases, and the disease should always be suspected when a patient has a red macule on the skin of the face, neck, forearm, or hands which becomes vesicular in the centre and later acquires satellite vesicles A history of exposure to infection helps in diagnosis, but as Dr Doig and Dr Gemmill show in their article this week, the chain of infection may need some unravelling Among those primarily exposed are dockers and others handling goat hair and animal tissues before these are decontaminated Soltys[2] has reminded us, too, that laboratory workers and students handling stained films of anthrax are also in a dangerous occupation The organism gains entry through skin abrasions, and methods which reduce the number of minor injuries, such as mechanical aids in handling and the wearing of gloves, are of preventive value People working with infected material should have ready access to 2% tincture of iodine or some other effective local application For treating malignant pustule Sclavo's antiserum appears more often in textbooks than in wards, and large doses of penicillin are now commonly used Ellingson et al[3] successfully treated 25 cases of cutaneous anthrax with 30,000 units of penicillin every three hours, the total dosage being between 1 and 2 million units 'Aureomycin' has also been found to be curative, and now Gold and Boger[4] have described 8 cases which were successfully treated with the newer antibiotics—2 with aureomycin, 4 with chloramphenicol, and 2 with 'Terramycin' Bacterial sensitivity tests showed that in each case the anthrax bacillus was fully susceptible to each of these antibiotics, which appeared to be equally useful in controlling cutaneous anthrax Local œdema and erythema did not increase 24–48 hours after treatment was started, but enlargement of the regional lymph nodes continued for several more days, moreover, anthrax bacilli were repeatedly recovered from lesions 2–3 days after the spread of local œdema had stopped, and the organisms disappeared somewhat more slowly with aureomycin, chloramphenicol, or terramycin than has been usual with penicillin All but 1 of the 8 patients were treated at home, this is one advantage of using drugs which are given by mouth Meanwhile, with at least four antibiotics effective against cutaneous anthrax, Sclavo's white asses can graze in peace

THE HIGH AND FAR-OFF TIMES

BEFORE man walked in on two feet, prehistory was occupied, for more than 500 million years, by a great deal of other livestock, and in his latest exhibition, "Prehistoric Man in Health and Sickness," at the Wellcome Historical Medical Museum, Dr E Ashworth Underwood has found it as hard as our primitive ancestors to keep out the mammoths and the sabre toothed tigers Even a dinosaur, who left the mortal scene some 70 million years before *Homo sapiens* came upon it, has wriggled his way into this fascinating exhibition, by dint of a hæmangioma affecting two vertebræ near the end of his tail This massive specimen in which the tumour is as big as a grapefruit and the vertebral bodies are almost wrist thick, does much to confirm the sapience of man To attempt to share a world with such a creature would have been foolhardy As it was, man had quite enough to contend with not the fauna only, but the weather (four ice ages in 300,000 years), and such common ills of the flesh as gall stones, arthritis deformans, periosteal sarcoma, osteomyelitis, and bad teeth Examples of all these are shown in the exhibition, alongside such interesting dental veterinary problems as a cystoma in the mandible of a four tusked mastodon, a dental abscess in a titanothere, and pyorrhœa in a three toed horse As man only left his bones and his calculi, it is hard to know what less durable ills he also suffered from, but as Dr Underwood points out in his scholarly introduction to the catalogue,[1] bacteria were ready and waiting for him A photomicrograph in the exhibition shows the oldest known bacteria—more than 520 million years old Being calcium precipitating, they have preserved themselves for study But, as usual, man was probably his own worst enemy active rather than thoughtful, he pressed forward to a cure without proper study of causation We have all heard of the neolithic enthusiasm for trephining the skull, and skulls in the exhibition, as well as a life like diorama of the primitive surgeon in action, illustrate the practice Usually the piece removed was roughly circular, and the method was to scrape it out with a flint tool The fragment was then bored with holes and probably worn as an amulet Skulls showing healing of such trephine holes are common, and so are those in which the operation had been performed on two or three occasions The theory is that it was done to relieve headache or to let out an evil spirit, and it seems to have been tried on men, women, and children, impartially Another neolithic operation was cranial cauterisation in a T shape, usually done with boiling oil and only on women

Public health had no place in prehistoric economy The floors of caves or other simple dwelling places consist of packed refuse, in which deceased members of the family were sometimes buried A model shows a pile dwelling such as men built on the shores of the Swiss lakes, and in the diorama mentioned there are huts built sturdily of stones below, with wattle and daub above and a thatched roof with a central smoke hole. Another diorama shows cave dwellers looking down from their cliff on an inexhaustible meat ration of mammoth, woolly rhinoceros, cave lion, reindeer, and horse. Horses figure more often than any other animal in carvings and decorations on tools and weapons—a tribute, no doubt, to their flavour.

---

[1] See *Lancet* Jan 13 1951 p 102

[2] Soltys M A *J Path Bact* 1948 60 253

[3] Ellingson H V Kadull P J Bookwalter H L Howe C *J Amer med Ass* 1946, 131 1105

[4] Gold H Boger W P *New Engl J Med* 1951 244, 391

[1] Published for the Wellcome Historical Medical Museum by Geoffrey Cumberlege Oxford University Press 1951 Pp 56 *2s 6d*

Whatever the shortcomings of primitive man as a surgeon and a sanitary inspector, his position as an artist is now established. This exhibition shows many splendid examples of his work—weapons (including a beautiful spear thrower carved from reindeer antler in the form of a horse), carved ornaments, and those wall paintings of bison and other animals which are now so familiar, though so recently discovered. These are shown beautifully on transparencies against the windows. The later primitive cultures produced delicately ornamented pots, combs, and jewellery, and an elegant display shows how early was the idea of the safety pin and how ornamentally it was used. Weaving came far earlier than we are apt to think; flaxen homespun has survived from the Swiss lake dwellings. Weapons and tools in great profusion show primitive man's skill with his hands—delicate flint knives like leaves, bone and ivory fish spears, stone axe heads, and all the necessities of an arduous and extraverted life. This is an exhibition not to be missed by anyone with the least curiosity about man's origins and career.

HEART SOUNDS AGAIN

LIKE all good things, the stethoscope has at times been misused; but this does not excuse the disdain with which it is now sometimes regarded. Curiously enough, it is our American cousins who, prompted largely by experience in the late war, have leapt to the defence of this Victorian insignia. These proponents have found a brilliant leader in Samuel A. Levine, of Harvard. His grouping of heart murmurs into six grades may be open to criticism, but it does provide the learner with a useful guide.

The importance attached to auscultation by the American Army is well exemplified by Johnson,[1] who remarks that men with a grade III or louder systolic murmur are rejected for military service regardless of other evidence. Similarly, the presence of a grade I apical systolic murmur is taken as ground for rejection if accompanied by an authentic history of rheumatic fever, while a grade II murmur which is not completely dispelled in certain phases of respiration will also cause rejection. An even firmer line is taken with murmurs in the aortic area; a localised systolic murmur of any intensity (unless grade I) is a cause for rejection. In the pulmonary area—the "area of auscultatory romance," as it has been described—a murmur can be disregarded if it is grade I or II in intensity and if there is no other sign of heart disease. Proven rheumatic heart disease is undoubtedly a sound reason for rejecting an army recruit, but it is no barrier to an active civilian life. Deciding the extent of physical activity permissible to a patient with rheumatic heart disease is a matter of sound clinical judgment in which are weighed a full clinical history and physical examination, and a knowledge of the patient's family background such as only the family doctor can attain.

In discussing the role of auscultation in cardiology certain practical considerations are too often neglected. The ear pieces must fit the ears comfortably, and rubber tubing must be of reasonable thickness (the tubing used for bunsen burners is ideal, and has the further advantage of cheapness) and length (an inch longer than the maximum jumping distance of the flea is a sound working rule). The question of end pieces is easily solved; two end-pieces (not a double one) should be bought—a bell and a diaphragm type—but many clinicians will prefer to adhere to one type, contending that with long experience skill becomes greater than with two. As an ancillary to the stethoscope, particularly for detecting early aortic diastolic murmurs, the advantages of direct auscultation should never be overlooked: many an early case of aortic incompetence has been missed because direct auscultation was not carried out to the left of the mid sternum with the patient leaning forwards and holding the breath in full expiration. Finally, the examination room must be quiet. If only doctors would refuse to examine patients in the bedlam of so many outpatient and examination centres, the authorities would be compelled to act.

The stethoscope will long remain an essential instrument for the clinician. As Levine[2] points out, "in the present era, where complicated apparatus, such as the X ray and the electrocardiograph, are often essential adjuncts in diagnosis and treatment, and when the cost of medical care is necessarily increasing, it is imperative to derive all possible help from such an inexpensive and expedient tool as the stethoscope."

CLEAN CATERING

THE caterer, who once chose proteins languidly from the joints of the world's herds, now wears the strenuous and devoted look of the collector of rare specimens. His profession is becoming more exacting in other ways, too, for the report of the Catering Trade Working Party,[3] under Sir William Savage, is helping to foster a common prejudice in favour of clean food. King Edward's Hospital Fund for London has long urged on the hospital caterer the advantages, from the point of view of patients, of clean well run hospital kitchens. Its School of Hospital Catering, which is shortly to open at St. Pancras Hospital, London, is to offer refresher courses to all categories of staff in hospital catering departments, and a useful innovation will be a basic cookery course for untrained staff. The Fund has already published several circulars on the problems encountered by the caterer. The latest of these[4] draws a comparison between the standard of cleanliness demanded, and maintained, in the operating theatre, and that countenanced, even accepted, in some hospital kitchens. The theatre staff are highly drilled in ritual cleanliness; the kitchen staff as a rule are not. The theatre staff, even the most junior nurse among them, have had specific teaching in bacteriology, whereas the head cook usually knows as little about germs as the junior kitchen-maid—possibly less.

> 'To maintain the best hygienic standard,' the circular reads, 'catering staff must be given proper facilities to carry out hygienic practices such as washing up in two sinks with adequate hot water of a sufficient heat to avoid the use of drying cloths, and practise personal hygiene such as washing the hands after visiting the toilet.'

For, as the circular goes on to point out, the most hygienic equipment and layout are useless if the staff fail to keep the rules of hygiene. Why should they keep rules which they do not understand? Why should they practise a piece of tedious and time consuming magic in answer to a notice on the wall? They need, as the circular insists (though not until the very last paragraph), to be taught underlying principles.

The introductory paragraphs of this well intentioned document set out the causes of food infection, but in such an elementary and telegraphic way that they will hardly impress an uninformed reader. The assertion that "fatal cases of food poisoning have occurred from infection of food from a sore on the finger of a Cook" needs at least one example to give it force Moreover, the circular abounds in vague phrases which badly need backing by descriptions, measurements, and figures Thus the washing of crockery must be carried out "under proper conditions," attention must be given to the "proper disposal" of swill, cold storage space must be "adequate," the standard of kitchen hygiene "satisfactory," the premises "large enough," and "adequately lit," hot water must be provided "for all requisite purposes," there must be a "sufficient" number of wash-basins for the staff, steam for sterilising food containers should be available under "adequate pressure" and "an adequate time of steaming is essential," and detergents should be used in "correct strength" These weaknesses apart, the circular gives much useful general information, noting that food infected with small numbers of food poisoning organisms may be harmless if eaten soon after preparation but dangerous if allowed to stand in a warm atmosphere for a few hours, that kitchen floors should be hard, uncracked, and easily washed, that water closets should have adjacent wash basins, and that kitchen sinks should not be used for hand washing, that dish washing machines should also sterilise, that staff should wear light coloured gowns and caps, and that vermin should be kept down It recommends that, in order to limit the infection of food, food handlers should report to the manager if they are suffering from a discharging wound, sores on hands or arms, discharging ears, diarrhœa, vomiting, or any other illness, and that the manager, should he learn of such illnesses, should send the affected member of the staff off duty Any applicant for a post who has suffered from typhoid or paratyphoid should be referred to the medical officer of health and not engaged without his approval. These sound proposals are part of a target code laid down by the Working Party—nothing short of which, the circular rightly asserts, should be entertained by hospital caterers

---

[1] Johnson R P U S Armed Forces med J 1951 11 13

[2] Levine S A Harvey W P Clinical Auscultation of the Heart Philadelphia and London 1949

[3] Hygiene in Catering Establishments H.M. Stationery Office, 1951 Pp 50 1s 9d See *Lancet* Feb 10 1951, p 333

[4] No 5 Hygiene in Catering Pp 12

TREATMENT OF BRUCELLOSIS WITH ANTIBIOTICS

UNTIL 'Aureomycin' and chloramphenicol were discovered the treatment of brucellosis was unsatisfactory Combined administration of streptomycin and sulphadiazine can apparently bring about a cure, but this method requires very careful supervision, and streptomycin is not free from toxic effects The response to aureomycin and chloramphenicol is rapid and toxic manifestations are few, but the relapse rate is high, this averages 22%, and Knight et al[1] have reported 6 relapses in a series of 13 cases

'Terramycin,' the antibiotic obtained by Finlay and his co workers[2] from cultures of *Streptomyces rimosus*, is also said to be effective against *Brucella melitensis* Killough et al[3] gave a daily total of 50 mg per kg body weight in divided doses every four hours, treatment was continued for one to two weeks after the patients became afebrile, and no serious side effects were noted Terramycin proved as effective as aureomycin or chloramphenicol in controlling pyrexia and the acute symptoms, the patients became afebrile within $3^1/_2$ days of starting treatment Unfortunately the clinical relapse rate was 50%, and a further 19% had a bacteriological relapse, making altogether 69% relapses This compared favourably, however, with two similar series treated with aureomycin and chloramphenicol, where the relapse rates were 73% and 66%

With these fairly small numbers comparison is difficult, but it does look as if terramycin is just as effective as aureomycin and chloramphenicol in the treatment of brucellosis The fairly high proportion of patients with bacteriological relapse without signs or symptoms underlines the value of repeated blood and urine cultures after stopping treatment The acute manifestations of brucellosis can be controlled by antibiotics the problem of preventing relapse has still to be solved Possibly a combination of antibiotics may be better than any one alone

LAST WORDS OF A TEACHER

To countless friends in many countries, Dr Alfred E Barclay became affectionately known as "Uncle B" His generous and friendly disposition made him always ready to help and encourage others, and his last book,[1] published posthumously, is not only a thought provoking account of a new technique, and of some older ones, employed in radiology, but an intentional legacy "to those who follow after"

On retiring he planned a long voyage to Bali, New Zealand, and elsewhere, with the prospect of indulging his bents towards music, fishing, golf, and gadget making in his private workshop on his return, but he was invited to come, for a trivial financial recompense, as radiologist to the newly founded Nuffield Institute for Medical Research at Oxford Almost without hesitation, he agreed to come as soon as his voyage was over, and from 1936 to his death in 1949 he served the institute in an honorary capacity, rounding off the achievements in clinical radiology of his earlier years with the even more remarkable research achievements of his later ones Though he never knew it, the use of the relatively short X rays which made micro arteriography possible was one of the technical possibilities listed in the original scheme for the radiological wing of the institute, and the problems involved came to be tackled by Barclay in his last few years They became specially obvious during the studies of the renal circulation, carried out during 1945–47, when radiological methods had led on to histological ones, and when these in their turn were proving to have their limitations Beginning as an adjuvant technique to the histology, the method of micro arteriography, thanks to the improved war time production of fine grain emulsions, emerged, in Barclay's skilled hands, relatively quickly as an independent method for a new appreciation of the more minute structures in the blood vascular system This last book contains accounts of its initial, very successful, application to the kidney, stomach, and testis (this section by Prof R G Harrison) illustrated with truly amazing radiographs Apart from its main subject, the book deals with research apparatus and protection, with cineradiography, and (in a chapter by Professor Harrison) with selection and injection of contrast media In general, therefore, it describes the radiological precautions and techniques employed at the Nuffield Institute for Medical Research during Dr Barclay's years there, and is his legacy, as a craftsman, to his successors But it contains also his thoughts on the bearings of his and his colleagues' researches Those who have learnt so much from him, and those who have still so much to learn, will always regret that it was not available in time for the International Radiological Congress in 1950, and that he did not live to see it appear

THE next session of the General Medical Council will be held on Tuesday, May 22, at 10 30 A M, when Prof DAVID CAMPBELL, the president, will deliver an address The Medical Disciplinary Committee is expected to sit on Thursday, May 24, at 10 30 A M

---

[1] Knight V Ruiz Sanchez F McDermott W *Amer J med Sci* 1950 219 627

[2] Finlay A C et al *Science* 1950 111 85

[3] Killough J H Magill G B Smith R C *J Amer med Ass* 1951 145 553

[1] Micro arteriography and Other Radiological Techniques Employed in Biological Research By ALFRED E BARCLAY MD FRCP FFR Oxford Blackwell Scientific Publications Pp 102 30s

Special Articles

OBSERVERS' ERRORS IN TAKING MEDICAL HISTORIES

A L COCHRANE
M B Camb

P J CHAPMAN
M B Brist

P D OLDHAM
M A Oxfd

From the Pneumoconiosis Research Unit of the Medical Research Council

ALTHOUGH medical disagreement has long been recognised as common and was publicised by Alexander Pope (1732), there appears to be some general reluctance to recognise it as due to the subjectivity of medical judgment and even more reluctance to investigate it quantitatively Certain recent tendencies have, however, made the recognition and measurement of medical error desirable

In the work of our unit, for instance, it is necessary to correlate medical observations on workmen with the physical characteristics and quantity of the dust they have breathed In doing this, just as the imprecision of the physical measurements must be allowed for, so, similarly, it is necessary to estimate how much one medical observer varies when he repeats his observations on the same material (intra observer error) and how much his observations differ from those of another (inter-observer error), for in large scale surveys several observers must cooperate and their results must be comparable

Although relatively few studies have been published on the subject of medical error, several different approaches can be distinguished In some cases—e g, in the study of cyanosis (Comroe and Botelho 1947)—it has been possible to compare a clinical estimate with some objective accurate measurement of the same characteristic Similar but less accurate measurements have been used by Birkelo and Rague (1948) and Cochrane et al (1949) to estimate the accuracy of radiological prognoses by following up minimal tuberculous lesions Cochrane et al introduce a slight refinement in technique in that an estimate was made of the number of prognoses that would have been made accurately by chance, the results being expressed as the percentage of the errors expected of a "blind" radiologist which were avoided by the reader Such a refinement is obviously necessary when there are relatively few possible choices

In other studies no objective standard was possible and attention was focused chiefly on the inter observer error These studies were mainly confined to estimates of human nutrition (Bean 1948, Derryberry 1938, Jones 1938), although Britten and Thompson (1926) and Sydenstricker and Britten (1930) have suggested that a similar error is attached to routine clinical examinations

Recently there have been several detailed studies of the intra observer and inter observer errors in the diagnosis of pulmonary tuberculosis (Birkelo et al 1947), pneumoconiosis (Fletcher and Oldham 1949), and pulmonary fibrosis (Hebert 1939) In all these cases the simple repeat technique was applicable, for the subjects of the examinations were not altered by the first investigation Difficulties arise when the first examination is likely to affect the results of the second, as is clearly the case in taking a medical history The general problem is discussed at some length by Kinsey et al (1948), who emphasise that the second interview is influenced by the first, and require a minimum of eight months between interviews

In large scale surveys of coalminers carried out by this unit we wished to know the proportions of men complaining of various symptoms and showing various degrees of radiographic abnormality at a particular time, and a method such as Kinsey's would be impossible

We have therefore approached the problem from a rather different point of view If a population is divided into groups by some purely random method, the proportion giving a positive answer to questions asked by the same observer should be very similar in each separate group The limits outside which the proportions have a small probability (say 5%) of falling by chance can be calculated If then the population is divided into groups at random and each group is seen by a different observer, proportions of positive answers differing by more than the amount expected will be assumed to show that observers are either obtaining different answers from patients in the same clinical state or are interpreting the patients' answers differently

MATERIAL AND TECHNIQUE

During a survey of an English coalmine 993 underground workers were interviewed Observers A, B, and C did the bulk of the interviewing Three other observers, who saw somewhat fewer miners, are called "observer D" The numbers of miners seen by each observer were as follows

Observer	*No interviewed*
A	261 (*26 3%*)
B	250 (*25 2%*)
C	300 (*30 2%*)
D	182 (*18 3%*)
Total	993

All the interviews took place in the same room under apparently identical conditions Usually a queue formed, and the men took the places in order as they fell vacant At slack periods it was rather difficult to tell whether the men chose the observer or the observer the man There was probably a little of both. Three observers were usually present in the room at the same time and could easily overhear each other's questions, and every effort was made to standardise technique The men were asked, in such a way that simple positive or negative replies could be made, whether they had cough, sputum, pain in the chest, tightness of the chest, or shortness of breath, and whether they had a history of bronchitis, pneumonia, pleurisy, or dyspepsia The interviewing had to be done very quickly, since miners were usually seen at the end of a shift, when they were anxious to get home The average time taken was about 5 minutes per man

TABLE I—AGE DISTRIBUTION OF MEN IN EACH GROUP

Age (yr)	No of men seen by observer				
	A	B	C	D	Total
14–19	21 (*8 0%*)	18 (*7 2%*)	14 (*4 7%*)	5 (*2 7%*)	58 (*5 8%*)
20–24	19 (*7 3%*)	20 (*8 0%*)	22 (*7 3%*)	23(*12 6%*)	84 (*8 5%*)
25–29	29(*11·1%*)	31(*12 4%*)	49(*16 3%*)	33(*18 1%*)	142(*14 3%*)
30–34	26(*10 0%*)	23 (*9 3%*)	34(*11 3%*)	23(*12 6%*)	106(*10 7%*)
35–39	40(*15 3%*)	44(*17 6%*)	48(*16 0%*)	29(*15 9%*)	161(*16 2%*)
40–44	35(*13 4%*)	38(*15 2%*)	42(*14 0%*)	27(*14 8%*)	142(*14 3%*)
45–49	36(*13 8%*)	41(*16 4%*)	39(*13 0%*)	19(*10 4%*)	135(*13 6%*)
50–54	20 (*7 7%*)	12 (*4 8%*)	24 (*8 0%*)	10 (*5 5%*)	66 (*6 6%*)
55–59	16 (*6 1%*)	12 (*4 8%*)	12 (*4 0%*)	7 (*3 8%*)	47 (*4 7%*)
60–64	11 (*4 2%*)	7 (*2 8%*)	12 (*4 0%*)	4 (*2 2%*)	34 (*3 4%*)
65–69	8 (*3 1%*)	3 (*1 2%*)	4 (*1 3%*)	2 (*1 1%*)	17 (*1 7%*)
70 or more	— —	1 (*0 4%*)	— —	— —	1 (*0 1%*)
Total	261	250	300	182	993

TABLE II—NUMBER AND PROPORTION OF MEN IN EACH GROUP WHO COMPLAINED OF CERTAIN SYMPTOMS

Symptom	No of men seen by observer				Probability (%)
	A	B	C	D	
Cough	61 (23 1%)	70 (28 0%)	121 (40 3%)	60 (32 9%)	<0 1†
Sputum	34 (13 0%)	50 (20 0%)	108 (36 0%)	76 (41 9%)	<0 1†
Tightness of chest	39 (14 9%)	42 (16 8%)	69 (23 0%)	40 (21 9%)	5 4
Pain	18 (6 9%)	16 (6 4%)	28 (9 3%)	30 (16 5%)	0 1–1 0†
Dyspnœa*	40 (15 5%)	45 (18 0%)	42 (14 0%)	18 (9 9%)	10–20

* Excluding three cases with no record of dyspnœa
† Significantly small

RESULTS

To discover whether observers A, B, C, and D had been interviewing similar samples of the total population, the age distribution of those seen by each observer was determined (see table I) Although the men seen by observer B had a slightly higher mean age than the others, the difference is not statistically significant, for it might occur once in eight times by chance alone Years underground and the prevalence of pneumoconiosis have found to be closely related to age, and it seemed reasonable to proceed on the assumption that the necessary random clinical composition of the groups seen by each observer had been attained

Fig 1 and table II show the percentages of men in each observer's group who gave a positive answer when asked whether they had cough, sputum, pain in the chest, tightness of the chest, or shortness of breath on exertion

Fig 2 and table III show the percentages of men in each group who gave a past history of bronchitis, pleurisy, pneumonia, and dyspepsia The probability that these differences were due to chance is given in the last column of each table Accepting as the level of significance that the difference would not have occurred more often than once in twenty times by chance, we find that there was a significant difference in the observers' recordings of the frequency of cough, sputum, pain in the chest, and dyspepsia

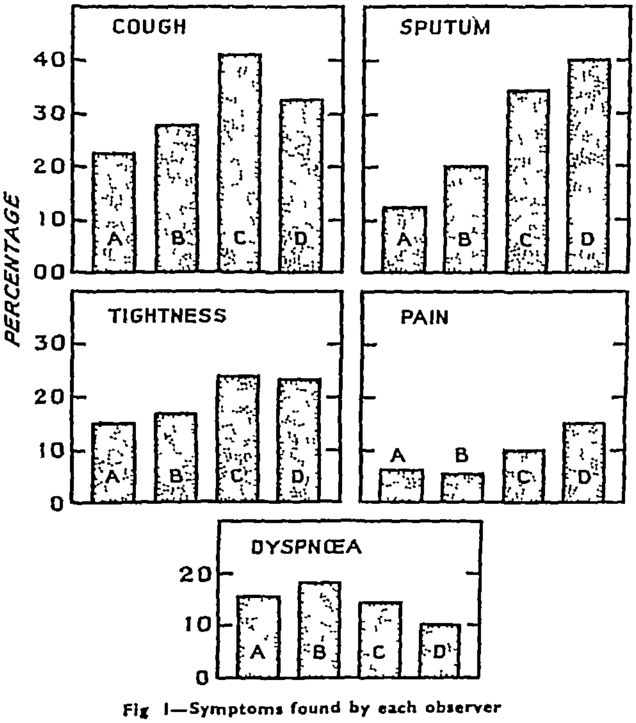


Fig 1—Symptoms found by each observer

DISCUSSION

Our results suggest that the recording of patients' answers to simple questions may, in some cases, give results that are unaffected by the observer In the case of a past history of bronchitis, pleurisy, or pneumonia the question "Have you ever had ?" is straight forward, and the answer in most cases will be "Yes" or "No," which will be thus recorded

The consistency between the observers' recordings, however, does not mean that the answers are necessarily correct Their accuracy must have depended on the memory and cooperation of the men who were asked the question, but men with good and bad memories or high and low levels of cooperation were presumably randomly distributed throughout the group In the other questions, however, the observer had to interpret the man's answer before recording it For instance, to the question "Have you a cough?" or "Do you spit?", the man might reply "Only an ordinary cough" or "Only after work" (for miners commonly cough up a little black phlegm after the shift) The observer would then have to ask supplementary questions to decide whether or not the severity of the cough constituted a symptom of chest disease, and his ultimate recorded answer would depend as much on his judgment as on the man's answer This is presumably why, in these cases, we find very different frequencies recorded by different observers

TABLE III—NUMBER AND PROPORTION OF MEN IN EACH GROUP WHO GAVE A HISTORY OF HAVING HAD CERTAIN DISEASES

Disease	No of men seen by observer				Probability (%)
	A	B	C	D	
Bronchitis	32 (12 2%)	26 (10 4%)	31 (10 3%)	21 (11 5%)	80–90
Pleurisy	24 (9 2%)	21 (8 4%)	31 (10 3%)	23 (12 6%)	50
Pneumonia	30 (11 5%)	36 (14 4%)	45 (15 0%)	24 (13 2%)	50–70
Dyspepsia	26 (9 9%)	40 (16 0%)	70 (23 3%)	49 (26 9%)	<0 1*

* Significantly small

In the case of shortness of breath on exertion, which is normal to some extent in health, the observers had agreed before the survey on a careful grading The miners were asked if they could keep up with their fellow workers of their own age while walking Our results seem to show that such a system helps to reduce observer error if it is properly used Errors due to faulty answers will remain

In the case of dyspepsia there is once more an infinite gradation from healthy men who feel bloated after Christmas dinner to the true case of peptic ulcer, hence the observer's judgment once more enters into his recorded answer Presumably the error that we have shown could have been lessened by more careful definition, as in the case of dyspnœa

We believe that our results demonstrate that, at least in this particular survey, the recorded answers to several questions commonly asked in taking clinical histories were not reproducible from one observer to another, so they could not be considered objective scientific observations Possibly if the observers had been more experienced clinicians, or if they had worked more slowly, their results would have been better Observer A was an experienced clinician of consultant physician status, and observers B and C could fairly claim to be well trained in academic scientific medicine, which might be considered at least as important as clinical experience for the accurate and consistent recording of men's answers The composite observer D would be expected to be exceptionally accurate, for the

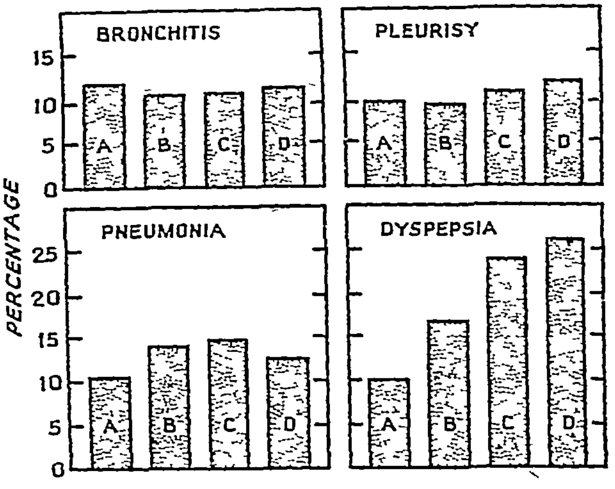


Fig 2—Past medical history found by each observer

proportions found by D are a kind of average of those found by the three observers included in D, the inter-observer error of the three being thus partially averaged out For this reason the discrepancies found are likely to be underestimated In view of the slightly higher mean age of the men seen by observer B it is interesting to observe that his results are in only one case more extreme than those of observers A, C, and D

The work was certainly done quickly, but little faster than some of the work done in hospital outpatient departments or in the consulting rooms of general practitioners Possibly miners are a particularly difficult group, because so many of them have the slight degree of cough and expectoration after work to which we have already referred

In spite of these reservations we believe that our findings have some general application, they are certainly important in clinical field surveys Unless different observers can obtain consistent answers to questions from comparable groups of witnesses their findings are of little scientific value If this were generally recognised, a great deal of misplaced research endeavour would be saved, and many publications would gain in validity what they lose in length We suggest that the technique we have adopted is suitable for investigating the reproducibility of clinical findings

The application of our results to history taking in general is less certain, but many doctors must remember certain curious discrepancies between the histories taken by them as students and those elicited later from the same patients by the house physician or the registrar This inter observer error of hospital history taking would merit investigation particularly if there were any possibility of the histories being used for research purposes later

A further possibility is in the field of medical education A great deal is taught about the art of history taking, its science is badly neglected It should not be difficult to arrange demonstrations for students to show the dangers of leading questions and the invalid deductions that can be made owing to the lack of reproducibility of clinical findings

SUMMARY

A clinical survey of a large number of coalminers was made by several medical observers who interviewed different groups of men The age distributions of the groups were similar The observers all asked the miners in their groups the same questions

The answers to some of these questions showed that the observer's bias was influencing the frequency with which a positive answer was recorded. Other questions were more consistently answered in the different groups

These results are discussed, and it is suggested that more attention should be paid to possible lack of reproducibility in the answers that patients give to questions commonly asked in clinical practice, and that, for research purposes, answers which are not reproducible are worthless

In such large-scale coöperative work it is difficult to apportion credit fairly We should however, like to mention Dr C M Fletcher, Dr J C Gilson, and Dr K J Mann, of this unit, and the 993 miners who answered our questions so patiently and so surprisingly

REFERENCES

Bean W B (1948) *J appl Physiol* 1, 458
Birkelo C C Chamberlain W E Phelps P S Schools P E Zachs D., Yerushalmy J (1947) *J Amer med Ass* 133 359
— Rague P O (1948) *Amer J Roentgenol* 60 303
Britten, R H Thompson L R (1926) *Publ Hlth Bull Wash.* no 162
Cochrane A L Campbell H W Stein S C (1949) *Amer J Roentgenol* 61 153
Comroe J H jun Botelho S (1947) *J Amer med Sci* 214 1
Derryberry M. (1938) *Publ Hlth Rep Wash* 53 263
Fletcher C M. Oldham P D (1949) *Brit J industr Med* 6 168.
Hebert, G T (1939) *Tubercle* 20 145
Jones R H (1938) *J roy Statist Soc.* 101 1
Kinsey A C Pomeroy W B Martin C E (1948) Sexual Behavior in the Human Male Philadelphia and London
Pope A (1732) Epistle 3 to Lord Bathurst London.
Sydenstricker E Britten R H (1930) *Amer J Hyg* 11 73

IMPERIAL CANCER RESEARCH FUND

In his summary of the work done during the past year in the laboratories of the Imperial Cancer Research Fund,[1] Dr James Craigie, F R S, the director, reports investigations on tumour transplantation, tumour induction and progression under hormonal influences, and chemical carcinogenesis in the liver

Dr A M Begg, Miss P E Lind, and Miss Margaret Hayward, PH.D, have collaborated with Dr Craigie in exploring the possibility of developing quantitative methods for the study of transplantable tumours For this purpose a better knowledge of conditions governing cell survival in vitro is essential It was found that tumours could be preserved as cell suspensions in the frozen state provided that dextrose solution was used It was noted that cell suspensions contained a small number of highly refractile bodies similar in size and contour to tumour cells Retention of viability in vitro depended on maintenance of this refractility as seen by phase microscopy Refractile cells were resistant to dextrose solution and to freezing and drying in dextrose—manipulations which kill normal tumour cells

The discovery of a resistant state raises many questions.

Doubtless before doing any further work along these lines, the facts have been taken into consideration that normal cells—liver for example—as well as tumour cells of all kinds actually develop this curious refractile change with obscured nuclear detail in dextrose sucrose and glycerin solutions that the appearance is completely reversible by washing out the sugars or glycerin that it is not to be confused with a similar but irreversible appearance natural to dead pyknotic cells that no normal liver cells whether highly refractile or not, are resistant to immersion in dextrose solutions, and to freezing and partial drying as measured by growth after animal grafting And therefore high refractility is not likely to underlie any property peculiar to tumour cells

Dr Leslie Foulds has extended his studies on the progression of tumours towards malignancy and on their responsiveness to various physiological conditions Observations extended over long periods of intermissions of breeding have confirmed the previous findings that some mammary tumours that regressed after parturition

---

[1] Imperial Cancer Research Fund 48th Annual Report 1950–51. Issued by the Fund. Royal College of Surgeons Lincoln's Inn Fields London W C 2

TABLE II—NUMBER AND PROPORTION OF MEN IN EACH GROUP WHO COMPLAINED OF CERTAIN SYMPTOMS

Symptom	No. of men seen by observer				Probability (%)
	A	B	C	D	
Cough	61 (*23.4%*)	70 (*28.0%*)	121 (*40.3%*)	60 (*32.9%*)	<0.1†
Sputum	34 (*13.0%*)	50 (*20.0%*)	108 (*36.0%*)	76 (*41.9%*)	<0.1†
Tightness of chest	39 (*14.9%*)	42 (*16.8%*)	69 (*23.0%*)	40 (*21.9%*)	5.4
Pain	18 (*6.9%*)	16 (*6.4%*)	28 (*9.3%*)	30 (*16.5%*)	0.1–1.0†
Dyspnœa*	40 (*15.5%*)	45 (*18.0%*)	42 (*14.0%*)	18 (*9.9%*)	10–20

* Excluding three cases with no record of dyspnœa
† Significantly small

RESULTS

To discover whether observers A, B, C, and D had been interviewing similar samples of the total population, the age distribution of those seen by each observer was determined (see table I). Although the men seen by observer B had a slightly higher mean age than the others, the difference is not statistically significant, for it might occur once in eight times by chance alone. Years underground and the prevalence of pneumoconiosis have found to be closely related to age, and it seemed reasonable to proceed on the assumption that the necessary random clinical composition of the groups seen by each observer had been attained.

Fig. 1 and table II show the percentages of men in each observer's group who gave a positive answer when asked whether they had cough, sputum, pain in the chest, tightness of the chest, or shortness of breath on exertion.

Fig. 2 and table III show the percentages of men in each group who gave a past history of bronchitis, pleurisy, pneumonia, and dyspepsia. The probability that these differences were due to chance is given in the last column of each table. Accepting as the level of significance that the difference would not have occurred more often than once in twenty times by chance, we find that there was a significant difference in the observers' recordings of the frequency of cough, sputum, pain in the chest, and dyspepsia.

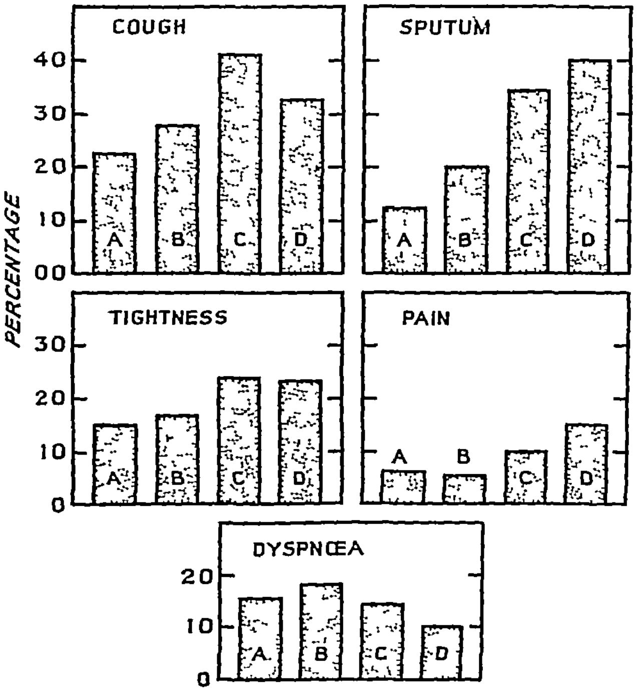


Fig. 1—Symptoms found by each observer

DISCUSSION

Our results suggest that the recording of patients' answers to simple questions may, in some cases, give results that are unaffected by the observer. In the case of a past history of bronchitis, pleurisy, or pneumonia the question "Have you ever had ...?" is straightforward, and the answer in most cases will be "Yes" or "No," which will be thus recorded.

The consistency between the observers' recordings, however, does not mean that the answers are necessarily correct. Their accuracy must have depended on the memory and cooperation of the men who were asked the question, but men with good and bad memories or high and low levels of cooperation were presumably randomly distributed throughout the group. In the other questions, however, the observer had to interpret the man's answer before recording it. For instance, to the question "Have you a cough?" or "Do you spit?", the man might reply "Only an ordinary cough" or "Only after work" (for miners commonly cough up a little black phlegm after the shift). The observer would then have to ask supplementary questions to decide whether or not the severity of the cough constituted a symptom of chest disease, and his ultimate recorded answer would depend as much on his judgment as on the man's answer. This is presumably why, in these cases, we find very different frequencies recorded by different observers.

TABLE III—NUMBER AND PROPORTION OF MEN IN EACH GROUP WHO GAVE A HISTORY OF HAVING HAD CERTAIN DISEASES

Disease	No. of men seen by observer				Probability (%)
	A	B	C	D	
Bronchitis	32 (*12.2%*)	26 (*10.4%*)	31 (*10.3%*)	21 (*11.5%*)	80–90
Pleurisy	24 (*9.2%*)	21 (*8.4%*)	31 (*10.3%*)	23 (*12.6%*)	50
Pneumonia	30 (*11.5%*)	36 (*14.4%*)	45 (*15.0%*)	24 (*13.2%*)	50–70
Dyspepsia	26 (*9.9%*)	40 (*16.0%*)	70 (*33.3%*)	49 (*26.9%*)	<0.1*

* Significantly small

In the case of shortness of breath on exertion, which is normal to some extent in health, the observers had agreed before the survey on a careful grading. The miners were asked if they could keep up with their fellow workers of their own age, while walking. Our results seem to show that such a system helps to reduce observer error if it is properly used. Errors due to faulty answers will remain.

In the case of dyspepsia there is once more an infinite gradation from healthy men who feel bloated after Christmas dinner to the true case of peptic ulcer; hence the observer's judgment once more enters into his recorded answer. Presumably the error that we have shown could have been lessened by more careful definition, as in the case of dyspnœa.

We believe that our results demonstrate that, at least in this particular survey, the recorded answers to several questions commonly asked in taking clinical histories were not reproducible from one observer to another, so they could not be considered objective scientific observations. Possibly if the observers had been more experienced clinicians, or if they had worked more slowly, their results would have been better. Observer A was an experienced clinician of consultant physician status, and observers B and C could fairly claim to be well trained in academic scientific medicine, which might be considered at least as important as clinical experience for the accurate and consistent recording of men's answers. The composite observer D would be expected to be exceptionally accurate, for the

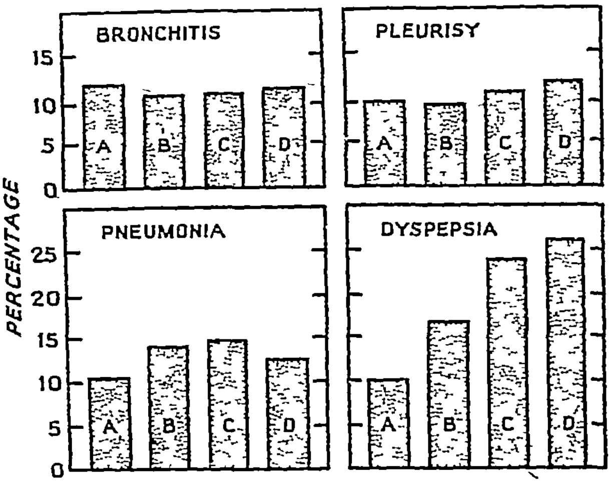


Fig 2—Past medical history found by each observer

proportions found by D are a kind of average of those found by the three observers included in D the inter observer error of the three being thus partially averaged out For this reason the discrepancies found are likely to be underestimated In view of the slightly higher mean age of the men seen by observer B it is interesting to observe that his results are in only one case more extreme than those of observers A, C, and D

The work was certainly done quickly, but little faster than some of the work done in hospital outpatient departments or in the consulting rooms of general practitioners Possibly miners are a particularly difficult group, because so many of them have the slight degree of cough and expectoration after work to which we have already referred

In spite of these reservations we believe that our findings have some general application, they are certainly important in clinical field surveys Unless different observers can obtain consistent answers to questions from comparable groups of witnesses their findings are of little scientific value If this were generally recognised, a great deal of misplaced research endeavour would be saved, and many publications would gain in validity what they lose in length. We suggest that the technique we have adopted is suitable for investigating the reproducibility of clinical findings

The application of our results to history-taking in general is less certain, but many doctors must remember certain curious discrepancies between the histories taken by *them as students and those elicited later from the* same patients by the house physician or the registrar This inter observer error of hospital history taking would merit investigation particularly if there were any possibility of the histories being used for research purposes later

A further possibility is in the field of medical education A great deal is taught about the art of history taking, *its science is badly neglected It should not be difficult* to arrange demonstrations for students to show the dangers of leading questions and the invalid deductions that can be made owing to the lack of reproducibility of clinical findings

SUMMARY

A clinical survey of a large number of coalminers was made by several medical observers who interviewed different groups of men The age distributions of the groups were similar The observers all asked the miners in their groups the same questions

The answers to some of these questions showed that the observer's bias was influencing the frequency with which a positive answer was recorded Other questions were more consistently answered in the different groups

These results are discussed, and it is suggested that more attention should be paid to possible lack of reproducibility in the answers that patients give to questions commonly asked in clinical practice, and that, for research purposes, answers which are not reproducible are worthless

In such large scale coöperative work it is difficult to apportion credit fairly We should, however, like to mention Dr C M Fletcher, Dr J C Gilson, and Dr K J Mann, of this unit and the 993 miners who answered our questions so patiently and so surprisingly

REFERENCES

Bean W B (1948) *J appl Physiol* 1 455
Birkelo C C Chamberlain W E Phelps P S, Schools P E Zachs D Yerushalmy J (1947) *J Amer med Ass* 133 359
— Rague P O (1948) *Amer J Roentgenol.* 60 303
Britten R H Thompson L R (1926) *Publ Hlth Bull Wash.* no 162
Cochrane A L Campbell H W Stein S C (1949) *Amer J. Roentgenol* 61 153
Comroe J H jun Botelho S (1947) *J Amer med Sci* 214 1
Derryberry M. (1938) *Publ Hlth Rep Wash* 53 263
Fletcher C M Oldham, P D (1949) *Brit J industr Med* 6 168.
Hebert G T (1939) *Tubercle* 20 145
Jones P H (1938) *J roy Statist Soc* 101 1
Kinsey A C Pomeroy W B Martin, C E (1948) Sexual Behavior in the Human Male Philadelphia and London
Pope A (1732) Epistle 3 to Lord Bathurst London
Sydenstricker F Britten R H (1930) *Amer J Hyg* 11 73

IMPERIAL CANCER RESEARCH FUND

In his summary of the work done during the past year in the laboratories of the Imperial Cancer Research Fund,[1] Dr James Craigie, F R S, the director, reports investigations on tumour transplantation, tumour induction and progression under hormonal influences, and chemical carcinogenesis in the liver

Dr A M Begg, Miss P E Lind, and Miss Margaret Hayward, PH.D, have collaborated with Dr Craigie in exploring the possibility of developing quantitative methods for the study of transplantable tumours For this purpose a better knowledge of conditions governing cell survival in vitro is essential. It was found that tumours could be preserved as cell suspensions in the frozen state provided that dextrose solution was used It was noted that cell suspensions contained a small number of highly refractile bodies similar in size and contour to tumour cells Retention of viability in vitro depended on maintenance of this refractility as seen by phase microscopy Refractile cells were resistant to dextrose solution and to freezing and drying in dextrose —manipulations which kill normal tumour cells

The discovery of a resistant state raises many questions

Doubtless before doing any further work along these lines, the facts have been taken into consideration that normal cells—liver, for example—as well as tumour cells of all kinds actually develop this curious refractile change with obscured nuclear detail in dextrose, sucrose, and glycerin solutions, that the appearance is completely reversible by washing out the sugars or glycerin that it is not to be confused with a similar but irreversible appearance natural to dead pyknotic cells that no normal liver cells, whether highly refractile or not are resistant to immersion in dextrose solutions and to freezing and partial drying as measured by growth after animal grafting And therefore high refractility is not likely to underlie any property peculiar to tumour cells

Dr Leslie Foulds has extended his studies on the progression of tumours towards malignancy and on their responsiveness to various physiological conditions Observations extended over long periods of intermissions of breeding have confirmed the previous findings that some mammary tumours that regressed after parturition recurred after many weeks without the stimulus of a new pregnancy, but that others did not recur although new tumours developed elsewhere in the mammary glands of the same mouse

---

[1] Imperial Cancer Research Fund 45th Annual Report 1950–51 Issued by the Fund, Royal College of Surgeons Lincoln's Inn Fields London W C 2

Dr E Vazquez Lopez has continued his study of the effect of thiourea in decreasing mammary tumour incidence in a strain of mouse with the Bittner agent Although œstrogenic secretion is interrupted for a long period during administration of thiourea, nevertheless the size and differentiation of the mammary glands are equal in treated and untreated animals The purely carcinogenic contribution of œstrogens in this type of tumour production can therefore be established and studied independently of any other manifestation of ovarian activity

Mr H G Crabtree has prepared a number of new azo compounds with the purpose of examining further the concept that p aminobenzoic acid and possibly folic acid may be determining factors in the genesis of liver tumours Experiments designed to test the concept will take many months to mature

ROYAL SANITARY INSTITUTE

Southport's sun, sea, sky, and too plentiful sand provided the physical background for a busy time last week for many practitioners of preventive and curative medicine Experts on tropical hygiene, occupational health, engineering and architecture in relation to hospital design, housing and town planning, veterinary hygiene, and the food industry helped to contribute to the forty seven addresses Also present were members of local authorities, engineers, surveyors, sanitary inspectors, health visitors, and not a few general practitioners —over 2000 members of the "health team" in the campaign against disease

THE RHEUMATIC DISEASES

Sir Henry Cohen, in the opening paper, gave an important classification of rheumatic diseases He protested against the domination of labels in diagnosis He estimated that in Great Britain there were not less than 250,000 arthritics—more probably there were twice as many He cautioned against the cry of "cortisone for all", for at $35 per gramme a quarter of a million patients could cost (even if the drug were available) over £112 million per annum He had caustic comment to make on the "meaningless" cry of prevention and on the many valueless contributions, statistical and otherwise, in the rheumatic field Nevertheless, he felt that "never in the history of rheumatic disease has the horizon been brighter"

Dr E T Conybeare followed with a careful scientific assessment of the problems of acute rheumatism and rheumatic heart disease Another quarter of a million persons under the age of 40 had hearts damaged by acute rheumatism The number of new cases every year might be 5000 He quoted Bywaters's recent summary of the now practically overwhelming evidence that infection with *Streptococcus hæmolyticus* (group A) is one of the causes of acute rheumatism and rheumatic heart disease Infection with this organism is, Bywaters says, the "prime factor, not exclusive of other factors, but without which the disease would not exist"

Dr Conybeare felt that overcrowding might be attacked to better advantage, sleeping and other accommodation in all residential communities (and especially those which were educational or military) should be arranged so as to diminish as far as possible the spread of respiratory infection and to control the frequency, weight, and variety of these infections among children and young adults With so much depending on early detection, especially with the sometimes insidious onset, the help of the general practitioner was of outstanding importance The special rheumatism supervisory centres were of help to him The hospital and specialist services, together with local health and education services could provide much useful help in carrying out the important recommendations of the Rheumatic Fever Committee of the Royal College of Physicians

VETERINARY HYGIENE

In the section on veterinary hygiene, Mr W S Davison, M R C V S, re stated the need for a central reference laboratory in investigating infestation of meat by parasites inimical to man

Mr E -R Callender, M R C V S, discussed the eradication of bovine tuberculosis and the financial inducements which were offered to the milk producer and stock rearer, his figures showed the apparent slow progress achieved

HOUSING

Mr Ronald Bradbury, PH D, pleaded for a more realistic basis of housing design to meet the varying needs of different families, from the newly married couple to the large number of aged persons living singly and occupying a big house

FOOD

There was much discussion on the control of manufacture of ice cream and other emulsified food products No one bacteriological test was reliable Miss Betty Hobbs, PH D, thought that risk of infection had been considerably reduced by the operation of the Ice cream Heat Treatment Regulations, 1947, but unnecessary outbreaks of infective disease, particularly those caused by *Salmonella paratyphi B* and other organisms of the salmonella group, still occurred Far stricter control over the manufacture of synthetic cream was needed Many foodstuffs, such as mayonnaise and salad cream, were relatively safer because of their low pH and their content of vinegar

HYGIENE IN INDUSTRY

Dr J N Morris, in the section on hygiene in industry, challenged his audience with the question "What is it we are trying to do?" In the discussion a speaker brought down the house by stating that "most troubles in industrial health are due to sheer laziness!"

ENGINEERING AND ARCHITECTURE

In considering the design of a premature baby unit, Mr P B Nash showed the plans of a new unit, containing 14 cots, designed to accommodate mothers and their babies The unit also provides for demonstration and feed rooms, six "warm" cubicles, and 8 "cool" cubicles

Lieut Colonel E G King described the problems of sewage disposal in seaside towns He emphasised the value of sterilising effluents before discharge into tidal waters in order that amenities on the beach should not be affected

MATERNAL AND CHILD WELFARE

Dr Alfred Torrie, in a human contribution on the problem of placement of children for adoption, said of adoption "the earlier the better" The child's interests were paramount Some neurotic adults wished to adopt children to compensate for the lack of love in their own lives and to try to cure their own neurosis Though breast feeding was in the best interests of the child, if we rigidly followed a rule that every unmarried mother should breast feed her child and then part with it we were placing a great strain on the mother The sooner the permanent alternative, mother was found and affectionate bottle feeding begun, the better it would be for the mental health of the child

Dr Torrie discussed the problems of backward children who were adopted His experience was that many children who were slower in development than others le up for it later on, those who kept height and ght charts of infants knew that these were helpful understanding week to week progress but were not essarily an indication of what the child would be en grown up To condemn a child to an institution instead of giving it an opportunity to be brought up a family was a very grave responsibility

The psychological problems in placement for adoption olved round the personalities of the adopting parents, ability of the mother to make her own decisions, and need for the child to be adopted at the earliest sible moment More study was required to determine criteria for successful adoption, so that magistrates d others might have something valid to guide them e problems of adoption required a considerable know ge of the factors making for mental health and bility of personality as well as of physical sanitation

Mrs **Austin Melford**, of the National Adoption Society, reiterated the doubts often felt as to whether the motives for adoption were the right ones. It was important to make a wise choice of adopters, and to avoid unhealthy, highly strung, or elderly couples Still greater care was necessary in placing a second child with the same family, and there was more risk of failure where adopters had a child of their own

In the last session, Prof A V **Neale** pleaded for the removal of the "iron curtain" between preventive and curative medicine and for greater knowledge of the normal child Undergraduates in particular should examine 'normals" because later they would encounter more normalcy than disorder The training in hospitals might lead to wrong views, for hospitals were filled with "medical failures" Students should have more teaching in the homes of the people

---

Public Health

PIDEMIOLOGY OF A SMALL OUTBREAK OF ANTHRAX

A T Doig
M.D St And, D.P.H
H M MEDICAL INSPECTOR OF FACTORIES

J S Gemmill
M B Glasg D.P.H.
SENIOR MEDICAL OFFICER, PUBLIC HEALTH DEPARTMENT, GLASGOW

In early summer, 1950, three cases of anthrax occurred Glasgow The first patient, who sickened in May, as a motor-van driver employed by a firm of purveyors nd caterers in a southern area of Glasgow some four niles distant from his home in the east end.

On May 16, 1950 the patient aged 35 returned from work nd, before entering his home had his hair cut at the local arber's shop While a towel was being adjusted he received scratch on the back of his neck which made him wince nd he remonstrated with the barber Before leaving he elt the same spot again painful when having his hair brushed On the following day there was a small pimple at the site of he injury which he covered with an adhesive dressing he area, however, continued to itch for some days

On May 21 he suffered from anorexia headache, generalised ains, and malaise, to which sweating was added on the 2nd when he stayed in bed On the 23rd his doctor visited im and treated him for influenza and a boil the dressing aving now been removed for the first time On the 24th e had pain in his left shoulder and now very ill he was een by another doctor who suspected anthrax from the ppearance of the neck lesion and took a smear in which the resence of anthrax bacilli was confirmed by animal inoculation. Penicillin treatment was begun and was at once ffective

The patient was seen at home on the 31st by one of us J S G) and was found to be convalescent The lesion onsisted of a healing ulcer on the left side of the back of the neck just above collar level the crater was covered by a dry black eschar which measured 1 in horizontally by $^3/_4$ in vertically The appearance was typical of a malignant pustule in the stage of resolution There was also firm discrete adenitis of the posterior triangle and supraclavicular region on the left side but none of the left axilla or on the right side anywhere He had not recently bought or used any new shaving brushes or hair brushes

The patient's place of work and his duties were investigated (A. T D), and these did not appear to bring him into contact with any known or likely source of anthrax infected material. The vans were all motor driven His main duties were to carry trays of foodstuffs from the bakery to his van and then deliver these The goods handled were almost all cooked or baked and seldom contained meat, although on occasion he had to collect meat from a butcher

At this time there was in Glasgow no other patient notified as a case of anthrax.

A visit to the hairdresser's shop showed this to be of a low order of hygiene and management The equipment was modern but the premises were generally dirty and untidy Scissors, clippers, brushes, combs, &c., were said to be sterilised by heat every night They were certainly not sterilised between each customer, the proprietor freely admitted that this was not practicable and was never done He had not recently bought any new brushes, his present stock of shaving-brushes had been in use for a year, and of hair-brushes for two years.

Many of this hairdresser's regular customers were known to be employed at a nearby tannery, and on June 1 two men employed at the tannery—neither of whom was a customer of this hairdresser—fell ill with anthrax These two patients, aged 47 and 50, were seen by us several days after the onset of their illness. In one the lesion was on the left arm and was extremely severe, while in the other it consisted of a typical malignant pustule at the angle of the right jaw, anthrax bacilli were isolated from both lesions Both patients recovered The severe case appeared to be penicillin-resistant but began to make slow progress under treatment with anti anthrax serum and 'Aureomycin', the other case responded well to penicillin alone

On June 6 one of us (J S G) visited the tannery and took samples for bacteriological examination These were (1) floor-sweepings from an area of the store on which a batch of suspected East African hides had been stacked since their arrival in the factory in February and March, 1950, (2) a sample of dry East African hide cut from the edge, (3) a sample of dry East African hide cut from the centre Sample 2 was negative for *Bacillus anthracis*, the guineapig having died of an intercurrent intoxication (*Clostridium welchii*) Samples 1 and 3 were both positive for *B anthracis* on guineapig inoculation Another batch of East Indian hides from the same cargo was responsible for a fourth case of anthrax occurring in another town

COMMENT

It seems reasonably certain that case 1 was infected indirectly in the barber's shop, by contaminated instruments or finger-nails, or both It also seems permissible to assume that this infection was introduced into the barber's shop *on or about* May 16 by a tannery employee whose hair or clothing was contaminated by infected dust, but who himself was not suffering and did not later suffer, from anthrax The assumed path of infection, then, is from the infected hides by means of dust to the hair or clothing of an unaffected worker, thence to the barber's instruments or finger-nails, and finally to the affected person

The facts supporting these *conclusions* are as follows (1) a certain batch of hides in the tannery was proved to be infected with *B anthracis*, which was also present in the dust arising from this batch, (2) a considerable number of employees at the tannery habitually patronised a nearby hairdresser, (3) a man having no other known, or likely, contact with infected material received a wound on the neck while having his hair cut at the same hairdresser's, and a malignant pustule developed at the site of the wound; (4) two cases of anthrax occurred in the third week after this incident in tannery employees who had contact with the infected hides, but had not patronised the hairdresser's shop.

Children in Glasgow

The average weights and heights of Glasgow schoolchildren have increased steadily in the last 18 years. The following figures for 1950[1] show the average increases for the different age groups since 1932:

Age (years)	*Increase in average weight and height* *Boys*	 *Girls*
5	2·91 lb 1·37 in	2·66 lb 1·30 in
9	4·84 lb 1·78 in	4·64 lb 1·44 in
13	8·63 lb, 2·30 in	9·46 lb, 1·92 in

Medicine and the Law

Parent's Refusal to allow Operation

In a recent case which must have given the hospital authorities a distressing anxiety a mother persistently refused permission for an operation to be performed upon her infant daughter. At the inquest[2] the coroner told the jury that they might have to consider returning a verdict of manslaughter or even murder. The jury's verdict was "death by misadventure"; they added the comment: "We feel that the mother did not sufficiently understand what was being asked of her." In recording the verdict the coroner observed that death was accelerated by lack of adequate treatment owing to the mother's refusal to consent to an operation.

The deceased baby, born in June last year, was admitted to the Ipswich Isolation Hospital (on transfer from the Borough General Hospital) with whooping-cough. Gastro-enteritis developed. Efforts were made to obtain the mother's permission for intravenous injection; she was told that the medical authorities said that the child's only chance of survival was by an operation. She had herself undergone two operations in hospital and had said that she would never have consented to them had she known how severe they would be. Since that experience she had dreaded operations. There was some conflict of evidence as to whether she had or had not, at one point, assented to the operation on the child; she maintained at the inquest that she had at all times said "no." The doctor in charge of the case, being informed that verbal consent had been given, started the intravenous drip; the operation was not complete when the mother arrived at the hospital and made it clear that she refused to allow it. The wound was closed and the operation was abandoned; the infant died next day. Medical witnesses could not say that the operation would have saved the child's life, but they considered that it would at least have prolonged it. The mother was told that the chances of survival in hospital, if the operation were performed, were fifty-fifty; without it they were nil. At the inquest the pathologist's evidence was that the recommended treatment was the only useful course; it was not always successful, but in many cases it gave the sole chance of recovery.

Apart from any common-law obligations to care for a child, the Children and Young Persons Act of 1933 (replacing section 12 of the Children Act of 1908) makes it an offence to neglect a child in a manner likely to cause unnecessary suffering or injury to health, and specifically states that it is neglect if the parent fails to provide medical aid. The Act declares that injury to health includes injury to, or loss of, sight or hearing or limb or organ of the body; these words, as Mr Justice Darling pointed out in Oakey *v.* Jackson in 1914, indicate that Parliament contemplated that medical aid might include surgical operation. In Oakey *v.* Jackson the alleged neglect was the failure to allow an operation upon a 13-year-old child for removal of adenoids. There was evidence that she suffered from mental dullness, impaired breathing, deafness, and some anæmia, and that, though it probably involved anæsthesia, the operation was not a dangerous one. The magistrates took the view that there was no legal compulsion upon the parent to allow the operation. The High Court held that the facts might amount to a failure to provide medical aid and that, if the facts justified it, the magistrates should have convicted the accused.

Two points have arisen in this class of prosecution. The fact that parents are poor and could not ordinarily afford to pay professional fees has been no defence to the charge; the medical aid could be obtained through public assistance and today through the National Health Service. Secondly, the intention of the accused person needs to be considered. The word "wilfully" was explained in 1899 by Lord Russell of Killowen, L.C.J., in R. *v.* Senior, where the parent had belonged to the sect known as the Peculiar People and had objected on religious grounds to calling in medical aid or the use of medicine. "Neglect," said Lord Russell, "is the want of reasonable care, that is, the omission of such steps as a reasonable parent would take—such as are usually taken in the ordinary experience of mankind." Mr Justice Avory, concurring in those observations, tersely added that one matter the justices ought to consider in such a case is "whether the person who advises the operation is a qualified medical practitioner or merely some irresponsible person."

Parliament

The Health Service Charges

The debate on the second reading of the National Health Service Bill swung between those who regarded the proposed charges for spectacles and dentures as safeguards of the whole service and those who regarded them as a breach of faith and principle. Mr Hilary Marquand in his lucid review of the Budget proposals declared that the new charges were not a tax on the service but a readjustment of its finances to enable it to meet rising costs. Nor were these the first adjustments to be made. For instance, economies involving cuts in the remuneration of dentists, opticians, and chemists had already been made; and patients' travelling expenses to hospitals had been curtailed. The Secretary of State for Scotland took a similar view, defending what he described as modest charges on the very periphery of the service.

Dr Santo Jeger, on the other hand, firmly denounced the new charges. They were, he said, deterrents rather than money-raisers. They would be a counterblast to health propaganda. Spectacles and dentures were not inessentials but an important part of treatment. If economies had to be made, could not old spectacle frames be used? Could not the patient be asked to provide his own bottle for his medicine? What about further adjustments of dental fees? Were not the sums paid to medical specialists rather inflated compared with those to other members of the medical profession? Dr Charles Hill joined Dr Jeger in the defence of dentures and spectacles. He deprecated any suggestion that the word cosmetic should be applied to them, for they were of real importance to health. On the other hand he accepted the need to fix a ceiling for our health service if other less glamorous but also important social services were not to suffer. But an over-all ceiling should also mean a series of ceilings within the service for the component parts. At present hospitals claimed two-thirds of the health service expenditure, and if this went on other parts of the service would have to be cut He thought there was insufficient control and economy in the hospital service and that this could only be remedied by allocating money at the lowest possible administrative level But though he agreed that charges must be made he regretted that they had been slapped on at administratively convenient points without consideration of their effect on health Thus two large obvious items had been chosen to bear the brunt It was true that until we had more dentists to safeguard our children's teeth, we must place a financial barrier between the public and the dental service But why place it four-square on the dental plate ? Turning to the ophthalmic service he reminded the House that nominally its present form was temporary He thought the best way to control it was to bring it as originally planned, under the ægis of the hospitals.

---

[1] Corporation of Glasgow Education Health Service Report on the Medical Inspection and Treatment of School Children for the Year ended July 31, 1950.

[2] *East Anglian Times*, April 19, 1951, p. 5.

Paying for Beds

On the motion for the adjournment on April 24, Brigadier J G SMYTH raised the question of pay beds in hospital, basing his remarks on the experience of one of his constituents

This constituent Mr Harris, had an income of £500–£600. Last August his wife was taken seriously ill and her general practitioner diagnosed an irreducible femoral hernia strangulation. The doctor had asked King's College Hospital, where Mrs. Harris had some years before been a patient if they had any public beds free, but they had none The doctor then suggested she should inquire if there were any private or semi private beds available she rang the hospital again and found there were The doctor warned Mr Harris that the fees would be about 13 or 14 guineas for the bed and that there would also be a surgeon's fee but Mr Harris maintains he was given no indication what the surgeon's fee would be He admits that he signed a form but he did not know what was written on it at that moment his wife was so ill he would have signed anything When Mrs Harris left hospital her husband was given a bill for £85—14 days in hospital at 12 guineas a week, surgeon's fee of £52 10*s* anæsthetist's fee of £7 7*s* Mr Harris was unwilling to pay, but both the hospital and the surgeon threatened to bring legal proceedings and after some months the account was settled

Brigadier Smyth felt that there should be a distinction between a patient who arranged for an operation in a private ward beforehand and knew what he was letting himself in for, and someone who was desperately and suddenly ill He felt there should be more give and take

Mr ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, said that the case raised an important principle for which he had much sympathy, it also raised problems which the Ministry had been trying to meet for some time There was a proviso in the Act that pay beds may be used without charge where there was urgent medical need, and during the last six months King's College Hospital had admitted 65 cases free to pay-bed accommodation. The proportion of pay bed as against free-bed accommodation was under discussion and he understood that before long a further 30 beds at King's would change over from pay-bed to amenity or free-bed accommodation In cases of this kind the normal procedure was for the practitioner to let the hospital know when no ordinary accommodation was available that the case should be regarded as an emergency He was satisfied that in this case the hospital did not understand the case was an emergency It was true that there was no general bed available at King's, but there might have been one in a nearby hospital—the Dulwich Hospital The service could not guarantee that admission can be made automatically to any particular hospital Occasionally it was found that admission had been made to a pay bed through misunderstanding, adjustments were then made later at a time when the anxiety was not so great Mr Harris was presented with his account at the end of the first week but he made no complaint and let it run on. Definite pledges had been given to the medical profession, Mr Blenkinsop pointed out that there should be some pay bed accommodation and as long as there was surely it was reasonable to try to ensure that it was put to the best use for the purposes for which it was intended, except under emergency conditions

QUESTION TIME

Health Centres and Group Practices

Mr SOMERVILLE HASTINGS asked the Minister of Health how many comprehensive health centres had been provided since 1948 how many were now under construction either by new building or adaptation, how many centres for group practice had been provided since July, 1948, how many were now under construction either by new building or adaptation.—Mr H. A. MARQUAND replied Nine premises taken over when the National Health Service began are being administered as health centres for groups of doctors and other services One large centre is under construction, and tenders for two smaller ones have been invited.

Mr HASTINGS Would the Minister not regard it as dangerous if when the time came to make it possible to build health centres and centres for group practice, there was no more experience of them than is suggested as possible in his answer ?—Mr MARQUAND I have every sympathy with this and I intend to encourage where suitable conditions are available the establishment of further group centres of this kind

Mr HASTINGS asked the Minister why he had refused the London County Council permission to provide at the Hampstead Health Institute a centre for group practice, and how far it was now his policy only to permit local authorities to make provision for group practice in under-doctored areas. —Mr MARQUAND replied In general I want to see some experiments in provision for group practice in suitable areas, but this area is already well supplied with doctors and surgeries Two centres are out to tender at the moment—one in Bristol and one in Farringdon Other proposals are under consideration. In Hampstead it is understood that the group of doctors wishing to practise at the centre intended to continue their existing practice at their own private surgeries and to seek new patients for their practice at the health centre

Hospital Accommodation

In answer to a question Mr MARQUAND stated that the total number of staffed beds in hospitals now in the National Health Service was 440,231 on June 30, 1948, and 458,363 on Dec 31, 1950

Of these about 6875 were pay beds or 1½% of the total number of staffed beds which were set aside at present under section 5 of the National Health Service Act 1946

Unsuitable Hearing-aids

SIR THOMAS MOORE asked the Minister how many National Health hearing aids had been returned by their recipients as unsuitable—Mr MARQUAND replied Precise figures are not available but the number is estimated at 2000

National Health Service Spectacles and Dentures

Mr GORONWY ROBERTS asked the Minister the number of persons issued with free spectacles and dentures in the years 1948 1949, and 1950 respectively—Mr. MARQUAND replied Precise information is not available but I estimate that in England and Wales the numbers of dentures and spectacles supplied (including those for which the patient paid a contribution) were approximately as follows

	Patients supplied with dentures	*No of pairs of spectacles*
1948	200,000	1 500 000
1949	2,300 000	7 250 000
1950	3 450 000	8 250 000
	5 950 000	17 000 000

Qualifications of Foreign Dentists

Mr S S AWBERY asked the Minister what steps were now being taken to utilise the services of experienced foreign dentists in this country who had been naturalised what discussions had taken place with the Dental Board on this subject and with what result—Mr MARQUAND replied The Government intend at a convenient opportunity to introduce a Bill which will include proposals for new methods of assessing the qualifications of foreign trained dentists I am satisfied that all that can be done under the existing law has been done

Replying to further questions Mr MARQUAND said that the number of dentists affected was a good deal fewer than 100 It was not possible to allocate to the school dental service personnel who were not qualified to practise dentistry under the law

Durham County Council

Miss IRENE WARD asked the Prime Minister whether, in view of the Durham County Council's decision to cease questioning teachers as to whether they are members of their appropriate unions, he would now take steps to ensure the adoption of a similar attitude with regard to other employees of the council —Mr CHUTER EDE replied the Prime Minister has no information that similar questions are put to other employees, but Ministers are concerned to intervene in the actions of local authorities only where these actions may endanger the efficiency of services for which the Ministers have responsibility

Accommodation for Mental Defectives

In answer to a question Mr MARQUAND stated that according to returns made by local health authorities on Jan 1, 1951, there were 5316 mental defectives awaiting admission to institutions There was no reason to think that the proportion of mental defectives was increasing, but the number increased yearly with the population Provision for these patients received high priority in the hospital service, within the limits of capital investment and staff available

In a written answer the Secretary of State for Scotland stated that 1200 names were on the waiting lists of mental defective institutions in Scotland

Boarding-out

Major NIALL MACPHERSON asked the Secretary of State for Scotland how many lunatics were boarded out in the year ending March 31, 1950, and how this figure compared with the number for the two previous years —Mr HECTOR MCNEIL replied 49 lunatics were boarded out during the year ending March 31, 1950 (27 males and 22 females) The numbers boarded out during the years ending March 31, 1949, and March 31, 1948, were 32 (19 males and 13 females) and 29 (15 males and 14 females) respectively

Major MACPHERSON Under what conditions are lunatics, boarded out and what supervision is exercised ?—Mr MCNEIL Lunatics are boarded out either with their own relatives or with unrelated guardians For lunatics boarded out with unrelated guardians the aim is to provide a home life in suitable surroundings, men are usually placed on small farms or crofts and women in cottages in villages Not more than four patients can be placed with any one guardian The homes are usually found by the local health authority, and the sanction of the General Board of Control must be obtained to the placing of any patient with the guardian selected The board exercise supervision over the patients, who are visited at least once a year, and oftener in special circumstances, by a deputy medical commissioner In addition the patient is visited four times a year by a doctor, and twice a year by the local authority welfare officer acting on behalf of the regional hospital board

Brussels Treaty Public Health Committee

Mr BARNETT JANNER asked the Secretary of State for Foreign Affairs what were the present purposes and terms of reference of the Brussels Treaty Public Health Committee, what was its composition, who were the representatives of Great Britain thereon, what were the main subjects of the committee's recent session at Marseilles, and what were the major recommendations of this committee which had been implemented up to date —Mr K G YOUNGER, Minister of State for Foreign Affairs, replied This is one of several committees set up to consider the development on corresponding lines of the social services of the five countries, in accordance with Article II of the Brussels Treaty Its members are administrative and medical officers of the health administrations of the five countries At the meeting to which my hon friend refers the committee discussed the control of foodstuffs and proprietary medicines and the protection of populations from the health point of view in war time The main recommendations of this committee to have been put into effect so far are those for treating the five countries as a single territory for the health control of sea and air traffic

Dentures and Spectacles for Servicemen

In answer to a question Mr JOHN STRACHEY, Minister of War, said that the question whether soldiers were affected by the new proposals for payment for dentures and spectacles was under consideration

In England Now

A Running Commentary by Peripatetic Correspond

FESTIVAL

When Stratford Will was on the boards (and did
writing on the side),
The Londoners would come in hordes, taking a
across the tide
A penny for the waterman, a penny to attend the
And for their sausages and ale another penny, let us
They hadn't got a lot to spend, but they en
themselves no end

The same South Bank which beckoned thus,
bearpit, Globe and Swan and Rose,
Now spreads a peacock tail for us of lights and
and wonder shows
And now from France and U S A , from Rio, Th
and Panama,
From Singapore and Mandalay, and even the U.S.
Come foreign visitors to be the guests of Lo
on spree

Now is the time to cock our hats, to set the mat
Cockney wits,
To sing like larks and leap like cats, to chaff with
and wink at chits
Now is the time to air our French, give "Oui" for "O
and "Non" for "Non,"
And dance upon the Bailey Bridge as people
Avignon

Let us forget that Cromwell came to quench
a native flame,
Let us put off with one consent the winter of
discontent,
And may the merry gods and mad give us the
our fathers had

* * *

A good anæsthetist is as skilful at protecting surgeon from the effects of mental trauma as he is protecting his patient's nociceptors from the of the surgeon The satisfactory performance of important psychological task calls for many go —or at any rate mythical—qualities in the He must be as calm as Jupiter, as patient as P as punctual as Apollo, as resilient as Anteus, as as Mercury, and on occasions as many-handed as He must be ready to assume the rôle of porter, plum electrician, note reader, brow-wiper, spectacle pol table adjuster, and fire fighter at a moment's noti He must suffer the little barbs of the surgeon with humour, but be ready nevertheless to make such spirited riposte as to keep the surgeon on his Clever sayings of the surgeon at the expense of anæsthetist have a wide currency, and they do no But the anæsthetist usually contents himself w remarking to his disciple "Of course you must pro the patient by adequate depth against surgery such this", or 'What is the treatment of surgical sho occurring late in the second hour of a simple hernio rhaphy ?"

But I recall one occasion when the anæsthetist as one might say, the gas out of the bag The surg was operating on a foot to whose leg he had (somewhat inexpertly) applied a tourniquet He having great difficulty in finding a foreign body, was the more incommoded by a constant ooze of pu blood "Doctor," he said at last, "he seems blue my end" "I know," the anæsthetist repl gleefully, "I can get only a little oxygen past yo tourniquet"

When the surgeon reproaches the anæsthetist beca he says, the patient is bleeding (or not bleeding), because he is coughing when he wants to sew or not coughing when he wants to find the hernia, because the anus is so tight he can't get his finger (or out), or so loose that he can't identify the The an the requisite action is very simple expresses sympathetic concern, and ostentatiously mak some adjustment to his apparatus. As soon as the surgeon's attention is withdrawn the status quo may be restored. The suggestion, confidently made a few minutes later, that the nuisance has now abated invariably elicits the correct response.

* * *

"When we have thousands and thousands of pounds in the bank" I said to my wife as we lay in bed on Sunday morning, "I shall have breakfast in bed every day with little triangles of thin toast and two sorts of marmalade. And somebody will say 'Will you have tea or coffee this morning?' without adding 'because we've run out of coffee.' And we shall say 'Shall we go to Bermuda *again* this winter and we shall live the Gracious Life, like the advertisements" I was dragged back from the Ambassador's reception by our First Child's insistent "Daddy! Daddy! Daddy!" "Yes, First Child?" "Why were you in the coffee?" "In the coffee? What do you mean?" "You said you came out of the coffee" "I said we *ran* out of coffee. That's different. It means we didn't have any. Look, First Child, go and help your sister put her dolly to bed" A moment later piercing screams indicated that Second Child had been inconvenienced in some way. "What's the matter now?" "First Child touched my baby!" A crash, followed by tinkling of glass and bellowings, took me out of bed and down the stairs. At the bottom I kicked the remains of my shaving mirror into a corner, picked up Third Child and mopped up the blood. 'And our puppy," I said, as I went back into the bedroom, 'will be *thoroughly* house-trained" I threw my slippers out of the window. "By then he will be a graceful Borzoi," I added, throwing the laws of genetics after them, "and you, my dear, shall stand on the terrace with your fingers resting lightly on his head" "Oh *do* get up, Daddy," said First Child. "No," I said, "it's only seven o'clock and it's Sunday morning" "But it's *quite light*," said First Child indignantly. I put my head under the bedclothes. "You'd better get up," said my wife unfeelingly, "and do something towards putting those thousands and thousands of pounds in the bank" Well, here it is.

* * *

As Lady Bracknell said so memorably, "To lose one parent may be a misfortune; to lose both looks like carelessness" But my recent experience with the R N and R M Recruiting Headquarters suggests that to lose not only one's parents but one's entire family and forebears is sometimes a patriotic duty. Their letter ran:

> 'You have been found Temporarily Medically Unfit for entry into the Royal Navy/Marines as a volunteer due to —
> Family history of T B
>
> Should you still wish to be considered as a candidate for the Royal Navy/Marines you should visit your own Doctor and endeavour to have this defect remedied.

The doctor, I suppose, will do the job for a small decapitation fee.

* * *

Well, I finished my wool rug and, against my better judgment, was persuaded to enter it in the local Arts and Crafts Exhibition, where it was awarded a "Highly Commended." This damning with faint praise might have been weathered had not my daughter—in another class, it is true—taken a 'First" This has led to the discharge of numerous shafts of juvenile wit and been wholly subversive of parental discipline. Most humiliating. Let other non surgically-fingered fathers take warning and avoid vulgar competition with their offspring. No good can come of it.

* * *

Our latest technique with flies in the operating theatre is simple, effective, and cheap. Induction is preferably by the anæsthetist, who fills a 10 ml syringe with ether and stands at the ready. Spotters report on the whereabouts of the fly, hissing and pointing as soon as it settles. The anæsthetist takes aim and, after allowing a little for gravity, smartly rams home the plunger of the syringe. If the resultant jet lands within a foot of the fly, it drops to the floor in coma. The rest can be left to Sister. The range can be anything up to 15 ft and the trajectory should avoid the surgeon.

Letters to the Editor

PSYCHIATRY AND THE LAW

SIR,—The nation wide publicity given in the press to the advice of the Lord Chief Justice, Lord Goddard, when he addressed the annual conference of the National Association of Probation Officers on April 20, and warned them against "the fashionable craze for sending children to psychiatrists" and urged more frequent punishment for young offenders, is only the most recent example of the avidity with which our newspapers blazon abroad the opinion of any authority who demands a return to such punitive measures as the birch or flogging.

Editors and their newspapers live by "giving the public what it wants," and their shrewd choice of this sort of subject reflects our uneasy social conscience. We are all relieved when we read that Lord So and so or Mr S Snooks, J P, regards the juvenile delinquent either as just a naughty boy (negligible) or as a precocious monster (alien). In either case, we need concern ourselves no more with the young rascal—let him be punished. His punishment gives us respectable citizens an opportunity for revenge, and makes us still more aware of the gulf separating him from ourselves.

The average man who says "I was well and truly thrashed by my father (or schoolmaster) and it did me the world of good" quite forgets that it did him good because he himself accepted the values held by the chastiser or by the society he represented. But the delinquent, whose whole attitude to society is conditioned by early separation or lack of emotional support from his parents, has no such inner assent. His attitude to punishment can only be visualised in terms of a prisoner-of war resisting and resenting the stern measures of his captors: they may cow him into submission but they can never win him to allegiance.

Society's best protection against the offender is so to win him. It is only by understanding and accepting our own antisocial tendencies—not ensconcing ourselves on judicial benches, in editorial offices, or psychiatrists' consulting rooms—that we can give the delinquent the understanding and acceptance he needs, so that he can accept us and our values and become our fellow citizen.

London W 1 F R C CASSON

COMBINED ABDOMINO-VAGINAL HYSTERECTOMY

SIR,—I was interested in Mr Ellsworth Laing's suggestion last week that the cavity left after removal of the vagina should be treated by Thiersch grafting after the fashion of Sir Archibald McIndoe. I have not actually done this as a primary procedure at the time of the operation, but there is one candidate for it as a secondary procedure. She is aged 29, and it is 16 months since her operation, which included total cystectomy and implantation of the ureters. I felt that a decent interval should elapse and that the prognosis should be fairly assessed before submitting her to further surgery. Mr Laing will therefore realise that in one case his suggestion will probably be adopted, but as a secondary operation.

I am not so sure about the advisability of primary grafting, for the following reasons: (1) the operation has already been considerable, and any further elaboration of it may be detrimental to the patient, (2) the cavity left by the removal of the vagina is bounded anteriorly by the bladder, posteriorly by the rectum, and laterally by a vague space from which the paravaginal tissues and the cardinal ligaments have been removed. The ureters are superolateral relations of this space, and the peritoneum of the newly formed pelvis makes the roof. The bladder and the rectum may to some extent have been damaged, and I should be a little hesitant to add the trauma produced by the pressure of a mould to these tender structures For example, the ureters have been denuded of their distal blood supply by the dissection and in about 5% of cases undergo avascular necrosis, so that any further insult to their blood supply is to be avoided I should say that the optimum time to apply the mould and the graft would be 2–3 weeks after the operation, when the cavity and its visceral boundaries are already protected with early granulations

One final point must be made Mr Laing slightly exaggerated by suggestion the inconvenience caused by the slow healing of the cavity In some of my most favourable cases this has been clinically complete in 4 weeks and has never caused the patient any inconvenience whatsoever It was only in the case mentioned above, where the uterus, vagina, and bladder were removed, that the cavity took 6 months to heal Perhaps the situation can best be summarised by saying that if the case goes well the cavity causes little or no trouble If it is slow to heal and the cause of this is not recurrent or unextirpated growth, then I think Mr Laing's suggestion of grafting should be considered In the young patient for whom vaginal function is important, secondary grafting by McIndoe's operation should be employed when the prognosis is reasonable—say, 18 months to 2 years after the primary operation

London W 1 JOHN HOWKINS

EMPYEMA THORACIS TREATED WITH PENICILLIN AND ASPIRATION ONLY

SIR,—We were interested to see that the experience of Dr Asher and Dr Davies, recorded in their paper last week, bears out our own experience of the efficacy of this treatment which we reported in a rather larger series of cases[1] The technique they employ is similar to ours except that the need to inject intrapleural penicillin in a large volume of fluid is not mentioned We regard this as an important practical point since penicillin does not mix readily with purulent exudates It should, therefore, be given intrapleurally in not less than 20 ml of normal saline

St Alfege's Hospital
London S E 10

W A ELLIOTT
B A YOUNG

EPILEPTIFORM FITS DURING CALCIFEROL THERAPY

SIR,—The article by Dr Beare and Dr Millar (April 21) implies that calciferol has been the cause of epileptiform fits , but in two cases reported in this article the evidence does not seem adequate

Case 2 is of a woman, aged 20, admitted on Feb 21 in status epilepticus Later it transpired that she had been treated with 'Sterogyl' 600,000 units orally on Feb 14 and again on the day of admission." Only in the last line are we told that "the patient's mother suffers from epilepsy" Two lines above, they say no cause except calciferol intoxication was found for the fits '

Two doses of 600,000 units pure calciferol at a week's interval have not, up till now, been shown to be capable of intoxicating an adult A blood calcium level of 14 mg per 100 ml is not a sign of intoxication at all , and vomiting, pain in the jaws, and colicky pains in the abdomen can occur without calciferol therapy

Case 1 concerns a man, aged 20, who, apparently for the first time, had one epileptiform attack on two consecutive days *As this accident occurred after taking more than 42 million units calciferol,* "severe calciferol intoxication was provisionally diagnosed" It is surprising, to say the least, that the patient tolerated 150,000 units daily for 9½ months and that the drug should then suddenly have a convulsant effect Epileptiform attacks certainly occur for the first time in adults who have never taken calciferol As regards the slight albuminuria, which cleared up completely in 9 days and recurred occasionally some months later when the patient was no longer under calciferol treatment, it would appear difficult to link the drug with possible renal impairment, but Dr Beare and Dr Millar suggest this connection repeatedly, and do not deny it anywhere In addition, "the state of renal function before calciferol was given is not known"

In conclusion, there does not seem to be adequate evidence that calciferol produces epileptiform fits either in non epileptic or in epileptic subjects

London N W 10

A E GREMEAUX
Director of Medical Department
Roussel Laboratories Ltd

ACCOMMODATION FOR MEDICAL STAFF IN HOSPITALS

SIR,—I was so interested in Dr Goodall's remarks (April 14) about the desirability of providing married quarters for hospital residents that I am tempted to record my own experience

Recently I was resident at a famous hospital in the Home Counties My self contained accommodation consisted of two bedrooms, a bathroom kitchen, and a living room When built during the war it was occupied by a doctor and his wife Having been separated once and, as a Reserve officer, likely to be again, I applied for permission for my wife to stay in the unoccupied room for limited periods during my term of office This request was refused without adequate reason, the impression being conveyed that the demand was outrageous and should not be mentioned again

It is to be hoped then that Dr Goodall's work will not only stimulate the creation of married quarters for residents, but also change the outlook of management committees and administrators towards the use of existing resources

London W C 1 F G HARDMAN

HYPERCALCÆMIC URÆMIA WITH NEPHROCALCINOSIS

SIR,—I read with interest the report (April 21) by Dr Fulton and Dr Paget, as I have seen a similar case

A 62 year old housewife was admitted to hospital on Oct 4, 1946 For the previous month she had been confined to bed with increasing weakness and abdominal pain She complained of aching pains in her limbs and persistent pain across the upper abdomen She had troublesome vomiting and diarrhœa, and was thirsty She was drowsy and her skin had a muddy appearance Her tongue was dry and covered with a brown fur, and her breath had a slightly urinous odour There was no abnormality in the heart and lungs, and the blood pressure was 170/80 mm Hg The abdomen was slightly distended and appeared to be tender all over No œdema was found

Investigations—Blood Hb 80% (Haldane), red cells, 4 460,000 per c mm , mean corpuscular diameter 7 6 μ, white cells 10,000 per c mm (neutrophils 53%, metamyelocytes 1%, lymphocytes 40%, monocytes 6%) Urine specific gravity 1010, slight trace of albumin and a few hyalogranular casts and pus cells no Bence Jones protein Blood urea 108 mg per 100 ml blood calcium 16 8 mg per 100 ml , blood phosphorus 2 7 mg per 100 ml , serum alkaline phosphatase 30 units The total serum protein was 5 75 g per 100 ml of which 3 24 g was albumin and 2 51 g was globulin. The erythrocyte sedimentation rate was 9 mm in the 1st hour

A *straight radiograph* of the abdomen did not show any renal calcification and a cholecystogram was normal *Secondary* deposits in the form of circumscribed areas of bone absorption were seen in the ribs, pelvis, spine, scapula and femora A biopsy specimen was obtained from the ilium by trephining and showed secondary deposits, probably from a hypernephroma

Progress—The patient's condition gradually deteriorated, and vomiting and dehydration increased She became restless and noisy, and died on Oct 31 Unfortunately permission for necropsy could not be obtained

---

[1] Elliott W A Young B A *Post-grad med J* 1948 24 175

Despite the objection raised by Dr McGowan last week, the lesson from these case histories surely is that hypercalcæmia and renal impairment should, in the absence of a history of vitamin D therapy, initiate a search for bone secondaries as well as for myelomatosis and hyperparathyroidism

Grays Essex. R N Herson

THE BODY'S IRON

Sir,—The reference in your leading article of April 14 to the case of iron encephalopathy described by Dr Till and myself[1] is, I think, misleading It does not mention that the preparation used was different from those previously injected although it was accepted at the time as their equivalent The total dose was low, and its damaging effect may have been due to the fact that it was "home-made" and not prepared strictly in the same way as other solutions known to be safe

Enfield Middx C Allan Birch

INTER-INNOMINO-ABDOMINAL AMPUTATION

Sir,—I make no apology for describing the following single example of the above operation

Six months before admission the patient, a boy aged 17 years, fell off his bicycle and injured his right hip, Ten days later he became unable to walk, and the upper part of his right thigh began to swell. He was put into plaster, which, as the swelling increased, had to be removed The presence of malignant disease was now obvious, and he was left to his fate

On admission the patient had a huge semi fluctuating swelling with distended veins involving the upper right thigh and encroaching on the symphysis The circumference at the groin was 76 cm, compared with 35 cm on the normal side *Radiographs showed that 14 cm of the shaft and neck of the* femur had been replaced by growth and spicules of bone could be seen invading the soft tissues up to the pubis only the shell of the head of the femur remained intact The lung fields were clear, but the liver and spleen were palpable

Three weeks were spent, or rather wasted, in applying radiotherapy getting the patient into suitable condition, and persuading the relatives that an operation offered the only hope Throughout this time he had a hectic fever and was obviously going rapidly downhill On admission his red blood cells numbered 3,400 000 per c mm., and the hæmoglobin was 11 5 g per 100 ml ten days later the figures had fallen to 2 315 000 and 10 Finally 2 5 litres of blood was collected and operation was undertaken.

Anæsthesia was by rectal ether intrathecal procaine and closed circuit oxygen and ether *During the operation* 500 ml of glucose solution was infused intravenously followed by the 2 5 litres of blood The operation took 3 hours 50 minutes Owing to invasion by the tumour along Poupart s ligament, the external iliac artery was ligated at its origin, after stripping back the peritoneum. Thereafter there was no appreciable hæmorrhage until the guide for the Gigli saw was being introduced through the sciatic notch The hæmorrhage from the gluteal muscles was then easily controlled by digital pressure on the common iliac artery The skin flap was dissected back at the last possible moment The external iliac vein was ligated just before removal of the limb The portion removed weighed 16 kg (the patient s weight *before* operation was 51 kg) Histological examination showed that the growth was an osteosarcoma

In the three weeks since operation the patient has gained 2 kg in weight, his temperature has fallen to normal his appetite has become ravenous and he is *already walking* with crutches

In such a case this formidable *operation* is amply justified I am grateful to my former teacher, Sir Gordon Gordon Taylor, who has done more than anyone else to bring this procedure within the realm of the feasible and the humane

Altounyan Hospital Aleppo
Syria
E H R Altounyan

MANAGEMENT OF FLEXION DEFORMITIES IN ARTHRITIS

Sir,—One of the problems facing those who have to care for patients with chronic arthritis is the treatment of flexion deformities, which are caused by increased tone of the flexor muscles and wasting of the opposed extensor muscles In the last few years we have treated nine bedridden arthritic patients with flexion deformities of the legs with combined physical and medical treatment, and all can now walk Five have been discharged from hospital, either to their homes or to a hostel where there is no nursing care The methods of treatment used are recorded so that others interested in this problem can use them and perhaps improve on them

It was assumed that the primary cause of the flexion deformity in these patients was joint pain, and every effort was made to relieve this Pain can arise from inside the joint, from the capsule, or from the periarticular tissues, and injection of a local anæsthetic into the site of origin gave relief for periods varying from two hours to five days For intra articular injection procaine with lactic acid was used for other sites, procaine alone Injections were given once a week, but more often if severe pain recurred The patients had spasm of the hamstrings and adductor muscles which caused pain when the knee was extended Tender spots were often present in the muscle bellies, and when these were anæsthetised extension became less painful At first these spots were injected with procaine but later we used neostigmine ('Prostigmin') 0 5 mg with better effect

The injections when used in conjunction with physiotherapy *stopped the pain in some patients, but others* needed tab codein co once or twice a day in addition If the tender spots were in the superficial tissues, 1% ephedrine cream, rubbed in thoroughly daily, was effective The combination of local anæsthetic, neostigmine, and ephedrine cream has given more relief than any other medical treatment in our experience

Before starting physiotherapy neostigmine 0 5 mg was injected to produce muscular relaxation, and a posterior plaster was then applied to the limb in extension This plaster was worn during rest and at night, and a new one applied when necessary The affected joint was then treated with short wave diathermy or infra red rays When a *painful spot in the soft tissues* resisted other treatments ionisation with histamine was often successful The patient was not allowed to walk until the quadriceps had been strengthened, and this was achieved by a combination of faradism and active exercises The exercises were carried out in general classes and also individually in the Guthrie Smith frame with slings and springs Neostigmine was always given beforehand as it allowed more freedom of movement during exercise Extension and abduction of the limbs were encouraged, but flexion and adduction movements were reduced *to a minimum* When the local pain diminished the joints were passively stretched, after a preliminary injection *of neostigmine* by *a sling loaded* with a 6 lb weight applied for ten minutes For greater effect the feet were kept at the same level as the body Gradually the weight and the time of application were increased up to 12 lb for thirty minutes The patients were also made to lie prone and practise straight leg lifting and knee extension

In some patients the patella was adherent to the lower end of the femur and this prevented full extension The patella was mobilised where possible by manipulation under local anæsthesia, and, if successful, movement increased and walking became easier Two patients in whom the patella remained fixed improved sufficiently to be included in this series

Close cooperation between physician and physiotherapist is essential. It has taken as long as four years of continued treatment to enable some of the bedridden patients to walk, and one woman relapsed three times before she was able to walk in comfort Treatment has failed in four other patients who are excluded from this series Three of these have an additional disease which prevented treatment, and the fourth was psychologically unsuitable for treatment

---

[1] Birch C A Till M Brit med J Jan 13 1951 p 62

Geriatric Unit St John s Hospital
London, S W 11

TREVOR H HOWELL

BILIVERDIN

SIR,—In reference to the letter last November from Dr Gairdner and his colleagues,[1] I wish to point out that biliverdin does not give a positive diazo reaction [2] Statements to the contrary are occasionally made, but such findings are due to the use of impure samples of biliverdin which contain bilirubin

Institute of Medical Research,
Royal North Shore Hospital
Sydney, Australia

R LEMBERG

PARAFFIN IN SYRINGES

SIR,—I read with concern Dr McCartney's statement (March 3) that the syringes supplied ready for use to a group of hospitals are lightly lubricated with liquid paraffin Surely this is quite unnecessary and very dangerous

I do not know whether it has been determined that there is a quantity of paraffin below which none will leave the syringe with an aqueous injection, nor whether those who assemble the syringes can be relied on never to exceed such an amount, but I have seen syringes, used for withdrawing blood samples, containing so much liquid paraffin that had they been employed for intravenous injection embolism would have been almost inevitable However, even small quantities may involve serious risk now that so many injections are of fat solvent substances (e g, oily penicillin), which will certainly dissolve the paraffin and carry it into the tissues On the same grounds, strong objection must be taken to the practice of "sterilising" syringes by rinsing with hot paraffin

It seems ironical that, after the creditably prompt action by doctors which led to legal prohibition of the use of mineral oils for cooking, we should now be injecting the stuff ourselves

Napsbury Hospital, St Albans

A C WOODMANSEY

METHONIUM FOR INTRACTABLE HICCUP

SIR,—Any effective therapy for intractable hiccup is welcome, and for that reason I should like to report briefly a case recently referred to me

A man, aged 76, had suffered from epigastric pain $^1/_2$-1 hour after meals since recovering from influenza one month before On Feb 16, for no obvious reason, hiccup set in and persisted despite treatment, including paraldehyde, morphine, carbon dioxide inhalations, and pressure on the eyeballs Hæmatemesis occurred on Feb 23, and the patient was admitted to hospital the following day In hospital there was no further hæmatemesis, but hiccup continued Routine clinical examination failed to reveal any abnormality to account for this distressing symptom

On Feb 26 treatment with hexamethonium bromide ('Vegolysin') by mouth was begun Two tablets, each containing 0 25 g of hexamethonium bromide, were given with no result, and four hours later three tablets were given Half an hour later the hiccup stopped completely, there has been no recurrence A subsequent barium meal revealed no abnormality in the gastro intestinal tract, the blood-urea was 42 mg per 100 ml

The ætiology of the hiccup in this case is uncertain, but the effect of hexamethonium bromide was so dramatic and immediate that others may be prompted to test the drug in similar cases

Lymington Hospital Hants

R J McGILL

---

[1] Gairdner, D , Laurie N R Hutchcon M *Lancet* 1950 ii 541

[2] Lemberg R Legge J W Hematin Compounds and Bile Pigments New York and London 1949 p 116

ACQUIRED IDIOSYNCRASY TO P A S

SIR,—Several descriptions of acquired allergy to para aminosalicylic acid (P A S) have appeared in your columns,[1 2] but the following case showed certain features that have not been previously described

A young man was admitted to Guy's Hospital on April 15, 1948, with bilateral tuberculous infiltration of the lungs and cavitation at the left apex Examination of the sputum revealed tubercle bacilli Soon after admission a pink, circinate, and slightly raised rash appeared on the anterior aspect of the chest, the upper arms, and the abdomen These lesions faded within forty eight hours but reappeared intermittently throughout the next month They were diagnosed as toxic allergic manifestations—i e , tuberculides

Six weeks after admission a phrenic crush was performed on the left side, and an artificial pneumoperitoneum was induced Two days later treatment with P A S was instituted, the patient receiving a total of 12 g in twenty four hours This dosage was found to maintain a blood level of about 12 mg per 100 ml At this time the erythrocyte sedimentation rate (E S R) was 25 mm , and the patient was apyrexial

On Aug 16, sixteen days after the start of P.A.S and eighteen days after the induction of an artificial pneumoperitoneum, the temperature rose to 100°F , it fell to normal until two days later when it rose again, with the accompaniment of a rigor, to 101°F The patient now complained of colicky pain, first in the mid abdomen and later in the right iliac fossa, which was tender White cells numbered 9000 per c mm The patient had given a history suggestive of attacks of subacute appendicitis, and the appendix was removed This showed submucosal fibrosis but no evidence of acute inflammation

The patient appeared to make a good recovery from the operation, but his temperature continued to swing between 105° and 99°F The total white cell count now was 9700 per c mm , with a normal differential count (eosinophils 2%) Blood culture was sterile, and the E S R —12 mm —was the lowest recorded up till then

On Aug 25, nine days after the onset of pyrexia, the patient complained of tinnitus and of pains in the back and limbs Next day a generalised pink maculopapular rash appeared, and the palpable lymph glands throughout the body were tender and moderately enlarged The total white cell count was 14,000 per c mm (polymorphs 58%, lymphocytes 31%, monocytes 2%, eosinophils 9%) The Wassermann reaction was negative

The administration of P A S was stopped , on the same day the blood level was 5 mg per 100 ml , and four days later nil Urticarial weals now appeared round the original skin lesions, which became confluent and highly irritating until five days later, when they faded leaving a generalised erythema with desquamation During this period excretion of urine was partly suppressed , despite a fluid intake of some 100 oz daily, output fell to below 20 oz and the urine contained a trace of albumin The blood-urea at the end of this period was 46 mg per 100 ml , and the blood pressure was normal

On the eighteenth day of illness, as the rash faded, swellings were noted in the regions of the parotid and submaxillary glands, whose buccal orifices were red , and at the same time angular stomatitis developed Next day the application of a sphygmomanometer cuff to the arm was followed by the appearance of large ecchymoses and many petechial spots over the congested area No spontaneous purpura was detected, but intracutaneous bleeding was initiated by the slightest trauma The white cell count at this time was 38,200 per c mm (polymorphs 42%, lymphocytes 39%, monocytes 5%, eosinophils 14%) , platelets numbered 105,000 per c mm , the clotting, bleeding, and prothrombin times were normal , the F S R was 10 mm

Next day (the twentieth) the patient complained of mistiness of vision and diplopia He was found to have right external rectus palsy, and in response to questioning he admitted to having felt numbness and tingling of his feet and fingers during the past three or four days No other neurological signs were discovered , and thrice-daily administration of aneurine hydrochloride 25 mg intramuscularly, nicotinic acid 50 mg , and riboflavine 2 mg , was started

---

[1] Cuthbert J *Lancet* 1950 ii 200 Climie H *Ibid* p 308 Morrison J B *Ibid* Livingstone R Street E W *Ibid* Little J D *Ibid* Jan 27 1951 p 238

[2] Livingstone, R Street, E W *Ibid* Feb 10 1951 p 353

Within two days the patient's temperature had fallen to normal, and in three days the neurological symptoms and signs had cleared By Sept 8 twenty four days from the beginning of symptoms the patient, still apyrexial, was feeling better, the swellings of his salivary glands had subsided, but his blood, with a total white cell count of 13,500 per c.mm, still showed an eosinophilia of 18%, while platelets numbered 100,000 per c.mm Plasma proteins at this time were 6 g per 100 ml with albumin 2 55 g, globulin 3 2 g, and fibrinogen 0 25 g per 100 ml There was thus a reversed albumin/globulin ratio of 0 8 1 On Sept 21 the total white cell count was 19,500 per c mm. with polymorphs 42%, lymphocytes 50%, monocytes 2%, and eosinophils 6% On Oct 2 plasma proteins were 7 7 g per 100 ml with an albumin/globulin ratio of 1 1

By the beginning of October the patient had apparently made a satisfactory recovery from his toxic illness, and he was subsequently transferred for sanatorium treatment

Affections of salivary glands as a result of P.A.S toxæmia have not previously been described, neither have neurological signs, though Heming and Stuart[3] reported a case with photophobia and headache The neurological symptoms and signs in the case described here are difficult to explain Lehmann[4] observed that *guineapigs treated with P.A.S developed toxic reactions* including anorexia, wasting, falling out of hair, and "symptoms suggestive of vitamin B deficiency" Feldmann et al.[4] failed, however, to confirm these findings

The blood P.A.S level, estimated immediately after the drug had been stopped, was not unduly raised, and although the total dosage before the appearance of symptoms had been only 192 g, its administration was continued for a further nine days This prolongation of treatment may, as Livingstone and Street suggest,[2] have conditioned the severity of the illness

Though jaundice was not a feature of this case, the inverted albumin/globulin ratio of the plasma proteins suggested hepatic damage Finally, the patient received, other than P A S, only anti histamine drugs These were given as soon as the rash appeared, but, apart from allaying the itching of the skin, they did not seem to influence the course of the illness

I wish to thank Dr E R Boland, under whose care this patient was treated, for his advice and for his permission to publish this report

Guy's Hospital
London S E 1

M. G THORNE

THE ECONOMIC VALUE OF THE DOCTOR

SIR,—In his letter of April 21, Dr Rabson, commenting on Dr Ffrangcon Roberts's article (March 24), points out that "premedical and medical training is now largely technical," with a resultant "personality inadequacy" in the doctor This defect in scientific training is not confined to medicine, and it might be of interest to quote from the foreword to the first number of the *British Journal for the Philosophy of Science* This journal, first published in May, 1950, is the official journal of the Philosophy of Science Group, which concerns itself with "an approach through the various special sciences to the philosophy of science" The foreword says

> "The young student of science has now no leisure to reflect on the meaning of his work. As soon as he has passed through the strenuous undergraduate days he enters a field where the race is to the swift and favour to men of skill who have no time to *become men of understanding* The probable consequences need no emphasis The deep personal problems which the reflective in all generations feel impelled to face become more and more intertwined with the knowledge that science brings and it becomes more and *more imperative* to understand the meaning of such knowledge and its relation to the religious, ethical æsthetic and other elements of our mental environment The faster knowledge grows and the more deeply it penetrates the more difficult becomes the work of assessing its ultimate significance Only the scientist can do it adequately, and he is becoming less and less capable of his task because the nature of his training and his preoccupation with the exigencies of his immediate calling do not, and are not intended, to fit him for this task"

Philosophical thought in this country has undergone *tremendous changes during the past fifty years—changes* which as yet have made little impact on medicine The sort of "revaluation of the doctor" which Dr Rabson thinks so desirable but so depressingly remote, will have to be based on a revival of the doctor's confidence this can only come when the doctor knows that the philosophical basis of his practice is sound For this to *happen*, he would be well advised to take into account the linguistic movement which now dominates the philosophy faculties of Oxford, Cambridge, and London Without enlarging on this rather sweeping statement, might I suggest that those who are interested should read A G N Flew's *Logic and Language* (Blackwell) as a general introduction to the subject

London S W 7

WILFRED BARLOW

UNICELLULAR SEBACEOUS GLANDS

SIR,—The "unicellular sebaceous glands in the basal layer of the normal human epidermis" described by Mr Wolff in your issue of April 21 are dendritic melanoblasts This can be proved by the "dopa" reaction, or *more conveniently* by using Masson's silver stain for melanin, which will blacken the granules already formed in some of the cells

These cells have been known for some time to contain a lipid such a lipid is not uncommonly found in the nævus cells of a benign melanoma In some circumstances melanoblasts produce more lipid than melanin Xanthelasma palpebrarum is merely a benign melanoma in which there is more lipid than melanin production, even so the superficial xanthoma cells may be seen to contain fine grains of melanin This has usually been explained by claiming a histiocyte origin for the xanthoma cells, but I am obtaining material which suggests that the correct explanation is that they are derived from melanoblasts

Department of Pathology
University of Bristol

OLIVER C LLOYD

MIND AND MATTER

SIR,—While reading Dr Russell Brain's delightful address in your issue of April 21, I could not help remembering the words of Whitehead "The safest general characterisation of the European philosophical tradition is that it consists of a series of footnotes to Plato"

For Plato the world is one, but from the point of view of knowledge we have to distinguish a physical aspect; the physical world in which we live and act, and the absolute aspect, the world of ultimate reality That such an ultimate and supreme reality transcending our physical being exists is shown by the consciousness we have of the transcendence of the physical world, by our ideas of good, of value, of God, and of immortality, by our *astonishment before the immensity of the Universe*, and by our intimate feeling of creativity, liberty, and power of choice

Knowledge of the physical world—always, according to *Plato*—is obtained through the perceptual conceptual mechanism, what we call today the scientific method, our "practical reason" bound up with the organisation of our nervous system, developed in the course of evolution to equip us in our struggle for physical life, and thus, although supreme for this particular object, not adapted for knowledge of the ultimate reality, the absolute world Knowledge of this absolute world is based on a different method, the Platonic dialectic, a complicated process of abstract thinking, in which after rubbing together conflicting hypotheses, living in our mind various alternatives, "the truth is brought to patients to walk, and one woman relapsed three times before she was able to walk in comfort Treatment has failed in four other patients who are excluded from this series Three of these have an additional disease which prevented treatment, and the fourth was psychologically unsuitable for treatment

---

[3] Heming M. Stuart C J *Ibid* 1949 ii 174
[4] Lehmann J cited by Feldmann W H Karlson A G Hinshaw H C *Proc Mayo Clin* 1947 22 473

Geriatric Unit St John s Hospital
London S W 11
TREVOR H HOWELL

BILIVERDIN

SIR,—In reference to the letter last November from Dr Gairdner and his colleagues,[1] I wish to point out that biliverdin does not give a positive diazo reaction [2] Statements to the contrary are occasionally made, but such findings are due to the use of impure samples of biliverdin which contain bilirubin

Institute of Medical Research
Royal North Shore Hospital
Sydney Australia
R LEMBERG

PARAFFIN IN SYRINGES

SIR,—I read with concern Dr McCartney's statement (March 3) that the syringes supplied ready for use to a group of hospitals are lightly lubricated with liquid paraffin Surely this is quite unnecessary and very dangerous

I do not know whether it has been determined that there is a quantity of paraffin below which none will leave the syringe with an aqueous injection, nor whether those who assemble the syringes can be relied on never to exceed such an amount, but I have seen syringes, used for withdrawing blood samples, containing so much liquid paraffin that had they been employed for intra venous injection embolism would have been almost inevitable However, even small quantities may involve serious risk now that so many injections are of fat solvent substances (e g, oily penicillin), which will certainly dissolve the paraffin and carry it into the tissues On the same grounds, strong objection must be taken to the practice of "sterilising" syringes by rinsing with hot paraffin

It seems ironical that, after the creditably prompt action by doctors which led to legal prohibition of the use of mineral oils for cooking, we should now be injecting the stuff ourselves

Napsbury Hospital St Albans
A C WOODMANSEY

METHONIUM FOR INTRACTABLE HICCUP

SIR,—Any effective therapy for intractable hiccup is welcome, and for that reason I should like to report briefly a case recently referred to me

A man, aged 76, had suffered from epigastric pain $^{1}/_{2}$–1 hour after meals since recovering from influenza one month before On Feb 16, for no obvious reason, hiccup set in and persisted despite treatment, including paraldehyde, morphine, carbon dioxide inhalations, and pressure on the eyeballs Hæmatemesis occurred on Feb 23, and the patient was admitted to hospital the following day In hospital there was no further hæmatemesis, but hiccup continued Routine clinical examination failed to reveal any abnormality to account for this distressing symptom

On Feb 26 treatment with hexamethonium bromide ('Vegolysin') by mouth was begun Two tablets, each containing 0 25 g of hexamethonium bromide, were given with no result, and four hours later three tablets were given Half an hour later the hiccup stopped completely, there has been no recurrence A subsequent barium meal revealed no abnormality in the gastro intestinal tract, the blood-urea was 42 mg per 100 ml

The ætiology of the hiccup in this case is uncertain, but the effect of hexamethonium bromide was so dramatic and immediate that others may be prompted to test the drug in similar cases

Lymington Hospital Hants
R J MCGILL

ACQUIRED IDIOSYNCRASY TO P A S

SIR,—Several descriptions of acquired allergy para aminosalicylic acid (P A S) have appeared in yo columns,[1 2] but the following case showed certain featu that have not been previously described

A young man was admitted to Guy's Hospital on April 1948, with bilateral tuberculous infiltration of the lungs a cavitation at the left apex Examination of the sputu revealed tubercle bacilli Soon after admission a pin circinate, and slightly raised rash appeared on the anter aspect of the chest, the upper arms, and the abdomen Thes lesions faded within forty eight hours but reappeared inte mittently throughout the next month They were diagnose as toxic allergic manifestations—i e, tuberculides

Six weeks after admission a phrenic crush was performe on the left side, and an artificial pneumoperitoneum was induced Two days later treatment with P A S was instituted, the patient receiving a total of 12 g in twenty four hours This dosage was found to maintain a blood level of about 12 mg per 100 ml At this time the erythrocyte sedimenta tion rate (E S R) was 25 mm, and the patient was apyrexial.

On Aug 16, sixteen days after the start of P.A.S and eighteen days after the induction of an artificial pneumo peritoneum, the temperature rose to 100°F, it fell to normal until two days later when it rose again, with the accompani ment of a rigor, to 101°F The patient now complained of colicky pain, first in the mid abdomen and later in the right iliac fossa, which was tender White cells numbered 9000 per c mm The patient had given a history suggestive of attacks of subacute appendicitis, and the appendix was removed This showed submucosal fibrosis but no evidence of acute inflammation

The patient appeared to make a good recovery from the operation, but his temperature continued to swing between 105° and 99°F The total white cell count now was 9700 per c mm, with a normal differential count (eosinophils 2%) Blood culture was sterile, and the E S R—12 mm—was the lowest recorded up till then

On Aug 25, nine days after the onset of pyrexia, the patient complained of tinnitus and of pains in the back and limbs Next day a generalised pink maculopapular rash appeared, and the palpable lymph glands throughout the body were tender and moderately enlarged The total white cell count was 14,000 per c mm (polymorphs 58%, lymphocytes 31%, monocytes 2%, eosinophils 9%) The Wassermann reaction was negative

The administration of P A S was stopped, on the same day the blood level was 5 mg per 100 ml, and four days later nil Urticarial weals now appeared round the original skin lesions, which became confluent and highly irritating until five days later, when they faded leaving a generalised erythema with desquamation During this period excretion of urine was partly suppressed, despite a fluid intake of some 100 oz daily, output fell to below 20 oz and the urine contained a trace of albumin The blood-urea at the end of this period was 46 mg per 100 ml, and the blood pressure was normal

On the eighteenth day of illness, as the rash faded, swellings were noted in the regions of the parotid and submaxillary glands, whose buccal orifices were red, and at the same time angular stomatitis developed Next day the application of a sphygmomanometer cuff to the arm was followed by the appearance of large ecchymoses and many petechial spots over the congested area No spontaneous purpura was detected, but intracutaneous bleeding was initiated by the slightest trauma The white cell count at this time was 38,200 per c mm (polymorphs 42%, lymphocytes 39%, monocytes 5%, eosinophils 14%), platelets numbered 105,000 per c mm, the clotting, bleeding and prothrombin times were normal, the E S R was 10 mm

Next day (the twentieth) the patient complained of misti ness of vision and diplopia He was found to have right external rectus palsy, and in response to questioning he admitted to having felt numbness and tingling of his feet and fingers during the past three or four days. No other neurological signs were discovered, and thrice daily adminis tration of aneurine hydrochloride 25 mg intramuscularly, nicotinic acid 50 mg, and riboflavine 2 mg, was started

---

[1] Gairdner D Laurie N R Hutchcon M *Lancet* 1950 ii 541
[2] Lemberg R Legge J W Hematin Compounds and Bile Pigments New York and London 1949 p 116

[1] Cuthbert J *Lancet* 1950 ii 209 Climie H *Ibid* p 308 Morrison J B *Ibid* Livingstone R, Street, E W *Ibid* Little J D *Ibid* Jan 27 1951 p 238
[2] Livingstone R Street E W *Ibid* Feb 10 1951 p 353

Within two days the patient's temperature had fallen to normal, and in three days the neurological symptoms and signs had cleared By Sept 8, twenty four days from the beginning of symptoms the patient, still apyrexial, was feeling better, the swellings of his salivary glands had subsided, but his blood, with a total white cell count of 13,500 per c mm, still showed an eosinophilia of 18%, while platelets numbered 100,000 per c.mm Plasma proteins at this time were 6 g per 100 ml with albumin 2 55 g, globulin 3 2 g, and fibrinogen 0 25 g per 100 ml There was thus a reversed albumin/globulin ratio of 0 8 1 On Sept 21 the total white-cell count was 19,500 per c mm with polymorphs 42%, lymphocytes 50%, monocytes 2%, and eosinophils 6% On Oct 2 plasma proteins were 7 7 g per 100 ml with an albumin/globulin ratio of 1 1

By the beginning of October the patient had apparently made a satisfactory recovery from his toxic illness, and he was subsequently transferred for sanatorium treatment

Affections of salivary glands as a result of P A S toxæmia have not previously been described, neither have neurological signs, though Heming and Stuart[3] reported a case with photophobia and headache The neurological symptoms and signs in the case described here are difficult to explain Lehmann[4] observed that guineapigs treated with P.A S developed toxic reactions including anorexia, wasting, falling out of hair, and "symptoms suggestive of vitamin B deficiency" Feldmann et al.[4] failed, however, to confirm these findings

The blood P.A S level, estimated immediately after the drug had been stopped, was not unduly raised, and although the total dosage before the appearance of symptoms had been only 192 g, its administration was continued for a further nine days. This prolongation of treatment may, as Livingstone and Street suggest,[2] have conditioned the severity of the illness

Though jaundice was not a feature of this case, the inverted albumin/globulin ratio of the plasma proteins suggested hepatic damage Finally, the patient received, other than P A.S, only anti histamine drugs These were given as soon as the rash appeared, but, apart from allaying the itching of the skin, they did not seem to influence the course of the illness

I wish to thank Dr E R Boland, under whose care this patient was treated, for his advice and for his permission to publish this report

Guy s Hospital
London S E 1

M G **Thorne**

THE ECONOMIC VALUE OF THE DOCTOR

Sir,—In his letter of April 21, Dr Rabson, commenting on Dr Ffrangcon Roberts's article (March 24), points out that "premedical and medical training is now largely technical," with a resultant "personality inadequacy" in the doctor This defect in scientific training is not confined to medicine, and it might be of interest to quote from the foreword to the first number of the *British Journal for the Philosophy of Science* This journal, first published in May, 1950, is the official journal of the Philosophy of Science Group, which concerns itself with "an approach through the various special sciences to the philosophy of science" The foreword says

> "The young student of science has now no leisure to reflect on the meaning of his work. As soon as he has passed through the strenuous undergraduate days he enters a field where the race is to the swift and favour to men of skill who have no time to become men of understanding The probable consequences need no emphasis The deep personal problems which the reflective in all generations feel impelled to face, become more and more intertwined with the knowledge that science brings and it becomes more and more imperative to understand the meaning of such knowledge and its relation to the religious, ethical, æsthetic and other elements of our mental environment The faster knowledge grows and the more deeply it penetrates the more difficult becomes the work of assessing its ultimate significance Only the scientist can do it adequately, and he is becoming less and less capable of his task because the nature of his training and his preoccupation with the exigencies of his immediate calling do not, and are not intended, to fit him for this task"

Philosophical thought in this country has undergone tremendous changes during the past fifty years—changes which as yet have made little impact on medicine The sort of "revaluation of the doctor" which Dr Rabson thinks so desirable but so depressingly remote, will have to be based on a revival of the doctor's confidence this can only come when the doctor knows that the philosophical basis of his practice is sound For this to happen, he would be well advised to take into account the linguistic movement which now dominates the philosophy faculties of Oxford, Cambridge, and London Without enlarging on this rather sweeping statement, might I suggest that those who are interested should read A G N Flew's *Logic and Language* (Blackwell) as a general introduction to the subject

London S W 7

Wilfred **Barlow**

UNICELLULAR SEBACEOUS GLANDS

Sir,—The "unicellular sebaceous glands in the basal layer of the normal human epidermis" described by Mr Wolff in your issue of April 21 are dendritic melanoblasts This can be proved by the "dopa" reaction, or more conveniently by using Masson's silver stain for melanin, which will blacken the granules already formed in some of the cells

These cells have been known for some time to contain a lipid such a lipid is not uncommonly found in the nævus cells of a benign melanoma In some circumstances melanoblasts produce more lipid than melanin Xanthelasma palpebrarum is merely a benign melanoma in which there is more lipid than melanin production, even so the superficial xanthoma cells may be seen to contain fine grains of melanin This has usually been explained by claiming a histiocyte origin for the xanthoma cells, but I am obtaining material which suggests that the correct explanation is that they are derived from melanoblasts

Department of Pathology
University of Bristol

Oliver C **Lloyd**

MIND AND MATTER

Sir,—While reading Dr Russell Brain's delightful address in your issue of April 21, I could not help remembering the words of Whitehead "The safest general characterisation of the European philosophical tradition is that it consists of a series of footnotes to Plato"

For Plato the world is one, but from the point of view of knowledge we have to distinguish a physical aspect; the physical world in which we live and act, and the absolute aspect, the world of ultimate reality That such an ultimate and supreme reality transcending our physical being exists is shown by the consciousness we have of the transcendence of the physical world, by our ideas of good, of value, of God, and of immortality, by our astonishment before the immensity of the Universe, and by our intimate feeling of creativity, liberty, and power of choice

Knowledge of the physical world—always, according to Plato—is obtained through the perceptual conceptual mechanism, what we call today the scientific method, our "practical reason" bound up with the organisation of our nervous system, developed in the course of evolution to equip us in our struggle for physical life, and thus, although supreme for this particular object, not adapted for knowledge of the ultimate reality, the absolute world Knowledge of this absolute world is based on a different method, the Platonic dialectic, a complicated process of abstract thinking, in which after rubbing together conflicting hypotheses, living in our mind various alternatives, 'the truth is brought to h in the soul suddenly like light which is kindled by a ping spark and thereafter sustains itself" (*Epistles*, c) This method, according to Plato, is vouchsafed very few and is obtained after years of mental training, it is the only method through which the real spiritual ies will be approached The intuition of the Neo tonists and of Bergson the existential thinking of ne de Biran and of Karl Jaspers, are in my opinion ects of this Platonic dialectic, this "transcendental son" Two worlds, one empirical, the other absolute, methods of knowledge, one adapted to the empirical ng, the other to the absolute This is the teaching which Plato inaugurated the first university in the ld—that of Athens—twenty four centuries ago

---

[3] Heming M Stuart C J *Ibid* 1949 ii 174
[4] Lehmann J cited by Feldmann W H Karlson A G Hinshaw H C *Proc Mayo Clin* 1947 22 473

r Russell Brain has rendered us a great service by nting out the limitation of the usual scientific method arding knowledge of the supreme reality We have ly heard too many fairy tales about the explanation ll great human values by the play of a few grey cells of a complicated network of white fibres It is time us physicians to strike a sound balance in our con tions by reintroducing the clear vision of the master hose who think—Plato

ondon W 1 A P Cawadias

ENERAL PRACTITIONER AND CONSULTANT

ir,—I think that in his letter last week Dr Bower missed the point of Dr Robertson's letter (April 14) one suggests that there is a cleavage between the and the consultant in the sense that they are refusing peak to each other, but the fact remains that there very hard and fast line of demarcation between the Many of the very best consultants in Dr Bower's town have reached specialist status from the ranks eneral practice Such a graduation is quite impossible

is good of Dr Bower to state that the medical ability he G P in Southampton is on a high level The level ll not high enough to prescribe an X ray examination

omsey Hampshire T P Lalonde

SYNCOPE DURING INJECTIONS

ir,—I have recently had to give a course of daily avenous calcium injections to a patient who on the two occasions had a syncopal attack when the needle introduced On the third day I decided to time the ulation of the solution, and I asked him to tell me his sation as the injection proceeded He became very rested in this and had no sign of faintness On sub ent occasions he has timed himself, and each time shown no signs of losing consciousness

suggest that in the susceptible subject mental concen ion by timing intravenous injections may prevent yncopal attack and so not prolong "surgery hours"

rrow L P Davies

CALLING ALL ATHLETES

ir,—At the request of the Amateur Athletic Associa , a small committee has been formed to advise and st athletes in their various problems and difficulties, h as the details comprised under "training," the motion and maintenance of fitness the treatment of ries incidental to sport and so on Such assistance, ch has for long been available in the United States on the Continent, has in this country been contributed y in a comparatively haphazard fashion by a few rested individuals Now for the first time a systematic roach is contemplated

t is clear that widespread cooperation of the profession essential, and I appeal for the help of colleagues oughout the British Isles The aim is to secure the hnical knowledge and professional experience of a siderable number who in their youth were famous letes They will be asked to give occasional advice to athletes in their neighbourhood, and, when convenient, to attend athletic contests In this way no great demands will be made on their time, and they will have the satisfaction of performing a national service and of preserving their contact with athletics under the most advantageous circumstances

Anyone interested is invited to communicate with Dr John Etheridge, of 73, Fitzjohn's Avenue, London, N W 3, who will in due course forward further information

London W 1 Adolphe Abrahams

CONGENITAL INDIFFERENCE TO PAIN

Sir,—With reference to the article of April 14 by Dr Farquhar and Dr Sutton, van Rooy has described 2 cases in which painless parturition led to the accidental death of the newborn infants In these 2 women he found a remarkable absence of pain sensitivity in the lower part of the body without other defects

Another case of congenital indifference to pain was seen by me in one of the Japanese "protection" camps. The patient was a 14 year old boy with mongolian idiocy His teeth were grossly carious, and extraction of two proved completely painless Thereafter he begged for further extractions because the experience had been so pleasant His infected skin was covered with boils and phlegmons, when we had to open them without any anæsthetic the same painlessness was evident We could find no other disturbances in the nervous system (tactile and thermal sensations were intact), his level of intelligence was that of a 6 year old child

Hilversum, Holland D P R Keizer

PENTAMETHONIUM AND SHOCK

Sir,—Increasing experience of pentamethonium induced hypotension during massive surgical procedures appears to show that shock is not encountered when this method is employed Should any substantial volume of blood be lost replacement by transfusion is, of course undertaken This is in accordance with the observation by Freeman et al[1] that totally sympathectomised dogs were resistant to shock It is not clear whether this action of pentamethonium in preventing shock is due to the great reduction of blood loss, or mainly to the abolition of circulatory reflexes (this latter may imply that vasodepressor material[2] is not produced)

Although established shock is at present regarded as a contra indication to the use of pentamethonium, it does appear that the effect of this agent in preventing the development of shock deserves further investigation

Department of Anæsthetics
Westminster Hospital,
London S W 1

C F Scurr

POLIOENCEPHALITIS, "ENCEPHALOPATHY," AND POLIOMYELITIS

Sir,—Dr Warren's case report in your issue of Jan 27, entitled Poliomyelitis and Polioencephalitis with Opso clonia Following Appendicectomy, is of considerable interest and bears upon several points I should like to comment only upon the interval of four weeks between onset of poliomyelitis and those findings interpreted as "polioencephalitis"

Clinical relapses of poliomyelitis with an interval as long as four weeks appear to be rare, and the findings in this patient raise the question of an "encephalopathy" rather than polioencephalitis The onset of convulsions, with loss of consciousness, cyanosis, and oscillation of the eyes, four weeks after paralysis is more suggestive of an "encephalopathy," perhaps associated with hyper tension The levels of blood pressure are not mentioned in the report

---

[1] Freeman N E Shaffer S A Schecter A E, Holling H E *J clin Invest* 1938 17, 359
[2] Chambers R Zweifach B W *Amer J Physiol* 1947 150 239

It is becoming increasingly apparent that arterial hypertension when sought is not uncommon in paralytic poliomyelitis. Although ordinarily it is transient, we have observed persisting changes for months associated with "hypertensive encephalopathy"

It has only been in recent years that the sphygmomanometer has pierced the isolation curtain around the patient Apart from paralysis itself, much clinical and environmental investigation remains to be done with *poliomyelitic patients*

Department of Pediatrics
University of Louisville Kentucky ALEX J STEIGMAN

PUBLICITY IN CANCER

SIR,—The importance of combating delays in the diagnosis and treatment of malignant disease at all levels from the patient to the hospital is clear The conclusion that by a publicity campaign a dramatic difference could be brought about in cancer results is, however, less certain

A strong case can be made out that with existing diagnostic methods our present methods of treatment are in general, effective only in the biologically less malignant examples of malignant disease A fallacy arises from a looseness in the use of the word "early," which in one place may mean early in point of time and in another early in point of spread of the disease, that the two are not the same is in *practice only too obvious* While therefore not neglecting any way of making present methods of diagnosis and treatment more effective, the real hope must be for an advance in our fundamental knowledge of the malignant process and its control factors

On the immediate practical plane I venture to suggest that more could be achieved by measures directed to strengthening the status and facilities of the general practitioner—as, for example, by providing him with radiodiagnostic and pathological centres—than by any publicity campaign I would, on the other hand have no objection to explaining to any intelligent layman or group of laymen, who wanted to know, the present position of the cancer problem provided that the explanation was true and based on a correct assessment of the situation

London W 1 DAVID H PATEY

AIR TRAVEL

Mrs A Clifford passenger relations officer of British Overseas Airways Corporation, writes

We were very sorry to read in your issue of March 24 that a peripatetic correspondent formed the impression that the sherry served as an aperitif to the meal was inferior to the quality of that supplied in the bar The truth, is that the difference is not one of quality but of taste The sherry provided free is a medium one intended to cater for all tastes as far as possible whereas probably he purchased a dry type Because of the limited stocks which can be carried on an aircraft the choice is necessarily limited, but there is no question of one being inferior to the other

It was decided *some time ago that the corporation* was entitled to a profit on bar sales and bearing in mind that the tots are doubles our prices are considerably less than *those applying elsewhere It must also be* remembered that drinks are provided free of charge with meals Linen towels are to be provided on all our aircraft as soon as supplies are available

With regard to the facilities at airports we are only too well aware that in certain cases these are below the standard which we would prefer but this is a matter for the various governments concerned and is outside the province of airlines

It is our policy to give as much information as possible to passengers when aircraft are delayed, sometimes, however, when technical problems arise it is difficult for the engineers to gauge exactly how long the work will take, and they hesitate to give a time of departure which for one reason or another may have to be extended or in more *fortunate* circumstances brought forward No doubt the same applies to other airlines.

Obituary

ALBERT RUSKIN COOK

Kt., C.M G , O B.E , B A. Camb , M D , B.Sc Lond

IT is a considerable achievement to walk for three months over 800 miles of African bush, to found a hospital at the end of the trek, to rebuild it three times within 7 years, and to live to see it stand as a widely renowned and active medical centre 54 years later That, in fact, is what Sir Albert Cook did during his long and distinguished life of service which ended at Kampala on April 23

Born in 1870, he was the son of a doctor and the nephew of a bishop At St Paul's School, at Trinity College, Cambridge, and at St Bartholomew's Hospital, he won prizes, scholarships, and exhibitions at every stage He graduated as M B in the University of London in 1895, and a year later he set out for Uganda, under the auspices of the Church Missionary Society

[Church Missionary Society

After an arduous journey on foot through difficult and dangerous country, he arrived at Kampala, where early in 1897 he established the Mengo hospital, a primitive structure of grass and reeds Within a few years this was replaced by a hospital built of wattle and daub, but this was destroyed by lightning in 1904 The buildings of sun dried brick which were then erected stand today, greatly extended and modernised, as a large and efficient hospital centre At first the hospital was something of a family affair, for Cook married the first matron, Miss Katharine Timpson, one of the original band of missionaries who came with him to Uganda, and two years after his arrival he was joined by his brother, Dr Jack Cook, an outstanding surgeon

In two wars Mengo Hospital opened its doors to the wounded It dealt with many casualties from the Sudanese rebellion of 1897, and again in 1914–18 it was the principal base hospital for Uganda, with Captain Albert Cook in command But peace brought opportunity for expansion of Mengo's real work A medical school for African auxiliaries was opened, and later, through the energy of Katharine Cook, the Lady Coryndon maternity training school was founded, and African girls from all over East Africa went to Mengo for training as midwives and nurses Together the Cooks wrote an illustrated handbook of midwifery in the vernacular, and Cook also compiled a medical phrasebook and vocabulary in Luganda

His work was by no means confined to the mission field, for he took an active part in the development of public health measures and of medical services in Uganda, and his advice was continually sought by the government medical department, who appointed him to every important medical board He and his brother were the first to diagnose sleeping sickness in Uganda and were indeed pioneers in many medical measures

It was natural that many honours should be given him After the first war, he was appointed O B.E and he was honoured by the Belgian government with the Order of Leopold In 1922 he was appointed C M G and in 1932 he was knighted In 1928 he received the silver medal of the African Society He retired from active medical work in 1934 The death of his wife four years later was a grievous blow but for many years his wide knowledge, his counsel, and his wisdom were at the disposal of those who required it, and he remained a consultant to the government hospital and a member of a number of boards In 1945 his book *Uganda Memories* was published by the Uganda Society, which he had served as president In 1947, the jubilee year of the foundation of Mengo Hospital, a fund was raised to rebuild the hospital, and the Uganda branch of the B M.A held a three-day interterritorial meeting to honour its founder

"To those of us who were concerned with medical education in East Africa," writes H J O'D B-G, "the Cook tradition was almost symbolic The vast medical library at Mengo, with its detailed records and case-sheets from the earliest days, is a monument to Cook's care and accuracy He was a simple man of simple faith—a missionary in the fullest sense, for he had a mission to fulfil and spared nothing of himself in its fulfilment His own words reveal the nature of that mission 'to attempt to heal the suffering body is much, to carry the water of salvation to thirsty souls is more, but to combine the two is the grandest work a man can have' Thousands of Africans are poorer for his passing, but healthier and happier for the care and wisdom and sympathy which he gave to them"

PAUL JENNER VERRALL

M B Camb, F R.C S

Mr Jenner Verrall, who died on April 22, was orthopædic surgeon to the Royal Free Hospital, and lecturer in orthopædic surgery at the London School of medicine for Women from 1926 to 1945 But he will also be remembered for his great experience of military orthopædic surgery For well over thirty years he was associated with the Ministry of Pensions, at first as orthopædic surgeon at two of their largest hospitals, and for the last ten years or so as orthopædic specialist at the regional offices in London At the beginning of the late war he was a member of the war wounds committee of the Medical Research Council

Born in 1883 at Brighton, the son of the late Sir Thomas Verrall, M R C S, he was educated at Winchester, Trinity College, Cambridge, and St Bartholomew's Hospital In 1908 he qualified, and two years later he took his F R C S The same year he was appointed to the orthopædic department at St Bartholomew's Hospital where he worked as assistant to Mr R C Elmslie In 1915 he volunteered for service with the R A M C, but he was invalided home after a year in Egypt He then became one of the original team of orthopædic surgeons whom Sir Robert Jones chose to help him in the task of organising the special surgical hospitals to deal with the many thousands of wounded whose injuries came under the somewhat elastic designation of "orthopædic" The biggest of these hospitals was set up at Shepherd's Bush, and it was to this hospital that Verrall was attached

After the war his orthopædic colleagues returned one by one to the ever-widening field of civilian orthopædics, but Verrall remained to carry on the work, at first at Shepherd's Bush and then, after 1925, at Queen Mary's (Roehampton) Hospital, to which the Ministry of Pensions had transferred all their surgical work in London Here to his orthopædic work was added the thousands of men with amputations attending the Roehampton limb fitting centre who for some reason or another were having trouble with their stumps Under his influence a close collaboration soon developed between the limb-fitting surgeons and the operating surgical staff, and from this collaboration was built up that body of amputation surgery which is now accepted practice Not only had the existing amputation cases to be dealt with, but many primary amputations had to be carried out, and on very unpromising material—for example, on limbs with chronic bone sinuses of many years' duration or with unrecovered nerve lesions Those were the days before the sulphonamide drugs or the antibiotics, and it speaks volumes for the high standard of Verrall's work at Roehampton that so few cases went wrong

Shortly after the outbreak of the second world war he gave up hospital work at Roehampton, and as orthopædic specialist to the Ministry in London examined and advised on many thousands of cases both from the 1914–18 war and the 1939 war One of his colleagues writes "His reports were always a pleasure to read—short and to the point, nothing of importance left out, no redundancies, answers given to all questions put to him, and a sound opinion expressed It is perhaps unfortunate that Verrall wrote so little of that branch of surgery on which he could have spoken with so much knowledge and authority, but those who knew him and worked with him can testify to the readiness which he always showed in passing on to others who went to him for guidance something from his own wide experience His work for the Ministry of Pensions continued uninterruptedly until the illness from which he died"

In 1908 Mr Verrall married Edmée, daughter of Comte Lostie de Kerhor de St. Hippolyte She survives him with their only daughter

EUSTACE JOHN PARKE OLIVE

O.B E, M.A, M D Camb, F R C.S

Dr E J P Olive, consulting physician to the Warneford Hospital, Leamington, died on April 14 at the age of 88

From St John's College, Cambridge, he entered St Bartholomew's Hospital, where he had a distinguished student career After qualifying in 1889 he held house appointments at Barts before he migrated to the General Hospital, Birmingham, where he was house-surgeon to Gilbert Barling Thence he went to Leamington, where he was appointed to the staff of the Warneford Hospital, and he spent his long life of professional service in that town In 1892 he took the F R C S, and two years later his M D

He was appointed O B E at the end of the first world war A colleague writes "During both wars Olive was actively employed, and at the end of hostilities he retired and well deserved the honour which was accorded him He was always ready for emergency work, and in his later years he equipped himself as a very competent anæsthetist In a full and valuable life he earned the gratitude of many"

Appointments

CHEATLE C A M R C S D A anæsthetist St Mary's group of hospitals London

LEVIS R D, M B Dubl D A anæsthetic registrar Frenchay Hospital Bristol

REID R D, M B Lond D T M & H morbid histologist (consultant) Colchester

TEES, J E, M R.C.S D A anæsthetist North Gloucestershire clinical area

TURTON E C, M A Oxfd M B M.SC Lond M R.C.P D.P M consultant physician in psychiatry with special knowledge of electro encephalography Bristol mental hospitals

WESTHEAD PAMELA M B Brist D.A anæsthetic registrar Frenchay Hospital Bristol

WILLIAMSON D M M B Aberd regional M O north western region of Ministry of Labour and National Service

Appointed Factory Doctors

HENDERSON I R M.B Edin Braemar district Aberdeenshire

MACKENSIE, G K M D Edin West Linton district, Peeblesshire

Births, Marriages, and Deaths

BIRTHS

BOYD—On April 21 at Lower Hutt, Wellington New Zealand the wife of Dr Edmond Boyd—a daughter

CHALMERS—On April 24 to Dr Mary Chalmers (née Evans) wife of Dr Kenneth Chalmers—a daughter

READ—On April 8, the wife of Dr A M Read—a daughter

TAYLOR—On April 22 in London the wife of Dr John Taylor—a daughter

MARRIAGES

BREBNER—SMILEY—On April 21, at Kingston on Thames Hugh Brebner M B to Cecilia May Smiley M B

HARVEY—BROOKS—On April 24 at Bury Lancs Peter Wynne Harvey M B to Margaret May Brooks

DEATHS

BURTON—On April 26 at Shanghai Thomas Menzies Burton M B Glasg

CAIRNIE—On April 29 at Largs Ayrshire Charles Cairnie M A M B Glasg

EDWARDS—On April 20 at Northwood Middlesex David Glyn Mason Edwards M B Lond D P H

EDWARDS—On April 29 at Harrogate Francis Henry Edwards M B Lpool, F R C S E

LITTLE—On April 24 in London Andrew Hunter Little M R C S

PORTER.—On April 25 at Eastbourne William Ernest Porter M D Edin D P H aged 88

POWELL.—On April 27, at Sudbury Suffolk Rhys Vaughan Powell F R C.S aged 60

STEVENSON—On April 9 in Sheffield Eliza Moira Kennedy Stevenson M D Glasg F R.F P S

VERRALL.—On April 22 in London Paul Jenner Verrall B A, M B Camb F R C.S

Notes and News

TREE OF HIPPOCRATES

A HISTORIC ceremony took place in the Chelsea Physic Garden on April 27 when a gift from the Greek government and the University of Athens was presented to the Royal College of Physicians of London The gift was a cutting from the famous plane tree of Cos under which Hippocrates is reputed to have taught and it was presented by Dr Gerasime Loverdos, endocrinologist and medical historian, in the presence of the Greek Ambassador, the chairman of the British Council the master of the Society of Apothecaries, the chairman of the board of trustees of the Physic Garden, and representatives of the Royal Colleges Dr W S C Copeman, accepting the gift on behalf of the Royal College of Physicians, said that the cutting would be a living memento of the great Greek teacher to whom modern medicine all over the world owes all that is sound in its origins, and would symbolise for future generations the traditional good will between Greece and Great Britain. Dr Loverdos was also thanked by Mr Walter Prideaux chairman of the board of trustees of the Physic Garden, and by Dr F D Howitt, master of the Society of Apothecaries The tree was planted by Dr Loverdos, Lord Webb-Johnson, Dr Copeman, and Dr Howitt

A second cutting has since been planted in the council garden at B M A House, in the presence of the president and council of the British Medical Association, and a third at Oxford

A UFAW JUBILEE

ON April 30, Major C W Hume, with twenty five years of animal welfare work to his credit, sat down to dine with the friends of the Universities Federation for Animal Welfare, to celebrate this pleasant jubilee Fougasse the dearly loved artist of UFAW, and in other manifestations Mr Kenneth Bird, and editor of *Punch*, was at the head of the table in this family party and toasted The Guests as wittily as he draws Mr W R Wooldridge PH.D, proposing the toast of UFAW, recalled its founding as ULAWS (the University of London Animal Welfare Society) in the days when Major Hume played hockey furiously for Birkbeck College and was tough with his opponents though tender with rats Funds were small in those days and new ideas Dr Wooldridge complained do not come easily to an educated community Major Hume won the university over brought in the veterinarians and invited the late Sir Frederick Hobday to become the first president In replying Major Hume noted that nearly half of the early supporters were present, and he mentioned others who would have been present if they could UFAW attracts people he said because of the sound underlying idea that science and learning have a duty to the subject of animal welfare It also attracts because as Mr John S Cripps said in replying for the guests it sees the problem whole and without undue sentiment All its friends wish it long life and more power to its elbow

CALL-UP OF AMERICAN DOCTORS

BECAUSE of the shortage of volunteers for the American army and air force the Department of Defence has announced[1] that compulsory call up of doctors will begin in July this year The department intends to call up 1202 doctors during July August, and September, but this figure may be reduced if the number of volunteers increases before then. As announced previously,[2] doctors will be selected from those who were trained at government expense in the late war and who served less than 90 days on active service, later additional doctors will be selected from those government trained doctors who served less than 21 months

University of Oxford

Dr R V Coxon, F R C S, has been appointed to the readership in human physiology

Ministry of Health

Mr J P Dodds has been appointed under secretary for finance and accountant general in the Ministry

R A F Appointment

Dr J C Sawle Thomas has been appointed civil senior specialist in psychiatry to the Royal Air Force

Royal College of Physicians of London

At a comitia of the college held on April 26, with Dr W Russell Brain, the president, in the chair, Mr Winston Churchill, O.M., C.H, F.R.S, was elected to the honorary fellowship of the college The following members were elected to the fellowship

H H STEWART Belfast B A HUNT Perth Australia W G PATTERSON Newcastle upon Tyne B F RUSSELL, London MOHAMED AHMED IBRAHIM Bey Cairo C E DOLMAN, Vancouver C J HACKETT London R T GRANT O B E F.R.S London, G H NEWNS London A H IMRIE Glasgow G R ELLIS Liverpool T M GREENAWAY Sydney K D KEELE, Staines J H KELLGREN, Manchester S A PROPERT, Colchester W S TEGNER, London J E G PEARSON Bristol, J W D BULL London, C R St. JOHNSTON Birmingham H J WALLACE London D H. DAVIES Bristol W W PAYNE, Watford J W CROFTON, London J D HAY Liverpool J B RENNIE Glasgow SHEILA SHERLOCK London WILLIAM MAYER GROSS Dumfries CLIFFORD WILSON London MELVILLE W ARNOTT, Birmingham and, under by law 39c, Brigadier J S K BOYD O B E F.R.S London

The following were elected to the fellowship under by law 39b which provides for the election of non members "who have distinguished themselves in any branch of the service or practice of medicine"

Viscount ADDISON K G London Sir ALAN DRURY C.B E, F R.S London Sir HOWARD FLOREY F.R.S Oxford

The following having satisfied the Censors Board were elected to the membership

Barbara M Ansell M.B Birm, A F Barnett, M B Lond, F T Bassadone L.R.C P J H Baylis M B Lond J H Bruce, M.D Belf W H Cary M B Sydney F S Cooksey O B.E M D Lond Philip Freedman M.D Lond. H R Gilmore, M B Adelaide Harry Greenburgh M.B Lond. P G Griffiths M.B Manc Fred Grundy M.D Leeds G W Hadfield M.B. Lond S P Hall Smith M D Edin J P Horder, B.M Oxfd A W MacLeod M.B Glasg Christopher Pallis B.M Oxfd, M. I M Pines M.B Camb Kenneth Rawnsley M B Manc J B Ryder M D Dubl J S I Skottowe M D Glasg J M K. Spalding B.M Oxfd Lionel Stein M.B Cape Town J D Stevens M B Lond K. B Taylor B.M Oxfd A W S Thevathasan L.M.S Singapore Louis Vogelpoel M.B Cape Town, C A C Wiggins M B N Z.

Licences to practise were conferred upon 194 candidates (164 men and 30 women) who have passed the final examination of the Conjoint Board

S W Albright Valerie M D Alcock A J Allen Barry Altman R A J Anthony G H. Apthorp, Joyce A Arscott, James Ashworth, G A E Baker, Katharine M. Baker A A Bapty W R Barrow, A P Barter P R Bateson Elizabeth L Batson T R Beatson T G L Bellis B W Betterton Geoffrey Birch Kenneth Biss Pauline M Bousquet A L C A M Bracchi A J Bridge A R Brighten N P Bronsdon William Brumfitt T A Bryant J A B Burn Jean M Burnett A. M Burnford A C Campbell, D S Carroll R D Catterall, P A Chapman J S Clayton, C J Cliffe, M K Coles, P H Connell B I Copeland Delia M H. H Cothay H T W Coupe P H E Courtenay B P Courtenay Mayers A. N Cowan W H. A. C Cox, M J Craft K. A Creamer, Mary D Daly Margaret E Darling D D Davies Joan R Davies J P Davies, D M Devane S H Dunce C E Durber F B D Easby Ralph Emery, F O Esiri G L Evans Stella Feldman Arrigo Ferrari P G Fildes A C Garnham Jean Claude Gazet, Hilda L Gibbs Michael Gibbs J S Gilbert Alan Gillespie G D Glennie Peter Goodall J W Goodfellow D J C Graff Pamela E Green David Greenbaum J D Hackett M H Hambling T R Hamilton J W Hamlett C R Harrison C B L Hart P D Harvey, M D A Heller C B Higgie F E P Higgins B W Holbrook J B Holland D C Hood J M Hood P T Hull Penelope C Humphries J H M James, G H Jantet J C Jelleyman G O Jenkins Marion J P Jenkins A H John B T Johnstone G A H Jones Zilla M Kaye Russell Keeley T D Kellaway, S W Kemp G C E King, R H. King Beryl J Lander J G Lewis R C Lewis W H J Llewellyn A L Lloyd Colin McKinna E J Masters William May Margaret B Mearns J W Mercer, P McK Middleton J L Montagnon, Ada C Morrison, F J Moynihan J W Murdoch Shirley E Nathan P J Nobes Zoila Nowiak P M J O Brien Mary Ogden J O Ojukwu J E O Malley G P C Orlay D R M P B O Sullivan J N Pachmayr P H Padwick, S A C Paget Jack Palmer J A Parrish R E H Partridge J T Patton P L Pelmear Jacqueline S Pennycuick R J Pett A R Phillips J M. Powley W J Prvn Adrian Raban Williams Mary T C Randall Ann Reader S H Richards R A A Rickett, J N Roper E J Ross F L Rowland D L Rugg Easey G C Saint Z R Salib Vitezslav Schoengut Dan Scott Rosamund O F Shanks M H Sheard C H Sheridan A J Sims D P Q Smith R G Smith Mia Ayoob Sorefan K. A. E Spence A G Spooner W J Stanley E H Stephenson G J Stott Joan M M Sutherland Maurice Sutton J A Szydzik, Joseph Taylor W N A Taylor Jack Terry J L Tester Frances M Thortont A W Tranter W M. E Tweed Vernon Udall J T Vorster D R H Walker M A T Waters Monica E Watkins M W B Watson A N E Watt P K. B White, B R Wilkinson W H Wilkinson D K. Williams J F Williams R A J Williams Frederick Wilson Vivienne L L Wolfson Robert Woodside E H Wyatt P A. Zorab

The following diplomas were also conferred conjointly with the Royal College of Surgeons

D C H—Harry Altman, J P Anderson G C Arnell Sunder Laxman Bale J S Beedie Mary T Behanan Samir Kumar Biswas Sisir Kumar Bose Lucy M C Boyd R J K Brown Hyman Chai Isabel A Cossar, Constance M Cowan G N H Cranswick Mary E Curling S B du Toit J S Ebsworth, R F E Edwards

---

[1] See *New York Times* April 24 1951 p 11

[2] See *Lancet* Jan 20 1951 p 178

Joseph Erulkar, D G Evans, Elspeth M Evans, Loveday A Farquharson, Ann Ferguson Prudence A FitzGerald, R M Forrester, J B Frost Angela D Fuller, Molly I Govier, A J Gray, Zaida M Hall Yuen Ho, C W Howden, Lionel Soubhkaran Jaikaran, Trilochan Kaur Jari, J G P Jones, Syed Mohamed Ali Khadri Percy Lancer, K W Lavers Lois M Leitch, Schneir Levin, Joan V Llewelyn, Archibald Macfarlane Lisa E Mandelbaum, Margaret G Martin, Joan M Milne, Mary D Milne L H Moffin, Judith Murray Jones, R W Nash Margaret I E Neave G F Newbold Joan R Nichols, Marjorie G Nisbet, T O Noble, Fakirbhai Hirabhai Patel, Kumaradasa Rajasuriya, Margaret P B Reid J D L Reinhold, Jean Robson, F C Rose Margaret M P Ryan Henry Sharma, Swasdi Skulthai, Mary G Southern Holt, Sybil H Stephens G J Sutin, H T Swan, Joyce M Teasdale, Joan P Tom Shabbarahmed Bashirahmed Vahidy Sarla Vaishnava, R H Vines Mary Vowles Daphne M L Walters B W Webb, J W Woodburn Audrey J Worman, Guan Eng Yeoh,

D O—G W Allen, C H Baker, H H W Bennett, G L Cantrell, Malcolm Cowan, J A Eustace E M L Evans, R H L Ferguson, Anwar Rouben Gabbay Foad Ahmed Hamdi, D R L Hart, J I Heany Hemanta Kumar Indra, Nem Chand Jain, John McLenachan J G Madden, K P Milne, T G O'Driscoll Winifred I Pearce R P Phillips Noe Pines, Muhammad Abdul Qayyum Mumtaz Quli Khan Raja, James Roche, J H Slade Mona A. Smith L C G L Trichard John Whitwell Kin Yip Wong

D T M & H—W G L Allan, Isaac Nnadiebulam Oparauwoma Asinobi J C Babbage, Kyaw Bo, Mohomed Ahmed Botawala, James Carswell, D W F Charlton, B J Chelmicki, V St E D'Abrera, C R Doering Anilkant Chhaganlal Doshi Fazal Elahi, Titus Fernando, L F Gunaratna, B P Harris Hans Herlinger J H Hobson Ma Hpay, Varaphon Israngura, Lakshmi Kant Ravindra Motichand Kapadia Isaac Shaoul Khutaina, Kali Das Lahiri Poo Ling, J A McDonald, W H McDonald, J A Mahoney, A L Meikle, H O L Murray R J Pitchford, Bermeshwer Prasad, Satwant Singh L P Spence Daniel Arianayagam Thamotheram, Muhtar Yildiz

D Phys Med—M Q Birkbeck B O Scott

D I H—David Crichton

D.L O—Coroth Madathankandy Leelavathi

D P M—J B Gordon Russell

Conference on A C T H

A conference on A C T H is to be held by Armour Laboratories in Harrogate on Sept 13 and 14 Medical speakers from this country will include Dr W S C Copeman and Dr O A. Savage, Dr, J J R Duthie, Dr J R Forbes, Dr F Dudley Hart, Dr G Kersley, Dr F T G Prunty, and Prof L J Witts Attendance will be confined to those doctors who have administered 'Acthar'

International Centre for Training in Anæsthesia

On April 27, ceremonies at the University of Copenhagen marked the successful conclusion of the initial course at the W H O international training centre for anæsthesiology, established a year ago by W H O and the university A second group of 30 medical fellows—from Finland, Greece, Norway, Sweden, France, Yugoslavia, and Denmark—arrive in Copenhagen this week for the second course of one year W H O provides for the maintenance and travel of the foreign medical fellows, and book allowances for the Danish students, it has also provided anæsthesia equipment

Society for General Microbiology

The following have been appointed as officers and committee for 1951–52

President Prof J W McLeod F R S, meetings secretary W E van Heyningen, general secretary J G Davis, treasurer, R. Lovell editors, B C J G Knight and A F B Standfast associate editors, G C Ainsworth W B Brierley, T Gibson, A T R. Mattick, A A Miles, K. M Smith, A W Stableforth, and D D Woods members of committee L A Allen, C H Andrewes, P W Brian H J Bunker, A W Downie, Betty Hobbs H B Maitland, N W Pirie, H Proom P M Frances Shattock and G Sykes, representing International Association of Microbiologists Sir Alexander Fleming, F R.S

The society, which was founded in 1945, now has 985 members and will hold its September meeting at Manchester Further information may be had from the general secretary, 35, Villiers Road, Southall, Middlesex

Kingston Victoria Hospital

The Ministry of Health announces that the Minister "considers that there is no justification for further delay in the conversion by the South West Metropolitan Regional Hospital Board of the Kingston Victoria Hosiptal to meet gynæcological needs Since the debate in the House of Commons on Jan 30 (see *Lancet* Feb 10, 1951, p 343) detailed discussions have taken place between the Minister and representatives of the hospital and of the regional board as well as direct between the board and the hospital All the alternative proposals put forward have, however, on examination proved to be unworkable The Minister has, therefore informed the board that they may now proceed to the conversion of the Kingston Victoria Hospital and to the opening of the Claremont Hospital which has been specially adapted for the use of general practitioners"

West London Medico-Chirurgical Society

On Monday, May 21, at 8 30 P.M, the Bishop of Birmingham, the Rt Rev E W Barnes, SC D, F.R.S, will deliver the Cavendish lecture to this society at 1, Wimpole Street, London, W 1 He is to speak on Overpopulation.

Harveian Society of London

The annual Buckston Browne dinner of this society will be held at the Hyde Park Hotel, Knightsbridge, London, S W 1, on Thursday, May 10, at 7 30 P M The principal guest will be Mr L S Amery, C H Further information may be had from the hon secretaries, 11, Chandos Street, London, W 1

Institute of Hospital Administrators

The annual conference of the institute is to be held at Eastbourne on May 17, 18, and 19 when papers will be read on Central Administration and Finance, on Regional and Local Hospital Administration, and on Administrative Problems within the Hospital Sir Wilson Jameson, F.R.C.P, will also open a discussion on the Needs of the Hospital Service Further particulars may be had from the secretary of the institute, 75, Portland Place, London, W 1

Scottish South-Eastern Regional Hospital Board

Owing to ill health Dr J R C Greenlees, D S O, has resigned from the chairmanship of the South Eastern Regional Hospital Board Sir Humphrey Broun Lindsay, D S O, D.L, J P, has agreed to accept appointment as chairman for the time being

---

Diary of the Week

MAY 6 TO 12

Monday, 7th

INSTITUTE OF OPHTHALMOLOGY, Judd Street, W C 1
5 30 P M Mr M H Whiting Sympathetic Ophthalmitis
MEDICAL SOCIETY OF LONDON 11 Chandos Street W 1
8 30 P M Sir Charles Symonds Migrainous Variants

Tuesday, 8th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East S W 1
5 P.M Dr T F Fox Professional Freedom (First of two Croonian lectures)
ROYAL EYE HOSPITAL, St George s Circus, Southwark, S E 1
5 P M Dr T H Whittington Non paralytic Strabismus
INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle Street, W C 2
5 P M Dr G B Dowling Tuberculosis of the Skin

Wednesday, 9th

INSTITUTE OF DERMATOLOGY
5 P M Dr H Haber Cellular Nævi and Melanomas
INSTITUTE OF OPHTHALMOLOGY
5 30 P M Mr H Ridley Recent Advances in Ocular Therapeutics
UNIVERSITY OF BIRMINGHAM
4 P.M (Medical School Hospitals Centre Birmingham, 15) Mr John Stallworthy Antepartum Hæmorrhage (First Ingleby lecture)
UNIVERSITY OF DUBLIN
4 30 P M (School of Physic, Trinity College) Prof J H Burn, F R S Importance of Noradrenaline (John Mallet Purser lecture)

Thursday, 10th

ROYAL COLLEGE OF SURGEONS Lincoln s Inn Fields W C 2
3 P M Mr J H Mulvany Exophthalmos
5 P M Prof Emile Holman Constrictive Pericarditis
UNIVERSITY COLLEGE Gower Street W C 1
4 45 P M Prof H A. Krebs F R.S Energy Transformations in Living Matter (Third of four lectures)
5 15 P M Prof G Liljestrand (Stockholm) Studies on the Regulation of Arterial Blood pressure
LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE Houghton Street, W C 2
5 P M Prof R M Titmuss Social Administration in a Changing Society (Inaugural lecture)
ST GEORGE S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S W 1
4 30 P M Dr Denis Williams Neurology lecture demonstration
INSTITUTE OF DERMATOLOGY
5 P M Dr Brian Russell Cutaneous Manifestations of the Reticuloses
ALFRED ADLER MEDICAL SOCIETY
8 P M (11, Chandos Street W 1) Dr A R Redfern The Neurotic Life style
UNIVERSITY OF BIRMINGHAM
4 P M Mr Stallworthy Antepartum Hæmorrhage (Last Ingleby lecture)
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place Edinburgh) Prof C Scott Russell Injuries of the Female Bladder and Urethra
UNIVERSITY OF ST ANDREWS
5 P M (Medical School Small s Wynd Dundee) Sir Lionel Whitby Realistic Approach to the Problem of Anæmia

THE PSYCHOSOMATIC APPROACH TO PULMONARY TUBERCULOSIS*

GEORGE DAY
M.A., M.D Camb
RESIDENT PHYSICIAN, MUNDESLEY SANATORIUM, NORFOLK

THE psychosomatic approach to pulmonary tuberculosis is beset with difficulties

First, in order to contract the disease it is necessary to be infected by the tubercle bacillus, and this bacillus is not quite so ubiquitous as it used to be Secondly, the result of the infection depends largely on inherent somatic resistance Thus the infected guineapig always dies of generalised tuberculosis, whereas the elephant inoculated with the human type of bacillus does not become diseased, and this has nothing to do with their respective psyches Thirdly, the human being who hails from a virgin uncivilised island has no racial immunity and will suffer the guineapig's fate if infected, for hereditary resistance to the disease takes generations to develop Fourthly, resistance to tuberculosis varies not only from race to race but even from family to family An identical twin shares his fellow twin's morbidity chances, his rate of progress in either direction, and his prognosis Even when twins have lived separate lives in entirely different circumstances, there seems to be a very high correlation between their behaviours towards tuberculous infection This correlation is said to be only a sixteenth as high when the twins are fraternal and not identical—which suggests that horoscopes should be cast at the hour of conception and not at the hour of birth

All the foregoing statements are observable facts, sanctified by statistics, which must not be overlooked when we talk about psychosomatic factors in the *onset* of tuberculosis We must not forget the guineapig, the elephant, the negro, and the twin

INFECTION

Let us now consider what happens when the body is invaded for the first time by the tubercle bacillus, and thence what on a purely physical or animal plane determines the course of events

Some tubercle bacilli enter the fastness of the body It is no new experience for them it is how they make their living It is not an entirely new experience for the body, which has already some degree of inherited resistance, or, to put it another way, some racial memory of how to cope with the situation What ensues, in brief, is a constitutional upset of short duration—rather like a mild attack of influenza—with tubercle formation at the focus of infection and inflamed and swollen lymph glands in the neighbourhood Generally this all settles down within six weeks or so, and the body resumes its normal health, which usually persists—so far as the absence of active tuberculosis goes—for the rest of its life Most of our bodies experience this primary infection before we reach the age of 21 In urban communities 60%, 70%—perhaps 80%—of the adults have been through this little illness, and only a small proportion of them seize the opportunity to develop wider spread disease or to die like guineapigs

Normal health, I have said, is regained, but thereafter there are three differences

1 The tubercle bacilli of the invading force are not exterminated but are, we believe, imprisoned in a fortress of living cells where they remain viable for many years

2 The chemistry of the body is changed It has become sensitised to tubercle bacilli and their toxins, and responds quite differently towards them the next time they drop in—or break out This biochemical change has taken place in every cell in the body, and from now onwards even the cells in the skin will react when tuberculin is instilled, thus giving us the positive Mantoux or Pirquet reaction Whereas at its primary infection the body took the bacilli in its stride in a comparatively methodical and sensible manner, its reaction now to any vagrant-bacillus is capricious and unpredictable sometimes it is indolent, but sometimes it is violent and aggressive even to the extent of self-destroying all contaminated living tissue Whereas the primary infection was self-limiting, to a matter of six weeks or so, the secondary disease-process is inconclusive—for more like six years

3 The body has developed some degree of immunity against reinfection with fresh bacilli

DEVELOPMENT OF TUBERCULOSIS

How then does ordinary adult type phthisis develop? There are two schools of thought One maintains that *generally*—owing to "lowered resistance" (that convenient legal fiction)—there is leakage of endogenous bacilli from the primary focus to other tissues (via blood stream, bronchial tree, or lymphatic channels) The other school says that *generally* it is due to a superinfection by a massive dose of fresh bacilli from outside, perhaps again helped by temporarily lowered resistance Such evidence as we have is sufficiently labile to support both schools I think we are agreed that both mechanisms operate, but we cannot agree which is the more usual

And it is a matter of some importance to the psychosomatic approach Under one scheme an individual *needing* pulmonary tuberculosis can develop it merely by lowering his resistance and allowing his primary lesions to leak, whereas under the other scheme he must, in addition, go out and find some more bacilli

What I want to emphasise is that tuberculosis differs from the ordinary run of so called psychosomatic diseases It is not so simply acquired as peptic ulcer, hyperpiesis, a gloomy facial expression, and other such occupational diseases, where presumably an emotional habit causes symbolic functional changes, which in turn, if persisted in, cause organic changes in the organ concerned Not everybody can develop tuberculosis, so to speak, to order Those members of the community who have never encountered the bacillus, and those with high inherent immunity, will have to content themselves with a substitute—if they really need an illness

It would therefore be unreasonable to expect to find tuberculosis affecting predominantly any particular personality type And we do not—apart from the compulsive obsessionals who are always asking for trouble in all directions. Tuberculosis, however, is to be found in all grades of intelligence from the genius to the mentally deficient in which again it differs from some of the more generally accepted psychosomatic afflictions, such as migraine and asthma, to qualify for which it is almost essential to be up to School Certificate standards

LOWERING OF RESISTANCE

Let me recapitulate To develop chronic active pulmonary tuberculosis a person needs some bacilli, some moderately inflammable lungs (not celluloid like the guineapig's nor asbestos like the elephant's), and some internal or external factor which *lowers the resistance to the disease*

We have now reached the weak link in the chain and must face it and expose our ignorance about it Certain external environmental factors, such as captivity, starvation, lack of fresh air and sunlight, and over-fatigue, we know predispose towards breakdown, and we therefore say they lower the resistance Again, certain internal factors, such as diabetes, measles, and whooping-cough, similarly lower the resistance But there always are and always have been healthy bodied people living in comfortable material circumstances who break down with tuberculosis What on earth caused their breakdown, we ask And we have to find out Our job is only half done if we patch them up under sanatorium conditions and then send them back to exactly the same circumstances (whatever they may have been) as brought about their breakdown It would be like resuscitating a near drowned child on the bank and then chucking him back into the deep end without making sure that he could swim

---

* Read before the quarterly meeting of the Royal Medico Psychological Association at Shrewsbury on May 18 1949

PSYCHOLOGICAL FACTORS

Now if in such cases we take a careful history we find in a great number that they have suffered some major psychological trauma or have experienced some increasing difficulty in adjustment during the previous 18–24 months And, of course, the cold voice of criticism says "But who hasn't ? Especially in war time, when major psychological traumata and increasing difficulties in adjustment were ten a penny Where are your controls ?" It is really most unsatisfactory We have no quantitative test of a person's resistance to tuberculosis, and no Admiral Beaufort's scale of his psychological maladjustment So there can be no really scientific correlation between the two

One has to admit the weakness of this concept that psychological factors can cause lowered physical resistance, and one has—like the clergyman dealing with an insuperable obstacle—to "face it fearlessly and march boldly on" All the same there is one argument in its favour Psychological factors can very often be observed working during the long months of treatment, influencing both the immediate course of the tuberculosis and the ultimate prognosis, and if they work during the flowering of the disease, surely we may reasonably infer that they were working at its germination ? That psychological factors can and do influence the course of tuberculosis, once it is established, can be witnessed by anyone who has the opportunity of watching a patient's progress over a reasonably long period

ILLUSTRATIVE CASES

By way of illustration I will give a couple of thumb nail sketches of patients who have been under my observation during the last two years

Case 1 —Ursula, aged 25, was admitted with bilateral tuberculosis, sarcoma of the upper jaw, and diabetes She had had a hard time keeping down a secretarial job, running the flat, and looking after her mother, who was getting more and more peculiar and was a great worry Her mother was the worst case of senile dementia I have ever seen out of hospital, and it was a great relief to the girl to sink back into a bed far from home

Her diabetes was got under control, her maxillary sarcoma (of which two maternal aunts had died before the age of 30) was radically excised and shows no signs (now after 2 years) of any recurrence But her tuberculosis hung fire, and after as much operative interference as we dared make at the time she stabilised at a very low level out of bed only from 2 0 to 4 30 P M, with tea downstairs and a minimal walk in the grounds And there she stuck—for months and months Whenever we tried to extend her hours or her walking exercise she had a slight setback her temperature and her erythrocyte sedimentation rate (E S R) climbed up, and she lost weight, and back to bed she would have to go It was like snakes and ladders without any ladders

All this time she was a good coöperative patient doing her utmost to get well But she knew that on her discharge she would be faced with the dire alternative of either returning to her mother and all the worries that "*brought about her breakdown*" (her own words) or cutting free from her mother—and suffering thereafter the reproaches of her own conscience and her relations' tongues What could one do ? One could only wait patiently and hopefully for one of Time's miracles

It was a deadlock that went on for more than a year Then her mother became hallucinated, was certified, and entered a mental hospital, where she is perfectly happy ar whence she will never emerge Ursula wept bitterly at tl news, which was not entirely unexpected, but since th day she has got on, has trebled her exertions with impunit and will, I am now hopeful, make a useful recovery An amazingly enough, her 18 month old half crown cavity ı her right lung has healed almost completely during the la 3 months Tomograms taken 4 days ago show in its plac a small area of fine honeycombing She will probably kee her diabetes as a memento

Postscript May, 1951 —She has now been at home mai taining perfectly good health for nearly two years She sti has her diabetes

Case 2 —Jennifer, aged 16, developed tuberculosis in bot lungs, and was treated at home for 2 years without muc progress in either direction Her tuberculous father wa already under treatment at home, having been discharged from a sanatorium as incurable Hers was an extremely indolent form of early tuberculosis Then she coughed up some blood and was sent in panic haste to the sanatorium, where she made practically no progress for the first 6 months in spite of streptomycin She, too, stabilised at a low level and any attempt at pushing her on was rewarded with ris of temperature and E S R —and back to bed again

This went on for 9 months Then her tuberculous manic depressive father, who for the past 10 years had cast a hecti gloom over the home, died At once the girl began to improve and in course of time was fit enough to go home on 10 days leave She returned in a state of hysteria and tears He mother, deprived of her invalid husband, focused all he anxious solicitude on her daughter "She worries and fusse over me and everything I do the whole time I've lost ever bit of the self confidence I had been gaining this past year" The girl was not so well and threatened to stagnate again at a low stability

What could one do ? Again hope for one of Time's miracles. It came Her mother became so depressed—so obviously depressed—that her doctor referred her to a psychiatrist who gave a course of electric convulsion therapy with dramatic effect She became hypomanic, jolly, and carefree The daughter rapidly completed her convalescence and went home I have since learnt that she is well and happy and is attending an art school—an ambition which her mother had vetoed before her electrocutions

I could go on almost indefinitely giving this sort of testimony about the conscious state of mind and the *course* of the disease

Personally—and in spite of the guineapig, the elephant, the negro, and the twin, and all the other reasonable arguments put forward by the sceptics—I am convinced that in some cases disturbance of the psyche can and does *precipitate* the active disease process But that conviction does not make life any easier My next difficulty is to decide on what level the disturbance is operating and on what level it should be tackled I can make this clearer by examples Take the compulsive obsessional type His behaviour pattern can most easily be accepted as tending directly on a somatic or near somatic level to lower his resistance to the disease In pure culture he slave drives himself at his work, undertaking other people's work as well as his own, neglects both bed and board, enjoys no relaxations, and refuses to give in to feelings of fatigue He builds his own Railway of Death On a purely physical plane he is lowering his resistance to the disease by flirting with the classical quartet—captivity, starvation, lack of fresh air and sunlight, and over fatigue But on another level I wonder whether his guilt feelings, which allow him no peace, welcome tuberculosis as yet another cross for him to bear, yet another form of self punishment ? There is undoubtedly a higher percentage of these obsessionals among the tuberculous than in the population at large (This may, of course, be equally true of other diseases, I do not know) They do not make good patients and they do not do very well on the milder forms of therapy They mostly come sooner or later to thoracoplasty Is it too fanciful to wonder whether the pain and mutilation and the sacrifice of a few ribs have a deeper significance to the patient—an expiation of his guilt feelings similar to that brought about (it is my contention) by electric convulsion therapy on the guiltily depressed?

Incidentally, among sanatorium patients there is a curious hierarchy. There are the Oldest Inhabitants, of course; they are the Prefects or Wise Men whose views carry much weight. Those who have successfully undergone major surgical operations are held in as much esteem as if they had gained their school colours. They are the Bloods. And so on down the scale. The patient whose treatment has been purely conservative—rest in bed followed by graduated exercise, without even a phrenic crush or a course of streptomycin—is very small beer indeed. It strikes me very forcibly that at some primitive level of the group unconscious the ordeal of suffering at the hands of the surgeon must be regarded as a ritual of initiation or perhaps of purification.

Another cause for breakdown on the near somatic level is unhappiness. I might call it Unhappiness in Captivity, where the fetters are an uncongenial job, a deadening family life such as obtained in the two cases I have described, or an unhappy marriage—something inescapable or with apparently only a fire awaiting him who might leap out of the frying pan. This sort of situation, taking as it does all zest out of life, all taste out of food, all repose out of sleep, must inevitably starve the body of some of its needs, alter its metabolism, and lower its resistance to disease. Can it be that on a deeper level the pent up and frustrated aggression is turned in on itself and sets about destroying the organism with whatever weapons are at hand—in this case the tubercle bacilli? Can it be that the patient is sick of his life, and the Death Wish replaces the helmsman?

This sort of case is easy to spot—where the conflict is on a conscious level. I doubt whether there is a sanatorium superintendent in the world who has not on some occasion exclaimed "If only someone would shoot this patient's mother (wife, husband, or father, as the case may be)." Moreover, this is the sort of case in which one can often do something to help, even though it only amounts to waiting patiently for Time to bring about its healing. A full frank discussion of the patient's whole life situation—not once but repeated at intervals; for repetition is just as important here as in any other form of remedial exercises—can help the patient to find a way of altering his emotional attitude towards it. Very often all he needs is time, a renewal of courage, and the feeling that he has a friend behind him in his new venture.

But it is not always as easy as that. The presence of a conscious conflict, or a rationalised anxiety, can be very misleading. It may be merely the visible expression of some deeper maladjustment which is ready to provide other conscious conflicts to replace the one we may successfully resolve. I remembered how annoyed I felt once when in Army psychiatry I successfully dispelled a tuberculophobia on a purely rational level, and after a few days' peace and gratitude the patient became convinced that he had cancer of the stomach. Thus I learned the truth of the platitude "fear is hydra headed."

Then there are those cases in which no psychological disturbance whatever can be found on a conscious level and yet there must be something amiss deeper down which is in some way connected with their tuberculosis. The obsessional type comes to mind at once in this connection. But there are others.

One patient, while enjoying normal physical health, began having a recurrent dream that he was being driven through lovely countryside on a late summer afternoon enjoying the beauties of cloud, field, and foliage as never before—very poignantly—because his destination was a prison from which he would never emerge again. Eventually, $3^1/_2$ years later the dream came true in every detail.

Another patient, a woman, developed a rather more subtle prescient dream which recurred several times during the months before she fell ill. She dreamed that she was on a railway station about to make a journey she knew not where. While looking for a seat she put down her suitcase, which contained all that she possessed, and when she looked round for it it had disappeared.

Then there are those quiet spoken, gentle, cheerful little patients, whose lives and circumstances seem the quintessence of normality but whose Rorschach reactions are terrifyingly full of high explosive stuff—battle, murder, sudden death, anxieties, destructive aggressive impulses, pain, and cruelty. I have learnt to make mental reservations when giving a prognosis in such cases, even though clinically and radiologically their disease appears to be of slight extent. They may get well enough to return home and to their work, but they are apt to break down again. I have also learnt to be far happier about them if their crust gives way and reveals an apparent deterioration of their personality in the matter of a depression or chronic anxiety. But I rather draw the line at frank psychotic episodes.

Sometimes I wonder if we are not barking up the wrong tree, and whether tuberculosis, cancer, and such destructive diseases should not sometimes be regarded as psychotic conversions. It is notorious that, if one succeeds in depriving an asthmatic of his asthma, there is a chance of his becoming schizophrenic. I have known depressed tuberculous patients who, when discharged, improved, and, improving, have gone home and committed suicide. The near suicide of a patient I had under my care jerked him out of his depression and set him up for five years before he tried again, next time successfully.

It is not a very attractive hypothesis, because it makes one feel more helpless than ever.

So far I have been talking as if the road from psyche to soma were a one way street. It is not. Neither is psyche always the horse and soma the cart. They are much more like horses in double harness, inasmuch as if one falls lame the other suffers and has to adjust to the situation. And this adds yet another difficulty to the study of sick patients. Their bodily illness affects their psyche—their whole personality—dynamically. They will not stand still but are undergoing change the whole time.

RECOVERY AND THE DOCTOR

The patient who falls sick with tuberculosis is quite often pretty anxious at first—even panicky. Emotionally he regresses and wants Daddy to Make Him Well Again. While he is lying in bed for several months with all his little wants attended to by Mother Figure nurses and God the Father doctors he is apt to regress further—if not quite to the womb, at least to cradlehood. This regression seems to be as necessary a phase in therapy as the transference situation (with which it is surely linked?) is in analysis. The Kingdom of Heaven, we are told, is open only to those who are born again.

In course of time he is born again; by the time he becomes ambulant he has become a member of the family and identifies himself with the group. This phase of group identification, too, I regard as highly desirable, if not absolutely essential, for psychological reorientation. It is a phase comparable to puberty or adolescence. The group, untutored and leaderless, is a much more powerful psychotherapeutic instrument than any half baked psychiatric doctor like myself. It is the patients who heal each other.

Does the doctor play no part whatsoever? Well, by joining with the group in its creative activities he can do a little to preserve harmony: drawing out some inhibited member, damping down the persistent struggle for group domination, and encouraging each individual to realise that the group cannot be quite the same if he does not participate—much as a play producer strives to achieve balance and integrity among his players

But I must confess, we cannot do much I learned at Northfield during the war that the hospital itself was the real therapeutic agent, and that patients in a ward with a good morale did better than others in a disgruntled bear garden Quite late I discovered, too, to my humiliation, that going swimming or playing basket ball with my patients brought about more therapy than if I had spent treble the hours in psychiatric interviews I did not tell the Commanding Officer this He might have commented drily, and with some justification, that it evidently suited *my* complaint Instead I wrote a little hymn, for use in Army psychiatric messes, which I still occasionally hum to myself The refrain goes

Grant us, Lord, a proper sense
Of therapeutic impotence
Keep us humble, Lord
AMEN

My ideas, and the patterns into which they fall, owe much to Dr S H Foulkes, Dr James L Halliday, and Dr Eric Wittkower To their writings, and to the lively discussions I have enjoyed with them, I make my grateful acknowledgments

PARALYSES FOLLOWING IMMUNISING INJECTIONS

MEASURES CALCULATED TO DIMINISH THE RISK

GUY BOUSFIELD
M.D , Lond
DIRECTOR, CAMBERWELL LABORATORIES

THE investigations described below were, in part, instigated by a remark made to me by Sir Allen Daley, who observed that paralytic poliomyelitis following injections of diphtheria prophylactic or combined diphtheria toxoid and pertussis vaccine seemed to occur less often in infants under 1 year of age than in older children

Although many infants are immunised between the ages of 8 and 12 months, relatively few are injected earlier If the incidence of post injection paralysis rises notably over the age of 1 year, it might diminish in an equally striking manner if the injections were given in the first month or two of life

Sir Allen's observation immediately suggested to me that small infants might have some form of immunity to poliomyelitis like the passive immunity to diphtheria possessed by many babies during the early months of life Despite the fact that there does not seem to be much serological evidence of antibodies in adults to show that there is any widespread immunity to poliomyelitis, it is just possible that some such immunity does exist, and that it is due to some at present undetermined factor The defence of the infant might well be impermeability of the mucosæ

In any attempt to estimate the risk of poliomyelitis in the earlier period of life, the first step seemed to be to study the incidence of the disease in children under 1 year of age, dividing the cases into three month groups, but before proceeding to this analysis it will be instructive to study the age incidence of notified cases compiled from the Registrar General's returns for 1946–49 (fig 1) It will be noticed that the morbidity is far less in children aged less than 1 year than in the older children, the period of greatest risk apparently falling between the 2nd and 5th years

These findings tend to fit in rather well with Sir Allen Daley's observation Unfortunately, official records of notifications do not break down the morbidity in children aged less than 1 year into any shorter periods Thus it became necessary to investigate this aspect Many medical officers of health kindly analysed notifications received by them during the 4 years 1946–49 and furnished this information privately In addition, the General Register Office collected data relating to the first three quarters of 1950 It has thus been possible to construct two separate curves (fig 2) and to plot the mean The figures which it has been possible to obtain are not large, but they are culled from widely distributed areas of these islands, and should be fairly representative. One difficulty in producing larger totals is the relative infrequency of poliomyelitis in small infants In perusing fig 2, to keep this low incidence in mind it is well to refer once more to fig 1, and to recollect that only the children aged less than 1 year are being studied In considering fig 2 certain facts must be borne in mind There may be more frequent errors in the diagnosis of poliomyelitis in infants under 6 months of age, and some cases of poliomyelitis may have been missed or attributed to other conditions Again, there has undoubtedly been unsatisfactory diagnosis and notification of poliomyelitis in the past, which may render statistics somewhat misleading Further, the really small child may not be so often exposed to infection as are older children However, even allowing for these factors, the steady trend of the curve in fig 2 is reminiscent, in reverse, of the natural immunity curve found in the case of diphtheria (fig 3)

Whether or not the curve in fig 2 is attributable to passive immunity to poliomyelitis seems to be immaterial The fact remains that the disease, in recognisable form, is relatively infrequent under the age of 6 months, and we ought to be able to take advantage of this fact in any attempt to avoid paralytic sequelæ to injections of diphtheria, and possibly other, prophylactics If such treatment can be shown to be both effective and durable, it seems that inoculation against diphtheria should be undertaken as early as possible in life

PRODUCTION OF IMMUNITY IN INFANTS

There is already considerable evidence that it is feasible to immunise infants against diphtheria during

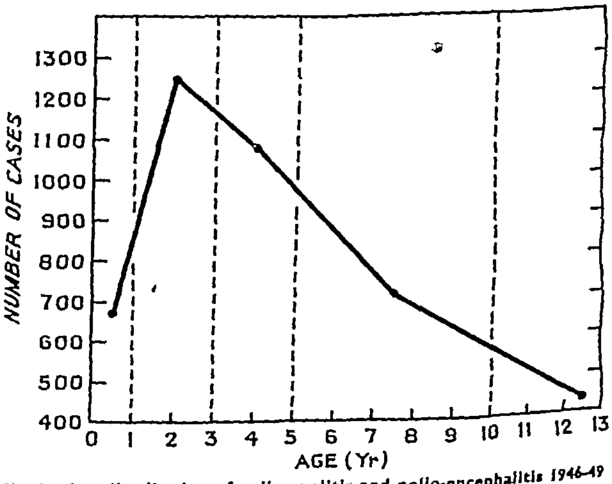


Fig 1—Age-distribution of poliomyelitis and polio-encephalitis 1946–49 The curve is constructed from the Registrar General's tables for infantile paralysis and polio-encephalitis in the civilian population for 1946–49 The interrupted vertical lines show the limits of the age-periods adopted in those tables To obtain a rough approximation of the trend of the curve of age-incidence the number of cases in each group has been divided by the number of years included in the group and the resulting figure has been plotted at the middle point in the age-group For example, there were 670 cases below the age of 1 year; and from the beginning of the 1st year to the end of the 2nd there were 2501 cases which figure divided by two gives 1250·5 This has been plotted on the line of the second year It is assumed that the numbers of children exposed to risk at each year of age within the grouped age-periods plotted, is about the same.

the first few months of life (Vahlquist 1949, Bousfield 1949, Barr et al. 1950, di Sant'Agnese 1950, Sauer and Tucker 1950)

It will be of interest to cite some figures published previously (Bousfield 1949), because it has now been possible to study these cases at relatively long range In the original article a description was given of 97 infants, of an unknown state of immunity of maternal origin, aged 2–5¹ months, who were treated by two different methods Reference to table I will show that a noteworthy proportion of these children would have been Schick negative at the time of inoculation.

Group A, comprising 46 children (aged 3–5 months) were given a single intramuscular injection of 1 0 ml of combined diphtheria toxoid and pertussis vaccine (P.D & Co) This contained 25 Lf units of diphtheria toxoid in the form of P T.A.P The children received post-Schick tests when they reached the age of 1 year The results were

Post Schick positive 3 negative 43 (post-Schick negative rate 93 5 %)

Group B, containing 51 children (aged 2–5 months) received two intramuscular injections of 0 5 ml of the same combined prophylactic at an interval of a month The diphtheria toxoid dosage was thus 12 5 Lf units on each occasion. These children were post-Schick tested at the age of 1 year The results were

Post Schick positive 0 negative 51 (post-Schick negative rate 100 %)

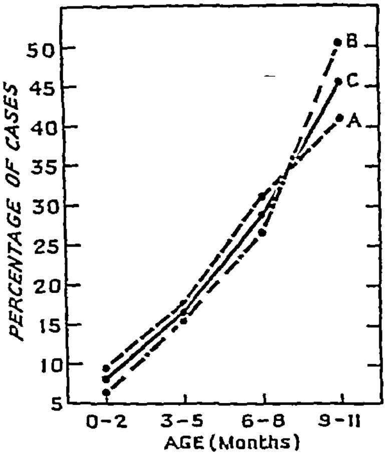


Fig 2—Incidence of poliomyelitis in infants aged less than 1 year A analysis of the General Register Office of 192 cases occurring in the first three-quarters of 1950 B information obtained by the author relating to 183 cases occurring between 1946 and the end of 1949 This information was supplied privately by medical officers of health, C average results obtained from the 375 cases contained in the two series.

To understand the significance of these figures, reference should be made to table I This gives the result of an investigation, in and around London, of the Schick-negative rate in untreated children aged 2–12 months It should here be mentioned that all Schick tests recorded here were done with Wellcome toxin and control The use of control is absolutely essential in post Schick testing, otherwise there will be erroneous positive readings

The data in table I have been set out in fig 3, and from this it will be noted that, at the age of 12 months, the age at which groups A and B were post Schick tested, practically every child would normally have lost any maternally bestowed immunity and become Schick positive, were it not for the inoculations carried out in the early months of life

The results of retesting groups A and B, when compared with the expectation in untreated children, show just how efficacious the immunisation was, especially in group B

DURATION OF IMMUNITY IN INFANTS

The question will be raised as to how long an immunity will last when infants are inoculated at a tender age It is now possible to provide some evidence on this point

Of the 97 children treated as described above it has now been possible to retest 52, some 2 years or slightly more after the original inoculation Group A (single injection only) provided 31 children for long range test, and group B produced 21 cases The results appear in table II

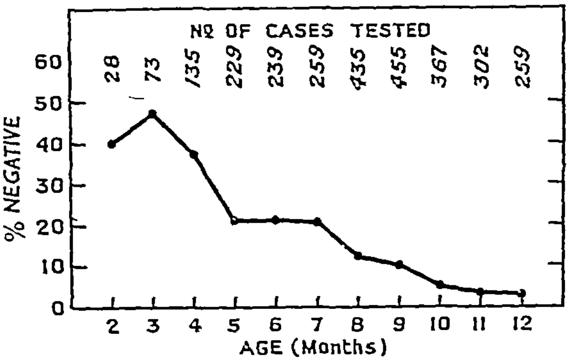


Fig 3—Primary Schick tests in 2781 infants Results related to age

These are the bare facts Their precise significance must now be considered During the 18 months or so which elapsed between the original post Schick tests and the long range tests there had been little, if any, diphtheria infection in the locality to boost the immunity of the infants Permanence of the Schick-negative state due to this cause can be discounted On the other hand, a Schick test is known to exercise a noteworthy boosting effect in persons who have previously been immunised or who have a basal immunity

Group A had one powerful primary stimulus, followed by the minute additional stimulus of the Schick test some 5–8 months later Thus accurate definition demands that these infants should be regarded as having been treated by a two injection procedure Had the Schick test, done at the age of 1 year, been replaced by a normal second dose of prophylactic the results of the long range test might have been better

By the same standard, group B must be considered to have received three injections two of P T.A.P and a Schick stimulus several months later The point at issue, however, is not how many injections have to be given to procure a lasting immunity in infants, but rather can it be done at all ? It is submitted that table II provides an affirmative answer over a reasonable period of time Judging from past experience, what lasts for such a time may well endure much longer It will be necessary to observe infants at longer range to prove this beyond all doubt Measures for immunising small infants are given below

TABLE I—PRIMARY SCHICK TESTS ON INFANTS

Age (mos)	No of cases	Positive	Negative	% Schick negative
2	28	17	11	39 3
3	73	39	34	46 6
4	135	85	50	37 0
5	229	180	49	21 4
6	239	187	52	21 8
7	259	206	53	20 5
8	435	385	50	11 5
9	455	409	46	10 1
10	367	350	17	4 6
11	302	291	11	3 6
12	259	252	7	2 7

Infant Immunity Curve—The form of curve in fig 3 is of some interest because it is based on 2781 primary tests and should therefore be fairly comprehensive Apart from the 2 month age group, which comprised only 28 infants, the decline in immunity is as would be expected, except for the abrupt fall to the 5th month, and the definite flattening of the curve covering the 6th and 7th months Weaning might have something to do with this, but it is difficult to see what mechanism could produce this effect It is, however, clear that, at does not participate—much as a play producer strives to achieve balance and integrity among his players

But I must confess, we cannot do much I learned at Northfield during the war that the hospital itself was the real therapeutic agent, and that patients in a ward with a good morale did better than others in a disgruntled bear garden Quite late I discovered, too, to my humiliation, that going swimming or playing basket ball with my patients brought about more therapy than if I had spent treble the hours in psychiatric interviews I did not tell the Commanding Officer this He might have commented drily, and with some justification, that it evidently suited *my* complaint Instead I wrote a little hymn, for use in Army psychiatric messes, which I still occasionally hum to myself The refrain goes

Grant us, Lord, a proper sense
Of therapeutic impotence
Keep us humble, Lord
AMEN

My ideas, and the patterns into which they fall, owe much to Dr S H Foulkes, Dr James L Halliday, and Dr Eric Wittkower To their writings, and to the lively discussions I have enjoyed with them, I make my grateful acknowledgments

PARALYSES FOLLOWING IMMUNISING INJECTIONS

MEASURES CALCULATED TO DIMINISH THE RISK

GUY BOUSFIELD
M.D, Lond
DIRECTOR, CAMBERWELL LABORATORIES

THE investigations described below were, in part, instigated by a remark made to me by Sir Allen Daley, who observed that paralytic poliomyelitis following injections of diphtheria prophylactic or combined diphtheria toxoid and pertussis vaccine seemed to occur less often in infants under 1 year of age than in older children

Although many infants are immunised between the ages of 8 and 12 months, relatively few are injected earlier If the incidence of post injection paralysis rises notably over the age of 1 year, it might diminish in an equally striking manner if the injections were given in the first month or two of life

Sir Allen's observation immediately suggested to me that small infants might have some form of immunity to poliomyelitis like the passive immunity to diphtheria possessed by many babies during the early months of life Despite the fact that there does not seem to be much serological evidence of antibodies in adults to show that there is any widespread immunity to poliomyelitis, it is just possible that some such immunity does exist, and that it is due to some at present undetermined factor The defence of the infant might well be impermeability of the mucosæ

In any attempt to estimate the risk of poliomyelitis in the earlier period of life, the first step seemed to be to study the incidence of the disease in children under 1 year of age, dividing the cases into three month groups, but before proceeding to this analysis it will be instructive to study the age incidence of notified cases compiled from the Registrar General's returns for 1946–49 (fig 1) It will be noticed that the morbidity is far less in children aged less than 1 year than in the older children, the period of greatest risk apparently falling between the 2nd and 5th years

These findings tend to fit in rather well with Sir Allen Daley's observation Unfortunately, official records of notifications do not break down the morbidity in children aged less than 1 year into any shorter periods Thus it became necessary to investigate this aspect Many medical officers of health kindly analysed noti cations received by them during the 4 years 194 and furnished this information privately In addition the General Register Office collected data relating to the first three quarters of 1950 It has thus been possible to construct two separate curves (fig 2) and to plot the mean The figures which it has been possible to obtain are not large, but they are culled from widely distributed areas of these islands, and should be fairly representative One difficulty in producing larger totals is the relative infrequency of poliomyelitis in small infants In perusing fig 2, to keep this low incidence in mind it is well to refer once more to fig 1, and to recollect that only the children aged less than 1 year are being studied In considering fig 2 certain facts must be borne in mind There may be more frequent errors in the diagnosis of poliomyelitis in infants under 6 months of age, and some cases of poliomyelitis may have been missed or attributed to other conditions Again, there has undoubtedly been unsatisfactory diagnosis and notification of poliomyelitis in the past, which may render statistics somewhat misleading Further, the really small child may not be so often exposed to infection as are older children However, even allowing for these factors, the steady trend of the curve in fig 2 is reminiscent, in reverse, of the natural immunity curve found in the case of diphtheria (fig 3)

Whether or not the curve in fig 2 is attributable to passive immunity to poliomyelitis seems to be immaterial The fact remains that the disease, in recognisable form, is relatively infrequent under the age of 6 months, and we ought to be able to take advantage of this fact in any attempt to avoid paralytic sequelæ to injections of diphtheria, and possibly other, prophylactics If such treatment can be shown to be both effective and durable, it seems that inoculation against diphtheria should be undertaken as early as possible in life

PRODUCTION OF IMMUNITY IN INFANTS

There is already considerable evidence that it is feasible to immunise infants against diphtheria during

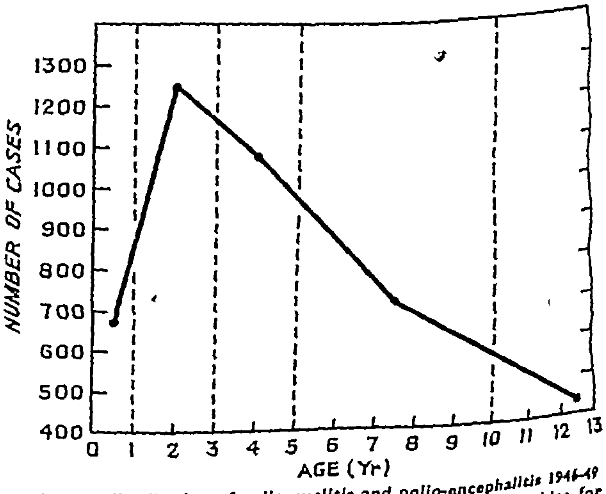


Fig 1—Age-distribution of poliomyelitis and polio-encephalitis 1946-49 The curve is constructed from the Registrar-General's tables for infantile paralysis and polio-encephalitis in the civilian population for 1946-49 The interrupted vertical lines show the limits of the age-periods adopted in those tables To obtain a rough approximation of the trend of the curve of age-incidence the number of cases in each group has been divided by the number of years included in the group, and the resulting figure has been plotted at the middle point in the age-group For example there were 670 cases below the age of 1 year; and from the beginning of the 1st year to the end of the 2nd there were 2501 cases which figure, divided by two gives 1250 5 This has been plotted on the line of the second year It is assumed that the numbers of children exposed to risk at each year of age, within the grouped age-periods plotted is about the same

the first few months of life (Vahlquist 1949, Bousfield 1949, Barr et al 1950, di Sant'Agnese 1950, Sauer and Tucker 1950)

It will be of interest to cite some figures published previously (Bousfield 1949), because it has now been possible to study these cases at relatively long range In the original article a description was given of 97 infants, of an unknown state of immunity of maternal origin, aged 2–5 months, who were treated by two different methods Reference to table I will show that a noteworthy proportion of these children would have been Schick negative at the time of inoculation.

Group A, comprising 46 children (aged 3–5 months) were given a single intramuscular injection of 1 0 ml. of combined diphtheria toxoid and pertussis vaccine (P.D & Co) This contained 25 Lf units of diphtheria toxoid in the form of P T.A.P The children received post-Schick tests when they reached the age of 1 year The results were

Post Schick positive 3 negative 43 (post Schick negative rate 93 5 %)

Group B, containing 51 children (aged 2–5 months) received two intramuscular injections of 0 5 ml of the same combined prophylactic at an interval of a month. The diphtheria toxoid dosage was thus 12 5 Lf units on each occasion These children were post Schick tested at the age of 1 year The results were

Post Schick positive 0 negative 51 (post-Schick negative rate 100 %)

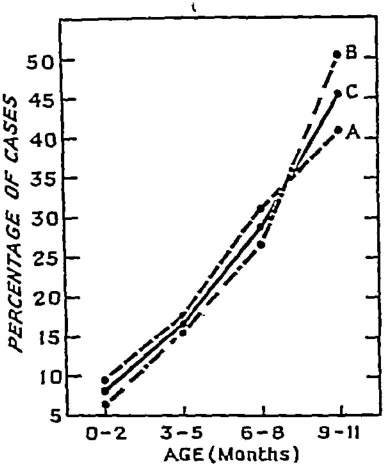


Fig 2—Incidence of poliomyelitis in infants aged less than 1 year A analysis of the General Register Office of 192 cases occurring in the first three-quarters of 1950 B, information obtained by the author relating to 183 cases occurring between 1946 and the end of 1949 This information was supplied privately by medical officers of health C average results obtained from the 375 cases contained in the two series.

To understand the significance of these figures, reference should be made to table I This gives the result of an investigation, in and around London, of the Schick negative rate in untreated children aged 2–12 months It should here be mentioned that all Schick tests recorded here were done with Wellcome toxin and control The use of control is absolutely essential in post Schick testing, otherwise there will be erroneous positive readings

The data in table I have been set out in fig 3, and from this it will be noted that, at the age of 12 months, the age at which groups A and B were post Schick tested, practically every child would normally have lost any maternally bestowed immunity and become Schick-positive, were it not for the inoculations carried out in the early months of life

The results of retesting groups A and B, when compared with the expectation in untreated children, show just how efficacious the immunisation was, especially in group B

DURATION OF IMMUNITY IN INFANTS

The question will be raised as to how long an immunity will last when infants are inoculated at a tender age It is now possible to provide some evidence on this point

Of the 97 children treated as described above it has now been possible to retest 52, some 2 years or slightly more after the original inoculation Group A (single injection only) provided 31 children for long range test, and group B produced 21 cases The results appear in table II

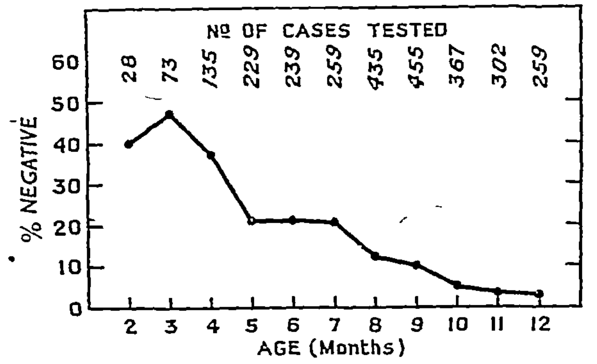


Fig 3—Primary Schick tests in 2781 infants Results related to age

These are the bare facts Their precise significance must now be considered During the 18 months or so which elapsed between the original post Schick tests and the long range tests there had been little, if any, diphtheria infection in the locality to boost the immunity of the infants Permanence of the Schick negative state due to this cause can be discounted On the other hand, a Schick test is known to exercise a noteworthy boosting effect in persons who have previously been immunised or who have a basal immunity

Group A had one powerful primary stimulus, followed by the minute additional stimulus of the Schick test some 5–8 months later Thus accurate definition demands that these infants should be regarded as having been treated by a two injection procedure Had the Schick test, done at the age of 1 year, been replaced by a normal second dose of prophylactic the results of the long range test might have been better

By the same standard, group B must be considered to have received three injections two of P T A.P and a Schick stimulus several months later The point at issue, however, is not how many injections have to be given to procure a lasting immunity in infants, but rather can it be done at all? It is submitted that table II provides an affirmative answer over a reasonable period of time Judging from past experience, what lasts for such a time may well endure much longer It will be necessary to observe infants at longer range to prove this beyond all doubt Measures for immunising small infants are given below

TABLE I—PRIMARY SCHICK TESTS ON INFANTS

Age (mos)	No of cases	Positive	Negative	% Schick-negative
2	28	17	11	39 3
3	73	39	34	46 6
4	135	85	50	37 0
5	229	180	49	21 4
6	239	187	52	21 8
7	259	206	53	20 5
8	435	385	50	11 5
9	455	409	46	10 1
10	367	350	17	4 6
11	302	291	11	3 6
12	259	252	7	2 7

Infant Immunity Curve—The form of curve in fig 3 is of some interest because it is based on 2781 primary tests, and should therefore be fairly comprehensive Apart from the 2 month age group, which comprised only 28 infants, the decline in immunity is as would be expected, except for the abrupt fall to the 5th month, and the definite flattening of the curve covering the 6th and 7th months Weaning might have something to do with this, but it is difficult to see what mechanism could produce this effect It is, however, clear that, at

TABLE II—PERMANENCY OF THE SCHICK NEGATIVE STATE IN INFANTS INOCULATED AT THE AGE OF 2–5 MONTHS RETESTS 2 YEARS AFTER INOCULATION

Group of infants	No of cases	Post Schick positive	Post Schick negative
Group A	31	2	29
Group B	21	0	21

Permanency of Schick negative state (both methods) 96 %

the age of 1 year, all but a few infants have lost their passive immunity

AGE AT WHICH IMMUNITY CAN BE PROCURED

The feasibility of immunising infants having been demonstrated, the next point which required study was how early in life active immunity could be shown to have been established For this purpose a further 174 small infants, all previously shown to be Schick positive, were treated by different methods All were aged 2–5 months at the start of the immunising course, and in each case post Schick tests were made about a month after the last injection Occasionally the interval was slightly longer

Group C received two intramuscular injections of 0 5 ml of combined diphtheria and pertussis prophylactic (P.D) at an interval of 28 days

Group D received two or three subcutaneous injections of 0 5 ml of fluid toxoid in buffered saline solution at intervals of 14 days, or 14 days and 28 days

Group E received a single subcutaneous injection of P T A.P mixed with fluid toxoid This mixture is later referred to as F.P T

The results are shown in table III

It is not suggested that the age of Schick conversion recorded in table III by any means necessarily constitutes the low limit of possibility The new experimental antigen, F P T, has made a good showing (see below) Clearly, if infants could be obtained for treatment at the age of 2 months or less, there is no reason why most of them should not have an effective potential immunity conferred on them, by a single subcutaneous injection of F P T, by the time they are 3 months old A secondary stimulus could be applied later at a convenient time

Part of the trouble in inquiries such as those embodied here is due to the difficulty in educating parents to bring infants for treatment at a tender age The idea of having children inoculated at the age of about 9 months has prevailed so long that it is difficult to change it Fig 3 shows that the vast majority of infants are brought to clinics at the age of 8–10 months

TABLE III—AGE AT WHICH IMMUNITY CAN BE SHOWN TO HAVE BEEN ESTABLISHED IN SCHICK POSITIVE INFANTS INOCULATED AT THE AGE OF 2–5 MONTHS

Group	No of cases	Post Schick positive	Post Schick negative	Average age at inoculation (mos)	Average age at post Schick test (mos)
C	112	2	110	4 0	6 3
D	20	0	20	4 5	7 0
E	42	0	42	4 5	5 7

Total cases in all groups 174 Conversion rate 98 9 %

Table III thus offers further evidence of the feasibility of immunising the small infant It also shows that this can be effected at the age of about 6 or 7 months, before the risk of poliomyelitis becomes significant Finally there is a little evidence that subcutaneous injections of purified toxoid produce a satisfactory response in very young infants, a point which will be found to be of possible significance later

ROUTE OF INJECTION AND CHOICE OF PROPHYLACTICS

It is now fairly generally accepted that intramuscular injections made when poliomyelitis is prevalent occasionally tend to be followed by paralysis of that muscle or of an associated group Probably persons so affected already have the virus in their systems, or become infected about the time of injection Intramuscular injections may possibly convert a non paralytic type of poliomyelitis into the paralytic form The diphtheria prophylactics which seem to be chiefly connected with such lesions after intramuscular inoculation are A P T combined with pertussis vaccine and, to a lesser extent, A P T given alone

A twofold change in procedure seemed to be indicated when these facts became known The first thing was to abandon intramuscular injection, and to try injecting by the shallow subcutaneous route The second point was to use a prophylactic which could be injected in such a manner, without the production of excessive local reaction, while at the same time providing an efficient immunity response These considerations absolutely ruled out combined diphtheria and pertussis prophylactic, and even rendered the injection of A P T *rather* undesirable

TABLE IV—EFFECTS OF TWO SUBCUTANEOUS INJECTIONS OF 0 3 ML OF P T A.P, GIVEN AT A MONTHLY INTERVAL, TO SCHICK POSITIVE CHILDREN UNDER THE AGE OF 2 YEARS

No of *cases*	Interval between last injection and post-Schick test (mos)	Post-Schick results		Conversion rate
		Positive	Negative	
62	2	0	62	100 %
231	3	1	230	99 6 %
293		1	292	99 7 %

In the course of considerable research into the optimal aluminium phosphate content of Holt's purified toxoid, aluminium phosphate precipitated (P T.A.P), large numbers of subcutaneous injections were given to investigate the relation between the formation of subcutaneous nodules and the antigenic response (Bousfield 1947a)

Parents having been warned not to worry if a small *hard lump came up under the skin, practically* no complaints of untoward reaction were met with after the injection of small Schick positive children with P T A.P by the subcutaneous route This preliminary experience paved the way for investigation of the effect of subcutaneous injections of standard P T A P on a group of 293 children aged less than 2 years All the infants were initially shown to be Schick positive They received two injections of P T A P 0 3 ml just under the skin, over the deltoid muscle in the arm, the interval between the inoculations being a month Retests were made at the intervals shown in table IV It will be agreed that these results are virtually perfect from the immunological aspect

At this point it may be well to consider how much progress has been made in building up a scheme for safe and efficient inoculation The age of theoretical least danger from poliomyelitis has been indicated with a degree of probability and the feasibility of inoculating very small infants has been shown, originally by intramuscular injections The durability of the immunity bestowed by injections given early in life has been shown to be reasonably good, and it has been shown that a very high Schick conversion rate is obtainable with two strictly subcutaneous injections of P T A P at a monthly interval

Here a word of warning must be given *The site for a* subcutaneous injection must be carefully chosen The skin over the fleshy part of the deltoid *in the arm*, well

TABLE V—EFFECTS OF SUBCUTANEOUS INJECTIONS OF FLUID TOXOID (HOLT—BATCH 3540). DOSAGE ON EACH OCCASION 0·5 ML. POST SCHICK TESTS DONE A MONTH AFTER FINAL INJECTION

No. of injections	Interval between doses (days)	No. of cases	Post Schick		Conversion rate
			Positive	Negative	
3	0–14–28	127	1	126	99·2%
2	0–14	124	9	115	92·7%
1	—	30	14	16	53·3%

clear of the shoulder, is probably as good a site as any. Areas in which the musculospiral nerve could be involved must be scrupulously avoided, or wrist drop may supervene. Injections over the deltoid have given no trouble whatsoever. These injections should be strictly subcutaneous, not shallow intramuscular.

This investigation of the use of subcutaneous P.T.A.P. and fluid toxoid was conducted during an epidemic of poliomyelitis, and many thousands of other subcutaneous injections were administered throughout this period, without a suspicion of any paralytic sequelæ. Working under similar conditions, but using intramuscular injections, during a previous epidemic of poliomyelitis, I had met with several cases of post-injection paralysis.

INVESTIGATION OF PROPERTIES OF AN ANTIGEN WITHOUT MINERAL CARRIER

Because some people feared that it was the aluminium hydroxide in prophylactics such as A.P.T. which might be the irritant involved in the production of post-injection poliomyelitic paralyses, it was resolved to try to dispense with any aluminium compound. The mind went back to those days when one used the old formol toxoid, of which three spaced injections were necessary. Excellent antigenic response was obtainable with this prophylactic, but some persons developed severe local reactions after its use. This was due largely to various impurities in the material.

Today the position is different, mainly owing to the pioneer work of L. B. Holt in the production of a diphtheria toxoid of extreme purity, such as is embodied in his P.T.A.P. (Holt 1947, 1950).

It was resolved to try the effect of injecting this pure toxoid without any mineral carrier, and it was considered that a reasonable toxoid content would be 50 or 60 Lf per ml. Holt kindly prepared a batch of his pure toxoid in buffered saline solution, the strength being 60 Lf per ml. Three groups of Schick positive children aged less than 2 years were treated with this prophylactic subcutaneously. This material is henceforth referred to as F.T. Details of various procedures adopted are given in table V.

The single injection series was curtailed, since it was clear that no useful purpose could be served by investigating the method at any greater length.

It is not claimed that the best method of administration of this prophylactic was used in these experiments. It did seem possible that two large doses given at a short interval might approximate, in their behaviour, to the relatively protracted stimulus afforded by an adsorbed toxoid such as A.P.T., though it was realised that both these first doses would be subject to rather rapid loss from the body. However, as we wanted to obtain information as rapidly as possible about the behaviour of this F.T., the fortnight interval between the first and second doses was adopted in the initial investigations. Work now in hand is directed to finding out what results are obtainable from two 0·5 ml. doses of F.T. given at an interval of a month, the post-Schick tests being performed 3 months later. The preliminary results are encouraging.

It may also be that the results in table V are rather flattered by the fact that the Schick tests were made only a month after the last injection. In the case of the three injection procedure, this need give rise to no apprehension that the method is not sound. Past experience has shown that all modes of inoculation which produce a high Schick conversion rate, whatever the circumstances, also show good durability of immunity at long range. An example of this is available (Bousfield 1947b).

Here it should be noted that complaints of objectionable local reaction following the subcutaneous inoculation of small Schick positive children with F.T. have been practically absent. The use of this material in older persons would have to be the subject of a further inquiry. In children there is absence of the subcutaneous nodule such as often follows the injection of prophylactics containing any form of aluminium compound at present in use.

One more weapon is thus added to the armoury of those desirous of continuing diphtheria prophylaxis in all circumstances. Three injections of F.T. in buffered saline solution, used in the dosage of 0·5 ml., and probably best at monthly intervals, can be given with excellent immunological results, without producing undesirable reactions. Perhaps even two monthly injections of this prophylactic will suffice, but this remains to be seen. Whatever method is adopted, it is necessary that it shall yield a high Schick conversion rate. Among the last 5–10% of persons who are difficult to immunise are to be found just those most likely to contract the disease severely if attacked by it, especially if antitoxin treatment is delayed.

EXPERIMENTAL DIPHTHERIA PROPHYLACTIC

To make immunisation of the very young infant as efficient as possible, it is necessary to consider the findings of Vahlquist (1949) and those of Barr et al. (1950) regarding a difficulty which may be encountered. Their various observations showed that an occasional child, having a fairly large amount of residual maternally bestowed antitoxin in its blood, proved relatively difficult to immunise, or responded to injections only tardily. It seems that the infant's antitoxin swamps the injected toxoid.

I think it likely that this difficulty can be overcome by the use of a powerful and appropriately constituted prophylactic. To this end a new type of material has been envisaged, and some early work with it is mentioned at this stage in the hope that the conception may appeal to other investigators, and thus provide information in the near future. It would take a lone worker a long time to produce adequate evidence.

It seems that one method of disposing of the undesirable passive immunity of an infant would be to inject a fairly large dose of F.T. This should fix the child's antitoxin by combining with it rapidly. If, therefore, at the same time as the F.T. is injected, adsorbed toxoid (P.T.A.P.) were introduced, the latter might be left free to exercise its more potent stimulus unhampered. Any T.A.F. formed from the combination of the child's antitoxin with the F.T. might even be helpful to a slight degree.

A reasonable composition for such a prophylactic seemed to be 100 Lf units of fluid toxoid and 25 Lf units of P.T.A.P. contained in 1 ml. Holt kindly prepared this material to the above specification in the Wright Fleming Institute of Microbiology, and a method has been found which ensures that a reasonable proportion of the F.T. remains unadsorbed on to the phosphate. A good abbreviation for this experimental prophylactic would appear to be F.P.T. (fluid and phosphate toxoid). Preliminary work on this prophylactic has been in progress, in the first instance on known Schick positive infants, to study its immunising properties.

In theory FPT should prove excellent as a primary and secondary stimulus, because it possesses optimal characteristics for both purposes

At the time of writing, 154 children, mostly aged only a few months, have been treated with a single subcutaneous injection of 0 5 ml of the material Schick tests a month later showed only two positive readings, both very faint, a conversion rate of 98 7% Only by study of the effect of single injections can the merits of a prophylactic be determined with any degree of accuracy No attempt is made to produce evidence that one injection will suffice In practice the 0 5 ml. dose should be followed by a secondary stimulus some months later This could consist of 0 5 ml of FPT or FT

The main investigation is somewhat different Primarily Schick negative infants of tender age are being treated with a single subcutaneous dose of FPT, and this is not being augmented by a secondary stimulus The post Schick tests on these children will not be done before they reach the age of 1 year Comparison of the results, when available, with the normal expectations and trends, as shown in fig 3, will afford a fairly good indication of the success or failure of the procedure

Yet another group of Schick negative infants is being treated with a single 0 5 ml injection of FPT, by the subcutaneous route, followed by a secondary stimulus of 25 Lf units some months later The post Schick tests will be done at the age of 1 year, as in the former group From other experiences it is confidently anticipated that this method will yield good results

No untoward results have been encountered in the subcutaneous use of FPT, but it is advisable to warn parents that a very small lump will come under the skin, that this is quite normal, and that there is nothing to worry about If this is done, no complaints at all are received

If any other seekers after knowledge are interested in cooperating in these investigations on tiny infants, using FPT, Mr L B Holt, of the Wright Fleming Institute of Microbiology, will be glad to furnish them with a supply

GENERAL REMARKS AND CONCLUSIONS

It is felt that one logical approach to the solution of the problem of post injection paralysis is to inoculate infants subcutaneously with suitable diphtheria prophylactics as early as possible in life, and certainly before the age of 6 months On the basis of work so far completed, FT in buffered saline solution, as three injections of 0 5 ml each at monthly intervals, should be an adequate treatment for small infants Alternatively, two well spaced subcutaneous injections of PTAP 0 3 ml should suffice A fairly long interval between the injections is probably best—up to 3 or 4 months—if infants are inoculated when extremely small, without preliminary Schick tests Such procedure is likely to be more effective in the small percentage of infants who are treated initially while they still possess maternally bestowed antitoxin in their blood

No mention has been made here of whooping cough prophylaxis Assessment of its value must await the results of extensive investigations undertaken by the Medical Research Council Nevertheless the demand for the treatment by the public is such that the matter cannot be ignored by any authority Combined prophylaxis constitutes an admirable bait for diphtheria immunisation, and many only accept this latter treatment to procure whooping cough injections But whooping cough or combined prophylaxis will have to be the subject of a separate inquiry

Finally, though it is admitted that only time can prove how correct are the conclusions reached above, I submit that the suggested approach is rational and worthy of an extensive trial Only by continued constructive thought and effort can the question of post injection paralysis be answered

SUMMARY

It is shown that poliomyelitis, in recognisable form, seems to occur much less often in the first months of life than in the next few years of childhood

As the risk of post-injection paralysis is probably proportional to the liability to contract poliomyelitis, it is suggested that immunisation against diphtheria should be undertaken as early as possible in life—e.g., at the age of 2–5 months

Evidence is offered that infants can be immunised successfully at this age, and that the immunity holds good some 18 months to 2 years later in the great proportion of cases

The primary Schick state of 2781 infants has been studied to determine the percentage possessing natural protection against diphtheria at each age from 2–12 months It has been shown that active immunity can be procured in 98 9% of Schick-positive infants by about the 6th or 7th month of life

For the present it seems advisable to avoid intramuscular injections of diphtheria prophylactics, and to adopt the strictly subcutaneous route In an experience covering a very large number of injections, there have been no paralytic sequelæ, even throughout danger periods, when diphtheria antigens have been administered under the skin

Holt's PTAP, given as two subcutaneous injections of 0 3 ml. at a monthly interval, to children aged 1 year or less, has yielded a Schick conversion rate of 99 7%, without the production of objectionable reactions

The behaviour of a highly purified toxoid in buffered saline solution has been investigated, and further work is in progress on this material Given as three subcutaneous injections of 0 5 ml , it has produced a Schick conversion rate of 99 2 in children aged 1 year or less

An experimental diphtheria prophylactic (FPT) is described It is hoped that this material will enable infants with excessive amounts of antitoxin of maternal origin to be actively immunised effectively Collaboration in this investigation is sought 154 small children, all initially Schick positive, showed a conversion rate of 98 7% a month after a single subcutaneous injection of 0 5 ml of the material

Prophylactics at present generally available, which should prove suitable for subcutaneous administration to infants aged 2–5 months, are fluid toxoid (purified toxoid in buffered saline solution) as three monthly injections of 0 5 ml., or two well spaced injections of 0 3 ml of PTAP In treating infants who have not been previously shown to be Schick-positive an interval of 3 or 4 months between the two injections of PTAP is advised

Thanks are due to Dr A. A. Anderson (medical officer, No 9 Middlesex Area) for many facilities and helpful discussion , to Dr V Russell, DMO , No 1 London Division , Dr H D Chalke, DMO , No 7 London Division , and Dr W H S Wallace, DMO , No 8 London Division, for many facilities , to Mr L B Holt, of the Wright-Fleming Institute of Microbiology, for the preparation of special antigens , to the General Register Office for investigating the incidence of poliomyelitis in infants during the first three quarters of 1950 , to the numerous medical officers of health throughout the country who have given me information and statistical evidence , and finally to Sir Allen Daley (medical officer of health, London County Council) whose chance remark was responsible for the production of much of this evidence

REFERENCES

Barr M , Glenny A T Randall, K J (1950) *Lancet*, i 6
Bousfield, G (1947a) *Ibid*, i 286
— (1947b) *Ibid*, ii 867
— (1949) *Ibid* i 1100
di Sant Agnese P A (1950) *Amer J publ Hlth* 40 671
Holt, L B (1947) *Lancet* i 282
— (1950) Developments in Diphtheria Prophylaxis London
Sauer L W Tucker W H (1950) *Amer J publ Hlth*, 40 681
Vahlquist B (1949) *Lancet* i 16

THE BACTERIOSTATIC EFFECTS OF THE NEWER DRUGS IN THE TREATMENT OF GENITO-URINARY TUBERCULOSIS

A REVIEW OF 51 CASES

J Cosbie Ross
M.B Lpool, F.R C.S
SURGEON

J G Gow
M.B Lpool, F R C S
SURGICAL REGISTRAR

C A St Hill
M.B Brist.
CLINICAL PATHOLOGIST

ROYAL SOUTHERN HOSPITAL, LIVERPOOL

> I hope I grow wiser every year —John Hunter.

The effects of streptomycin and other substances, both alone and in combination, on tuberculosis of the genito urinary tract have been investigated. The following drugs were used

(1) Streptomycin alone in a dosage of 0·5 g b d. up to a total of 90 g

(2) Streptomycin and para aminosalicylic acid (P.A.S) together, streptomycin 0·5 g b d up to a total dosage of 90 g, and P.A.S 15 g daily

(3) Streptomycin and P.A.S alternately for six months, each being given for a month alone, streptomycin 0·5 g b d., and P.A.S 15 g daily

(4) Streptomycin and P.A.S alternately as in (3) plus thiacetazone ('Thioparamizone') 50 mg daily to begin with and gradually increasing to 200 mg daily, the whole course lasting six months.

The genito urinary tuberculosis was divided into five types (the classification suggested by the Medical Research Council)

(1) An early unilateral lesion of the renal parenchyma.

(2) A unilateral renal lesion with cystitis and nephrectomy

(3) A bilateral renal lesion with nephrectomy of the worse kidney

(4) Cystitis and involvement of the remaining kidney after nephrectomy

(5) Major bilateral severe disease

All the patients were treated at Wrightington Sanatorium, and were kept for several months under a strict sanatorium régime The diagnosis depended entirely on the isolation of tubercle bacilli from the urine by cultural methods, or by guineapig inoculation The urine was repeatedly examined, but one of the major difficulties was the inability to demonstrate tubercle bacilli either by culture or by guineapig inoculation once the course of treatment had begun.

Cystoscopy and bilateral retrograde pyelography were done whenever possible, and the urine from each kidney was cultured and inoculated into guineapigs The capacity of the bladder was estimated at each cystoscopy and intravenous pyelography was repeated at three-month intervals A close watch was kept for toxic manifestations

ASSESSMENT OF IMPROVEMENT

We consider that certain basic principles should be emphasised at the outset First, in our present state of knowledge, we should not speak of a cure of tuberculosis but merely control of the disease Follow up investigations have not been made for a sufficiently lengthy period, and the number of relapses which are occurring now will almost certainly tend to increase during the succeeding years Secondly, we have no accurate knowledge yet of the precise action of streptomycin and the other drugs on the tubercle bacillus Thirdly, resistance of the organisms may develop very rapidly, particularly in an acid medium Lastly, resistance of the human body must play a large part in the action against the tubercle bacillus, but to what extent as yet remains unsolved It is an undoubted fact that some patients seem to carry on for many years without any sanatorium or specific treatment One of us (J C R) sees at six month intervals a patient in whom bilateral renal tuberculosis was diagnosed thirteen years ago, after the organism had been obtained from each ureter after ureteric catheterisation The patient has steadfastly refused any treatment but is apparently well, except for frequency of micturition

An attempt has been made to assess progress under the following headings

(1) Micturition (*a*) alteration in frequency, (*b*) presence or absence of pain during micturition.

(2) Cystoscopic appearances of the bladder

(3) Alteration in capacity of the bladder

(4) Sterilisation of the urine

(5) Alteration in intravenous or retrograde pyelograms.

STREPTOMYCIN ALONE

So much has already been published about the pharmacology, dosage, efficiency, and toxicity of streptomycin that it is enough for us to say that the total dosage in this series was 90 g given as 0 5 g b d. for ninety consecutive days, and that the urine was made alkaline before treatment with streptomycin was begun, and was kept so throughout the course of treatment We were particularly careful to keep the urine alkaline throughout the course because streptomycin resistance appears more rapidly in an acid medium, and sometimes appears within a few days (Finland et al. 1946, Harris et al. 1947) One of our great difficulties was to keep the urine alkaline, even after large doses of potassium citrate the urine occasionally remained neutral.

The results are shown in table I and are similar to those obtained by Jacobs and Borthwick (1950) and Lattimer (1948) and Lattimer et al. (1949) In none of the severe cases was there sufficient improvement to allow surgery Streptomycin seemed to have some effect on the cystitis, but this usually depended on removal of the primary focus

STREPTOMYCIN AND P.A.S TOGETHER

In view of these poor results, and of the fact that it was considered at that time undesirable to increase the dosage of streptomycin owing to possible toxicity, it was decided to use a combination of streptomycin and P.A.S Table II shows the results thus obtained.

STREPTOMYCIN AND P.A.S ALTERNATELY

At this stage of our investigation we had great difficulty in giving P.A.S and potassium citrate together, because of the tendency to nausea and vomiting We felt that since it was important to keep the urine alkaline during streptomycin therapy, we should try some other method, and decided to administer streptomycin and P.A.S alternately, giving the potassium citrate at the same time as the streptomycin. In support of this we knew that streptomycin resistance increased rapidly after 30 g had been given (M. E Florey, personal communication) No case of streptomycin resistance in an alkaline medium has been reported in less than 28 days, when streptomycin had been given at the rate of 1 g a day, on the other hand, 30% were resistant after 42 g had been given, and 60% were resistant after 60 g Further support of this method of treatment was afforded by Cayley's (1950) report of serum potassium deficiency following protracted administration of P.A.S

Table III shows the results of cases treated by this method

STREPTOMYCIN, P.A.S, AND THIACETAZONE

After considering these results we were still dissatisfied, although there appeared to be slight improvement with alternate streptomycin and P.A.S We therefore tried

In theory F P T should prove excellent as a primary and secondary stimulus, because it possesses optimal characteristics for both purposes

At the time of writing, 154 children, mostly aged only a few months, have been treated with a single subcutaneous injection of 0 5 ml of the material Schick tests a month later showed only two positive readings, both very faint, a conversion rate of 98 7% Only by study of the effect of single injections can the merits of a prophylactic be determined with any degree of accuracy No attempt is made to produce evidence that one injection will suffice In practice the 0 5 ml dose should be followed by a secondary stimulus some months later This could consist of 0 5 ml of F P T or F T

The main investigation is somewhat different Primarily Schick-negative infants of tender age are being treated with a single subcutaneous dose of F P T, and this is not being augmented by a secondary stimulus The post-Schick tests on these children will not be done before they reach the age of 1 year Comparison of the results, when available, with the normal expectations and trends, as shown in fig 3, will afford a fairly good indication of the success or failure of the procedure

Yet another group of Schick negative infants is being treated with a single 0 5 ml injection of F P T, by the subcutaneous route, followed by a secondary stimulus of 25 Lf units some months later The post Schick tests will be done at the age of 1 year, as in the former group From other experiences it is confidently anticipated that this method will yield good results

No untoward results have been encountered in the subcutaneous use of F P T, but it is advisable to warn parents that a very small lump will come under the skin, that this is quite normal, and that there is nothing to worry about If this is done, no complaints at all are received

If any other seekers after knowledge are interested in cooperating in these investigations on tiny infants, using F P T, Mr L B Holt, of the Wright-Fleming Institute of Microbiology, will be glad to furnish them with a supply

GENERAL REMARKS AND CONCLUSIONS

It is felt that one logical approach to the solution of the problem of post injection paralysis is to inoculate infants subcutaneously with suitable diphtheria prophylactics as early as possible in life, and certainly before the age of 6 months On the basis of work so far completed, F T in buffered saline solution, as three injections of 0 5 ml each at monthly intervals, should be an adequate treatment for small infants Alternatively, two well spaced subcutaneous injections of P T A P 0 3 ml should suffice A fairly long interval between the injections is probably best—up to 3 or 4 months—if infants are inoculated when extremely small, without preliminary Schick tests Such procedure is likely to be more effective in the small percentage of infants who are treated initially while they still possess maternally bestowed antitoxin in their blood

No mention has been made here of whooping cough prophylaxis Assessment of its value must await the results of extensive investigations undertaken by the Medical Research Council Nevertheless the demand for the treatment by the public is such that the matter cannot be ignored by any authority Combined prophylaxis constitutes an admirable bait for diphtheria immunisation, and many only accept this latter treatment to procure whooping cough injections But whooping cough or combined prophylaxis will have to be the subject of a separate inquiry

Finally, though it is admitted that only time can prove how correct are the conclusions reached above, I submit that the suggested approach is rational and worthy of an extensive trial Only by continued constructive thought and effort can the question of post injection paralysis be answered

SUMMARY

It is shown that poliomyelitis, in recognisable form, seems to occur much less often in the first months of life than in the next few years of childhood

As the risk of post injection paralysis is probably proportional to the liability to contract poliomyelitis, it is suggested that immunisation against diphtheria should be undertaken as early as possible in life—e.g, at the age of 2–5 months

Evidence is offered that infants can be immunised successfully at this age, and that the immunity holds good some 18 months to 2 years later in the great proportion of cases

The primary Schick state of 2781 infants has been studied to determine the percentage possessing natural protection against diphtheria at each age from 2–12 months It has been shown that active immunity can be procured in 98 9% of Schick-positive infants by about the 6th or 7th month of life

For the present it seems advisable to avoid intramuscular injections of diphtheria prophylactics, and to adopt the strictly subcutaneous route In an experience covering a very large number of injections, there have been no paralytic sequelæ, even throughout danger periods, when diphtheria antigens have been administered under the skin

Holt's P T A.P, given as two subcutaneous injections of 0 3 ml at a monthly interval, to children aged 1 year or less, has yielded a Schick conversion rate of 99 7%, without the production of objectionable reactions

The behaviour of a highly purified toxoid in buffered saline solution has been investigated, and further work is in progress on this material Given as three subcutaneous injections of 0 5 ml, it has produced a Schick conversion-rate of 99 2 in children aged 1 year or less

An experimental diphtheria prophylactic (F P T) is described It is hoped that this material will enable infants with excessive amounts of antitoxin of maternal origin to be actively immunised effectively Collaboration in this investigation is sought 154 small children, all initially Schick positive, showed a conversion rate of 98 7% a month after a single subcutaneous injection of 0 5 ml of the material

Prophylactics at present generally available, which should prove suitable for subcutaneous administration to infants aged 2–5 months, are fluid toxoid (purified toxoid in buffered saline solution) as three monthly injections of 0 5 ml., or two well spaced injections of 0 3 ml of P T A P In treating infants who have not been previously shown to be Schick-positive an interval of 3 or 4 months between the two injections of P T A.P is advised

Thanks are due to Dr A A. Anderson (medical officer, No 9 Middlesex Area) for many facilities and helpful discussion, to Dr V Russell, D M O, No 1 London Division, Dr H D Chalke, D M O, No 7 London Division, and Dr W H S Wallace, D M O, No 8 London Division, for many facilities, to Mr L B Holt, of the Wright-Fleming Institute of Microbiology, for the preparation of special antigens, to the General Register Office for investigating the incidence of poliomyelitis in infants during the first three quarters of 1950, to the numerous medical officers of health throughout the country who have given me information and statistical evidence, and finally to Sir Allen Daley (medical officer of health, London County Council) whose chance remark was responsible for the production of much of this evidence

REFERENCES

Barr M, Glenny, A T, Randall K J (1950) *Lancet* i, 6
Bousfield G (1947a) *Ibid* i 286
— (1947b) *Ibid* ii 867
— (1949) *Ibid* i 1100
di Sant Agnese P A (1950) *Amer J publ Hlth* 40 671
Holt, L B (1947) *Lancet* i 282
— (1950) Developments in Diphtheria Prophylaxis London.
Sauer L W Tucker W H (1950) *Amer J publ Hlth*, 40, 681
Vahlquist B (1949) *Lancet* i 16

TABLE V—STERILISATION OF URINE

Treatment	No of cases	Result
Streptomycin alone	18	13 became and remained sterile 3 remained persistently positive 2 became initially sterile but reverted to positive later
Streptomycin and P.A.S together	7	4 became and remained sterile, 1 remained positive 2 became initially sterile but reverted later
Streptomycin and P.A.S alternately	20	19 became and remained sterile 1 remained constantly positive no reversions occurred up to six months after cessation of treatment
Streptomycin, P.A.S and thiacetazone	6	6 have remained sterile up to date

Comparison Between the Four Groups—Treatment groups 3 and 4 seemed to offer the best promise of success Although the severe lesions were disappointing in their response to any method of treatment, there was some improvement in group 4 Seven cases of progressive hydronephrosis were encountered in the whole series Of these, one was in group 1, two in group 2, two in group 3, and two in group 4. This might possibly be taken to indicate that there is an increased fibrosis at the lower end of the ureter, brought about by healing, thus causing an increase in the hydronephrosis We have also found that cases in which hydronephrosis is present at the start of treatment rarely show any response in any of the four groups, and eventually require ureteric transplant into the colon

Comparison Between Single and Multiple Lesions—Out of 51 cases there were 26 in which the lesion seemed to be confined to the genito urinary tract, and 25 in which it was an incident in a generalised disease affecting other systems of the body There has been no significant difference between the response to treatment in the two divisions

Comparison Between the Five M.R.C Types—Type 1 seems to respond equally well to streptomycin alone and in combination Type 2, if anything, responds best to streptomycin and P.A.S given alternately Type 3 responds equally well to either of these methods of treatment Types 4 and 5 are disappointing, and are unpredictable in their response Treatment with the three drugs seems to be the most helpful in these advanced cases If hydronephrosis is present, however, the outlook is poor in any event

Sterilisation of Urine—The results are given in table V

Intravenous Pyelograms—The results are given in table VI.

SURGICAL TREATMENT

Nephrectomy has been done in twenty-two cases in this series, always under a "screen" of streptomycin In no case was the wound drained, and it is not our practice to remove the lower end of the ureter With this technique all the cases healed by first intention, and so far it has not been necessary to remove the lower end of the ureter later We believe that, provided there is adequate drainage of the ureteric stump into the bladder the ureter ultimately heals, becoming a solid fibrous cord The type of ureter which may require excision is the tortuous fixed indurated one that does not drain freely We deprecate the common practice of doing a nephrectomy for tuberculosis at a general hospital, and subsequently transferring the patient to a sanatorium for continuation of treatment The nephrectomy is a single, although a most important, incident in the treatment of a generalised disease, and requires careful timing if primary healing is to be achieved in every case

Epididymectomy was done on many occasions by Ross's (1948) technique The scrotum was not drained, and all the wounds healed by first intention We suggest that a tuberculous epididymis may lead to the appearance of tubercle bacilli in the urine, and that, until this source has been removed, it is impossible to be certain that a subclinical focus is present in either kidney The prostate gland has been massaged before and after epididymectomy, and in four cases the urine, which contained tubercle bacilli before the operation, has remained persistently sterile after epididymectomy

Ureteric transplant has been done on eight patients three by the extraperitoneal technique, and five by Cordonnier's (1949) intraperitoneal method There was no immediate postoperative mortality, but the former three patients (in each of whom the ureter of a remaining kidney was transplanted) died of uræmia within six months Of the latter five patients two died eight weeks after operation with an ascending infection, both of them had had the ureter of a solitary kidney transplanted and had severe cystitis and a contracted bladder The three other patients were well and improved after operation, the hydronephrosis being much reduced in size

Ureters were transplanted for (1) increasing hydronephrosis, (2) severe cystitis and contracted bladder, (3) severe intractable frequency of micturition, and (4) tuberculous stricture of the urethra

In view of the report by Baggenstoss (1949) that streptomycin does not penetrate the fibrous wall, and hence does not enter the cavities, of ulcero cavernous lesions—we tried to grow cultures of tubercle bacilli from the pus of cavities after nephrectomy, which was done always towards the end of the treatment period If we were successful, the organism was tested for sensitivity or resistance to streptomycin The streptomycin content of the pus from which these bacilli were obtained was also estimated.

TABLE VI—INTRAVENOUS PYELOGRAMS

Treatment	No of cases	Result
Streptomycin alone	18	15 remained unchanged 3 deteriorated 1 showing hydronephrosis and 2 involvement of more calyces
Streptomycin and P.A.S together	7	4 remained unchanged 3 deteriorated 2 showing increase in hydronephrosis and 1 involvement of additional calyces
Streptomycin and P.A.S alternately	20	16 remained unchanged 2 deteriorated both showing increase in hydronephrosis, 1 hydronephrosis improved 1 showed healing of an ulcero-cavernous lesion
Streptomycin, P.A.S and thiacetazone	6	4 unchanged 2 deteriorated, showing increase in hydronephrosis

The results (table VII) are discouraging, and only in case 13 could we grow a tubercle bacillus sensitive to a lower percentage of streptomycin than was present in the pus The resistant organisms were resistant to concentrations of streptomycin much in excess of those we found in the cavities, the greatest being 8 5 units per ml. in case 3 Probably the reason for this is the acidity of the pus which predisposes to the rapid emergence of a resistant strain of bacillus It is significant, however, that some streptomycin does penetrate the walls of the cavities

The variation in concentration is unexplained at present, but it may depend on the timing of the nephrectomy in relation to the last injection of streptomycin

It is also important to ascertain whether there is any difference in sensitivity between the organisms in the urine and those located

etazone in conjunction with streptomycin and
Since all three drugs may exercise their effect
e tubercle bacillus in a different manner, it seemed
al to assume that a combination of all three might
uce better results

e thiosemicarbazone drugs, discovered in 1946,
shown by Domagk et al (1946) to be active against
ubercle bacillus, and have been extensively studied
ermany since then In vivo experiments have
n that some of them have a suppressive action on
rowth of this organism Their action is apparently
effective than that of streptomycin, but more
sive than that of P A S (Donovick 1949) Toxic
ions may develop, the commonest being anorexia,
ea, vomiting, agranulocytosis, and hæmolytic
nia Such reactions are relatively infrequent,
ded the dose does not exceed 200 mg a day
haw and McDermott (1950) and Mertens and
e (1950), summarising the extensive clinical trials
rmany, reported that about 70% of lesions through
he body were improved They issued a warning,
ver, that these results were obtained against
ng nutritional and social standard According to
these workers, the cases responding most favourably were those in which the infection was confined to mucosæ—i e, tracheobronchitis, bronchitis, laryngitis, enteritis, and cystitis They thought that thiosemicarbazone was *not* sufficiently powerful by itself, but that in combination with other drugs it might prove of value in the treatment of tuberculosis In the German investigation few cases of genito urinary tuberculosis were included Hurni (1949) studied the effects in vivo of various combinations of thiacetazone, streptomycin, and P A S He showed that, though combinations of thiacetazone with P A S, and of thiacetazone with streptomycin, had no additive effect, combinations of all three drugs in therapeutic doses had some increased effect in mice So far we have only treated six cases by the combined method, but all the patients concerned showed encouraging improvement, although falling into the most severe type of case

Table IV shows the results in this small group

DISCUSSION OF RESULTS

We emphasise again that the final results of treatment can only be assessed after many years

TABLE I—RESULTS OF THERAPY WITH STREPTOMYCIN ALONE

C e	No of cases	Clinical improvement		Bladder		Sterilisation of urine	Intravenous pyelographic changes	Remarks
		Frequency of micturition	Pain on micturition	Appearance	Capacity			
	1	1 improved	1 improved	1 no change	1 no change	1 sterile	1 no change	
	7	5 improved (1 slight)	5 improved	4 improved	5 improved	5 sterile 1 constantly positive, 1 initially sterile but reverted later	7 no change	
	2	2 improved	2 improved	2 improved	2 improved	2 sterile	2 no change	
	4	4 improved (2 slight)	4 improved (2 slight)	1 improved 3 no change	1 improved 3 no change	3 sterile, 1 initially sterile, but reverted later	2 no change 2 deteriorated	The case which showed cystoscopic improvement deteriorated later despite treatment
	4	2 improved (slight) 2 no change	3 improved 1 no change	3 no change 1 deteriorated	3 no change 1 deteriorated	2 sterile, 2 remained positive	3 no change, 1 deteriorated, increase in hydronephrosis	

TABLE II—RESULTS OF THERAPY WITH STREPTOMYCIN AND P A S TOGETHER

	1	1 improved	1 improved	1 improved	1 improved	1 sterile	1 no change	
	2	2 improved	2 improved	2 improved	2 improved	1 sterile, 1 initially sterile but reverted later	2 no change	
	2	1 no change 1 deteriorated	1 no change 1 deteriorated	2 no change	2 no change	1 positive, 1 initially sterile but reverted later	2 deteriorated	Both showed increased hydronephrosis and had ureteric transplantation into the bowel
	2	1 improved slightly 1 no change	2 improved	1 improved 1 no change	1 improved 1 no change	2 sterile	1 no change 1 deteriorated	

TABLE III—RESULTS OF THERAPY WITH STREPTOMYCIN AND P A S ALTERNATELY

	6	6 improved	6 improved	6 no change	6 no change	6 sterile	1 improved 5 no change	This case showed healing of an ulcerocavernous lesion
	7	7 improved	7 improved	5 improved 2 no change	5 improved 2 no change	7 sterile	7 no change	
	3	3 improved	3 improved	1 improved 2 no change	1 improved 2 no change	3 sterile	2 no change 1 deteriorated	Increase in hydronephrosis
	4	3 improved 1 deteriorated	3 improved 1 deteriorated	2 improved 1 no change	2 improved 1 no change	3 sterile, 1 consistently positive	1 improved 2 no change 1 deteriorated	This improvement was manifested by a decrease in hydronephrosis the deterioration was an increase in hydronephrosis

TABLE IV—RESULTS OF THERAPY WITH STREPTOMYCIN, P A S, AND THIACETAZONE

	1	1 improved	1 improved	1 improved	1 improved	1 sterile	1 deteriorated	Increase in hydronephrosis
	5	3 improved 2 no change	3 improved 2 no change	4 improved 1 deteriorated	4 improved 1 deteriorated	5 sterile	4 no change 1 deteriorated	Increase in hydronephrosis

melæna He had about six months' history of upper abdominal discomfort after meals and some loss of appetite

On admission he had collapsed after severe melæna, and his hæmoglobin was 46%

Treatment and Progress—Under treatment, including blood transfusion, he improved Recurrence of bleeding called for a further transfusion of 2 pints of blood on June 10, after which he again improved till June 15, when at 9 30 A.M. he had severe upper abdominal pain and was once again collapsed and pale His hæmoglobin was then 60% Abdominally he was a typical case of perforated peptic ulcer In view of the bad prognosis of the combination of perforation and hæmorrhage from gastric ulcer I felt that suture of the perforation alone held very little hope of recovery, and I decided on partial gastrectomy, after restorative measures, which lasted four hours This seemed a very hazardous undertaking in a patient so ill, but I thought the risk justifiable Gastric suction was instituted, 3 pints of blood was given, and morphine gr $^1/_2$ and atropine gr $^1/_{100}$ were injected as premedication

At operation free gas and much free fluid was found in the abdomen. A perforated ulcer was present on the anterior wall of the stomach $2^1/_3$ in from the pylorus and just off the lesser curve The perforation was rapidly closed, and the free fluid removed by suction There was nothing in the appearance of the ulcer to suggest that it was not benign A partial gastrectomy was done rapidly but it had to be a high one because of a second ulcer high on the posterior wall adjacent to the lesser curve This ulcer I suspected of being the source of the hæmorrhage The abdomen was closed without drainage A blood drip had been continued throughout the operation, and the anæsthetic (thiopentone, gas oxygen, and curare), given by Dr J Piney, caused so little upset that the general condition of the patient had improved when he left the operating theatre

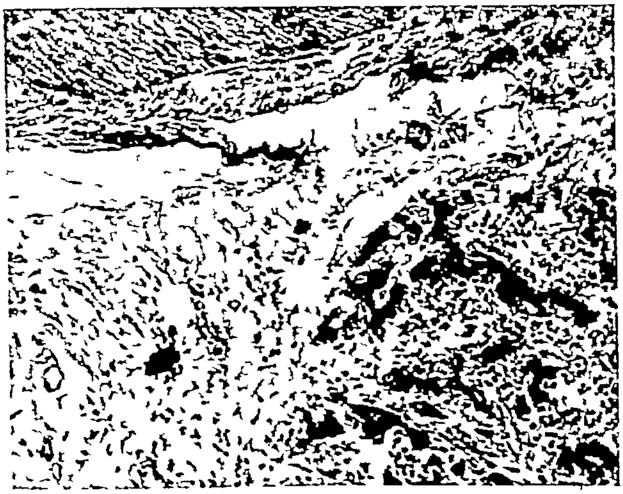


Fig. 2 (case I)—The floor of the ulcer at the extremity of invasion by carcinoma cells at the level of the artery seen in fig I The wall of this artery can be seen at the top of the figure the carcinoma cells at the right, and the fibrous tissue of the floor of the pre-existing ulcer on the left (× 100)

Postoperative Treatment and Progress—Chemotherapy was given and a further 2 pints of blood and the patient's condition steadily improved He was discharged on July 11, 1949, able to enjoy a normal diet He returned from convalescence very fit, and when seen about a year later was in the best of health On April 27 1951 he was still in excellent health and working as a policeman in the R A.F constabulary

Pathological Report (Dr M. O Skelton)— The stomach presents two chronic ulcers, one is 6 cm. proximal to the pylorus on the anterior surface, with one edge 3 mm. from the lesser curvature This ulcer measured 2 × 1 cm, with the long axis longitudinally, and has perforated and been sutured with catgut There is another ulcer, 5 cm proximal to the first, on the posterior wall 5 mm. from the lesser curvature This ulcer measured 1 5 × 5 cm Microscopically the perforated ulcer from the anterior wall has a partially necrotic floor covered by granulation tissue overlying the muscularis, which shows fibrous replacement of some of the muscle tissue There is a small artery in the floor of the ulcer plugged with fresh thrombus At one edge of the ulcer the mucosal glandular epithelium has undergone malignant change, and short columns of poorly differentiated carcinoma cells are insinuating themselves between the muscle-bundles and the fibrous tissue strands of the ulcer, and are seen lying beneath its floor (figs 1 and 2) The malignant change appears to have begun at one end and to be sweeping across the ulcer from one side. Microscopic examination of the second ulcer (figs 3 and 4) shows a chronic peptic ulcer with undoubted carcinomatous change at both edges—groups of malignant cells are seen invading the stomach wall A section across the mucosa between the ulcers shows chronic gastritis but no carcinoma cells Lymph nodes from the left gastric group show no tumour invasion There are two separate carcinomata developing in chronic gastric ulcers'

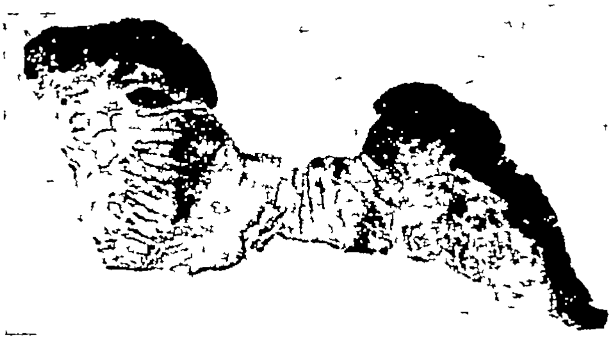


Fig 3 (case I)—Ulcer on lesser curve of stomach showing the infiltration of the fibrous floor of the chronic gastric ulcer by carcinoma cells on the right. The infiltration has invaded the wall of the stomach fairly deeply but has not traversed it so extensively as in the ulcer shown in fig I (× 4)

The gratifying result in this desperately ill patient fully justified the formidable operation, and has convinced me that, for perforation after hæmorrhage, gastrectomy should be done if a skilled team and an able and experienced anæsthetist are available The report of Mr W J Ferguson's two successful cases (Ives 1950) stimulated me to report this case in support of more radical measures for this grave condition.

The pathological report is of considerable interest because both ulcers were malignant and separated by a considerable area of stomach showing no malignant change Two separate carcinomatous ulcers in one

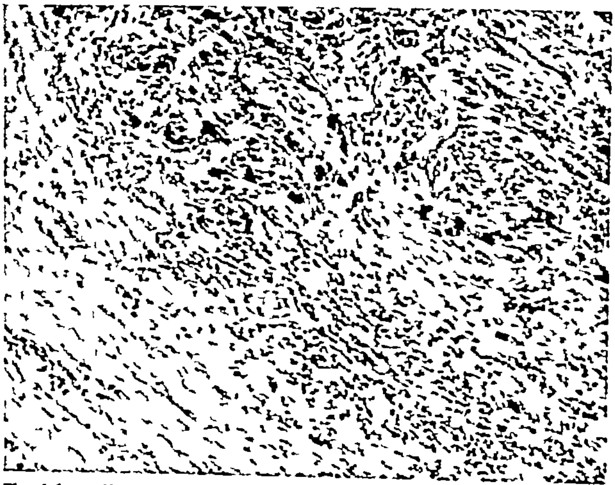


Fig 4 (case I)—The floor of the ulcer shown in fig 3, at the junction of invading carcinoma cells (top right) and the fibrous tissue of the floor (× 100)

TABLE VII—CULTURES FROM PUS OF NEPHRECTOMY CAVITIES

Case no	Culture of tubercle bacillus isolated from pus in cavity	Sensitivity to streptomycin per ml	Streptomycin per ml of pus in cavities
1	Positive	Resistant to 64 u	None present no streptomycin for three weeks
2	Positive	Resistant to 64 u	5 u
3	Negative	Not estimated	8 5 u
4	Negative	Not estimated	4 u
5	Negative	Not estimated	None present, no streptomycin for four weeks
6	Positive	Resistant to 64 u	2 5 u
7	Positive	Sensitive to 8 u	2 u
8	Positive	Sensitive to 1 u	No pus
9	Positive	Sensitive to 1 u	No pus
10	Positive	Resistant to 64 u	No pus
11	Negative	Not estimated	3 5 u
12	Negative	Not estimated	2 u
13	Positive	Sensitive to 1 u	4 u
14	Negative	Not estimated	5 u
15	Positive	Resistant to 64 u	4 9 u

cavities Possibly the organisms excreted in the urine are sensitive to streptomycin, whereas those in the cavities (owing to the acidity) have become resistant The great difficulty of prosecuting this line of investigation is that, once the streptomycin course has been started, cultures of tubercle bacilli from the urine are difficult to obtain

CONCLUSIONS

In established cases of severe renal disease treatment with streptomycin alone seemed to have no apparent effect, except for some symptomatic improvement If the disease is unilateral nephrectomy remains the method of choice

Of the four treatment groups, group 4 seemed to give the most encouraging results

In M R C types 1, 2, and 3 the prognosis is good, in types 4 and 5 poor

The three drugs used are not substitutes for surgery, but will prove of value in combination with the usual surgical measures

The sanatorium régime is still an essential part of the treatment, and should be insisted on in every case

There is no significant difference in the results of treatment between those cases in which the genito urinary lesion is the only manifestation of the disease and those in which there are also lesions in other systems

Patients presenting initially with hydronephrosis respond badly, whatever the treatment, and usually require transplant of the ureter With the Cordonnier (1949) technique the hydronephrosis is definitely improved by operation

Surgery should always be done under a "screen" of streptomycin

Ureterectomy is not essential as a general rule

Calcification is no proof that the disease is inactive

The results of a preliminary investigation into the relation of the amounts of streptomycin in ulcero cavernous lesions to the sensitivity of the bacilli are discouraging

FUTURE POLICY

In view of the fact that more encouraging results have been achieved with streptomycin, P A S, and thiacetazone, we intend to use this treatment in all cases in future We have increased the dosage of streptomycin to 2 g a day (Lattimer et al 1949) and are using a possibly more active and less toxic thiosemicarbazone—i e, 'Ethizone' (Herts Pharmaceuticals Ltd) Woody and Avery (1948) have shown the value of potassium iodide in increasing the effectiveness of streptomycin against the tubercle bacillus in laboratory animals and in pulmonary lesions We are therefore adding 5 g of potassium iodide to the alkaline mixture given as a routine during the administration of streptomycin

We wish to thank Dr J Dobson, superintendent and resident orthopædic surgeon, Wrightington Sanatorium, for his coöperation and keen interest, Prof A W Downie for his help with estimations of streptomycin sensitivity, and Herts Pharmaceuticals Ltd for technical assistance, and supplies of thioparamizone and ethizone

REFERENCES

Baggenstoss, A H (1949) Streptomycin and Dihydrostreptomycin in Tuberculosis New York
Cayley F E de W (1950) *Lancet*, i, 447
Cordonnier, J J (1949) *Surg Gynec Obstet* 88, 441
Domagk G, Behnisch R, Mietzsch, F, Schmidt, H (1946) *Naturwissenschaften*, 33, 315
Donovick R (1949) *Amer Rev Tuberc* 60, 539
Finland, M, Murray, R, Harris, H W, Kilham, L, Meads, M (1946) *J Amer med Ass* 132, 16
Harris, H W, et al (1947) *Amer J Med* 2, 229
Hinshaw, H C, McDermott, W (1950) *Amer Rev Tuberc* 61, 145
Hurni, H (1949) *Schweiz Z Path Bakt* 12, 596
Jacobs, A, Borthwick, W M (1950) *Proc R Soc Med* 43, 453
Lattimer, J K Stearns, W H, et al (1948) *J Urol* 60, 974
— Amberson, J B, Braham, S (1949) *Ibid*, 62, 875
Mertens, A, Bunge, R (1950) *Amer Rev Tuberc* 61, 20
Ross, J C (1948) *Brit J Urol* 20, 173
Woody, E jun, Avery, R C (1948) *Science*, 108, 501

ASSOCIATED PERFORATION AND HÆMORRHAGE FROM UNSUSPECTED GASTRIC CARCINOMA

JAMES JEMSON
F R C S
CONSULTANT SURGEON, LEWISHAM HOSPITAL, LONDON

THE combination of perforation and hæmorrhage from gastric ulceration is rare (Ives 1950) and carries a very grave prognosis In twenty five years' surgical work in hospitals I have encountered several such cases and have been impressed by the fatal termination of most of them

Case 1, which came under my care on June 15, 1949, presented additional unusual features

Case 1—A man, aged 52, was admitted to Lewisham Hospital on June 7, 1949 He had suddenly collapsed while having a drink three days previously and had subsequently had

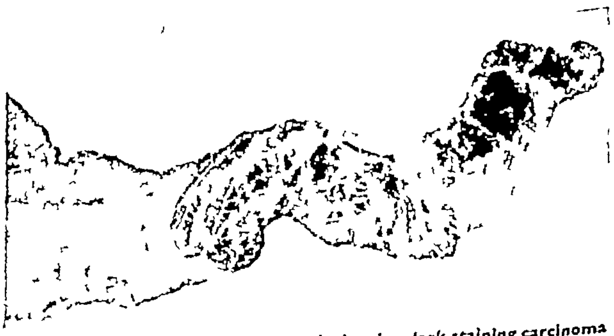


Fig 1 (case 1)—Ulcer in pyloric canal, showing dark staining carcinoma cells infiltrating the fibrous floor of the ulcer from the right. The malignant cells have traversed the floor of the ulcer as far as the large artery (× 4) possible, they still average about 50 a day No doubt similar conditions and a similar volume of work are to be found at most large hospitals in the country

Without large and extensive buildings and a very numerous and highly trained staff, major operating-theatre ritual for the treatment and dressing of wounds with such a volume of work is impossible In devising a practical method of treatment and dressing of wounds we *have to compromise* I have worked on the principle that cross infection from other patients is the most important factor to avoid, the organisms carried by the patient are considered to be of secondary importance in causing clinical infection of his wound To prevent cross infection it means that every instrument or pair of hands that touches one patient must be sterilised before it is used to dress the open wound of another patient

A no touch technique at first sight seems to be the answer to this, but I have yet to meet the person so dexterous with forceps that he can bandage a finger without touching the patient Washing the hands between each patient is a snare and a delusion Either the hands are washed so perfunctorily that the washing is of no value, or the hands become raw when many dressings have to be done, and cause infection on their own account To overcome this human element, in 1940, while serving in the Nigerian Medical Service, I devised an "assembly line" or "mass production" routine for doing dressings When I returned to Leeds to take charge of the casualty department, this method was introduced with only such modifications as the better equipment allowed

"ASSEMBLY LINE" ROUTINE

The routine now carried out in Leeds for dressings is as follows When the patient returns for a dressing, as he enters the department the old dressing is removed and a temporary dressing of sterile gauze is applied to the wound The patient holds this in place and walks over to the bench at the side of the casualty surgeon's table The patient lifts up the gauze, the surgeon inspects the wound, and the gauze is immediately replaced The surgeon records progress on a chart Tickets describing the dressing to be used and any other after treatment are given to the patient, who then passes behind a screen to the dressing team The tickets, each of which is of a different colour for each different treatment, are a great help in reducing contact between patient and dresser, for the dresser soon learns the significance of the different colours and can see at a glance what is required without having to read a card

The dressing team basically consists of three people—the server, dresser no 1, and dresser no 2 As the patient comes into the dressing line he sits down opposite dresser no 1, and as he does so the server places a sterile kidney dish, containing three pairs of forceps, pledgets of wool, and gauze dressing, on the table in front of the dresser With one pair of forceps the dresser removes the temporary dressing, and this pair of forceps is then discarded. With the remaining two pairs, one in each hand, the dresser swabs the wound with 1% cetrimide and places the next dressing on the wound The wound now being covered, the patient holds the dressing in place and moves down the bench to dresser no 2, who bandages the hand Meanwhile the server has removed the soiled kidney dish used for the first patient, and produces a new set of instruments as the next patient moves into place opposite dresser no 1 The soiled kidney dish of instruments is placed in the steriliser for use in turn later

It was found that patients with many stitches to be removed caused some delay to the main stream They were therefore diverted to dresser no 1a, who received from the server a standard set of instruments plus scissors, with which he cleaned the wound and removed the stitches, again using a no touch technique The patient then returned to the main stream for a bandage to be applied Often two dressers no 2 were required to do the bandaging so that no delay occurred after the dressing had been applied The server, usually the junior sister, was in charge of the team The dressers were from the general surgical firms, coming in teams of three, each team coming about once in 10 days Once they had learnt this routine, the teams became very quick in dressing, and, subject to the critical eye of the sister, there was a certain amount of competition The "prize" went to a team of three dressers and a nurse who did 45 dressings in 45 minutes This rapidity alone is a great help in preventing air contamination of the exposed wound, but, apart from this, it will be observed that no one handles the patient until the wound is covered, and so there was no need for dresser no 1 to wash his hands between each case When dresser no 2 bandages the patient, the wound is already covered, and so there is little chance of cross infection from this dresser's hands, and again there is no need for dresser no 2 to wash his hands between each case

The rapidity which the early morning dressing queue is disposed of also reacts on the efficient initial treatment of lacerations. The wounds are almost entirely sutured by the student dressers Therefore, as the wounds come in during the day, the students are free to proceed with them with the smallest possible delay On arrival in casualty the wounds are cleaned with 1% cetrimide Originally we used swabs for this, but now we use a soft 'Nylon' pastry brush Commonly we leave the patient to clean the wound and the surrounding skin by himself The arbitrary time of 10 minutes is fixed so that all the grease and dirt which may be present in the factory injuries can be adequately removed The wound is next inspected by the casualty officer, who grades it according to the amount of laceration and/or contamination (see figure) and possibly advises

HAND INJURIES

NAME NUMBER DATE

HOURS NATURE OF INJURY LACERATION 0 1 2 3 4 CRUSH

LOCAL ANÆSTHETIC Yes/No

Treatment

PENICILLIN DATE OUT

STITCHES Nylon GAPING 0 1 2 3 4

Silk PUS PRESENT 0 1 2 3 4

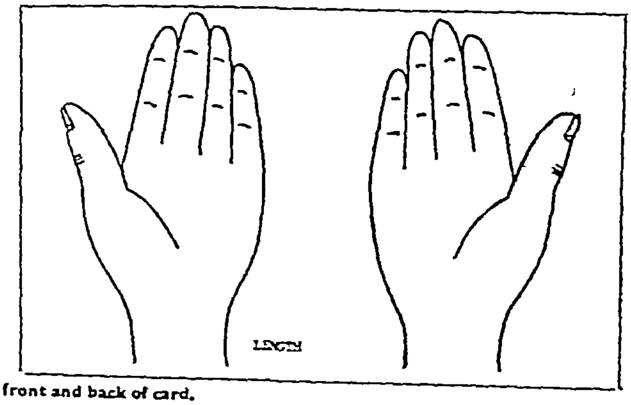
REDNESS 0 1 2 3 4

DATE FULLY HEALED DATE

GAPING 0 1 2 3 4

PUS PRESENT 0 1 2 3 4

REDNESS 0 1 2 3 4



Treatment pro forma, front and back of card.

stomach must be very rare, and the complications of hæmorrhage from one ulcer and perforation of the other is even rarer

It is known that malignant cells may become implanted in a suture line after conservative resection of the rectum, but this patient had not had any previous surgical interference, and so I do not think there is any parallel here, especially since the lower ulcer showed a more extensive infiltration by malignant cells than did the upper one If grafting of malignant cells had taken place, it might be reasonable to suggest that it took place from the lower ulcer to the upper one In the stomach this is theoretically possible if malignant cells can survive after detachment in the gastric juices My feeling in this case is that, with a more advanced stage of malignancy in the lower ulcer, grafting of malignant cells, though possible, is unlikely

This case lends support to Doll's (1950) warning that a gastric ulcer which perforates may not be a simple ulcer, and that if the patient is over 40 years of age he should be kept under observation Some cases of perforated carcinomatous ulcers are fairly easily recognised, but the fact that in 7 of 86 male cases reported by Doll (1950) a carcinoma was present in the stomach within three years after perforation confirms the view that a malignant ulcer may perforate long before it is possible to recognise it as malignant at operation

It was only the combination of perforation and hæmorrhage that decided me to undertake a gastrectomy and so incidentally gave the patient a much greater chance of cure from a deadly disease which otherwise might only have come to light much later when definitely incurable

Two other cases operated on by me have impressed on me the necessity of a careful follow up of cases of perforation One should submit them to early gastrectomy if suture of the perforation is not followed by complete relief from symptoms

Case 2 —A man, aged 66, had a prepyloric ulcer which perforated on April 14, 1949 At operation the ulcer appeared to be non malignant, but the patient returned with a recurrence of symptoms in January, 1950, when radiography suggested a neoplasm A further operation, on Feb 1, 1950, revealed an undoubted carcinoma of the pyloric antrum, and a high gastrectomy was done On March 8, 1951, the patient was in excellent health

In his pathological report Dr Skelton says that he thinks it very probable that the tumour (a poorly differentiated adenocarcinoma, penetrating the stomach wall deeply) has arisen in a pre existent chronic peptic ulcer The highest lymph node from the lesser curvature shows no evidence of tumour invasion

Case 3 —A woman, aged 66, who had a perforated gastric ulcer two and a half years ago, has had persistent symptoms for the last twelve months Laparotomy revealed an inoperable carcinoma of the stomach

CONCLUSIONS

Partial gastrectomy has a definite place in the emergency treatment of gastric ulcers in which both hæmorrhage and perforation have taken place

An apparently simple gastric ulcer which has perforated may be malignant

Early gastrectomy should be done if the patient still has symptoms after a perforated gastric ulcer has been sutured

In any case a careful follow up should be made of such cases

I am indebted to Mr J E Andrews, of the Southern Group Laboratory, Hither Green, for the photomicrographs

REFERENCES

Doll, R (1950) *Brit med J* i 215
Ives L A (1950) *Lancet* i 246

OUTPATIENT TREATMENT OF THE INJURED HAND

MAURICE ELLIS
M B Camb, F R C S, D T M & H
From the Casualty Department, General Infirmary at Leeds

THE efficient treatment of the lacerated hand, so that the patient returns to work at the earliest date with a soundly healed wound, is of increasing importance Probably the biggest factor retarding healing is sepsis. This inquiry was instituted to find out the incidence of sepsis in lacerated hands treated in the busy casualty department of a general hospital Results of such an inquiry would then serve as a yardstick by which the merits of new methods could be measured Towards the end of the inquiry the Medical Research Council (1949) reported on this subject, dealing largely with the bacteriological aspect of infection Our inquiry dealt purely with the clinical aspect, and this account of methods and results is published as complementary to the M R C report

INFECTION AND SEPSIS

In the control of sepsis in wounds a considerable number of factors must be taken into account, but they may be placed in two large groups The first group of factors are those that have to do with the organisms and their entry into the wound The second group are those that have to do with the patient and his ability to prevent these organisms from gaining a foothold—i e, causing an infected wound The bacteriologist almost wholely concerns himself with the first group

The means whereby the infecting organism can reach the wound are

1 The organism can be carried into the wound at the time of wounding either on the wounding agent or from the surrounding skin

2 From the hands, implements, or covering used at the first aid dressing

3 From the air, the pharynx, or the hands of the surgeon in the operating theatre

4 From the implements or dressings used in the operating theatre

5 From sources 3 and 4 at the times of subsequent dressings and removal of stitches

In theory all these factors except the first should be capable of elimination, but theory and practice often differ widely The M R C report shows how infecting organisms can appear in the wound that were not there at the time of wounding Without doubt, if each minor lacerated wound was treated from its origin, and during its subsequent dressings until it was healed, with full major operating theatre ritual, the low incidence of infection from extraneous sources would please even the bacteriologist But practical realities and even sheer economic necessity preclude our using such a ritual for minor cases At the Birmingham Accident Hospital they deal only with accident cases and their problems are not so complicated as most other hospitals. Like the casualty department in all general hospitals, the casualty department in the General Infirmary in Leeds, is the receiving room for all emergency cases, besides accidents we have to deal with septic hands, abscesses of different kinds, and all other ambulant surgical infections The casualty officer has also to examine and dispose of acute surgical and medical admissions There is constant traffic in and out In Leeds, admittedly one of the busiest casualty departments in the country, there are about 34,000 new cases a year and over 80,000 attendances. The number of operations done in the one casualty theatre is over 600 a month In spite of the fact that dressings are done as infrequently as

SUMMARY

The causes of sepsis in lacerated wounds of the hand are discussed; cross infection is suggested as the chief danger to the wound

An "assembly line" method of dressing wounds in a busy casualty department is described.

The incidence of sepsis in 555 cases of lacerated hand sutured in the casualty department of the Leeds General Infirmary is shown to vary with the initial amount of laceration or contamination and with the skill of the student dressers

REFERENCE

Medical Research Council (1949) *Spec Rep Ser med Res Coun Lond.* no. 266

PULMONARY AND PERIPHERAL CIRCULATION TIMES IN HÆMORRHAGIC SHOCK*

S R MUKHERJEE
M.B, M.S Calcutta
RESEARCH ASSISTANT IN EXPERIMENTAL SURGERY, WILKIE SURGICAL RESEARCH LABORATORY, UNIVERSITY OF EDINBURGH

S ROWLANDS
B Sc, Ph.D Lpool, F.Inst.P
SENIOR LECTURER IN MEDICAL PHYSICS IN THE UNIVERSITY

In shock a well recognised feature is slowing of the peripheral circulation, but little is known about the extent of this slowing in the capillaries Accordingly we have measured the time taken by blood to traverse the whole of a peripheral capillary bed

METHOD

The experiments were made on cats The circulation time between two points in a circuit was determined by injecting radioactive red blood-cells at one point and then taking samples of blood at the other point, at known intervals, and examining them for radioactivity The circulation time was taken to lie between the time of appearance of the first sample which showed radioactivity and the time of its immediate precursor which did not The positions of the injection and sampling points are shown in figs 1 and 2 It will be noted that, if these are the femoral artery and the carotid artery, the labelled blood has traversed a peripheral bed and the pulmonary circuit, giving the total circulation time (T C T) If the points are the femoral vein and the carotid artery, only the capillaries of the lung are traversed, giving the lung circulation time (L.C T) These times were measured both in normal and in shocked animals As the results have been consistent, it has been possible to calculate the peripheral circulation time (P C T) as the difference between the T C.T and the L.C T (figs 3 and 4)—i e, T C T—L.C T = P C.T Owing to the low blood pressure on the venous side, it was impossible to measure the P C T directly by taking samples of blood from a vein at short intervals

TABLE I—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL ARTERY TO CAROTID ARTERY WITH BLOOD VOLUME NORMAL

Expt no	Body-weight (kg)	Blood-pressure (mm Hg)	Circulation time (sec)
1	3·0	95	9–11
2	2·5	90	9–10
3	3·0	80	9–10
4	3·4	110	10–11
5	3·0	105	10–11
6	3·4	150	9–11
			(limits 9–11)

EXPERIMENTAL PROCEDURE

Although other substances have been used to measure circulation time, there is no doubt that radioactive substances give the most reliable values. In our experiments red cells have been labelled with the radioactive

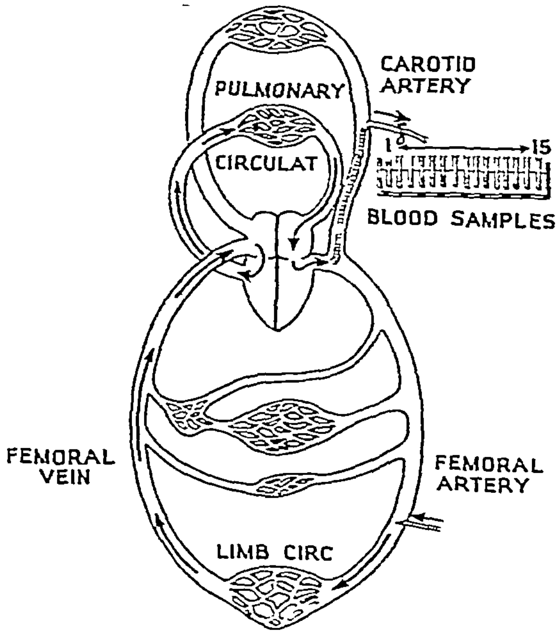


Fig 1—The labelled blood is injected into the femoral artery and traverses the limb (peripheral) capillary bed and the pulmonary capillary bed. The blood samples are collected from the cannula in the carotid artery The cannula is inserted down to the level of the arch of the aorta. (*Based on Best and Taylor 1944.*)

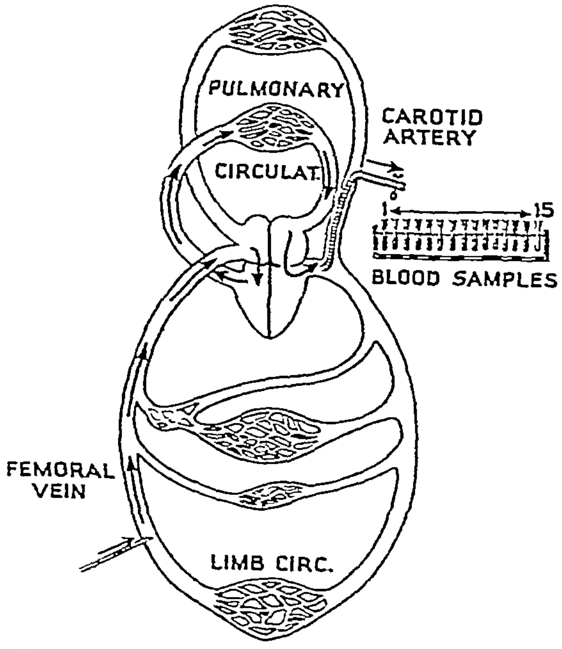


Fig 2—The labelled blood is injected into the femoral vein and traverses only the pulmonary capillary bed before the blood samples are collected.

---

*Paper presented to the Scottish Society for Experimental Medicine in Dundee on Oct 14 1950 the dresser on the placing of the sutures Penicillin procaine injections were given as required The dressing was left in place for 5 days, and then the wound was inspected In most cases the stitches were now removed, the dressing was reapplied, and the patient was told to attend again for a final inspection on the 10th day At the inspection any clinical signs of sepsis were noted, together with any gaping of the wound margins

It should be realised that in these subsequent dressings of lacerated wounds, septic fingers and other abscesses were inspected and dressed in turn with the lacerations This practice is probably common to very many casualty departments As previously explained, with the volume of work in the casualty department of any busy general hospital, from the practical point of view this is to some extent inevitable

The figures presented here represent consecutive cases as they came to the casualty department over about 6 months There has been no selection of cases, except for two fortuitous short gaps of about a week each, which occurred while we were waiting for a fresh supply of the special chart on which the results were recorded Twenty patients who did not come back for inspection after the wound had been sutured have been excluded

The chart, both sides of which are shown in the figure, was devised to make the recording of pertinent facts as easy and simple as possible The term "hours" represents the time interval between the receipt of the injury and treatment The wounds were divided into lacerations and crushed wounds, in the assessment of the results no significant difference was found in the healing of these, and they have therefore all been classified together The lacerations were graded as follows grade 0 was a wound such as might be produced by a surgical incision, grade 1 represented a wound slightly more ragged than this, and the grading then proceeded with increasing laceration and/or contamination up to grade 4, where this was very severe I had four different junior casualty officers working with me during this inquiry, and after a short time our independent grading of the degree of lacerations usually coincided

At the first inspection of the wound, when the stitches were usually taken out, the amount of pus or sepsis present and any gaping of the skin edges were also graded In those wounds in which gaping was noticed a special search for the clinical signs of sepsis was made at the next inspection of the wound Any case showing sepsis at any time was regarded as a septic wound We tried to be as severe in our criticisms as possible

RESULTS

There were 555 cases in the series In 23 (4 1%) of these the wound was classed as septic The analysis of the wound according to the grading reveals some interesting features

Grade	*No of cases*	*No septic*
0	40	0
1	226	4 (*1 8%*)
2	186	10 (*5 4%*)
3	77	3 (*4 0%*)
4	27	6 (*22 2%*)

At first sight these figures show what might be expected With little or no tissue damage (grade 0 and 1) the incidence of sepsis was very small, with greater laceration (grades 2 and 3) about 5% of wounds turned septic, and with severe laceration (grade 4) about 25% did so

As already mentioned, these wounds were sutured almost entirely by student surgical dressers In the middle of the inquiry the surgical appointments finished for one batch of dressers, and the new batch appeared in casualty to take over their work The first batch of dressers were responsible for 324 cases, and the second batch for 231 cases After the inquiry had been proceeding for several weeks, an interim check on the discharged cases was made to find out the approximate incidence of sepsis 199 cases had been discharged, and of these 13 (6 5%) had shown sepsis These results were communicated to the students, and encouraging talks were given to them to improve on this Of the next 125 cases 2 (1 6%) became septic

When a new batch of students came they had little or no experience of sutures and dressings The methods of suturing were demonstrated to them by myself or my junior casualty officers, and the students were encouraged to practise using needles and forceps to sew cloth or other material at home Of the first 50 cases treated by the new batch of students 6 (12%) became septic Further demonstrations of encouragement were given, and as a result only 2 (1 1%) of the next 185 cases became septic

These figures show quite clearly the results achieved after skill and experience had been acquired by the students and after they had been stimulated to attend to the minor points of detail in cleaning and dressing the wounds The number of students in each batch was over thirty, therefore each student would not have attended very many cases, and even with this small experience an adequate level of competence was soon reached

Effects of Penicillin

After the first batch of students had left, the incidence of sepsis in their cases was checked against the use of penicillin In grade 0 cases penicillin was rarely used, but none of these cases became septic Of 143 cases in group 1 78 had been given 600,000 units of procaine penicillin at the time of suture and the remaining 65 had no penicillin There were 2 septic wounds in the penicillin cases and 2 in the non penicillin cases, and all these 4 cases had occurred in the first 199 cases It was therefore felt that, with careful suturing, penicillin was unnecessary, and it was therefore decided not to use penicillin for grades 0 and 1 until a further review had been made In the next 83 cases in grade 1 there were no septic wounds In grade 2 cases 600,000 units of procaine penicillin was given at the time of suture and no more until the wound was inspected for the removal of stitches on the 5th day In grades 3 and 4 it was considered that the full use of penicillin should be made, and we aimed to give 600,000 units of procaine penicillin on alternate days until the wound was soundly healed, the patients did not all attend for these injections That this precaution was necessary is shown in two cases in grade 3 The wound had been inspected on the 5th day, when the stitches were removed The wound was inspected again on the 10th day and considered to be soundly healed Penicillin had been given on days 0, 2, 5, and 8 On the 10th day both patients were discharged On the 13th day, however, they returned with lymphangitis spreading up the arms from the wound, which had not broken down The lymphangitis was rapidly cured with penicillin I suggest that in these cases a secondary streptococcal invader had appeared in the wound, and while penicillin was present this streptococcus had not had a chance to multiply When the effect of the penicillin had worn off, the streptococcus multiplied and produced clinical infection These two cases quite clearly bear out the danger of secondary streptococcal invasion of the wound, which the M R C report showed bacteriologically to be quite common

CONCLUSIONS

The rate of sepsis in lacerated wounds of the hand depends on the degree of laceration and/or contamination at the time of wounding, and the degree of skill used in the initial treatment and subsequent dressings of the wound

If a reasonable degree of skill is used at the initial suturing, the method of dressing by the "assembly line" principle is adequate to keep down the infection-rate of the wounds to less than 2%

SUMMARY

The causes of sepsis in lacerated wounds of the hand are discussed, cross infection is suggested as the chief danger to the wound

An "assembly line" method of dressing wounds in a busy casualty department is described

The incidence of sepsis in 555 cases of lacerated hand sutured in the casualty department of the Leeds General Infirmary is shown to vary with the initial amount of laceration or contamination and with the skill of the student dressers

REFERENCE

Medical Research Council (1949) *Spec Rep Ser med Res. Coun Lond.* no 266

PULMONARY AND PERIPHERAL CIRCULATION TIMES IN HÆMORRHAGIC SHOCK*

S R MUKHERJEE
M.B , M.S Calcutta
RESEARCH ASSISTANT IN EXPERIMENTAL SURGERY,
WILKIE SURGICAL RESEARCH LABORATORY,
UNIVERSITY OF EDINBURGH

S ROWLANDS
B.Sc., Ph.D Lpool, F.Inst.P
SENIOR LECTURER IN MEDICAL PHYSICS IN THE UNIVERSITY

In shock a well recognised feature is slowing of the peripheral circulation, but little is known about the extent of this slowing in the capillaries Accordingly we have measured the time taken by blood to traverse the whole of a peripheral capillary bed

METHOD

The experiments were made on cats The circulation time between two points in a circuit was determined by injecting radioactive red blood-cells at one point and then taking samples of blood at the other point, at known intervals, and examining them for radioactivity The circulation time was taken to lie between the time of appearance of the first sample which showed radioactivity and the time of its immediate precursor which did not The positions of the injection and sampling points are shown in figs. 1 and 2 It will be noted that, if these are the femoral artery and the carotid artery, the labelled blood has traversed a peripheral bed and the pulmonary circuit, giving the total circulation time (T C T) If the points are the femoral vein and the carotid artery, only the capillaries of the lung are traversed, giving the lung circulation time (L C T) These times were measured both in normal and in shocked animals. As the results have been consistent, it has been possible to calculate the peripheral circulation time (P C T) as the difference between the T C T and the L C T (figs 3 and 4)—i e, T C T—L C T = P C.T Owing to the low blood-pressure on the venous side, it was impossible to measure the P C T directly by taking samples of blood from a vein at short intervals.

TABLE I—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL ARTERY TO CAROTID ARTERY WITH BLOOD VOLUME NORMAL

Expt no	Body-weight (kg)	Blood pressure (mm Hg)	Circulation time (sec.)
1	3.0	95	9–11
2	2.5	90	9–10
3	3.0	80	9–10
4	3.4	110	10–11
5	3.0	105	10–11
6	3.4	150	9–11
			(limits 9–11)

EXPERIMENTAL PROCEDURE

Although other substances have been used to measure circulation time, there is no doubt that radioactive substances give the most reliable values In our experiments red cells have been labelled with the radioactive

---

*Paper presented to the Scottish Society for Experimental Medicine in Dundee on Oct 14 1950

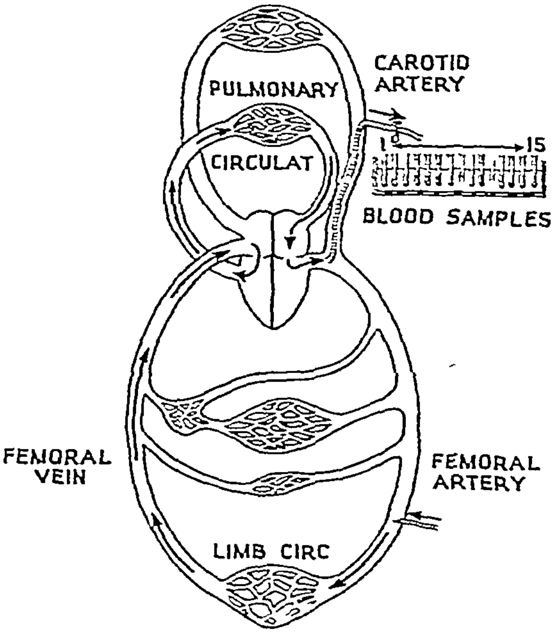


Fig. 1—The labelled blood is injected into the femoral artery and traverses the limb (peripheral) capillary bed and the pulmonary capillary bed. The blood samples are collected from the cannula in the carotid artery The cannula is inserted down to the level of the arch of the aorta. (Based on Best and Taylor 1944.)

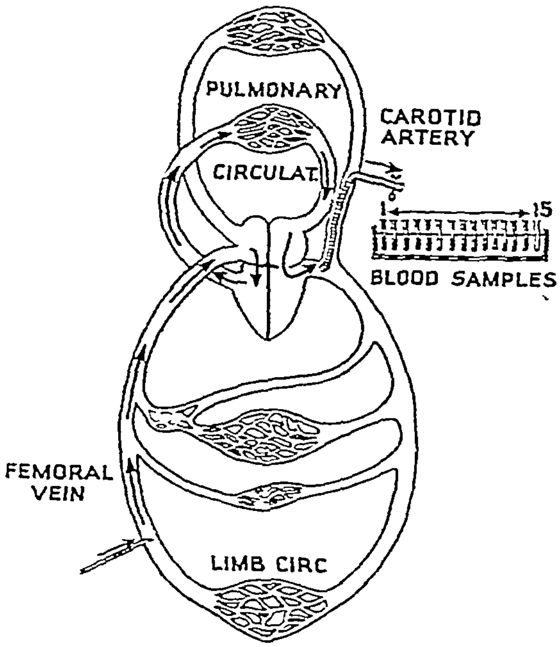


Fig 2—The labelled blood is injected into the femoral vein and traverses only the pulmonary capillary bed before the blood samples are collected.

TABLE II—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL VEIN TO CAROTID ARTERY WITH BLOOD VOLUME NORMAL

Expt no	Body weight (kg)	Blood pressure (mm Hg)	Circulation time (sec)
1	3 0	110	3–4
2	2 5	100	3–4
3	3 0	120	4–5
4	3 5	110	3–5
			(limits 3–5)

isotope P³² by the method described by Hevesy and Zerahn (1942), which has the advantage that the test substance is whole blood and not some substance foreign to the circulation In addition, the radioactive substance is firmly attached to the red cells, and the quantity lost to the plasma or tissue fluids in the course of an experiment is negligible

The animal is anæsthetised with 'Nembutal' and laid on its back Blood pressure is recorded from the right femoral artery Immediately before an injection is made, the speed of the drum is increased to record in seconds The labelled red cells in whole blood are injected into the left femoral vein or the left femoral artery at a time recorded on the drum with a mechanical time marker For 2 minutes samples are taken at intervals of 1–2 seconds from the left carotid artery into small tubes, the time of each sampling being recorded

To assay the samples, 0 1 ml of blood is withdrawn from each tube and dried in a thin uniform layer on a standard nickel counting planchet The activity of each sample is then estimated with a Geiger Müller counter

It was found unnecessary to make any correction for the fraction of a second taken by the blood to pass through the cannula in the carotid artery

RESULTS

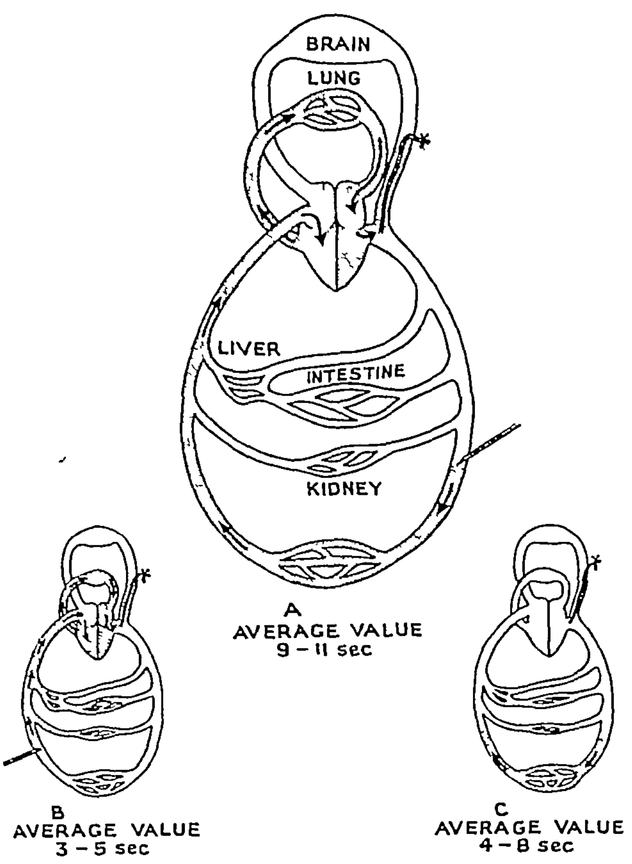
In the first series the blood volume was normal and the circulation time was measured in six cases from the femoral artery to the carotid artery (table I) and in four cases from the femoral vein to the carotid artery (table II)

TABLE III—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL ARTERY TO CAROTID ARTERY WITH BLOOD VOLUME REDUCED

Expt no	Body weight (kg)	Initial blood pressure (mm Hg)	Amount of blood lost (ml per kg)	Final blood pressure (mm Hg)	Duration of hypo tension (min)	Circulation time (sec.)
1	3 0	130	25 0	55	45	22–25
2	5 0	140	22 0	55	45	32–34
3	2 4	100	14 0	65	90	19–31
4	3 2	110	13 5	60	45	23–25
5	4 0	120	20 0	60	120	32–34
6	3 0	130	20 0	40	45	53–55
7	2 2	95	18 0	50	120	36–38
8	3 0	130	27 0	60	60	46–48
9	3 5	140	22 5	80	120	26–29
10	4 2	100	28 0	45	180	55–58
						(limits 19–58)

In the second series shock was produced in twenty cases by graded and controlled hæmorrhage In ten cases circulation time was measured from the femoral artery to the carotid artery (table III), and in ten cases from the femoral vein to the carotid artery (table IV)

Tables I and II show that the T C T lies between 9 and 11 seconds and the L C T between 3 and 5 seconds

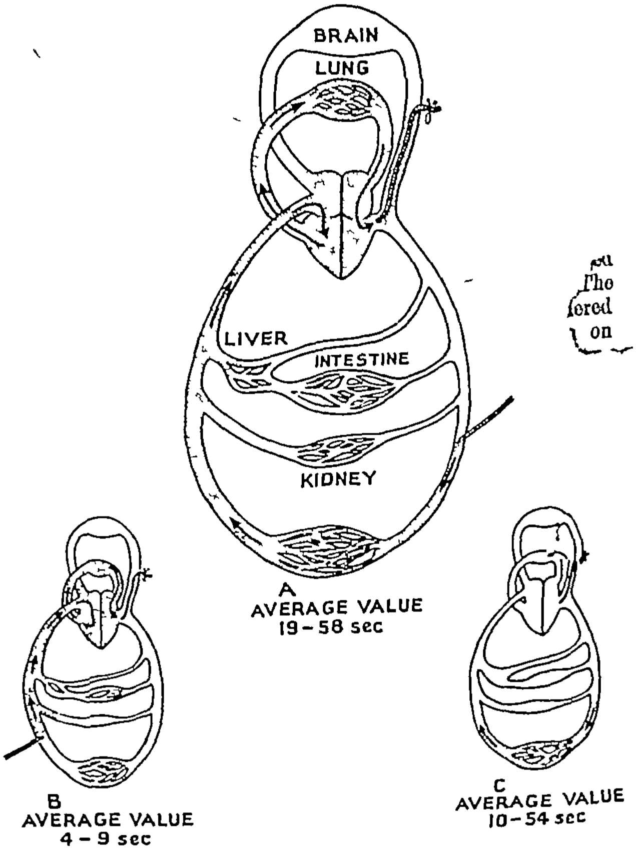


A
AVERAGE VALUE
9 – 11 sec

B
AVERAGE VALUE
3 – 5 sec

C
AVERAGE VALUE
4 – 8 sec

Fig 3—Limits of normal circulation time : A, from femoral artery to carotid artery (see fig 1); B from femoral vein to carotid artery see fig 2) C, peripheral



A
AVERAGE VALUE
19 – 58 sec

B
AVERAGE VALUE
4 – 9 sec

C
AVERAGE VALUE
10 – 54 sec

Fig 4—Limits of circulation time in hæmorrhagic shock : A from femoral artery to carotid artery ; B from femoral vein to carotid artery ; C, peripheral

TABLE IV—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL VEIN TO CAROTID ARTERY WITH BLOOD VOLUME REDUCED

Expt. no	Body weight (kg)	Initial blood pressure (mm.Hg)	Amount of blood lost (ml per kg)	Final blood pressure (mm.Hg)	Duration of hypotension (min)	Circulation time (sec.)
1	2 6	95	30	60	45	4–5
2	2 8	120	21	40	60	4–5
3	3 2	125	21	60	60	4–5
4	3 0	120	20	70	50	4–5
5	3 0	115	25	50	90	5–6
6	3 5	120	25	45	120	7–8
7	2 4	150	36	45	60	7–8
8	3 2	85	17	45	90	6–7
9	3 4	140	27	70	150	8–9
10	4 3	150	36	50	120	8–9 (limits 4–9)

P C T lies therefore between 4 and 8 seconds (fig 3) The data obtained are not yet sufficient for statistical analysis, but these limits serve the present argument well enough

The figures in tables III and IV suggest that the circulation time is definitely increased in hæmorrhagic shock, the L C T has limits of 4–9 seconds but the T C T varies between 19 and 58 seconds These results are plotted in fig 5, which shows that the T C T tends to increase with falling blood pressure, whereas the L C T is little changed Thus it is possible to set a range for the peripheral circulation times after hæmorrhage by subtracting from the limits of the total circulation time the limits for the lung circulation time In this way the P C T after hæmorrhage is seen to lie in the range 10–54 seconds (fig 4) When more data have been collected, it may be possible to express circulation time quantitatively in terms of blood lost per kg of body-weight Even with the present data, if the figures for the oligæmic animals are compared with the figures for those with a normal blood volume, a striking difference is apparent between the pulmonary and peripheral circuits (table V)

TABLE V—PULMONARY AND PERIPHERAL CIRCULATION TIMES WITH NORMAL AND REDUCED BLOOD VOLUMES

Group of animals	Pulmonary circulation time limits (sec.)	Peripheral circulation time limits (sec)
Normal animals	3–5	4–8
Animals in hæmorrhagic hypotension	4–9	10–54

reas in shocked animals the lung circulation time is er doubled, the peripheral circulation time may increase more than six times, a discrepancy which seems to have escaped notice In previous measurements of circulation time, the test substance injected intravenously has been detected in the lung, in the carotid sinus, or in the peripheral vessels before it has traversed the whole of the peripheral capillary bed. Such methods cannot detect the greatly increased peripheral circulation time in hypotension The relatively small effect on lung circulation time of hæmorrhagic hypotension is confirmed by the results of Wang et al. (1947) Using sodium cyanide as the test substance, they measured lung circulation time in dogs in hæmorrhagic hypotension, and observed only a slightly increased time after a hæmorrhage severe enough to be fatal. It is clear that in hæmorrhagic shock the lung circulation is not subject to the same changes as is the peripheral circulation

The relationship between circulation time and percentage reduction in blood pressure is shown in fig 5, which distinguishes between points relating to long and short periods of hypotension It will be noted that in four out of five cases of hæmorrhagic hypotension of short duration the lung circulation times lie within normal limits With prolonged hypotension they show an increase which is small compared with the increase in peripheral circulation time Further experiments will be necessary before it is certain that the duration or severity of hæmorrhagic shock has a significant effect on lung circulation time

When the other points on the graph are examined, it is evident that there is a correlation between percentage fall in blood-pressure and peripheral circulation time, and that the peripheral circulation time increases with the duration of hypotension, because the points relating to prolonged hypotension lie above those relating to short hypotension Further experiments have been planned to investigate the relationships between degree and duration of hæmorrhagic hypotension and peripheral circulation time

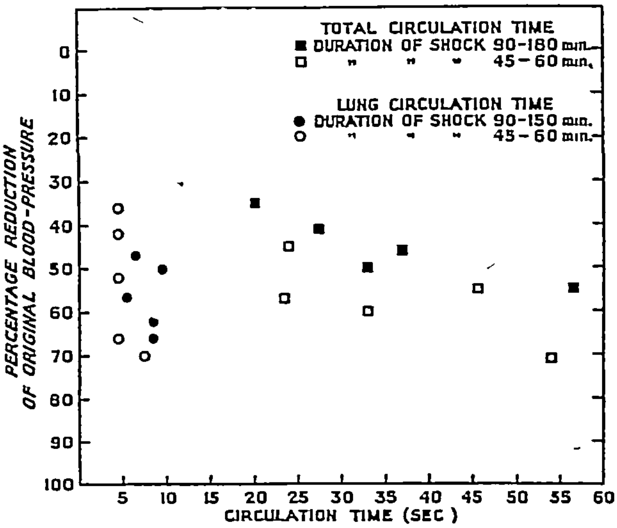


Fig 5—Effect of hæmorrhagic hypotension of long or short duration on lung circulation times (circles) and on peripheral circulation time (squares)

SUMMARY

The blood circulation times have been measured in cats by using red blood cells labelled with a radioactive isotope

In hæmorrhagic hypotension the peripheral circulation time increases considerably with fall in blood-pressure, whereas the increase in the lung circulation time is relatively small.

Peripheral circulation time is increased by prolonging the state of hypotension

One of us (S R M.) was assisted by a Government of India scholarship

REFERENCES

Best C H Taylor N B (1944) The Living Body London plate III
Hevesy G Zerahn K. (1942) *Acta physiol scand* 4 376
Wang S C Painter E E Overman R R (1947) *Amer J Physiol.* 148 69

The medical planners express deep concern that the general practitioner should be tempted to tackle work outside his competence,' a loose phrase typical of many in common use today In this connection it can at once be pointed out that errors of judgment and technique cling to a general practitioner, who lives amongst his patients far more tenaciously than to a consultant protected as he is by his status and grading the fear of bad results makes it extremely unattractive for the general practitioner to attempt things outside and, often enough well within his competence I wonder if the specialist is not more likely to attempt things outside his competence than the general practitioner is to attempt things outside his '—C J L WELLS, *Postgrad med J* 1951 27, 237

TABLE II—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL VEIN TO CAROTID ARTERY WITH BLOOD VOLUME NORMAL

Expt no	Body weight (kg)	Blood pressure (mm Hg)	Circulation time (sec)
1	3 0	110	3–4
2	2 5	100	3–4
3	3 0	120	4–5
4	3 5	110	3–5 (limits 3–5)

isotope P^{32} by the method described by Hevesy and Zerahn (1942), which has the advantage that the test substance is whole blood and not some substance foreign to the circulation In addition, the radioactive substance is firmly attached to the red cells, and the quantity lost to the plasma or tissue fluids in the course of an experiment is negligible

The animal is anæsthetised with 'Nembutal' and laid on its back Blood pressure is recorded from the right femoral artery Immediately before an injection is made, the speed of the drum is increased to record in seconds The labelled red cells in whole blood are injected into the left femoral vein or the left femoral artery at a time recorded on the drum with a mechanical time marker For 2 minutes samples are taken at intervals of 1–2 seconds from the left carotid artery into small tubes, the time of each sampling being recorded

To assay the samples, 0 1 ml of blood is withdrawn from each tube and dried in a thin uniform layer on a standard nickel counting planchet The activity of each sample is then estimated with a Geiger Müller counter

It was found unnecessary to make any correction for the fraction of a second taken by the blood to pass through the cannula in the carotid artery

RESULTS

In the first series the blood volume was normal and the circulation time was measured in six cases from the femoral artery to the carotid artery (table I) and in four cases from the femoral vein to the carotid artery (table II)

TABLE III—TIME TAKEN FOR RADIOACTIVE RED CELLS TO CIRCULATE FROM FEMORAL ARTERY TO CAROTID ARTERY WITH BLOOD VOLUME REDUCED

Expt no	Body weight (kg)	Initial blood-pressure (mm Hg)	Amount of blood lost (ml per kg)	Final blood pressure (mm Hg)	Duration of hypo tension (min)	Circulation time (sec.)
1	3 0	130	25 0	55	45	22–25
2	5 0	140	22 0	55	45	32–34
3	2 4	100	14 0	65	90	19–31
4	3 2	110	13 5	60	45	23–25
5	4 0	120	20 0	60	120	32–34
6	3 0	130	20 0	40	45	53–55
7	2 2	95	18 0	50	120	36–38
8	3 0	130	27 0	60	60	45–46
9	3 5	140	22 5	80	120	26–29
10	4 2	100	28 0	45	180	55–58 (limits 19–58)

In the second series shock was produced in twenty cases by graded and controlled hæmorrhage In ten cases circulation time was measured from the femoral artery to the carotid artery (table III), and in ten cases from the femoral vein to the carotid artery (table IV)

Tables I and II show that the T C T lies between 9 and 11 seconds and the L C T between 3 and 5 seconds

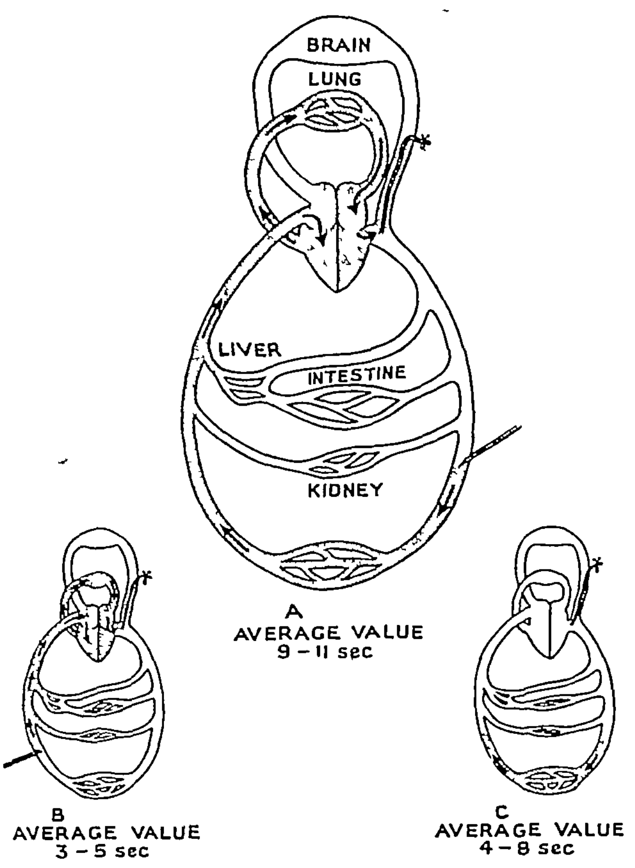


Fig. 3—Limits of normal circulation time: A from femoral artery to carotid artery (see fig 1); B from femoral vein to carotid artery see fig 2) C peripheral

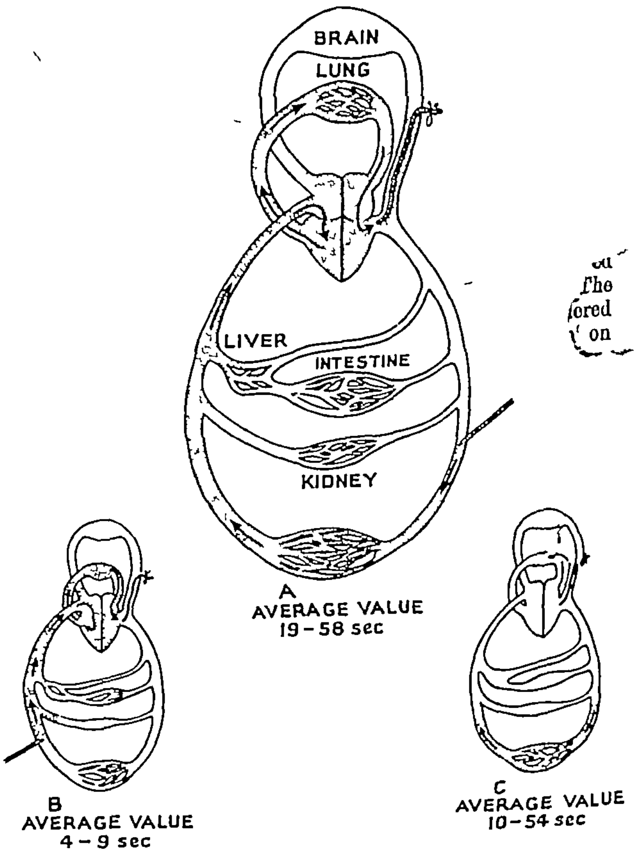


Fig 4—Limits of circulation time in hæmorrhagic shock: A, from femoral artery to carotid artery; B from femoral vein to carotid artery C peripheral

in the tube and saturated with carbon monoxide or coal gas Water is added to the 100% mark and gently shaken. The ratio of the photo-electric readings (test standard) is multiplied by 100 and by the N.P.L factor to give the concentration of hæmoglobin in percentage of Haldane normal, or by 14 8 x the factor to give g. of Hb per 100 ml of blood.

INSTRUMENTS

Visual Photometer—This was the Medical Research Council grey wedge photometer described by King (1947) and King et al. (1948c) It was made by Keeler Optical Products and fitted with an Ilford 625 bright spectrum yellow-green filter

Spectrophotometer—This was a Beckman DW instrument with which 1 cm. cells were used. Measurements were made at 540 mμ, and the density scale was checked with a calibrated grey screen

Photo-electric Photometers—A Spekker absorptiometer manufactured by Hilger & Watts was equipped with 1 cm. cells and Ilford 625 filters. The same filter was also used in a single-cell test-tube colorimeter made by EEL Measurements were made with the normal cuvette (equivalent light-path about 1 3 cm.) on all solutions except carboxyhæmoglobin The last-named was used as described above

Conversion Factors—The experimental results were converted into hæmoglobin content (g per 100 ml.) by the following means

(1) the Hüfner factors were used for the iron and gas analyses—i.e Hb contains 0·334% Fe 1 g Hb ≡ 1 34 ml. O_2 or CO

(2) the readings at 540 mμ on the Beckman instrument were divided by the specific extinctions given by Donaldson et al. (1951) and the calculated extinction coefficients given in that paper (for coloured solutions from 100% bloods, as measured through the 625 filter) were used to convert the Spekker values to g of Hb per 100 ml.,

(3) the M.R C photometer and the carboxyhæmoglobin method with Haldane tubes provided results on the Haldane scale (the equivalent 100% ≡ 14 8 g of Hb per 100 ml. was used), and

(4) the EEL photo-electric instrument with the normal size cuvette had previously been calibrated with a series of normal blood samples of known iron content

RESULTS

The results are given in the accompanying table In each group the mean value of the hæmoglobin content found by each method has been calculated. The figures in parentheses are the coefficients of variation of each result from the iron analysis of the corresponding blood sample

DISCUSSION

The base-line results (iron and gas capacity) show a pattern already familiar from the earlier papers in this series dealing with normal blood samples. Iron analysis and total hæmoglobin measured by CO capacity after reduction are in good agreement The oxygen capacity is about 3–5% lower, presumably because it does not measure inactive hæmoglobin (and methæmoglobin if present) In the present samples these inactive pigments seem to be present in normal amounts

In the colorimetric methods there is also good agreement between the average hæmoglobin values and the iron results Many of the coefficients of variation are higher than those found using similar methods on normal blood samples. However, the average hæmoglobin concentrations of this present series are much lower than those found previously The coefficient of variation is calculated by expressing the standard deviation as a percentage of the mean hence the diminished mean values have correspondingly increased the coefficient of variation

The calculation of the results has involved the use of factors extinction coefficients, &c, which had been determined in experiments with normal blood. It is apparent that these coefficients are appropriate to the pathological blood samples studied here The earlier papers in this series presented conclusions drawn from hæmoglobin methods applied to samples of blood from healthy laboratory personnel and other normal people These conclusions seem applicable also to the estimation of hæmoglobin in pathological blood samples.

SUMMARY

The hæmoglobin content of 56 blood samples has been estimated. Most of the blood samples were drawn from patients with diseases affecting the blood.

Agreement was good between the results obtained by accurate analytical methods and the results obtained by colorimetry

The extinction coefficients, &c, calculated on normal blood can be used in work on samples of pathological blood.

The average hæmoglobin values, as determined with instruments calibrated purely from an optical-density basis, are in as good agreement with the value derived from iron as are the results from an instrument calibrated by means of material standards

This investigation has been made for the Medical Research Council s subcommittee on analytical methods The expenses were partially defrayed by a grant from the Medical Research Council, to whom grateful acknowledgment is made Our thanks are due to Sir Charles Harington, chairman of the subcommittee, for much valuable advice.

REFERENCES

Donaldson R. Sisson R B King E. J Wootton, I D P Macfarlane R. G (1951) *Lancet* i 874
King E J (1942) *Ibid.* i, 511
— (1947) *Biochem. J* 41 xxxii
— (1951) Micro-analysis in Medical Biochemistry 2nd ed. London.
— Gilchrist M. Wootton, I. D P., O'Brien J R P., Jope H. M. Quelch, P E., Peterson, J M. Strangeways, D H., Ramsay W N M. (1948a) *Lancet* i 478.
— — — Donaldson, R. Sisson, R B Macfarlane, R. G Jope. H. M., O'Brien J R P Peterson J M., Strangeways, D H. (1948b) *Ibid* ii, 563
— Wootton, I. D P., Donaldson R Sisson R. B, Macfarlane, R G (1948c) *Ibid* p 971
Macfarlane, R. G., King E J Wootton, I D P Gilchrist, M. (1948) *Ibid* i 282
Trevan J W (1925) *Biochem. J* 19 1111
Van Slyke, D D, Neill J M. (1924) *J biol. Chem.* 61, 523.
— Weisiger J R. Van Slyke K. K. (1949) *Ibid.* 179 743
Wootton I. D P King E. J (1949) *Biochem J* 44 xli

CORONARY OCCLUSION IN YOUNG ADULTS

REVIEW OF A HUNDRED CASES IN THE SERVICES

MAURICE NEWMAN
M.D Lpool M.R C P
PRINCIPAL MEDICAL OFFICER, MINISTRY OF PENSIONS

In a previous paper (Newman 1946) I collected and analysed the Service records of 50 cases of coronary occlusion in Service personnel aged up to 35 The analysis showed that severe degenerative changes can exist in the coronary arteries at an early age, and that coronary disease is not so rare in the young as was formerly thought

I report here a further 50 similar cases in men and women since discharged or released from the Services, and review the whole series of 100 cases As before, only those cases have been selected where the diagnosis was beyond doubt—i.e., either proved by necropsy or where the electrocardiogram supported the clinical diagnosis All doubtful cases have been excluded. Of the 50 cases in the present series the diagnosis was established clinically in 9 and at necropsy in 41

AGE INCIDENCE

The youngest patient in this series was aged 21, and 11 of the 50 patients were in their twenties As in the previous series the frequency of coronary occlusion

DETERMINATION OF HÆMOGLOBIN

VIII ACCURACY OF METHODS APPLIED TO ABNORMAL BLOODS

E J King R J Bartholomew M Geiser
S Ventura I D P Wootton
Postgraduate Medical School of London
R G Macfarlane
Radcliffe Infirmary, Oxford
R Donaldson R B Sisson
National Physical Laboratory, Teddington

THE determination of hæmoglobin has been studied, and described in previous papers of this series, with clinical instruments (Macfarlane et al. 1948), by iron analyses, oxygen and carbon monoxide capacities (King et al 1948a), by several colorimetric and photometric procedures (King et al 1948b), and with a simple grey-wedge instrument, the M R C photometer (King et al 1948c), and the photometric measurement of the various coloured derivatives of hæmoglobin by visual and photo electric means was critically reviewed by Donaldson et al. (1951)

The net conclusion of these investigations has been that it is possible to determine hæmoglobin with a high degree of accuracy by analysis of blood for a constituent of the hæmoglobin molecule (i e , iron) , by measurement of a chemical reaction in which hæmoglobin takes part (i e , carbon monoxide combining capacity after reduction, but not so accurately by oxygen capacity) , and by accurate photometry of the concentration of coloured derivatives of hæmoglobin—oxyhæmoglobin, carboxyhæmoglobin, cyanmethæmoglobin, acid and alkaline hæmatin, and cyanhæmatin—provided that the chemical reaction takes place under suitable conditions and is given sufficient time to go to completion (e g , with acid hæmatin) All the coloured derivatives studied yielded satisfactory results when their light absorptions were accurately assessed, but it was concluded that, for simplicity of preparation and closeness of agreement with base line measurements of iron and carbon monoxide capacities, the oxyhæmoglobin and the cyanhæmatin procedures were to be favoured, the former for visual assessment and the latter for photo electric

All these previous studies have been concerned with the investigation of samples of blood procured from normal healthy people It has remained to test the methods, and the conclusions reached, on blood samples taken from persons with the more important diseases in which the blood pigment may be abnormal The present paper describes this work

METHODS

Blood Samples —25 ml specimens were taken from an antecubital vein and transferred to bottles containing the residue from four drops of 30% potassium oxalate In most cases the analyses were made on the same day Iron titrations and, occasionally, other manipulations were completed next day The samples were all obtained from patients in Hammersmith Hospital They have been placed in five groups (see table) Group A were normal bloods—i e , from patients with conditions not affecting the blood—and B and C were from patients with various forms of anæmia The specimens in group D were from jaundiced patients, and group E contained miscellaneous conditions, including six cases of methæmoglobinæmia

Iron analyses were made by titanous chloride titrations of ashed samples with the all glass microburette modified by Wootton and King (1948) from Trevan (1925) The method is described in full by King et al (1948a) and King (1951)

Gasometric Estimations —With the manometric Van Slyke apparatus, oxygen capacity was estimated by the method of Van Slyke and Neill (1924) The carbon monoxide method after reduction with hydrosulphite was done by the recent modification described by Van Slyke et al (1949)

Hæmoglobin Derivatives —The methods for making the coloured solutions have been described by Macfarlane et al (1948) Two modifications must be given in detail

Cyanhæmatin —For making the cyanhæmatin solutions 0 5 ml of blood was added to 49 ml of water in a 100 ml volumetric flask, followed by 0 5 ml of 10 *N*HCl The mixture was allowed to stand for 10 min Sodium phosphate solution (40 ml of 10% Na_3PO_4 $12H_2O$) was added to buffer the solution at an alkaline pH, and then 10 ml of 10% NaCN and water to the mark.

Carboxyhæmoglobin —The Haldane method was used with photo electric colorimeters (EEL, Gallenkamp, Hilger) fitted with micro adapters for the Haldane tubes The Haldane standard, and tube marked only at the 2 ml mark (i e , 100%) (Messrs Hawksley & Son) were given a factor, which takes into account the capacity and the diameter of the tube, for conversion to true hæmoglobin percentages of the readings of test and standard (National Physical Laboratory) Blood (0·02 ml) is washed into about 1 ml of ammonia water 0 4%

COMPARISON OF HÆMOGLOBIN METHODS, WITH COEFFICIENTS OF VARIATION FROM IRON ANALYSES AVERAGES FOR GROUPS OF HOSPITAL PATIENTS , RESULTS IN G OF HÆMOGLOBIN PER 100 ML OF BLOOD, WITH COEFFICIENTS OF VARIATION AS PERCENTAGES IN PARENTHESES

Group diagnosis and no of cases	Methods and results								
	Iron analysis	CO capacity	O_2 capacity	Colorimetric methods					
				Instrument	HbO_2	HbCO	Acid hæmatin	Alkaline hæmatin	Cyan hæmatin
A Normal (12)	14 6		14 2 (3 0 %)	M.R C photometer	14 7 (1 8 %)				
				Spekker	14 6 (2 3 %)	14 6 (2 8 %)		14 6 (1 7 %)	14 5 (2 1 %)
				Beckman	14 6 (1 4 %)	14 3 (3 0 %)		14 6 (2 9 %)	14 6 (2 3 %)
B Anæmia (10)	9 8		9 2 (6 3 %)	M R C photometer	10 3 (4 8 %)				
				Spekker	9 7 (2 9 %)	9 6 (5 1 %)		9 7 (4 8 %)	9 7 (3 3 %)
				Beckman	9 6 (1 9 %)	9 7 (2 6 %)		9 8 (2 0 %)	9 8 (3 5 %)
C Anæmia (11)	10 9	10 6 (5 0 %)	10 4 (5 6 %)	M.R C photometer	10 8 (3 9 %)				
				Spekker	10 8 (5 0 %)	10 7 (5 1 %)	10 7 (4 2 %)	10 8 (3 3 %)	10 7 (5 1 %)
				EEL	10 8 (4 1 %)	11 0 (4 3 %)	10 8 (3 5 %)	10 8 (3 5 %)	10 6 (5 4 %)
D Jaundice (10)	13 6		13 2 (3 9 %)	M.R C photometer	13 9 (3 2 %)				
				Spekker	13 6 (1 4 %)	13 6 (2 8 %)		13 6 (2 0 %)	13 6 (2 4 %)
				Beckman*	13 6 (1 9 %)	13 6 (1 9 %)		13 6 (1 3 %)	13 6 (1 8 %)
E Miscellaneous (13)	12 9	12 8 (2 0 %)	12 3 (5 0 %)	M.R C photometer	13 0 (2 7 %)				
				Spekker†	12 8 (2 7 %)	12 8 (3 2 %)	12 8 (3 6 %)	13 0 (3 4 %)	12 8 (4 0 %)
				EEL ‡	12 8 (2 3 %)	13 1§ (3 2 %)	12 9 (2 8 %)	13 0 (3 5 %)	12 9 (2 4 %)

* Spectrophotometer † Photo electric absorptiometer 2-cell balanced circuit. ‡ Photo-electric colorimeter simple single-cell instrument of type described by King (1942) § Micro adapter and Haldane standard.

with lesions of the conducting bundles. There was no evidence of rheumatic disease. The coronary arteries showed very advanced atheroma, which (the pathologist said) "at his age can only be described as precocious in the extreme." There was also shortening or deficiency in the cusps of the valves, not inflammatory.

The association of congenital morbus cordis with advanced atheroma of the coronary arteries in this case implies a congenital weakness of the coronary arterial system, and supports the contention that genetic influences play a more important part than extraneous factors in coronary disease in young adults.

All the 9 patients in the second series who have survived the initial attack of coronary occlusion are still alive 3–6 years after the occlusion. They are all working in similar occupations to their pre-Service ones, but symptoms such as shortness of breath on effort, pain, and tightness in the chest on exertion are complained of by all.

NECROPSY FINDINGS

The necropsy findings in the present series of 41 deaths were similar to those in the previously published cases. The left coronary arteries were much more frequently affected than the right—13 left and 3 right. Both coronary arteries were affected in 20 cases. In the remaining it was not stated which coronary arteries were affected. In 18 of the 41 cases the heart was enlarged, and in 1 patient, aged 32, the heart was very large, owing to aneurysmal dilatation of the left ventricular wall. The heart muscle was very thin and there was much fibrous tissue. Both coronary arteries showed considerable atheroma, and the first half-inch of the descending branch of the left coronary artery was completely occluded by atheroma. This man had died suddenly, four months after release while working as a stone finisher. He had to lift heavy weights. A thrombus was found in only 12 cases. In 8 cases myocardial infarction was found either recent or old standing.

In the total series of 80 deaths, the left coronary artery was affected in 30 cases, the right in 8 cases, and both were involved in 36 cases. The heart was enlarged in 38 cases—i.e., in about half. Myocardial infarction, either recent or old, was found in 25 cases. A thrombus was found in only 22 of the 80 cases. The degenerative changes found in the coronary vessels were similar to those found in the older age groups, the arteries being thickened, tortuous, and calcified. Occlusion took place in the non-thrombus cases as the result of the gross atheroma or of an atheromatous plaque blocking the lumen. Atheroma of the aorta was also present in most cases.

These findings do not support Leary's (1941) view that in the younger age group the pathological changes differ from those in the older age group (over 45), thrombosis being more common, and calcification not occurring, in the younger group.

DISCUSSION

This further series of 50 cases of coronary occlusion in young people confirms my previous view that advanced degenerative changes in the coronary arteries may exist at an early age, and that coronary occlusion is not so rare as was formerly thought. It is remarkable that, in spite of the advanced degenerative changes present in their coronary arteries, these patients appear to be in excellent health and can serve as grade I men for several years, many overseas in combatant units, without any symptoms or signs of cardiac inadequacy until occlusion takes place. Full clinical examination, even a few hours before the occlusion, as happened in 2 cases, revealed no indication of the underlying degenerative arterial disease with its impending crisis. In only 1 case was the coronary occlusion preceded by angina pectoris which in view of the youth of the patient and normal radiogram and electrocardiogram was not diagnosed as true angina but as an irritable heart with no organic lesion.

Coronary disease in young people seems to be predominantly confined to males, only 1 female occurring in the 100 cases. Body-build is an interesting factor because most of the patients were above the average weight for age and height, and such terms as "powerfully built," "well developed," and "muscular" were often used in the necropsy reports.

The second 50 cases do not confirm that infection is an important ætiological factor in coronary disease in young adults, for there was no such history in any. No cases of syphilis occurred in this series, although 2 cases occurred in the previous published series, which confirms that syphilis is a very infrequent cause of coronary disease, as in the older age groups. Hypertension is recorded in 5 out of the 9 surviving cases of the second series. In the previous series it was noted in 3 cases. In view of the fact that in most of the fatal cases the patients had had no illness necessitating investigations during life, the blood pressure was only occasionally recorded in these cases, as on routine examination, and so it is impossible to give the true incidence of hypertension, or discuss its influence as a factor in the ætiology of coronary disease in the young.

Most of these cases of coronary disease in the young fall in the Registrar-General's social classes IV or V, and there seems to be little evidence of any relationship to heavy responsibilities or mental stress. Ryle and Russell (1949), on the other hand, in a study of the epidemiology of coronary disease in the older age groups, found that the incidence of coronary disease was much greater in the business and professional classes, and suggested this was related to mental rather than physical stress. In discussing my first 50 cases these workers state: "Where extraneous factors in early life are far to seek it may possibly be shown that genetic influences play a more important part than habits of life and work."

The high mortality, 80%, is a striking feature in coronary disease in the young. So is the rapid onset of death: sudden death occurred in 74 out of the 80 fatal cases.

The necropsy findings are similar to those found in the older age groups, the coronary arteries showing all stages of atheroma, including calcification and occlusion by atheromatous plaques, with or without thrombus formation, and indicating that, in spite of the youth of the victims, the pathological process has been present for years.

These pathological findings at such an early age, the predominance in males, the body build, and the lack of relationship to mental stress or other extraneous factors support the view that genetic influences are the most important factors in the ætiology of coronary disease in young people.

SUMMARY

100 cases of coronary occlusion in young adults in the Services or following release therefrom are reviewed.

All the patients but one were males, and of good physical development and previous good health.

Infection rarely seems to be an ætiological factor. ✓

The great majority of cases fall in the Registrar-General's social classes IV or V, and there is little evidence of any relationship to heavy responsibilities or mental stress. Physical stress occurred in less than half the cases.

The mortality was 80%, with sudden death in 74 of the 80 fatal cases.

At necropsy the atheromatous changes in the coronary arteries were similar to those usually described in the older age groups. A thrombus was found in only 22 of the 80 fatal cases.

TABLE I—AGE INCIDENCE

Age (yr)	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
No of cases	1	3	4	3	3	3	1	4	9	2	9	8	10	11	12	17
No in 4 yr groups	11				11				28				50			
No in 8 yr groups	22								78							

increased with age, as in the older age groups The age incidence of the combined series is shown in table I It will be noted that half the cases occurred in persons aged less than 32, and that 33 cases were in persons aged less than 30, the youngest being aged 20

SEX-INCIDENCE

In the first 50 cases there was only 1 female, and in the present series there were no females, hence the incidence of female cases was only 1 in 100 Even allowing for the greater number of males to females in the Services —10–15 males to 1 female—there seems no doubt that coronary disease in the young is very rare in females

BODY BUILD

In the earlier report I remarked on the good physical development and nourishment of these young adults, 43 of the patients weighing more than 126 lb on entry into service, and many more than 150 lb In the second 50 only 8 weighed less than 126 lb on entry into service, 28 weighed more than 140 lb, and 16 more than 150 lb The highest weight was 202 lb on entry which increased to 240 lb at the time of the occlusion Physical fitness was again shown by the fact that 46 of the second 50 were graded A1 or fit on entry, and of the 4 exceptions 3 were downgraded for minor defects (flat foot and poor vision), the heart and general development being recorded as normal In the remaining case the man was graded II owing to enlargement of the heart shown on radiological examination He was accepted for service because there were no symptoms Subsequent necropsy showed he had congenital morbus cordis Since 45 of the first 50 were graded fit, or I, on entry, 91 of the 100 were graded fit, or I, on entry

PREVIOUS INFECTION

In the first 50 cases 3 patients gave a history of rheumatic fever and 2 of scarlet fever before entry into service In the second 50 none gave such a history Hence it seems that previous infection is rarely, if at all, a causal factor of coronary disease in young people

PRE SERVICE OCCUPATION

Of 49 recorded occupations in the second 50 cases only 6 were sedentary Of the 43 non sedentary occupations 25 would be considered as heavy work, 16 patients being labourers Of the 46 recorded occupations in the first 50 cases 8 were sedentary and 23 were heavy work Hence in the total series of 100 cases 14 patients had sedentary occupations before joining up, and 48 did heavy work, 33 being labourers Only 9 out of the 100 patients were officers, and all of these, apart from a doctor and an instructor lieutenant in the Royal Navy, had begun their service as rankers None of the commissioned officers were of higher rank than lieutenant, and they would not have been subject to sustained mental stress with heavy responsibilities Most of the cases of coronary occlusion in young people therefore fall in the Registrar General's social classes IV and V

PHYSICAL STRESS

Half of the second 50 patients had their coronary occlusion after release from service and therefore cannot be directly associated with Service stress The intervals between release from service and the onset of coronary occlusion, together with the post Service occupation, are shown in table II

It will be observed that the interval following release from service varied from 10 days up to 6 years As regards occupations at the time of the occlusion, 3 patients had not yet begun work, and, although 2 were students, none of the occupations could be said to involve mental stress asssociated with responsibility

Of the other 25 patients who had the coronary occlusion during Service, 24 had served more than three years, and 16 more than five years, before the occlusion, and 22 had served in the Middle East The 1 patient who had not served three years had his coronary occlusion three weeks after entry into service, while training In only 9 of these 25 cases did the occlusion come on while the patients were performing duties involving physical stress

TABLE II—ONSET OF CORONARY OCCLUSION IN RELATION TO RELEASE FROM SERVICE AND TO OCCUPATION *

Case no	Interval after service	Post Service occupation	Case no	Interval after service	Post Service occupation
51	1 yr 6 mos	Clerk	79	2 yr 9 mos	Motor mechanic
52	6 yr	Warehouseman	80	3 yr	Flour-packer
53	4 yr	Light labourer	81	10 days	No work
54	4 mos	Stone finisher	82	3 yr	Warehouse foreman
55	3 weeks	No work	83	4 yr 8 mos	Motor driver
56	3 yr 1 mo	Packer	85	3 yr 6 mos	Shop assistant
62	2 yr 6 mos	Medical student	86	3 yr	Shop manager
63	3 yr 3 mos	Store keeper	87	1 yr 6 mos	Carpenter
72	1 yr	Joiner	89	3 yr	Lorry driver
75	1 yr 9 mos	Street cleaner	90	9 mos	Painter and decorator
76	3 yr	Bricklayer			
77	3 yr 6 mos	Clerk	95	2 yr 6 mos	Postman
78	20 days	No work	100	3 yr 9 mos	Law student

PROGNOSIS

In my previous report I remarked on the high mortality (30 deaths) and of the tendency to die quickly after a coronary occlusion (33 patients were found dead, or died almost immediately after a collapse) The second 50 cases show a similar high mortality—41 deaths, making the mortality 80 in the 100 cases

In all 41 fatal cases in the second 50 death took place suddenly and, with 2 exceptions, in apparently fit and healthy men In one case the man, a motor-driver since release from service, called at a hospital because of sudden pain in his chest and vomiting The hospital case sheets record "Despite a thorough physical examination nothing abnormal was detected, and he was sent home" He collapsed on the way home and dropped dead

In the 2 exceptions, one complained of angina pain following release from service, but, since the radiogram and the electrocardiogram were normal, he was diagnosed as having an irritable heart with no organic lesion He died suddenly three years later, and necropsy showed complete occlusion of the left coronary artery, with atheromatous plaques

In the other case, a bank clerk, aged 18, was graded II on entry into service, owing to clinical enlargement of the heart, confirmed by radiography, which showed a globular heart consistent with right sided preponderance

There was no history of rheumatism, he had no symptoms, and the exercise tolerance test was good After three years' uneventful service in this country as an equipment assistant, he was investigated in hospital owing to concussion following a lorry accident The electrocardiogram showed a left bundle-branch block, and the man was invalided with this disability A Kahn test was negative After discharge the patient continued his pre Service occupation as a clerk for three and a half years without any discomfort or need for medical attention, when he suddenly collapsed and died at the age of 25, while out walking with his wife Necropsy disclosed a large heart, wholly diseased with severe fibrosis of the type associated with fusion of the remaining cusps. There was no evidence of rheumatic disease. The coronary arteries showed very advanced atheroma, which (the pathologist said) "at his age can only be described as precocious in the extreme." There was also narrowing or calcification in the cusps of the valves not inflammatory.

The association of congenital morbus cordis with advanced atheroma of the coronary arteries in this case implies a congenital weakness of the coronary arterial system, and supports the contention that genetic influences play a more important part than extraneous factors in coronary disease in young adults.

All the 9 patients in the second series who have survived the initial attack of coronary occlusion are still alive 3–5 years after the occlusion. They are all working in similar occupations to their pre-Service ones; but symptoms such as shortness of breath on effort, pain, and tightness in the chest on exertion are complained of by all.

NECROPSY FINDINGS

The necropsy findings in the present series of 41 deaths were similar to those in the previously published cases. The left coronary arteries were much more frequently affected than the right—13 left and 3 right. Both coronary arteries were affected in 20 cases. In the remaining it was not stated which coronary arteries were affected. In 18 of the 41 cases the heart was enlarged, and in 1 patient, aged 32, the heart was very large, owing to aneurysmal dilatation of the left ventricular wall. The heart muscle was very thin and there was much fibrous tissue. Both coronary arteries showed considerable atheroma, and the first half-inch of the descending branch of the left coronary artery was completely occluded by atheroma. This man had died suddenly, four months after release, while working as a steel-finisher. He had to lift heavy weights. A thrombus was found in only 12 cases. In 8 cases myocardial infarction was found, either recent or old-standing.

In the total series of 80 deaths, the left coronary artery was affected in 30 cases, the right in 8 cases, and both were involved in 36 cases. The heart was enlarged in 38 cases—i.e., in about half. Myocardial infarction, either recent or old, was found in 25 cases. A thrombus was found in only 22 of the 80 cases. The degenerative changes found in the coronary vessels were similar to those found in the older age-groups, the arteries being thickened, tortuous, and calcified. Occlusion took place in the non-thrombotic cases as the result of the gross atheroma or of an atheromatous plaque blocking the lumen. Atheroma of the aorta was also present in most cases.

These findings do not support Leary's (1941) view that in the younger age-group the pathological changes differ from those in the older age-group (over 45), thrombosis being more common, and calcification not occurring in the younger group.

DISCUSSION

This further series of 50 cases of coronary occlusion in young people confirms my previous view that advanced degenerative changes in the coronary arteries may exist at an early age, and that coronary occlusion is not so rare as was formerly thought. It is remarkable that, in spite of the advanced degenerative changes present in their coronary arteries, these patients appear to be in excellent health and can serve as graded-I men for several years, many overseas in combatant units, without any symptoms or signs of cardiac inadequacy until occlusion takes place. Full clinical examination, even a few hours before the occlusion, as happened in 2 cases, revealed no indication of the underlying degenerative arterial disease with its impending crisis. In only 1 case was the coronary occlusion preceded by angina pectoris, which in view of the youth of the patient and normal radiogram and electrocardiogram was not diagnosed as true angina but as an irritable heart with no organic lesion.

Coronary disease in young people seems to be predominantly confined to males, only 1 female occurring in the 100 cases. Body-build is an interesting factor because most of the patients were above the average weight for age and height, and such terms as "powerfully built," "well developed," and "muscular" were often used in the necropsy reports.

The second 50 cases do not confirm that infection is an important aetiological factor in coronary disease in young adults, for there was no such history in any. No cases of syphilis occurred in this series, although 2 cases occurred in the previous published series, which confirms that syphilis is a very infrequent cause of coronary disease, as in the older age-groups. Hypertension is recorded in 5 out of the 9 surviving cases of the second series. In the previous series it was noted in 3 cases. In view of the fact that in most of the fatal cases the patients had had no illness necessitating investigation during life, the blood-pressure was only occasionally recorded in these cases, as on routine examination, and so it is impossible to give the true incidence of hypertension, or discuss its influence as a factor in the aetiology of coronary disease in the young.

Most of these cases of coronary disease in the young fall in the Registrar-General's social classes IV or V, and there seems to be little evidence of any relationship to heavy responsibilities or mental stress. Ryle and Russell (1949), on the other hand, in a study of the epidemiology of coronary disease in the older age-groups, found that the incidence of coronary disease was much greater in the business and professional classes, and suggested this was related to mental rather than physical stress. In discussing my first 50 cases these writers state: "Where extraneous factors in early life are far to seek it may possibly be shown that genetic influences play a more important part than habits of life and work."

The high mortality, 80%, is a striking feature in coronary disease in the young. So is the rapid onset of death: sudden death occurred in 70 out of the 80 fatal cases.

The necropsy findings are similar to those found in the older age-groups, the coronary arteries showing all stages of atheroma, including calcification and occlusion by atheromatous plaques, with or without thrombus formation, and indicating that, in spite of the youth of the patients, the pathological process has been present for years.

These pathological findings at such an early age, the predominance in males, the body-build, and the lack of relationship to mental stress or other extraneous factors support the view that genetic influences are the most important factors in the aetiology of coronary disease in young people.

SUMMARY

100 cases of coronary occlusion in young adults in the Services or following release therefrom are reviewed.

All the patients but one were males, and of good physical development and previous good health.

Infection rarely seems to be an aetiological factor. ✓

The great majority of cases fall in the Registrar-General's social classes IV or V, and there is little evidence of any relationship to heavy responsibilities or mental stress. Physical stress occurred in less than half the cases.

The mortality was 80%, with sudden death in 70 of the 80 fatal cases.

At necropsy the atheromatous changes in the coronary arteries were similar to those usually described in the older age-groups. A thrombus was found in only 22 of the 80 fatal cases.

The findings support the view that genetic influences are more important factors than habits of life and work

I wish to thank Col F T Rees, Director General of Medical Services of the Ministry of Pensions, for permission to publish

REFERENCES

Leary T (1941) *Arch Path* 32 507
Newman M (1946) *Lancet* ii 409
Ryle J A Russell W T (1949) *Brit Heart J* 11, 370

SIMMONDS'S DISEASE (HYPOPITUITARISM) IN A MAN

DUE TO TRAUMATIC HÆMORRHAGE INTO THE PITUITARY GLAND

J Douglas Robertson
M D, D Sc St And F R C P, F R I C, D P H
DIRECTOR

H F W Kirkpatrick
B Sc, Ph D, F R I C
CHEMICAL PATHOLOGIST

DEPARTMENT OF CLINICAL INVESTIGATION, THE LONDON CLINIC

THE following case presented certain features suggesting Simmonds's disease, caused by hæmorrhage into the pituitary gland Simmonds's disease is not common in men, and an acute lesion such as hæmorrhage into the anterior pituitary has rarely been reported

CASE RECORD

A man, aged 44, was admitted to the London Clinic in August, 1947, with an illness which had begun at the age of 39, when he was a brigadier on active service and was leading a vigorous outdoor life At that time he was athletic, and for a height of 71½ in weighed 178 lb

History

He felt absolutely fit and well until Jan 31, 1943, when during a game of deck tennis he jumped to catch a high quoit and felt a sharp crick at the back of his neck, as if a red hot needle had been driven into the nape Momentarily he howled with agony and held his hand to the back of his neck He then tried to continue the game but he began to feel "groggy" and had to stop playing He could not eat dinner, was violently sick and developed a severe headache Throughout the night this headache continued, with vomiting every half hour From midnight to 1 A M he had diarrhœa At 5 30 A M a doctor was called The patient's temperature was then 100°F (37 8°C) and he was feeling very ill At 7 A M he was examined by a medical consultant who ordered his removal to hospital Fluid removed by lumbar puncture was said to be normal He was told that he did not have meningitis or a fractured skull A diagnosis of cerebral dengue was made and he remained in hospital six weeks, spending a further two weeks in a convalescent home

On April 1, two months after the accident, he returned to camp feeling far from well, listless, and lacking in energy He had lost about 28 lb in weight On May 2 he went on sick leave, but on June 2 he was readmitted to hospital because of his failure to improve Encephalitis was tentatively diagnosed, and an attempt to increase his body weight by giving him insulin was discontinued because of coma He remained in hospital for two months After a severe attack of headache and vomiting, lasting eight days, he was again admitted to hospital on Sept 1 His condition deteriorated, and he lost consciousness for about ten days His weight had now fallen to 110 lb, a loss of 68 lb in eight months Recovery from the coma left him exhausted, but at the same time he had a peculiar sense of well being He felt no longer toxic, and he formed the impression that the disease had run its course and that he was going to get better

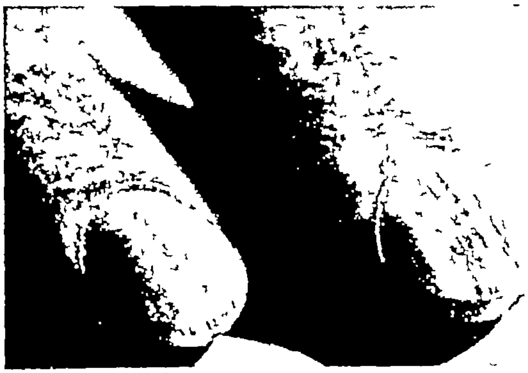


Fig 1—Longitudinal striæ on nails.

There is little of relevance in the later history, except that he had two attacks of pleurisy (February and August, 1944), and that in April, 1944, his teeth, previously in excellent condition, began to loosen and decay, those in the upper jaw being removed He was discharged from the Army in August, 1944, and three months later he returned to civilian occupation His condition remained static until his admission to the London Clinic in August, 1947

Complaints

On admission the patient complained that for the past few years he had lost all energy He tended to collapse after exercise, felt cold easily, had lost much weight, and was subject to severe attacks of headache and vomiting, lasting three days at a time During these attacks he could not eat but craved for water and passed about five litres of urine daily These attacks were said to occur almost regularly every month, and to be so severe that he could not leave his bedroom The last severe attack had been in April, 1947 They were worse in the winter than in the summer

He also complained of constipation, loss of sexual powers, and difficulty in swallowing solid food without sipping liquid His mouth had become dry, with little saliva

Clinical Examination

His height without shoes was 70½ in Before the accident his height had been 71½ in. This apparent loss of height was confirmed by the patient and by his wife and family (three children aged 19, 17, and 15) He weighed 128 lb, being 50 lb (23 kg) below his weight before the accident but 18 lb heavier than he was when his illness passed its acute phase He looked undernourished, and there was a loss of fullness at the terminal phalanges of the fingers, which tended to point, showing an absence of pads The nails were brittle and showed longitudinal striæ (fig 1)

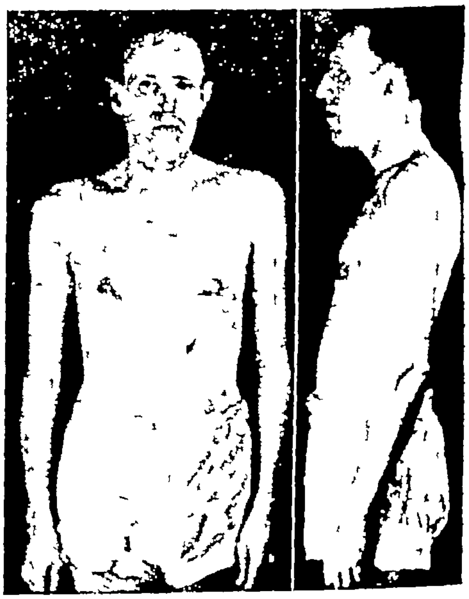


Fig 2—Patient on admission in 1947

Hair—The axillary and pubic hairs were scanty but present as a soft down Before his accident he had had a heavy hard beard, required to shave in the evening if attending any social functions After the accident his beard was soft and he shaved on alternate days The hair of his head had tended to fall out after the accident, and though it was still thick in texture it did not grow so quickly There was considerable thinning of the eyebrows and hair was absent from the outer third of each There was no hair on the first phalanx of each hallux, and hairs in his ears and nose were very scanty, although before the accident it had been necessary for the barber to trim the hair growing in the ears and nose.

The skin was dry over the whole of the body

Facies.—The patient looked ill and much older than his years (fig 2) His lips were thin and slightly parted His face was expressionless (fig 3) yet distinctive and unlike that seen in any other disease It could be described as mummified or like that of an old man asleep with his eyes open No puffiness was seen under the eyes

Cardiovascular System.—The basal pulse rate was 38 (regular) and the basal blood pressure 85/50 mm. Hg Radiographically the heart and aortic shadows were normal. Electrocardiography showed sinus bradycardia with P summits flat in II and III, and T summits inverted in III (fig 4)

Alimentary System.—The tongue was clean, and the six teeth in the lower jaw were loose and carious.

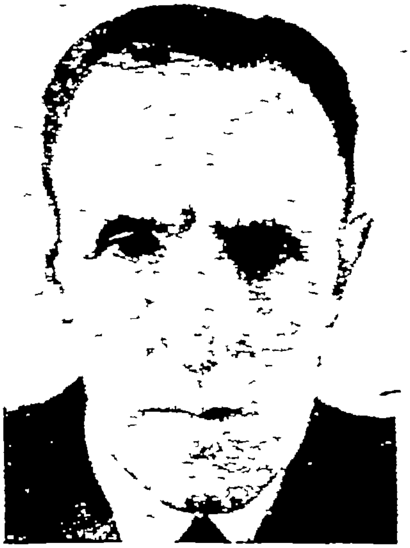


Fig. 3—Expressionless face on admission.

Body temperature.—97 F (36 C) The thermometer was left in the mouth for six minutes

Radiography.—The pituitary fossa was normal in size and shape and there was no radiological evidence of a lesion in the skull. The whole of the spine was examined for evidence of fracture but none was found.

Ophthalmological Report.—There were no ocular signs to indicate any abnormality in the central nervous system.

Investigations

Hæmatology.—Examination of the blood showed Hb 78% (11 3 g per 100 ml.), red cells 4,050 000 per c.mm., colour index 1 0, white cells 4400 per c.mm. (neutrophils 50%, lymphocytes 40%, monocytes 6%, eosinophils 4%) The red cells were normochromic but showed slight anisocytosis. The erythrocyte sedimentation rate (E.S.R.) was increased to 31 mm. in 1 hour (Wintrobe)

Serology.—The Wassermann reaction of the serum was negative

Relating to the Thyroid Gland.—The basal metabolic rate (B.M.R.) was −40 (standards of Aub DuBois) and the blood-cholesterol level 130 mg per 100 ml., suggesting that this was not a case of primary myxœdema, and that the fall in basal metabolism was due to a secondary dysfunction of the thyroid gland.

Relating to the Adrenal Gland.—The serum sodium was 355 mg per 100 ml the serum potassium 28 mg and serum-chlorides 585 mg The urinary excretion of chlorides was 9·3 g and of potassium 2 8 g in twenty four hours.

Relating to the Adrenal Gland and the Kidney.—The Robinson-Power Kepler index (Robinson et al. 1941) with extension of biochemical investigations, is shown in the accompanying table

After drinking 20 ml. of water per kg of body weight (1160 ml.) the patient passed only 130 ml. of urine—a phenomenon noted by Rosenow (1925) in Addison's disease Estimations of urea and chlorides in the urine showed a concentration of these crystalloids after a large intake of water although the net output per hour fell. All these findings were in complete contrast to those obtained in a normal person (see table) The urea-clearance gave a mean of 67%, a figure not uncommonly obtained in normal healthy people A urea-clearance of 54%, was obtained later

Relating to the Pancreas.—Several fasting blood sugar estimations on different occasions gave 60–70 mg. per 100 ml. A glucose tolerance test gave the following results

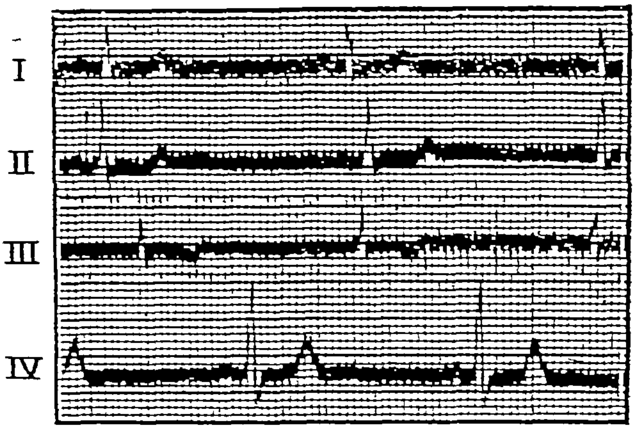


Fig 4—Electrocardiogram showing sinus bradycardia, P summits flat in II and III and T summits inverted in III

Resting blood sugar	70 mg per 100 ml
½ hour after glucose 50 g	110 mg "
1 hour	100 mg
1½ hours	65 mg
2 hours	60 mg

It was decided not to proceed with the standard (Fraser and Smith 1941) insulin tolerance test in view of the previous history of hypoglycæmia and the low fasting blood sugar level (This fortunate decision will be discussed elsewhere Recently, in a case of Simmonds's disease the intravenous injection of insulin 0·03 unit per kg of body-weight brought on severe hypoglycæmia with a blood sugar level of 15 mg per 100 ml in twenty five minutes and large doses of glucose by mouth did not prevent coma.)

Hormone Excretion.—The excretion of 17 ketosteroids was less than 1 mg in twenty four hours

Gastric Function.—A fractional test-meal showed a concentration of free hydrochloric acid reaching a maximum of the equivalent of 57 ml of N/10 NaOH and an emptying time of 1½ hours

Renal Function.—Three hours after the drinking of 1 litre of water 105 ml. of urine contained 2 08 g of urea per 100 ml

ROBINSON-POWER-KEPLER INDEX AND OTHER FINDINGS

Time	Urine					
	Volume (ml)	Urea clearance (%)	Urea (g per 100 ml)	Hourly excretion of urea (g)	Chlorides (g per 100 ml)	Hourly excretion of chlorides (g)
NORMAL CONTROL						
10.30 P.M.–7.30 A.M.	325	150	2 70	0 97	0·60	0 22
8.30 A.M.	1400 ml of water by mouth					
8.30–9.30 A.M.	165	101	0 72	1 19	0 27	0·45
9.30–10.30 A.M.	740	133	0 21	1 55	0·09	0 67
10 30–11 30 A.M.	470	96	0 24	1 15	0 11	0 52
11.30 A.M.–12 30 P.M	45	96	1 55	0 70	0 73	0 33
PATIENT						
10.30 P.M –7 30 A.M	605	58	0 88	0 59	0 32	0 21
8 30 A.M.	1100 ml of water by mouth					
8 30–9.30 A.M.	36	63	1 30	0·47	0 36	0 13
9 30–10 30 A.M.	36	70	1 45	0 52	0 40	0 14
10.30–11.30 A.M	30	71	1·65	0 50	0 43	0 13
11 30 A.M.–12.30 P.M	28	75	1 75	0·49	0 45	0 13

	Blood		
	Blood urea (mg per 100 ml)	Plasma-chlorides (mg per 100 ml.)	Index
NORMAL CONTROL	26	580	229 0
PATIENT	30	580	3 2

and the blood urea level was 35 mg per 100 ml, giving a normal urea clearance of 84%, impairment of water elimination being compensated for by a high concentration of urinary urea A urine concentration test gave the following figures

Time (A M)	*Volume* (*ml*)	*Sp gr*
6 30	530	1 014
7 30	415	1 012
8 30	70	1 020

The very restricted fluid intake caused no concentration of the urine, but instead urine with a diminished specific gravity was passed A urea concentration test gave the following figures

Specimen	*Volume* (*ml*)	*Urinary urea* (*g per 100 ml*)
Resting	26	1 3
	Ingestion of urea 15 g	
1 hour	60	2 3
2 hours	50	2 7
3 hours	52	2 1
4 hours	55	2 1

Treatment

After preliminary treatment with graduated doses of deoxycortone acetate, testosterone propionate, and thyroid gland for five weeks, and a high intake of salt and glucose, 400 mg of deoxycortone acetate and 400 mg, of testosterone propionate was implanted into the anterior abdominal wall

Progress

Two months after treatment was begun, the patient's condition had improved He weighed 140 lb, a gain of 12 lb (5 5 kg) The B M R was −19, the basal pulse rate 50, and the blood pressure 140/90 mm Hg The urinary excretion of 17 ketosteroids was 4 6 mg, of potassium 4 7 g, and of chlorides 9 9 g in twenty four hours Plasma chlorides 620 mg, serum sodium 355 mg, and serum potassium 23 mg per 100 ml The fasting blood sugar remained low, about 70 mg per 100 ml There was no change in the blood picture, but the E S R had fallen to 20 mm in 1 hr (Wintrobe)

The patient felt very much better, and said he had never felt so well since the accident He could walk two or three miles without fatigue For business reasons he had to return home after treatment had been in progress two months

Follow up —A note from him three months later said he was feeling almost normal and was driving his car, which he had been unable to do since the accident, driving as much as 200 miles a day without fatigue He has had no more attacks of headache, sickness, and vomiting since treatment was started Advice was given that reimplantation every six months might be necessary, according to his clinical condition

DISCUSSION

Simmonds's disease is not very common in the male It was some ten years after Simmonds * (1914) first described a case in a woman that Lichtwitz (1924) described a similar condition in a man Lichtwitz also suggested that the name "Simmonds's disease" be given to the pathological syndrome that Simmonds (1916) in his third communication had called "cachexia of hypophyseal origin," because, according to Lichtwitz, as a result of different degrees of damage to the pituitary gland, a varied clinical picture was found

Simmonds's disease caused by trauma has only rarely been reported There are two main causes a fractured skull and a bullet wound

Five, possibly six, cases due to a *fractured skull* have been reported (Cyran 1918, Reverchon et al 1921, Scherescheweky 1927, Berblinger 1934, Lisser and Curtis 1945, and possibly Lerman and Means 1945, case 2)

Two cases of *bullet wounds* of the pituitary gland have been reported Frank's (1912) case was questioned by Leschke (1919), who saw the X ray films and said that the bullet was lodged above the sella turcica Further, signs of damage to the anterior lobe of the pituitary gland were not clearly described Lerman and Means's (1945) case 1 is clear cut, and all the signs and symptoms of Simmonds's disease developed shortly after the accident

A further possible cause of Simmonds's disease is hæmorrhage into the pituitary gland De Costobadie and Ryrie (1924) described a case with an extensive hæmorrhage into the pituitary, but it was the hæmorrhage and not the Simmonds's disease that caused death.

The history is vague, but during the previous year the patient, a man aged 49, had complained of headache, failing vision, and hairlessness (which takes time to develop) The patient died six weeks after the acute lesion, during which time he was practically comatose At necropsy the pituitary showed a recent hæmorrhage, causing the pituitary, five times its normal size, to bulge up outside the sella turcica, and there was clear evidence of encephalitis lethargica

Our case presented all the signs, symptoms, and laboratory evidence typical of true Simmonds's disease The history and the findings at the time of the accident make it clear that there was an acute trauma, and that probably the lesion was a hæmorrhage into the pituitary gland, involving chiefly the anterior lobe With improvement in clinical and laboratory diagnosis it seems reasonable to diagnose Simmonds's disease at an early stage, thanks mostly to Sheehan (1939, 1940, 1948) and his colleagues (Sheehan and Summers 1949, Cooke and Sheehan 1950), who have pointed out that many cases of emaciation are misdiagnosed as Simmonds's disease

The differential diagnosis seemed to be between anorexia nervosa, Addison's disease, myxœdema, and Simmonds's disease Against anorexia nervosa were the sudden onset, the extreme weakness and reduction of activity, the normal appetite, the patient's age, the very low 17 ketosteroid excretion, and the loss of hair and teeth Against Addison's disease were the lack of pigmentation of the body and mucosæ, the normal plasma chloride and serum sodium levels, the normal excretion of urinary chlorides and potassium, and the bradycardia Against myxœdema were the low blood cholesterol level and other biochemical observations Thus Simmonds's disease was the most probable, and in favour of this were the sudden onset following an accident, the typical signs and symptoms, the failure of function of the thyroid, adrenals, and gonads, and the degenerative changes in hair, skin, and teeth

The tests commonly used showed no renal impairment, but an attempt to concentrate the urine by the usual procedure of Volhard as modified by Fishberg (1939) failed, leading to a large output of urine of low specific gravity—the opposite of what happens in normal people With the increased concentration of urinary urea and chlorides and diminished urine output following the ingestion of a large amount of water, it is tempting to postulate, in the present case, an increased accumulation of an antidiuretic substance (A D S) Our finding not dissimilar from those obtained by Birnie et al in a study of the A D S in normal and in adrenalect rats The A D S may act by increasing tubular reabso tion of water or diminishing glomerular flow If, as Birnie and his colleagues suggest, the A D S has its origin in the posterior lobe of the pituitary, the lesion our case affected only the anterior lobe

The insulin tolerance test, even when done w nty but small an intravenous injection of insulin as 0 03 u d had a kg of body weight, is not without risk, a da tending hypoglycæmia can develop, the blood sugar level was soft from 75 to 15 mg per 100 ml in twenty five ead had even when the procedure of Engel and Scott (1949), designed to prevent hypoglycæmic coma by giving glucose by mouth half an hour after intravenous insulin 0 1 unit per kg of body weight, is used

---

* Simmonds is given the credit for being the first to draw attention to a clinical syndrome due to post partum necrosis of the pituitary gland, afterwards limited by Fraenkel (1916) to the anterior lobe An abstract of a paper by L K Glinski of Poland, published in 1913 has been found in which he described three cases of pituitary necrosis following puerperal sepsis An attempt is being made to trace the original paper or papers, and these may show that Glinski anticipated Simmonds (Robertson 1951)

SUMMARY

A case of Simmonds's disease in a man was caused by an acute lesion, probably due to hæmorrhage, in the pituitary gland No similar case has been traced

The patient improved considerably on treatment with deoxycortone acetate, testosterone propionate, and thyroid gland

It is a pleasure to thank Mr A V Bridgland, chairman of the Trustees of the London Clinic for generously providing all facilities for this investigation, Mr J A Roberts for much technical assistance, Dr M Frisch for assistance in translations, and our patient for his most willing coöperation

REFERENCES

Berblinger W (1934) *Endocrinologie*, 14 369
Birnie J H, Eversole W J Boss W R Osborn C M. Gaunt, R (1950) *Endocrinology*, 47 1
Cooke R. T Sheehan H L (1950) *Brit med J* i 928
Cyran E (1918) *Dtsch med. Wschr* 44, 1261
De Costobadie L P, Ryrie, B J (1924) *Lancet* ii 1007
Engel F L Scott, J L (1949) *J clin Invest* 28 779
Fishberg A. M. (1939) Hypertension and Nephritis. 4th ed Philadelphia.
Fraenkel, E (1916) *Dtsch med Wschr* 42, 1369
Frank E (1912) *Berl. klin Wschr* 49 393
Fraser R Smith P H (1941) *Quart J Med.* 10 297
Lerman J Means J H (1945) *J clin Endocrinol* 5, 119
Leschke E (1919) *Z klin. Med* 87 201
Lichtwitz, L (1922) *Klin Wschr* 1 1877
Lisser H Curtis L E (1945) *J clin. Endocrinol.* 5, 363
Reverchon L Worms G Rouquier A (1921) *Pr med* 2 741
Robertson J D (1951) *Brit med J* i, 921
Robinson F J Power M H Kepler E J (1941) *Proc Mayo Clin* 16 577
Rosenow G (1925) *Med Klin* 21 203
Schereschewsky N A. (1927) *Rev franç Endocrinol* 5 275
Sheehan H L (1939) *Quart. J Med* 8 277
— (1940) *Lancet*, ii, 321
— (1948) *Irish J med Sci* 270 241
— Summers V K. (1949) *Quart J Med.* 18 319
Simmonds, M (1914) *Dtsch med Wschr* 40, 322
— (1916) *Ibid* 42 1369

METHÆMOGLOBINÆMIA DUE TO SODIUM NITRITE

T E Oppé
M B Lond, M.R C P
LATE CHILDREN'S HOUSE PHYSICIAN, GUY'S HOSPITAL, LONDON

Cyanosis in infancy is usually due either to congenital heart disease, or to respiratory-tract disease caused by congenital malformation, obstruction, or infection Occasionally cyanosis is due to alteration in hæmoglobin with methæmoglobinæmia or sulphæmoglobinæmia

In the case described here cyanosis was due to sodium-nitrite poisoning

CASE RECORD

A male baby, aged 2 months, was admitted to Guy's Hospital with cyanosis of 3 hours duration He was the only child of healthy parents, and there was no history of cyanosis in the family He had been delivered by forceps at home His birth weight was 7³/₄ lb, at birth he cried vigorously, and was not cyanosed He was breast-fed for 10 days and then put on bottle feeding Owing to mild dyspepsia—wind and colicky pain—the parents had been advised to give m sodium citrate gr 4 at each feed On the evening before sion a new supply of tablets had been obtained from emist and two tablets of this new supply were used for ly morning feed on the day of admission

t 7 A.M he had a normal feed with two tablets added to it this he took well At 8 20 A M he went "almost black", there was some retching but no vomiting The cyanosis persisted soon the hands and feet became blue, and at 0 A.M. he collapsed with drowsiness and rapid respirations was immediately taken to the local practitioner, who him collapsed and duskily cyanosed, with tachycardia hypnœa

dmission at 12 30 P M the child had a peculiar slate anosis unlike that of congenital heart-disease He did ear distressed and had no pyrexia

was only slight dyspnœa, and no signs of respiratory obstruction. Examination of the chest and cardiovascular system disclosed no abnormality The abdomen was soft and the liver and spleen were not palpable There was no neck rigidity, and the fontanelle was normal

Toxic methæmoglobinæmia was diagnosed, and the remaining tablets, which the mother had fortunately brought, were sent for analysis

The baby was placed in an oxygen tent, which did not relieve his cyanosis, and the stomach was washed out with sodium bicarbonate, since potassium chlorate poisoning was suspected

Blood examination Hb 61% (Haldane), red cells 3,200,000 per c mm, with no nucleated red cells Spectroscopy of a solution of whole blood after hæmolysis showed the characteristic absorption band of methæmoglobin, confirmed by its disappearance after the addition of alkali It was later reported that the tablets each contained sodium nitrite gr 1, the amount ingested therefore being gr 2—the amount named in the *British Pharmacopœia* as the maximum dose for an adult

That evening cyanosis was still present, although less severe, blood that was withdrawn was brownish 0 3 ml of a 5% solution of methylene blue was injected intravenously *Immediately the baby's colour became chocolate brown* but during the next 20 minutes his colour returned to normal

Cyanosis did not recur, and the patient was discharged, well, 5 days later

DISCUSSION

Toxic methæmoglobinæmia in infancy and childhood, which is not uncommon, should be considered in all cases of unexplained cyanosis Lately this condition has received much attention because of outbreaks associated with nitrate-contaminated well water or aniline derivatives in marking ink Isolated cases of methæmoglobinæmia, due to accidental absorption of other toxic compounds, occur occasionally in infants and children

Nitrite poisoning has been previously reported in a girl, aged 5 years, who, with her mother and father, ingested a large quantity of sodium nitrite in mistake for table salt, with a fatal outcome (McQuiston 1936) Roe (1933) reported several cases of methæmoglobinæmia in infants treated with bismuth subnitrite, with one death

Aniline derivatives are used in the manufacture of some wax crayons, and acute methæmoglobinæmia has been caused in children by their ingestion (Jones and Brieger 1947, Clark 1947) An interesting case in a schoolboy of 14, who accidentally came into contact with pure aniline during a chemistry lesson and suffered from almost fatal poisoning, is described by Sterning (1951)

Poisoning with nitrobenzene has been reported in twins, aged 3 weeks, by Stevens (1928), the source was a proprietary disinfectant used to kill bed bugs in the children's mattress Leader (1932) described a case of toxic methæmoglobinæmia in a 20 month old girl, the cause was poisoning with nitrobenzene mistakenly prescribed for almond oil, and the patient was treated successfully by exsanguination transfusion

The clinical picture of slate grey cyanosis, collapse, and vomiting without evidence of respiratory or cardiac disease should suggest methæmoglobinæmia If the cyanosis is unrelieved by oxygen therapy, and blood withdrawn from a vein shows the characteristic chocolate-brown coloration, the diagnosis is certain Methylene blue 1–2 mg per kg body-weight should at once be injected intravenously, and the causal substance must be sought and eradicated

SUMMARY

An infant with cyanosis due to accidental sodium-nitrite poisoning was successfully treated by intravenous injection of methylene blue

I wish to acknowledge gratefully Dr R C Mac Keith's interest in this case, and his help and encouragement in preparing this report

REFERENCES

Clark, E B (1947) *J Amer med. Ass* 135 917
Jones J A Brieger H (1947) *J Pediat* 30, 422
Leader S D (1932) *Arch Pediat* 49 245
McQuiston, T A C (1936) *Lancet* ii 1153
Roe H E (1933) *J Amer med Ass* 101 352
Sterning S E L (1951) *Med J Aust* i 578
Stevens A M (1928) *J Amer med Ass* 90, 116

HYPERPYREXIA WITH CEREBELLAR DAMAGE IN ACUTE RHEUMATISM

ERIC K. CRUICKSHANK
M.D. Aberd., M.R.C.P.
LECTURER IN MEDICINE IN THE UNIVERSITY OF ABERDEEN

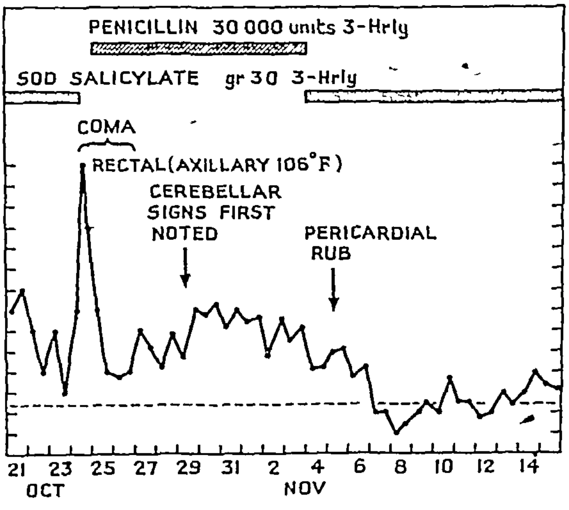
HYPERPYREXIA seems nowadays to be rare as a complication of acute rheumatism, but it was quite familiar to the physicians of the latter part of last century. So far as I know, cerebellar damage following hyperpyrexia has not been recorded in rheumatism, although it is a recognised sequel to the hyperpyrexia of heat stroke. The case reported here presented both these features.

CASE RECORD

A tractor driver, aged 20, was admitted to Woodend Hospital, Aberdeen, on Oct. 21, 1948, with the history that he had been fit until six weeks before admission, when he had had a sore throat, which had lasted two or three days. He had been well again until fourteen days before admission, when he had had a recurrence of sore throat with some swelling of the neck glands. Seven days later he had developed pain in the right shoulder. Thereafter pain and stiffness had occurred serially in the right elbow, right wrist and fingers and on the day before admission both knees had become swollen, stiff, and painful. He had been sweating profusely. He had received sulphapyridine 7 g. from his own doctor.

On examination he was a well built man with a flushed face and injected conjunctivæ and was sweating profusely. His temperature was 103°F. His right wrist and elbow were swollen and painful. There was some limitation of abduction of the right shoulder, some pain on flexion of the right hip, and stiffness of both knees, especially the left. The heart-rate was 76. The apex beat was palpable 4 in. from the mid sternal line in the 4th left intercostal space, and a soft systolic murmur was audible at the apex. The blood pressure was 138/46 mm. Hg. These findings were not regarded as indicating active carditis. No abnormalities were demonstrable in other systems. He was bright and coöperative. His speech was slow, but his voice and articulation were normal. A white cell count showed 19,450 per c.mm., and the erythrocyte sedimentation rate (E.S.R.) was 115 mm. in one hour (Westergren). The urine contained albumin, numerous pus cells, a few red cells, and some hyaline casts. A blood culture was sterile. Urine culture was not done. The patient therefore presented a classical picture of a moderately severe case of acute rheumatism with a low grade urinary infection.

Treatment.—He was treated with sodium salicylate gr. 30 three hourly and an alkaline mixture of potassium citrate and sodium bicarbonate, $\overline{\text{aa}}$ gr. 30 four hourly, with a high fluid intake.



Treatment and temperature chart.

Progress.—During the next three days the joint pains almost went, the temperature was settling, and the abnormal urinary findings disappeared. But on the morning of the fourth day after admission the patient complained of a black cloud in front of his eyes and buzzing noises in his ears, and said he felt funny and that "it was the last." Salicylates being thought to be responsible, the next dose was omitted. That afternoon at 4.15 P.M. the patient got out of bed and stood waving his arms about and talking incoherently. He was put back to bed and lay smiling, grimacing, and screwing up his eyes. There was occasional rhythmical twitching of his arms, lasting a few minutes. The axillary temperature was 106°F and rectal temperature 110°F. He next developed generalised clonic movements going on to intermittent tonic spasms with arching of the back. Between spasms he was deeply comatose, with widely dilated fixed pupils, flaccid limbs, absent reflexes, and extensor plantar responses.

The windows were opened. The patient was stripped and wrapped in sheets dipped in cold water. Oxygen was administered and nikethamide 6 ml. given intramuscularly. These measures reduced the rectal temperature to 104°F and were continued for the next twelve hours. Lumbar puncture produced a clear fluid not under pressure and containing protein 30 mg. per 100 ml. and no increase in cells.

The patient remained comatose during the night, but his blood pressure rose to 100/70 mm. Hg, with a pulse rate of 110. Occasional clonic twitching of the arms and legs continued. As he could not swallow he was given 8 pints of glucose saline solution intravenously during the next forty eight hours. On the evening of Oct. 25, 1948, he mumbled something to the night nurse, and by the morning of Oct. 26 he was conscious, but his speech was slow and mumbling. He was moving all his limbs; the deep reflexes were brisk and equal, and the plantar reflexes flexor. Unfortunately his central nervous system was not fully examined until Oct. 29, when scanning speech, a gross intention tremor of both arms, and incoordination of the legs were found. There was no nystagmus and no evidence of damage to the sensory system or the upper and lower motor neurones.

The patient continued to have fever for thirteen days after the hyperpyrexial attack (see figure). Penicillin 1,000,000 units in ten days was given to prevent a respiratory infection. Sodium salicylate was withheld for ten days because it was regarded as possibly responsible for the hyperpyrexia. It was given again on the tenth day after the hyperpyrexial attack, and the temperature fell to normal in three days. A transitory pericardial rub was noted on Dec. 5, 1948. The intention tremor of the arms and incoordination of the legs gradually disappeared in the next three weeks, but the speech disorder persisted.

During the next three months the patient had three recrudescences of the rheumatic infection; there was a pericardial rub and a transient diastolic murmur during one episode, and another was associated with a patchy consolidation of the left lower lobe.

Thereafter the E.S.R. remained below 3 mm. in one hour, and there was no clinical evidence of permanent cardiac damage. The speech remained slightly scanning. A brother said he had not noticed any mental changes since the illness, but the patient's speech was slightly but definitely altered. There was no evidence of ataxia or incoördination of the limbs when he was last reviewed in June, 1949, and he had again been working as a tractor driver for six months.

DISCUSSION

Hyperpyrexia was such a common and dramatic complication of acute rheumatism in the last century that in 1879 a special committee of the Clinical Society of London was nominated to investigate it. Their detailed report (Committee on Hyperpyrexia in Rheumatic Fever 1882) reviewed 67 cases in various London hospitals in 1871–80. They found that hyperpyrexia was commonest in first attacks of rheumatic fever, where it might suddenly supervene in apparently favourable cases, and that half the patients died. At that period salicylates were not in general use in the treatment of rheumatic fever; this therapy was first used in this country by Maclagan in 1874, and he did not publish his results until 1876. It therefore seems likely that salicylates have been mainly responsible for the extreme rarity of hyperpyrexia in rheumatic fever in recent years.

The committee described among the neurological manifestations muscular tremors, tonic spasms, convulsions, a silly manner, and hesitating speech, all of which were features of the present case in the early stage, but they did not mention signs of cerebellar damage persisting after recovery

Destruction of the cells of the hypothalamic nuclei in heat stroke have been demonstrated by Morgan and Vonderahe (1939) There is good evidence that these cells, among other functions, act as the thermostat of the body, and damage to them may produce gross disturbance of temperature regulation It is therefore reasonable to assume that the hyperpyrexia of acute rheumatism is the result of damage to these cells from the encephalitic changes which may complicate that disease Winkelman and Eckel (1932) reviewed these changes and concluded that they were not greatly different from those occurring in any severe infection Frisch (1934) reported a case of rheumatic encephalitis complicating a typical attack of rheumatic fever, which had initially responded to salicylate therapy

Seventeen days after admission signs of severe chorea with maniacal outbursts developed. The temperature was 103–106°F and later rose to 108 4°F when the patient became comatose and cyanotic The cerebrospinal fluid was under slightly increased pressure and contained an increased amount of globulin and 70 cells per c.mm , 80% of which were lymphocytes. Signs of diffuse brain damage with maximal involvement of the basal ganglia appeared thereafter These gradually disappeared, and eight weeks after the onset no abnormality was demonstrable in the nervous system

Alpers (1928) and Dobbs and de Saram (1938) describe acute hæmorrhagic encephalitis in acute rheumatism

The patient of Dobbs and de Saram was a girl, aged 8 years, with moderately severe rheumatism who, after responding satisfactorily to salicylates, suddenly developed nervous symptoms and hyperpyrexia (108°F) and died in coma eighteen hours later Histological examination of the brain showed numerous small and large ball and ring shaped hæmorrhages scattered generally throughout the substance None of the changes were regarded as specific to acute rheumatism.

Bourne (1936) and High and Aegerter (1945) record cases of acute rheumatism with features of meningo-encephalitis, but none of them mentions clinical or histological evidence of damage to the cerebellum Lhermitte and Pagniez (1930) and van Gehuchten (1931), however, noted predominant lesions in the dentate nucleus and Purkinje cells of the cerebellar cortex in patients dying in the course of acute chorea

Changes in the cerebellum as well as elsewhere in the brain have been demonstrated histologically in fatal cases of heat stroke, and the damage may be maximal in the region of the Purkinje cells (Brouwer 1913, Schwab 1925, Hartman 1937, Freeman and Dumoff-Stanley 1944)

Nonne (1907, cited by Weisenberg 1912) gave one of the first clinical records of cerebellar damage following heat-stroke Weisenberg (1912) described a patient who had gross ataxia of the limbs head, and tongue after coma with a temperature of 107°F due to heat-stroke Nystagmus was not present Stewart (1918) gave details of another case where the temperature reached 109 2°F and was accompanied by clonic convulsions and deep coma After recovery gross incoördination of the limbs nystagmus, and mental deterioration were still present sixteen months later Clinical evidence of gross cerebellar damage without nystagmus was also found by Freeman and Dumoff Stanley (1944) in a patient whose axillary temperature had reached 108°F

McAlpine (1946) gives a brief account of three soldiers who had recovered from heat-stroke All three were dysarthric and showed ataxia and unsteadiness in walking None showed nystagmus. In two the signs cleared in a few weeks, but in the third they persisted McAlpine describes a further case presenting features very similar to those seen in advanced disseminated sclerosis, the patient had made no improvement two months later

It is therefore apparent that in some people the cells of the cerebellum are particularly susceptible to damage from hyperpyrexia, and such damage may be temporary or permanent In the published cases the cause of the hyperpyrexia has been "heat stroke" In our patient the hyperpyrexia occurred during acute rheumatism and was probably due to damage to the nuclei of the hypothalamus from the encephalitic changes that may take place in acute rheumatism An unusual toxic action of sodium salicylate may have been responsible, but no such toxic action has been reported Moreover hyperpyrexia has become a very rare complication in acute rheumatism since the introduction of salicylates as the routine remedy, and in our patient pyrexia continued when sodium salicylate was withheld, but rapidly disappeared when sodium salicylate was given again The only evidence of any permanent damage to the central nervous system in this patient is the persistence of some hesitancy of speech

SUMMARY

A case of acute rheumatism complicated by hyperpyrexia is described

After the patient had recovered from the resultant coma, signs of cerebellar damage were demonstrable These signs disappeared in three weeks, but some hesitancy of speech persisted

REFERENCES

Alpers B J (1928) *Arch. Neurol Psychiat* 20 497
Bourne G. (1936) *Brit med J* ii 1017
Brouwer B (1913) *Arch. Psychiat Nervenkr* 51 539
Committee on Hyperpyrexia in Rheumatic Fever (1882 *Trans clin Soc Lond.* 15 261
Dobbs R. H de Saram G S W (1938) *J Path. Bact.* 46 437
Freeman W Dumoff-Stanley E (1944) *Arch Neurol Psychiat* 51 67
Frisch I A (1934) *J Pediat* 5, 654
Hartman F W (1937) *J Amer med Ass* 109 2116
High R. H. Aegerter E E (1945) *J Pediat* 27 343
Lhermitte J Pagniez P (1930) *Encéphale,* 25, 24 *Arch. méd Enfant* 33 156
McAlpine D (1946) *Proc R Soc. Med* 39 169
Maclagan, T (1876) *Lancet* i 342, 383
Morgan L O Vonderahe A R (1939) *Arch Neurol Psychiat.* 42 83
Schwab W (1925) *J Amer med Ass* 84, 712
Stewart R M. (1918) *Rev Neurol Psychiat* 16 78
van Gehuchten P (1931) *Rev. neurol.* 1 490
Weisenberg J (1912) *J Amer med Ass* 58, 2015
Winkelman, N W Eckel J L (1932) *Arch. Neurol. Psychiat* 28 844

A C T H IN DERMATOMYOSITIS

REPORT OF A CASE

A Alun Williams
M.D Lond , M.R C.P.E
ASSISTANT PHYSICIAN

D P Bowler
M.D Lond , M.R C.P.
LATE REGISTRAR

NUMBER TWO MEDICAL CLINIC TEES SIDE HOSPITALS

DERMATOMYOSITIS is classified as one of the collagenoses Dowling (1950) states that nothing is known of its ætiology, and classifies it with the sclerodermas In 1939 he drew attention to the presence of lymphorrhages in the muscle, and to a possible relationship with thyroid disease (Dowling 1940)

O'Leary (1949) holds that the most probable cause is infection culture of the affected muscle during an acute phase has revealed streptococci, staphylococci, or both, and occasionally a vaccine made from the organisms cultured has led to improvement He thinks that the histological changes in the muscle are inflammation (this may correspond to the lymphorrhages of Dowling) followed by degeneration

According to Selye (1950) dermatomyositis is one of the many manifestations of the adaptation syndrome and responds to adrenocorticotropic hormone (A C T H).

CASE RECORD

A married woman aged 34, was admitted to hospital on March 15, 1950, with eighteen months history of shortness author's obvious enthusiasm for his operation, and his minute description of preoperative and postoperative treatment, are delightful The opinions of any expert, writing on his own subject, are all the more interesting when he compares his own methods and results with those of others Professor Hryntschak has obviously absorbed every detail of Harris's work and more recently that of Millin, and put it to very good effect All urologists will derive pleasure from reading this detailed book and may learn much from it It is a pity that the publishers have included advertisements in the text and have relegated the illustrations to an envelope within the back cover

Conference on Problems of Aging

Editor Dr NATHAN W SHOCK New York Josiah Macy, Jr, Foundation 1950 Pp 258 $3 75

AT present, when so many doctors in Great Britain are considering the processes of ageing, it is interesting not only to learn something of the ideals and work of the Josiah Macy Foundation in gerontology, but also to appreciate the wide field reviewed at this conference Subjects ranged from scientific details of research methods, on the one hand, to matters of principle, or practical policy, in developments of geriatric services on the other, and the speakers spoke with authority

Most of the discussions were scientific, relating to biological research on regeneration of the liver in old age, sexual regeneration in elderly women, nutritional factors, long term hæmorrhage anæmia in dogs, life span experiments with rats, and like subjects Others dealt with social problems such as the age of retirement, and with the organisation of research units in gerontology, and the chances of coöperation between gerontological societies in Europe and America Discussions started all manner of fascinating hares, among them the recruitment of young people for work in geriatrics, the development of geriatric services in connection with hospitals, and the psychology and psychiatric care of the old The volume should be widely read, not only for information but for the vigorous exchange of ideas it presents

Terminal Care for Cancer Patients

WILLIAM F PETERSEN, M D, chairman of the advisory committee, Central Service for the Chronically Ill Chicago, Ill Institute of Medicine of Chicago Pp 211

THIS is the record of an inquiry by a specially appointed "survey staff" into "the facilities and services available and needed for the terminal care of cancer patients in the Chicago area," made in 1947–49 The field work was clearly excellent the facts disclosed have been recorded and correlated and the problems that emerged are thoughtfully and imaginatively considered The report itself is less admirable long words, awkward or obscure phrases, and much repetition make tedious reading of what should be a stimulating recital of facts to be faced None the less it deserves to be read and considered, and the work might well be repeated in some comparable district here

The survey distinguishes between the "terminal phase" of a cancer—the phase in which curative treatment is no longer possible and the disease is progressing towards death—and the "terminal carestage," in which the patient can no longer fend for himself It is with the latter that the writers are mainly concerned, though they observe that, despite the new therapeutic weapons, the average length of the terminal phase has not increased since 1921 The average length of the terminal care stage, as determined in this survey, is 93 days It varies with the site of the growth from 60 days' average for respiratory to 631 days for skin cancers For every four cancer deaths per annum in a community one patient, at any given time, is needing terminal care, and he needs an average of 4 hours' bedside care a day 20% of all cancer patients, these workers find, can remain at home to the end and prefer to do so The 80% who die in hospital will on an average, spend over half the terminal care stage at home, so at any one time about two-thirds of these patients will be at home and needing some care there. As to the kind of care, it is often as much housekeeping as nursing, and the nursing needed is often very simple The report urges that "practical nurses" and nurse housekeepers should be trained and made available in much greater numbers than at present their usefulness would extend far beyond the terminal care of cancer The provision of special homes or hospitals for late cancer is roundly condemned, and the writers find with satisfaction that general hospitals would willingly accept these patients if they had the beds The formidable financial difficulties of making appropriate or acceptable provision for them are examined in detail, as are the equally formidable emotional difficulties, due largely to misconceptions about the clinical features of cancer in its commoner forms

A final chapter gives an encouraging account of recent progress towards adequate provision for these unhappy patients in and about Chicago, but it is clear that there is still a long way to go Whether things are better or worse in this country probably only a similar survey could show

---

British Encyclopædia of Medical Practice (2nd ed London Butterworth Medical Publications 1951 Vol 5 Pp 680 £3)—Publication of the new edition of this important work is proceeding apace, the fifth volume, which sustains the high standard of its predecessors, carries forward this alphabetically devised compendium from Ecthyema (by Dr J E M Wigley and Dr O L S Scott) to Gassing and Poison Gases (by Lieut Colonel C A de Candole) This volume includes an unusually clear exposition, by Sir Adolphe Abrahams, of Etiquette and Ethics in medical practice

A Manual of Psychiatry (Christchurch, N Z N M Peryer 1950 Pp 294)—The work of Dr K. R Stallworthy, medical superintendent of Porirua Hospital, this textbook of psychiatry covers the syllabus for the New Zealand psychiatric nurse but should also prove of value to students and general practitioners in the Dominion It is clearly written, and the attitude to the patient which it both enjoins and exemplifies is altogether admirable

A Complete Outline of Fractures, including Fractures of the Skull (3rd ed London Heinemann *Medical* Books 1951 Pp 671 42*s*)—Mr J Grant Bonnin's justly popular textbook has reached its third edition without any serious increase in girth His deliberate attention to the needs of undergraduate and postgraduate students has kept him, as he says in the preface, from including exuberant detail, or "the peculiar fractures which appeal to the connoisseur" Instead, he has revised some judgments, added to the illustrations, and put in new matter about such things as the Küntscher nail, the operative treatment of hand and finger injuries, and streptomycin The line drawings are his own, and show him as an excellent draughtsman

Clinical Parasitology (5th ed London Henry Kimpton 1951 Pp 1032 84*s*)—Colonel C F Craig and Prof E C Faust have sifted the vast amount of information published on medical parasitology since their fourth edition, and present the results in this completely revised volume New drugs for the treatment of malaria, filariasis, and several of the diseases transmitted by arthropods, and new insecticides for slaughter of the transmitters, have been given due space and Prof Albert Miller contributes a chapter on the control of 'medically important arthropods" which reminds readers that this phylum includes such large direct attackers as scorpions, centipedes, and biting spiders as well as those smaller trouble bearers, lice, mites, and the like

Doctors of the Mind (London Robert Hale 1950 Pp 327 15*s*)—This book has the subtitle "The Story of Psychiatry", and a very dramatic story Miss Marie B Ray has made of it She has evidently read widely, and she acknowledges the help of no fewer than 27 psychiatrists whom she has interviewed or consulted. She begins by tracing the evolution of mind from the unicellular organism to the primates, describing Kohler's work with apes and then going on to Broca's discovery of the speech centre, and the growth of psychotherapy, via Charcot, Bernheim, and Liebault to Freud Adler, and Jung A full account is given of physical methods of treatment from Wagner-Jauregg to Meduna, Sakel, and Davidoff The style is colourful and over optimistic, and weighty problems are over simplified but the material is all there

THE LANCET

LONDON SATURDAY, MAY 12, 1951

More Discretion for Hospitals

In his report[1] accompanying the summarised accounts of the National Health Service for 1949–50 Sir **Frank Tribe**, the Comptroller and Auditor-General, remarks that some hospital authorities had not adjusted, or had declined to adjust, salaries in excess of the approved scales He goes on to say that the Ministry of Health tells him that, as a number of boards have not complied, the question of making regulations under section 66 of the National Health Service Act is being considered

The brevity with which the matter is handled in Sir **Frank**'s report lends colour to the opinion expressed in the press—that here we have a simple clash between the principle of central control and some recalcitrant hospitals But actually the position is probably more complex Judging by the few instances of which something has been heard, the point at issue is whether hospitals may use their free moneys to supplement salaries Some hospitals have sought permission to supplement certain salaries out of their free moneys, honestly believing that such a course would be in the public interest, but this permission has been refused, no doubt because the Ministry foresees a chaotic state of affairs and is apprehensive of wholesale evasion of the centrally regulated salary scales Nettled by this refusal, relying on the undoubted general intention of the Act that hospitals should be encouraged to accept real responsibility for their own affairs, and conscious of the extent to which they themselves control public moneys, some hospitals have paid, or continued to pay, the excess out of public funds It seems a pity that no compromise has been found possible, and for our part we should feel happier if we knew from the Ministry whether any via media has been seriously considered For example, where a hospital can find the money to do so, might it not be allowed to supplement the salaries of certain senior officers by a sum not exceeding such and such per cent of their salaries —subject, if necessary, to the Ministry's explicit approval in the particular circumstances, and also perhaps subject to compliance with certain known conditions, of which length of service with the hospital might be one ? Would it not be very much in the general interest to allow this degree of discretion to the employing authority, so that a man would feel some sort of debt to his board and the board in turn enjoy a slight, but valuable, hold over its servant ?

As matters stand—or will stand if the threatened regulation is made—the hospitals will be brought into line with the Civil Service This solution should not, we think, be tamely accepted The analogy with the Civil Service is far from complete, indeed, it is little more than superficial The individual hospital authorities are not branches of a Department, but separate units with power to appoint and dismiss, and the status of their officers is quite unlike that of a Civil Servant who is promoted from one post to another throughout his career There are other branches of the public service where rates are centrally negotiated—as for example the recently published scales for chief officers of local authorities—where a real and important discretion is allowed to the local unit In that field it has obviously been thought important not to destroy by uniformity the element of dependence of the officer on the good opinion of his authority, with all the incentive that is involved therein. In the hospital world very similar circumstances apply, and some sort of inquiry into the principles involved is desirable before the matter is settled We are, or should be, concerned not so much with avoiding trouble today as with devising a plan which will make for the excellence of the service tomorrow

---

[1] Report of the Comptroller and Auditor General on National Health Service Accounts H M Stationery Office Pp 37 1s 3*d*

The Influenza Virus

"I could be bounded in a nut shell, and count myself a king of infinite space"

Sir **Macfarlane Burnet** takes Hamlet's words for his text in the Herter lectures for 1950[1] His theme is Some Biological Implications of Studies on Influenza Viruses, and he attempts to show how the detailed study of a nutshell can provide us with knowledge of infinite space—not a simple task in this expanding universe

The first lecture describes the process of infection by influenza viruses Understanding of the initiation of influenza infection is due in large part to the work of **Hirst** in America and of **Burnet** and his colleagues in Australia **Hirst**[2] noticed that when allantoic fluid from chick embryos infected with influenza virus was mixed with chick blood, the red cells became agglutinated He was quick to appreciate that this would provide not only a most valuable laboratory technique for measuring the concentration of influenza virus and antibody, but also a model, suitable for study in test-tubes, of the method which the influenza virus adopts in order to enter respiratory cells **Burnet** describes how the Australian workers started with the red-cell model and then adapted their results to the study of the early processes of infection in the fertile egg and the mouse Largely as a result of this work, the "receptor substance" on red cells to which the virus adheres has been shown to be a mucopolysaccharide An enzyme from *Vibrio cholerae* filtrates, usually known as R D E (the receptor-destroying enzyme), can inactivate the receptor substance on red cells so that influenza viruses can no longer be adsorbed **Stone**[3] has shown that R D E will also prevent the adsorption of influenza virus to the cells lining the allantoic cavity and the respiratory tract of the mouse In these sites, R.D E can therefore prevent influenza infection from making a start Once the virus has entered the cells, however, it is no longer susceptible to attack by agents of this type, so let us leave the nutshell and join **Burnet** in his attack on the kernel.

The second lecture deals with reproduction and variation in influenza viruses, and the lecturer adopts a genetic approach to the problem of how the influenza virus multiplies. Recent work on bacterial virus genetics has introduced the disciplines of mathematics into what was once considered a biological field. But the application of similar techniques to animal virus genetics meets with many difficulties. It is comparatively simple nowadays to study the behaviour of a single bacterium infected with a single bacteriophage particle, but it is not yet possible to examine isolated animal cells in this way. This has not deterred BURNET from tackling the problems of virus genetics, and he summarises the results of recent investigations for us. Details of the work have lately been published.[4] Of great interest is the demonstration of combination of characters of two similar viruses—a sort of hybridisation. Two strains of influenza virus were injected together into mice intracerebrally—e.g., strain NWS which has neurotropic properties and MEL which is non-neurotropic. Under certain conditions it was possible to isolate virus with the neurotropic properties of NWS and the serological characters of MEL. Control experiments failed to show that MEL produced neurotropic variants spontaneously. One possible explanation is that the phenomenon is analogous to the transformation of serological types of pneumococci. Recently it has been shown that a desoxyribonucleic acid fraction, isolated from type 3 pneumococci, is capable of conferring type 3 specificity on a pneumococcus of another type. The new hereditary characters are then maintained in the absence of further added desoxyribonucleic acid. A second possibility which BURNET favours, is the hypothesis advanced in order to explain recombination of virus characters in bacteriophages. It is suggested that the influenza virus particle, on entering the infected cell, breaks up into a number of discrete genetic units, that these replicate independently, and that towards the end of the period of multiplication they recombine to form complete virus particles. Such a hypothesis proposes a basically different method of multiplication of viruses from that of bacteria and higher organisms, and has evolutionary implications of the greatest interest. It is clear that important developments in virus genetics are to be expected in the near future.

---

[1] Burnet F M. *Bull. Johns Hopk Hosp* 1951 88 119

[2] Hirst, G K *Science*, 1941 94 22

[3] Stone J D *Aust J exp Biol Med Sci* 1948, 26 49

The third lecture is concerned with the ecological approach to virus diseases—what might be called a virocentric point of view. How does the virus survive in nature? One of our main methods of defence against virus infections is the production of specific antibody. Those viruses whose primary point of attack is in the respiratory tract—e.g., influenza and the common cold—have found a weak spot in our defences, where specific antibody is not readily available to meet them; poliomyelitis may come into the same category. Infection does not produce a life-long immunity to these successful viruses, and it is not a coincidence, therefore, that these diseases are among the most troublesome of the infections of today.

BURNET concludes with the suggestion that the academic study of viruses can furnish an approach to many of the fundamental problems of biology. Like the biochemist, he feels that living matter is made of fairly uniform bricks, and that information obtained from the careful study of one brick will be found to apply to the other bricks of the building. This is a question which only the experimentalist can decide, for theories are but the shadow, and facts the substance, of the scientist's daily life.

Dietary Treatment of Laennec's Cirrhosis

THE usual methods of controlling ascites in patients with cirrhosis of the liver—repeated paracenteses and the injection of mercurial diuretics—have proved unsatisfactory. Drawing off the ascitic fluid depletes the body of protein and aggravates the inanition commonly present in cirrhosis patients. The mercurial diuretics, on the other hand, when given alone often do not mobilise water from the peritoneal cavity. In combination, the two procedures can be extremely dangerous, for they may precipitate acute depletion of electrolytes and death from the "low-salt syndrome." Our ideas about treatment need revision in the light of the newer knowledge of the pathology of ascites in cirrhosis.

The classical concept that the ascites results from portal hypertension and hypo-albuminæmia is certainly not wholly true and may even be wholly false. Raising the low serum albumin levels to normal by infusions of human serum albumin is usually ineffective in these patients, and may sometimes make the ascites worse. It has been shown that albumin infused into the blood-stream may pass into the patient's swollen peritoneal cavity, where, by osmosis, the albumin will bind the water and salt it has carried from the blood-stream. This passage of albumin, salt, and water from the circulation to the peritoneal cavity will produce a rapid and distressing increase in the amount of ascitic fluid. As for portal hypertension, reducing the pressure in the portal vein to a normal level, by means of portacaval or splenorenal venous shunts, cannot be relied on to relieve the ascites. Some patients have had successful shunts made for indications other than ascites—such as hæmorrhage from œsophageal varices—and these patients have later developed ascites although their portal pressure was within normal limits.

The primary factor in the genesis of ascites in cirrhosis may be a disturbance in the patient's sodium metabolism. In 1948, FARNSWORTH[1] noted that in cirrhotics with ascites or œdema the urinary excretion of sodium was abnormally low, and this observation has since been confirmed many times. EISENMENGER et al.[2] demonstrated that these cases also excrete an abnormally small amount of sodium in their sweat and saliva, though their fæcal excretion is normal. At Yale, GOODYER and colleagues[3] have demonstrated with salt-and-water loading tests and renal clearance estimations that in cirrhotics dietary sodium is retained as a result of increased renal tubular reabsorption. These various disturbances in the sodium metabolism are probably associated with overactivity of "11-desoxycorticosterone-like" hormones, and both EISENMENGER et al.[4] and KARK[5] have found an abnormally high urinary excretion of cortical hormone in cases of cirrhosis with ascites. The cause may be in a failure of the liver to detoxify the mineral retaining adrenal hormones of the blood stream or in excessive secretion by the adrenals In any case the disturbances in sodium and adrenal metabolism provide, at last, a rational basis for the use of low-sodium and high-protein diets in the management of cirrhotic patients with ascites, whose tissues are notoriously depleted of protoplasm The results obtained by **Eisenmenger** et al ,[5] **Ricketts**,[6] and **Kark**,[7] leave no doubt that this regimen is an advance over previous treatments

---

[4] Burnet F M Lind P E J gen Microbiol 1951 5 59

[1] Farnsworth, E B Krakusin J S J Lab clin Med 1948, 33 1534

[2] Eisenmenger W Blondheim S Bongiovanni, A Kunkel, H J clin Invest 1950 29 1491

[3] Goodyer A V N Relman A S Lawrason F D Epstein F H Ibid p 973

[4] Bongiovanni A Eisenmenger W Proceedings of the Second A.C.T.H. Clinical Conference 1951 Philadelphia.

[5] Kark R M Ibid

In practice, diets high in protein and low in sodium are difficult to plan without using specially prepared protein or amino-acid supplements from which the sodium has been removed by dialysis or otherwise **Kark**'s paper should be consulted for details of management, diets, recipes, and low sodium food supplements Before long, however, it should be possible to discard the present rigid sodium restriction and allow the patient fairly normal food, merely following each meal with a dose of the appropriate kation exchange resin, which will remove sodium in exchange for hydrochloric acid during its passage down the bowel

Medicine and Society

THE measure of the statesman is the gap left by his going The chairman and the two principal medical speakers at a discussion on social medicine held by the section of epidemiology and State medicine of the Royal Society of Medicine on April 20 referred to the debt of inspiration which they owed to the late Prof **John Ryle** To **Ryle** social medicine meant the application of medicine to man in society with a view to understanding and alleviating his health problems, and not merely to removing or relieving a present disorder A wide concept of this kind holds within it various elements for study An interest in ætiology draws attention to the interactions between man and his environment which influence his mental and physical health Diagnosis requires measurement of important manifestations of health and disease as they appear in different groups of the community Rational treatment involves not only the development of social policies to meet needs which have been carefully measured, but also the study of individual and group attitudes to these policies, and measurement of their effects once they have been introduced The elements are easy to state but less easy to practise The neat order of the laboratory experiment is not readily paralleled in a complex social environment Ethical considerations may forbid controlled studies , and emotion and expediency may colour policy, almost unknown to its proponents Policies adopted to meet a certain set of circumstances are apt to roll on through decades without any careful estimation of what they have achieved or of how they should be modified to meet new needs The challenge is there and opportunity is not lacking There is advantage in the present situation where the National Health Service has set us all by the ears More and more doctors are brought daily to ponder on social policies as they relate to health , and the politicians, now closely concerned with social welfare, need advice in dealing with anticipated health problems Moreover the new administrative machine, if fully used, can provide invaluable data, not only for assessing its own efficiency, but also for basic studies of our people's well-being

It was a happy thought that brought together a politician, a general practitioner, and a medical officer of health at the meeting of the Royal Society of Medicine Mr **Arthur Blenkinsop**, parliamentary secretary to the Ministry of Health, pointed out the need he feels for guidance through the study of major social changes and the problems they will involve The politician must, for instance, prepare to deal with an ageing population , and unless he is helped by those aware of the requirements of the elderly he may frame policies from expediency rather than with an eye to the true interests of the people Twenty years ago, because economic necessity appeared to demand it, early retirement was glibly recommended as a double blessing to solve unemployment and confer leisure on the elderly Today economic pressure impels us in the opposite direction, and equally glibly we assert that the solution lies in extending the working life of the ageing and so conferring on them the boon of prolonged usefulness There is a danger that slogans on health may become instruments of casuistry unless we base claims on evidence rather than impression , and this evidence should come from the researches of academic social medicine If it is true that men benefit by a prolonged working life, then it may be necessary to plan for change of employment rather than retirement But what is the best age at which to make the change ? We may be too late if we wait until the traditional time of retirement Mr **Blenkinsop** set us other questions over which the policy-maker needs guidance for example, the impact of the stress of contemporary life on mental health, and the hazards to this country from the rapidity of air travel (As to the speed of air travel, he suggested that enlightened self-interest might force us to develop a more moral attitude to the health of less privileged countries) He saw danger in the prevalent popular belief that a solution to all social problems may be expected from the wonders of science rather than from pursuing the harder road of social adjustment Dr G O **Barber**, too, appealed for help from the exponents of social medicine , but he appealed as a general practitioner, and therefore a field-worker dealing from day to day with problems which are raw material for its studies As Dr **Barber** remarked, the general practitioner holds the data of morbidity research in his hands he has first impressions of changing stresses on health, but he must look to the professors for guidance on how to ask his questions and order his material, and on how to process this when it has been collected Dr **Greenwood Wilson**, medical officer of health for Cardiff, described steps he has taken to meet medicosocial needs as a result of suggestions from Professor **Ryle** In Cardiff they experimented first with a service of aftercare for diabetic patients This is provided by specialist health visitors who bridge the gap between hospital and home by maintaining contact with both , and that this experiment has succeeded is suggested by the falling proportion of cases readmitted in coma Aftercare services have been developed for peptic ulcer, pædiatric, and asthma cases , and plans are under way for a similar service in mental health virus multiplies Recent work on bacterial virus genetics has introduced the disciplines of mathematics into what was once considered a biological field But the application of similar techniques to animal virus genetics meets with many difficulties It is comparatively simple nowadays to study the behaviour of a single bacterium infected with a single bacteriophage particle, but it is not yet possible to examine isolated animal cells in this way This has not deterred BURNET from tackling the problems of virus genetics, and he summarises the results of recent investigations for us Details of the work have lately been published [4] Of great interest is the demonstration of combination of characters of two similar viruses—a sort of hybridisation Two strains of influenza virus were injected together into mice intracerebrally—e g , strain NWS which has neurotropic properties and MEL which is non neurotropic Under certain conditions it was possible to isolate virus with the neurotropic properties of NWS and the serological characters of MEL Control experiments failed to show that MEL produced neurotropic variants spontaneously One possible explanation is that the phenomenon is analogous to the transformation of serological types of pneumococci Recently it has been shown that a desoxyribonucleic acid fraction, isolated from type 3 pneumococci, is capable of conferring type 3 specificity on a pneumococcus of another type The new hereditary characters are then maintained in the absence of further added desoxyribonucleic acid A second possibility which BURNET favours, is the hypothesis advanced in order to explain recombination of virus characters in bacteriophages It is suggested that the influenza virus particle, on entering the infected cell, breaks up into a number of discrete genetic units, that these replicate independently, and that towards the end of the period of multiplication they recombine to form complete virus particles Such a hypothesis proposes a basically different method of multiplication of viruses from that of bacteria and higher organisms, and has evolutionary implications of the greatest interest It is clear that important developments in virus genetics are to be expected in the near future

---

[6] Ricketts W *Ann intern Med* 1951 33 37
[7] Kark R M *Med Clin N Amer* 1951 35 73

The third lecture is concerned with the ecological approach to virus diseases—what might be called a virocentric point of view How does the virus survive in nature ? One of our main methods of defence against virus infections is the production of specific antibody Those viruses whose primary point of attack is in the respiratory tract—e g , influenza and the common cold—have found a weak spot in our defences, where specific antibody is not readily available to meet them , poliomyelitis may come into the same category Infection does not produce a life long immunity to these successful viruses, and it is not a coincidence, therefore, that these diseases are among the most troublesome of the infections of today

BURNET concludes with the suggestion that the academic study of viruses can furnish an approach to many of the fundamental problems of biology Like the biochemist, he feels that living matter is made of fairly uniform bricks, and that information obtained from the careful study of one brick will be found to apply to the other bricks of the building This is a question which only the experimentalist can decide, for theories are but the shadow, and facts the substance, of the scientist's daily life

Dietary Treatment of Laennec's Cirrhosis

THE usual methods of controlling ascites in patients with cirrhosis of the liver—repeated paracenteses and the injection of mercurial diuretics—have proved unsatisfactory Drawing off the ascitic fluid depletes the body of protein and aggravates the inanition commonly present in cirrhosis patients The mercurial diuretics, on the other hand, when given alone often do not mobilise water from the peritoneal cavity In combination, the two procedures can be extremely dangerous, for they may precipitate acute depletion of electrolytes and death from the " low salt syndrome " Our ideas about treatment need revision in the light of the newer knowledge of the pathology of ascites in cirrhosis

The classical concept that the ascites results from portal hypertension and hypo albuminæmia is certainly not wholly true and may even be wholly false Raising the low serum albumin levels to normal by infusions of human serum albumin is usually ineffective in these patients, and may sometimes make the ascites worse It has been shown that albumin infused into the blood stream may pass into the patient's swollen peritoneal cavity, where, by osmosis, the albumin will bind the water and salt it has carried from the blood stream This passage of albumin, salt, and water from the circulation to the peritoneal cavity will produce a rapid and distressing increase in the amount of ascitic fluid As for portal hypertension, reducing the pressure in the portal vein to a normal level, by means of portacaval or splenorenal venous shunts, cannot be relied on to relieve the ascites Some patients have had successful shunts made for indications other than ascites—such as hæmorrhage from œsophageal varices—and these patients have later developed ascites although their portal pressure was within normal limits

The primary factor in the genesis of ascites in cirrhosis may be a disturbance in the patient's sodium metabolism In 1948, FARNSWORTH [1] noted that in cirrhotics with ascites or œdema the urinary excretion of sodium was abnormally low, and this observation has since been confirmed many times EISENMENGER et al [2] demonstrated that these cases also excrete an abnormally small amount of sodium in their sweat and saliva, though their fæcal excretion is normal At Yale, GOODYER and colleagues [3] have demonstrated with salt-and-water loading tests and renal clearance estimations that in cirrhotics dietary sodium is retained as a result of increased renal tubular reabsorption These various disturbances in the sodium metabolism are probably associated with overactivity of " 11-desoxycorticosterone like " hormones, and both EISENMENGER et al [4] and KARK [5] have found an abnormally high urinary excretion of cortical hormone in cases of cirrhosis with ascites The cause may be place for the higher grade child; and when children under 2 years of age are certified as "ineducable" before they have had an opportunity to be educated, it is no wonder that some institutional waiting lists are distressingly long.

---

[4] Burnet F M Lind P E J *gen Microbiol* 1951 5 59

[1] Farnsworth E B Krakusin J S *J Lab clin Med* 1948 33 1534

[2] Eisenmenger W Blondheim S Bongiovanni A Kunkel, H *J clin Invest* 1950 29 1491

[3] Goodyer A V N Relman A S Lawrason F D Epstein F H *Ibid* p 973

[4] Bongiovanni A Eisenmenger W *Proceedings of the Second* A.C.T.H. Clinical Conference 1951 Philadelphia

[5] Kark R M *Ibid*

Many of those dealing with adult defectives have a static conception of mental deficiency. Social conditions have changed so much in the last 20 years that our standards of what the defective can do and cannot do in society must be radically revised. Social security legislation, National Assistance, the disabled persons register, and the abolition of mass unemployment have all greatly altered the problems with which the defective in the community has to cope. Often patients who have spent many years in an institution can be returned to the community to earn their living under the friendly supervision of welfare workers, and many institutions are arranging for them to do this. The Board of Control have wisely encouraged this development, but some institutions are not yet taking full advantage of the changed situation.

The following charges have been made by the National Council for Civil Liberties and given wide publicity: that wrongful certification and detention exist today; that the legal safeguards, which should protect the rights of the individual, are not, in some cases, being applied; that the type of testing used is not adequate to distinguish between temporary educational backwardness and permanent deficiency; that the law is being applied in a far from humane manner; that the use of patient labour creates a vested interest, so that many are detained as useful workers and employed at substandard rates of pay; and that the law itself needs complete revision. These allegations should be thoroughly investigated, and evidence taken from both sides. Misconceptions can then be corrected, and if changes are needed they can be made boldly, with the coöperation of the whole service.

FLUORESCENCE IN GYNÆCOLOGY

THE changes occurring in the vulval skin in health and disease are far from being fully understood, and some useful information may emerge from the studies of Benson and his colleagues[1] in San Francisco or from developments of their technique. This method is based on fluorescence—the property of converting ultraviolet or other radiations with wave-lengths shorter than the blue violet of the visible spectrum into visible light, the advertising potentialities of which are being rapidly explored in England though the fluorescent materials for the poster paints now enlivening the London hoardings are, we understand, all imported from the U.S.A. In medicine fluorescence is no new tool. For many years dermatologists have examined possible cases of ringworm of the scalp under light from a mercury-vapour lamp filtered through Wood's glass, which contains oxide of nickel and transmits very little light outside the ultraviolet range (3600–3300 Å). Healthy hair and skin fluoresce very slightly under this irradiation—looking in the darkroom as if they had been lightly dusted with flour—but the finger nails glow more brightly, and hairs infected with the small spored ringworm give off a brilliant green light for as long as the ultraviolet lamp is turned on them. (If they continued to glow after it was switched off they would be called phosphorescent.)

The vulva is viewed by ultraviolet light that has passed through a complex system of filters. The fluorescent colours seen range from yellow before puberty, through green, to the light-purple of the reproductive period and the deep purple of advanced pregnancy, which soon fades after delivery or if pregnancy is previously terminated. At the menopause the vulva fittingly turns an autumnal brown. These appearances seem to reflect the activity or otherwise of the ovarian hormones. In bleeding states the vulva fluoresces bright red or orange, through the action of porphyrins formed from the decomposition of hæmoglobin which the day's ablutions have not removed. A similar fluorescence due to porphyrins is observed on the tongue[2] in healthy young people and tends to disappear in pernicious anæmia, sprue, vitamin-B deficiencies, and old age; the porphyrins are formed by bacteria and disappear with local applications of antibiotics.

The remarkable colour-changes on the vulva have yet to be explained. It would be interesting to know whether they show any correlation with variations in vascularity demonstrable by infra-red photography, which have been studied in the case of the breasts in pregnancy.[3] Fluorescence of the vulva is unlikely to rival the existing tests for pregnancy, either in accuracy or in consideration for the patient's feelings; and as an indication of missed abortion or intra-uterine fœtal death it is not likely to be taken very seriously. But there is a group of conditions in which the results would be worth studying—those atrophies of the vulva, loosely termed chronic atrophic leukoplakic vulvitis, leukoplakic kraurosis, and the like, whose ætiology, pathology, and hormonic underlay, if any, are still undecided.

HERPANGINA

LESIONS on the mucosa of the mouth and throat are common in many infectious diseases; but, apart from glandular fever and the primary stomatitis of herpes simplex, we know little about the viruses causing sore throat. In 1920 Zahorsky described several cases of an illness that did not fit the pattern of any of the usual bacterial infections, and four years later[4] he suggested that it should be called "herpangina." The name is confusing, for it seems pretty certain that the condition has nothing to do with either herpes simplex or zoster. Similar outbreaks were later described by Levine et al.[5] and Breese,[6] who thought they might possibly be of herpetic origin. Lately Huebner et al.[7] have gone far to establish herpangina as a separate and specific infection, commonly seen in the neighbourhood of Washington, D.C. Last summer the five-year-old daughter of a doctor was taken suddenly ill with fever, headache, and abdominal pain, and when she complained of sore throat her father saw many small ulcers on the anterior pillar of her fauces. Two days later the child was well again; but in the next fortnight 5 of her playmates developed a similar illness, with small punched-out ulcers, having a greyish base and surrounded by a reddened areola, on the fauces, soft or hard palate, and occasionally the tongue. The lesions were not painful and there was no œdema, though one child's ulcers were over 5 mm. in diameter, and persisted for a week. All the children were afebrile within three days. No growth was obtained from the throat swabs taken in 4 of the cases; and if there had not been an epidemiological team working in the area the small outbreak would have joined the thousands of other unexplained outbreaks in the lumber-room of clinical experience. As it was, the throat swabs were examined for viruses, and from 3 of the patients an organism related to group A Coxsackie virus was recovered; it was also recovered from the fæces of all 6 cases, though it had not been present a month before. The virus was shown to be present in the fæces in large amounts in the acute stage of the illness, in decreasing amounts during convalescence, and not at all a month

---

[1] Benson, R. C., Strait, L. A., Chappell, L. C. *Surg. Gynec. Obstet.* 1951, 92, 14.

[2] Tomaszewski, W. *Brit. med. J.* Jan. 20, 1951, p. 117.

[3] Bowes, K., Riterband, S. H., Andrews, J. E. *J. Obstet. Gynæc.* 1948, 55, 285.

[4] Zahorsky, J. *Arch. Pediat.* 1924, 41, 181.

[5] Levine, H. D., Hoerr, S. O., Allanson, J. C. *J. Amer. med. Ass.* 1939, 112, 2020.

[6] Breese, B. B. *Amer. J. Dis. Child.* 1941, 61, 669.

[7] Huebner, R. J., Cole, R. M., Beeman, E. A., Bell, J. A., Peers, J. H. *J. Amer. med. Ass.* 1951, 145, 628.

The chairman, Dr W H **Bradley**, reminded us of an exhortation by Johann Peter Frank over a century and a half ago

> "Let the Government expel from our province the people's misery, most powerful mother of diseases! Then the wife's fertile womb will produce strong and numerous children The fields cultivated by sinewy arms will thrive The diseases will return to the cities that are rotten with debauchery Joy, virtue, patriotism and the former health of the citizens, secured by labour will be restored "[1]

When this phrase was first uttered, strong words had to be used and little governmental action could be expected Today the danger lies not in lack of action but in action misdirected from lack of knowledge The discussion showed that policy-makers and field-workers alike may appreciate this danger The door is open and help is invited Now it is for the experts of social medicine to respond

Annotations

BLOOD COLLECTION BY MACHINERY

Accustomed though we are to machines that calculate and remember and to the rest of cybernetics, it nevertheless comes as a shock to learn that a machine has been perfected that takes in blood and turns out separated red cells, white cells, gamma globulins, and plasma proteins, all without human handling Yet such, according to the *New York Times*,[2] is the achievement of Prof. Edwin J Cohn and his colleagues at Harvard This team has done notable work in the separation of blood fractions, and what they support must be taken seriously According to the *New York Times* correspondent, the whole processing takes place in a closed system which operates automatically from the donor's vein to the plastic containers for the various fractions All tubes, needles, and so on are either made of, or coated with, a non wettable material—presumably silicone or plastic As soon as possible the blood is passed over an exchange resin that removes the calcium and so obviates troubles from clotting A heat exchange unit then cools the blood, which passes on through a continuous centrifuge that separates cells and plasma The separated plasma is first passed over another exchange resin that removes prothrombin, then a trace of zinc glycine is added that causes precipitation of gamma globulins and fibrinogen, and these are removed by further centrifuging After this there remains a "stable plasma protein solution", the zinc is removed by passage over yet another exchange resin, and the solution is sterilised by "cathode rays" and passed to a final sterile container in which it is frozen and dried The red and white cells are collected into a "protein salt sugar" solution and are separated from one another by centrifuging at different speeds The machine is said to produce 4 pints of plasma an hour, and can presumably deal with 6–8 pints of blood an hour It is described as "portable," presumably meaning movable since it comprises three, if not four, centrifuges and a heat exchange unit among all the other gadgets, and this is probably a small scale pilot model since an output of 4 pints an hour is not very rewarding for all the trouble

We shall await with interest the full description of this remarkable machine, which might well enable the Minister of Health to dispense with much of the staff of the Blood Transfusion Service Meanwhile it is important to note the modern techniques employed in it, for they may well have applications elsewhere An unusual feature is the extensive use of ion exchange resins to remove unwanted substances like calcium and prothrombin, without the addition of chemicals, such as oxalate or barium salts, that would be harmful if they got into the final product, the use of resins obviates elaborate steps for subsequent removal of these chemicals This technique clearly has important applications in blood coagulation studies, especially as it is possible by suitable methods to elute, say, prothrombin that has been removed by a resin The days of oxalated blood may well be numbered, but relative costs will, we suspect be a determining factor Professor Cohn considers that his "stable plasma protein" preparation will replace the usual plasma preparations, and it should keep well It may be an advantage to have red cells separated, their value for transfusion depends on the composition of the "protein salt sugar" solution in which they are suspended

A NEW DEAL FOR DEFECTIVES

Mental deficiency, that usually placid backwater of psychiatry, has had its mud rudely stirred by a report issued by the National Council for Civil Liberties[1], the popular press has taken up the cause with the result that the public is disturbed and the medical and nursing professions self righteously indignant It is natural that those working in the mental deficiency service, which is virtually a law unto itself, should resent strongly the criticisms of a lay body, and probably their first reaction to this report will be to dismiss it as an unjust and exaggerated misrepresentation of the truth Nevertheless, the National Council for Civil Liberties, however sensational their prose style, have evidently gone into the question seriously, and the cases quoted—which they say are only a representative few out of 200 which have already been brought to their notice—are sufficiently disturbing to indicate that a full inquiry into the present administration of the mental deficiency services would not be amiss Many professional and other associations and committees have recently discussed bringing the Mental Deficiency Act up to date, and the ferment produced by this report may activate new ideas

The provisions of the Mental Deficiency Act have continued, with only minor amendments as to definitions, since it was passed in 1913 Nothing corresponding to the Mental Treatment Act, 1930, with its revolutionary concept of the voluntary patient has been incorporated into the Mental Deficiency Act The nearest approach is in section 3, whereby a patient may be "placed" in a mental deficiency institution by his parent without a magistrate's order, but for some obscure reason he is seen by two justices and recertified in the ordinary way at the end of the first year Even during the first year the parent cannot withdraw his child without the permission of the Board of Control The position of the child thus bears no resemblance to the position of the voluntary patient

Because all adult defectives were once children, it is particularly important that "borderline" defective children should not be certified too early Our schools for the educationally subnormal have places for only 15,000 pupils, though they are expected to cater for our 28,000 educationally subnormal children In other words, insufficient educational facilities are being provided for this type of child, and some of them are inevitably reported as ineducable If their home conditions are bad they may then be certified as mental defectives and ordered to a mental deficiency institution Under present conditions of overcrowding this may not be the best

---

[1] The people s misery mother of diseases An address delivered in 1790 by Johann Peter Frank. Translated from the Latin with an introduction by H E Sigerist *Bull Hist Med* 1941 9 100

[2] New York Times, April 17, 1951

[1] 50 000 Outside the Law an examination of the treatment of those certified as mental defectives. National Council for Civil Liberties, 16, Westbourne Grove London W 2 1s 3d

Special Articles

SINGLE ROOMS IN HOSPITAL

ESTIMATE OF THE MEDICAL NEED

J W D GOODALL
M D Edin, F R C P E
MEMBER OF TEAM INVESTIGATING FUNCTIONS AND DESIGN OF HOSPITALS (NUFFIELD PROVINCIAL HOSPITALS TRUST AND THE UNIVERSITY OF BRISTOL)

THE proportion of beds to be provided in single rooms within the ward unit has an important bearing on ward design Single rooms may be needed as an amenity, for privileged or paying patients, or on medical grounds This paper is concerned solely with the medical reasons for giving patients special accommodation

Studies of the present practice in hospitals do not give a clear indication of what proportion of beds should be in single rooms, or which patients should have them It is, I think, fair to say that at present the provision of single rooms is inadequate The large open ward, which is still the commonest type in this country, has usually one or two single rooms (or in some cases double rooms) attached to it These rooms are often used for convalescent patients of a different social class who would be ill at ease in a large ward, and it is quite common to find the single rooms occupied by sick members of the medical or nursing staff or their near relatives But this, of course, is by no means always the case, and many of the patients in single rooms are there on purely medical grounds For example, the hyperthyroid patient who is very nervous and sometimes irritable, the infectious patient or the patient suspected of infection, and in maternity hospitals the pre eclamptic

Single rooms are also occupied by "nuisance" cases—e g, patients suffering from lung abscess or gangrene of the lung, patients who shout or use foul language, and unsociable or quarrelsome patients, though these latter categories are rather rare In some instances the dying or seriously ill are removed from large wards to single rooms, but more often they are "screened off" in the open ward at a place convenient to the nursing staff for observation

If the above description of present practice in hospital wards is accepted, it will be evident that the claims of the doctor, the nurse, and the patient are all being considered in rather a haphazard way

Since most hospitals were built great advances have been made in medical knowledge We now know more of the causes of infections, and how to control or cure them Consequently, many more tuberculous patients and more infectious patients who would formerly have been sent to isolation hospitals are being treated in general hospitals, and they usually require single rooms or segregation in small wards In addition we have learnt that there are certain groups of patients who are particularly susceptible to infection—especially infants, patients suffering from burns, and those undergoing plastic operations—and they must be isolated

Thus there are overriding medical reasons for providing single rooms Naturally, in so far as segregation of patients increases the work of the nurses and makes observation of patients more difficult, the medical demands may have to be modified But it is essential to know what they are

CLASSIFYING THE REASONS

I began my investigation by asking a number of clinicians, drawn from all specialties, on what medical grounds they would place their patients in single rooms The reasons given by 24 specialists can be summarised under five headings

(a) Infective cases (patients liable to infect others)
(b) Infectable cases (patients particularly susceptible to infection)
(c) Dying and seriously ill cases
(d) Nuisance cases (patients likely to disturb others or be disturbed by others)
(e) Cases requiring special attention.

Each specialist was also asked to indicate the proportion of beds which he thought should be provided in the form of single rooms, and to state approximately how long a patient would be required to stay in a single room for each reason. Only a minority attempted such estimates, but a few were very definite Two superintendents of fever hospitals said that *all* infectious patients must have single rooms The specialist in the treatment of burns also required 100% single rooms for his patients, and the pædiatrician asked for single rooms for all babies from birth to two years of age Some surgeons wanted their patients to stay in single rooms for 24–48 hours after operation Other specialists estimated the proportion of single rooms required as between 2 and 20%

In order to obtain more precise information on this point I drew up a schedule of conditions warranting single room accommodation, based on the replies from the 24 specialists Each qualification for a single room was given a number, so that when records came to be made a number could be entered for each patient who qualified The 31 conditions fall into the five categories shown above, but it became apparent that patients requiring separate accommodation can also be divided into two main groups (1) those who have to be kept under close observation, and (2) those who require to be separated but who do not necessarily need constant supervision by the nursing staff Examples of the former, which I shall call type A, are dying or seriously ill patients, and cardiac patients needing peace and quiet, examples of the latter (type B) are patients suspected of infection and patients who are smelly or socially unpleasant The division is important from the ward planning point of view, since type A single rooms must be situated for easy observation, and therefore near the centre of the ward, whereas type B single rooms can if necessary be placed at the periphery of the ward

The schedule was as follows

	All dying cases
A	Dying cases
	Infective cases
B	Exanthemata chickenpox, &c
B	Tuberculosis all open cases all meningitis cases all cases receiving special treatment.
B	Venereal disease in infectious stage
B	Ringworm of scalp
B	Mastoid cases
B	Sinus infections.
B	All hare lips cleft palates and major skin losses
B	Suspected cases of infection (likely to infect others)
B	Other infections
	Seriously ill cases
A	Pre-eclamptic and eclamptic cases
A	Bacterial endocarditis
A	Other seriously ill cases
	Infectable cases
B	All burns, for whole period in hospital
A	All infants from birth to age of two years for whole period in hospital
B	Other infectable cases (particularly susceptible to infection)
	Nuisance cases
A	Nervous restless irritable patients—e g cerebral irritation and severe hyperthyroid
B	Smelly or otherwise unpleasant cases—e g lung abscess fistula in perineum offensive discharge
A	Cardiac cases needing peace and quiet
A	Severe vomiting
A	Post traumatic psychosis—e g, foul language indecent behaviour (mainly in association with head injuries and operations)
B	Other nuisance cases
	Cases requiring special attention
A	Eye cases with complications—e g pneumonia
A	Cases receiving special treatment—e g oxygen tent.
A	Postoperative cases (other than very minor operations), and all fenestration cases for 48 hours unless longer period thought necessary

successfully propagated in suckling mice, and in the convalescent sera of 4 of the human cases high levels of neutralising antibody were demonstrated against H_1 but not against other strains of virus

The epidemiologists soon established that doctors in the Washington area had seen many young children in the summer of 1950 with a mild uncomplicated fever and the typical vesicular or ulcerated lesions in the throat These might have been examples of herpetic, aphthous, or Vincent's stomatitis, so fæcal and other specimens were obtained from 31 of the cases and the virus of herpangina was isolated from 26 of them In suckling mice all the strains produced lesions which were indistinguishable from those caused by known strains of group A Coxsackie virus The immunological relationships of these viruses have yet to be worked out, but four H types (H_1–H_4) have already been differentiated by complement fixation and cross immunity tests Two previously known types of Coxsackie virus—group A type 2 and the High Point Texas type—have recently been isolated from more typical cases of herpangina, and this is probably only a beginning In the original epidemiological study the H virus was seldom recovered from people who were not known to have been in recent contact with cases of frank herpangina, and it was rare to find it in people with other illnesses Thus we have yet another disease to add to summer grippe, paralytic and non paralytic poliomyelitis, epidemic myalgia, and other conditions thought to be associated with the Coxsackie viruses In this diagnostic morass it is well to remember that some of the reports are of doubtful value, and that Dalldorf is cautious about the part these viruses play in causation Nevertheless, the experience and critical tests applied by Huebner et al strongly suggest that these viruses are intimately associated with herpangina, and this illness may well turn out to be the chief, if not the only, clinical manifestation of human infection with the A group of Coxsackie viruses

METHÆMOGLOBINÆMIA IN INFANCY

IN infants cyanosis is a common sign, and usually there is no difficulty in discovering its cause in the heart or lungs In the absence of cardiac or pulmonary disease, however, diagnosis is less easy, and the solution may be found by examining the blood for evidence of the abnormal pigments, methæmoglobin and sulphæmoglobin Simple inspection of the blood will reveal the characteristic chocolate colour of methæmoglobinæmia

The causes of methæmoglobinæmia can be grouped under the headings of toxic, hæmolytic, and idiopathic For several years pædiatricians have been intrigued by the toxic causes These are aniline derivatives, the sulphonamides, especially sulphapyridine and sulphanilamide, acetanilide, phenacetin, phenazone, methyl sulphonal and sulphonal, potassium chlorate, and the nitrites The newer sulphonamides do not cause methæmoglobinæmia, and there seems no reason to prescribe any of the other drugs to infants Roe[1] has reported a fatality from administration of bismuth subnitrite There are two main sources of accidental poisoning The first of these to be recognised was the aniline derivatives in ink used to mark napkins[2], and several outbreaks in maternity units have been traced to this cause[3] Prevention is secured by laundering all napkins before use The second source of accidental poisoning was brought to light in 1945 by Comly,[4] who first recognised methæmoglobinæmia in bottle fed babies under two months of age whose drinking water came from wells contaminated by nitrates Since then the con

Canada,[5] and in Belgium[6] Dr Ewing and Dr Mayon White[7] have described the first cases in England, a further case is reported in this issue by Dr Evel Jones Prevention of this well-water cyanosis is difficult but Krueger[8] has described two methods of removing nitrate from water by anion exchange resin Some rare causes of methæmoglobinæmia are mentioned by Dr Oppé in his article on p 1051

The reason why only infants under two months of age should develop methæmoglobinæmia is not clear Cornblath and Hartman[9] suggested that, owing to the gastric hypochlorhydria of infancy, the nitrate nitrite reducing organisms inhabit the upper as well as the lower bowel, and thus the area for reduction of nitrates and absorption of nitrites is greatly increased Lecks,[10] on the other hand, believes that the capacity of fœtal hæmoglobin to reduce methæmoglobin is less than that of adult hæmoglobin The poor excretory power of the infantile kidney, and a possible deficiency in ascorbic acid, have also been named as contributory causes. Toxic methæmoglobinæmia can be treated very effectively In experimental methæmoglobinæmia methylene-blue (methylthionine chloride) in a dosage of 1–2 mg per kg body weight intravenously will convert all the methæmoglobin into active hæmoglobin within forty five minutes[11] In man its use was introduced by Williams and Challis[12] and Steele and Spink[13] with equally satisfactory results. This forms the mainstay of treatment, although blood transfusion and oxygen therapy are valuable adjuvants. Ascorbic acid, which also reduces methæmoglobin, acts too slowly to be useful in acute poisoning[14]

Hæmolytic methæmoglobinæmia may be found in phenylhydrazine poisoning and in severe infections. Cyanosis with hæmoglobinuria and jaundice has been noted in outbreaks among neonates, and has been given the title Winckel's disease[15], but this is probably a manifestation of intense septicæmia and not a specific entity Idiopathic methæmoglobinæmia is rare and may exist only in a familial form, but Schwartz and Rector[16] could find no cause for their non familial cases. The familial group is well defined[17] Breakey et al.[18] have shown in two cases that the erythrocytes have an abnormally low capacity to reduce methæmoglobin in the presence of glucose and lactate, and that the activity of diaphorase I (co enzyme I) is deficient, thus proving the long suspected metabolic abnormality in the disease[19] In this condition cyanosis can be controlled by ascorbic acid in large doses or methylene blue by mouth.

The few tragedies due to methæmoglobinæmia in infancy could have been avoided if the diagnosis had been made and the simple treatment more widely known The recognition of "well water methæmoglobinæmia" in England should increase our awareness

Air Vice-Marshal J MACCONNELL KILPATRICK has been appointed director-general of Royal Air Force Medical Services in succession to Air Marshal Sir PHILIP LIVINGSTON, who retires on June 30

---

1 Roe H E *J Amer med Ass* 1933 101, 352
2 Rayner W *Brit med J* 1886 i 294
3 See annotation *Lancet* 1945 ii 503 Howarth B E *Ibid* April 28 1951 p 934 Etteldorf, J N *J Pediat* 1951 38 24
4 Comly H H *J Amer med Ass* 1945 129 112 See annotation *Lancet*, 1948 i, 956
5 Medovy H *Canad med Ass J* 1950 62 228
6 Ferrant M *J Pediat* 1946 29 585
7 Ewing M C Mayon White R M *Lancet*, April 28, 1951 p 931
8 Krueger G M *J Pediat* 1949, 35 482
9 Cornblath M Hartman S A F *Ibid* 1948, 33 431
10 Lecks H I *Amer J Dis Child* 1950 79 117
11 Wendel W B *J clin Invest* 1939, 18, 179
12 Williams J R Challis, F E *J Lab clin Med.* 1933 19, 166
13 Steele C W Spink W W *New Engl J Med* 1933 208 1159
14 Gibson Q. H *Biochem J* 1943, 37 615
15 Feldman W M *Brit J Child Dis* 1927 24 113
16 Schwartz A S Rector E J *Amer J Dis Child* 1940, 60 652
17 Bensley E H Rhea, L J Mills E S *Quart J Med* 1938 7 325 Deeny J Murdaik E T Rogan J J *Brit med J* 1943, i 721
18 Breakey V K St G, Gibson Q H Harrison D C *Lancet* April 28, 1951 p 935
19 Barcroft H Gibson, Q H Harrison D C McMurray, J *Clin Sci* 1945 5 145 King E J White J C Gilchrist M *J Path Bact* 1947 59 181

SUMMARY

A survey was undertaken to determine what proportion of beds in a ward should reasonably be provided in single rooms in order to satisfy the medical needs of the patient

After reference to a number of consultants, a list of 31 conditions qualifying patients for accommodation in single rooms was compiled

This schedule of conditions was used by housemen, in 29 wards of 8 general hospitals, to record each day over a period of a month whether the patients in the ward qualified for single rooms

An analysis of these records enabled conclusions to be drawn about the most desirable provision of single rooms For wards of sixteen beds these are

General medical wards	4 single rooms
General surgical wards	3 ,, ,,
Gynæcological wards	3 ,, ,,
Maternity wards	2 or 3 single rooms

For larger wards the proportion of single room beds to total beds would be somewhat less and for smaller wards it would be somewhat greater

I should like to thank the staff of the 8 hospitals who kept such painstaking records on their daily rounds, and Mr Bailey for his invaluable statistical work on analysing the records.

WINTER ADMISSIONS TO LONDON HOSPITALS

Work of the Emergency Bed Service, 1950-51

As is generally known, in the past winter great difficulty was experienced in London in the admission of acutely ill patients to hospital. These difficulties caused great hardship to patients as well as extra work for their doctors But it is not easy to turn these generalisations into facts and figures There are no figures to show the total number of urgent cases requiring admission to the London hospitals, though many of the hospitals keep a note of their own figures Thus the figures of the Emergency Bed Service (E.B S) seem to be the only ones covering greater London as a whole

The E.B S is an auxiliary service intended to help doctors who have made an unsuccessful direct application for the admission of a patient to the hospital of their choice What proportion of the acute cases in London are admitted through such direct applications by their doctors could only be discovered by putting a lot of extra work on hospital officials Random checks have shown that some hospitals admit three or four acute cases direct from doctors to every one admitted through the E.B S , in others the proportion is about equal, and on the average the ratio of direct to E.B.S seems to be about 2 1 But these proportions apply to total admissions, and it must be remembered that the doctor who cannot get his patient admitted direct can apply to the E.B S , who may be more fortunate , whereas if the E.B S fails to find a bed for a patient the failure is usually final. Thus, though only about a third of all the admissions are arranged through the E.B S , the service s failures represent a much larger proportion of the total—indeed, if all London doctors make a rule of trying the E.B S. before resigning themselves to keeping the patient at home then the E.B S failures will be the total failures in London. Broadly speaking, then, the E.B S experience will give a reasonably representative picture of the position in London

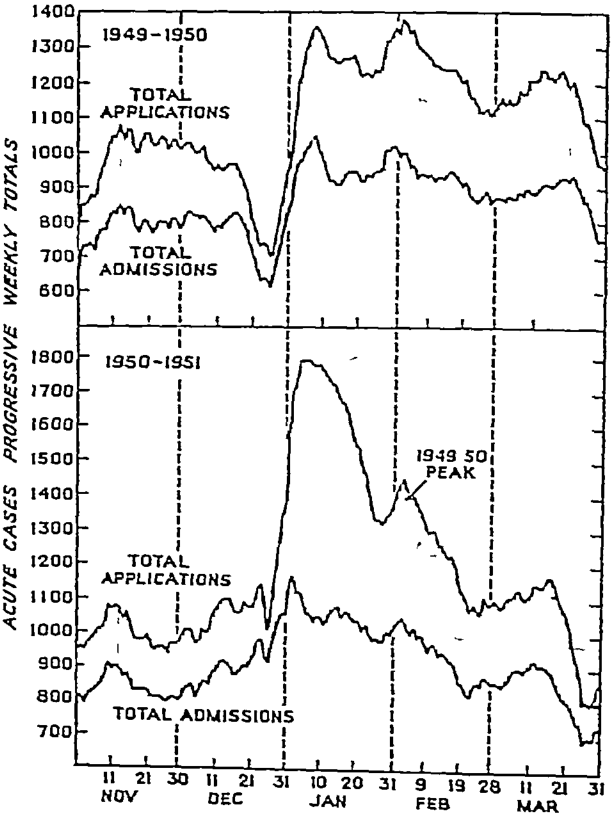
THE WINTER'S WORK

The work of the E.B S followed normal lines until Dec. 9, 1950, when, presumably owing to the influenza epidemic, it began to increase rapidly, instead of slackening, as is usual, before Christmas For the first time in the 13 years since the service started, Christmas Day, 1950, was a busy day, 106 applications being received for the admission of acute cases compared with 68 on Christmas Day, 1949 Thereafter the curve of applications rose steadily, as it always does after Christmas , and on Jan 1, 1951, the total reached its peak figure of 293—the highest number yet recorded on one day This exacerbation lasted for about 10 days, after which the demand began to fall steadily , even so, January's applications were 35% higher than the total for January, 1950

The accompanying chart shows that the admissions kept up fairly well with the applications until Christmas, but thereafter the admissions rapidly fell behind , for the whole of January the E.B S found a bed in only two thirds of the cases applying for admission In other words, one applicant out of every three could not get into hospital. For February and March the proportions of successful applications were 75 7% and 80 5% , and by the end of March the E B.S was once again working pretty well normally

What do these figures mean in actual cases ? At the worst time the failures amounted to 100 a day In January applications for admission were received for 7064 acute medical and surgical cases, of which 4632 were admitted and 2432 could not be placed Among the patients for whom beds could not be found were 247 whose applications were withdrawn, and these should not be counted among the failures Without them the month's daily average of failures was 70 5

If we assume that an application is received by the E.B S for 1 in every 3 urgent cases and that the remainder are all admitted direct—for otherwise the doctors will surely try the E.B S —then the total number of patients applying for admission to the London hospitals in January was three times the total E.B.S applications, or about 21,200 , all except the E.B S failures were admitted, so the failure rate for London as a whole can be estimated as 11 6% The E.B S served an area containing 200 hospitals, not counting fever hospitals



A	Epilepsy and all cases of ' fits
A	Shock cases having drip treatment
A	Cases in labour a long time with ruptured membranes
A	Failed forceps
A	Cases requiring constant supervision
A	Other cases requiring special attention'

THE SURVEY

In the main survey (undertaken after a preliminary pilot survey) residents in 8 hospitals cooperated by recording on their daily rounds those of their patients who qualified for a single room according to the schedule I had prepared Returns were made by residents in 29 wards over a period of at least a month There were 10 surgical wards, 10 medical, 4 gynæcological, 3 maternity, and 1 each of children, and of ear, nose, and throat patients The total number of beds covered was 1010

The records showed that, of the 31 possible reasons for wishing to place patients in single rooms, some were given much more often than others For example, patients often qualified for single rooms because their condition was smelly, infectious, or otherwise unpleasant Comparatively few needed separate accommodation because they had sinus infections, eclampsia, or eye complications This was to be expected, because most of the records were made in general hospitals and not in hospitals or wards for special diseases

It was found that the demand for separate accommodation fluctuated widely from day to day in all the wards, but except for two surgical wards, both in the same hospital, the types of demand for single rooms appeared to be roughly comparable within a given specialty Because of these considerable fluctuations in daily demand, a simple estimate of the *average* requirement fails to give a correct estimate of the number of rooms that should be provided The data therefore needed statistical analysis, and this was undertaken by Mr N T J Bailey, statistician to the Department of Medicine, University of Cambridge, with the results set out below

Because of the daily fluctuations in demand it is important to distinguish between how much of the demand can be met (efficiency of provision), and to what extent the single rooms available are occupied for their proper purpose (efficiency of utilisation) The former efficiency can be made very high only at the expense of the latter, and vice versa, for if enough single rooms are provided to cope with all requirements on "peak" days, many of them will not be used for their proper purposes on other days Mr Bailey found it possible to construct a simple mathematical model of the situation, from which the two efficiencies could be calculated in terms of ward size and the average chance of a patient selected at random requiring separate accommodation (approximately constant for a given specialty), for different numbers of single rooms provided The statistical theory employed takes account of the fact that data may be drawn from wards of different sizes, and it can be used to calculate tables, similar to those below, for wards of any size Results for 16 bed medical and surgical wards are shown in tables I and II From such tables the two efficiencies can be read off for different numbers of single rooms provided If a proper balance is to be struck between medical requirements and the necessity for economy of space—and finance—the hospital planners will choose that number of single rooms which gives the highest value for the efficiency of provision, consistent with a reasonably high value for the efficiency of utilisation

TABLE I—MEDICAL WARD, 16 BEDS BASED ON DATA FROM 10 WARDS

No of single rooms	Both types of single room		Type A rooms only	
	Efficiency of provision (%)	Efficiency of utilisation (%)	Efficiency of provision (%)	Efficiency of utilisation (%)
2	47	97	65	86
3	67	92	84	74
4	82	84	94	62
5	92	75	98	52
6	97	66		

Medical Ward

Table I shows that in a sixteen-bed medical ward four single rooms, three of type A and one of type B, should be able to deal with 84% of the type A requirement and 82% of the total requirement for single rooms These four single rooms would be appropriately occupied 84% of the whole time The three type A rooms would be used for type A cases only 74% of the time, but for some of the rest of the time they would obviously be employed to cope with excesses of type B patients

Surgical Wards

The data for 2 of the surgical wards (both in the same hospital) were so widely different from those from the other 8 that after careful consideration they were rejected as anomalous Table II is accordingly based on the data for the 8 only It shows that in a sixteen bed surgical ward, three single rooms, two suitable for type-A and one suitable for type B patients, should be able to deal with 84% of total requirements and with 76% of type A requirements This scale of provision, though satisfactory from the medical standpoint, will be somewhat wasteful of ward space since the rooms will be appropriately occupied only 74% of the time Similarly the two type A rooms would be used for type A patients only 73% of the time, though for the rest of the time they could, of course, be used for excesses of type B patients or for other purposes

TABLE II—*SURGICAL WARD, 16* BEDS BASED ON DATA FROM 8 WARDS

No of single rooms	Both types of single room		Type A rooms only	
	Efficiency of provision (%)	Efficiency of utilisation (%)	Efficiency of provision (%)	Efficiency of utilisation (%)
1	36	95	45	87
2	65	86	76	73
3	84	74	92	59
4	94	62	98	47
5	98	52		

Gynæcological Wards

Data were available from 4 wards and suggest a total of three single rooms out of sixteen, two for type A and one for type B patients This would satisfy 75% of the total demand and use 86% of the accommodation provided At the same time 80% of type A demand would be satisfied with a utilisation efficiency of 67% (Though this could be increased to 83% by having only one type A room, this would satisfy less than half the demand)

Maternity Wards

There were data from only 2 wards Two single rooms out of sixteen are probably the best provision, satisfying 71% of the demand and using 79% of the accommodation Some might prefer to use three rooms, satisfying 88% of the demand but using only 66% of the accommodation In either case, if we are to satisfy more than 66% of the type A demand two rooms would have to be of type A

Children's Wards

For this category data are available on only 1 ward and it would be unsafe to give more than a very tentative indication The total requirement is perhaps seven single rooms out of sixteen, of which two would be for type-A patients consistently outwits mere human opponents in an arithmetical game called Nim. Genetics is generously represented with large-scale translucent models of a unicellular organism in which movements of the chromosomes can be followed, and the ground is prepared for the introduction of the concept of mutations and their evolutionary significance. This theme is developed using drosophila as an illustration, but a much more striking example of a genetic variant is provided by a pair of waltzing mice who circle madly round their little arena while the normal mice next door doze peacefully. Genetics leads naturally to embryology, which lends itself well to explanation by models. In other corners are to be found exhibits to demonstrate the rôle of enzymes in the life cycle, the mechanism of the human and insect eye, and the appearance of common bacteria and viruses.

The descriptions of each exhibit are so worded as to be comprehensible to an uninitiated viewer, but simplification is surely overdone by such phrases as "The earthworm is simply a sac full of fluid." The display in general is influenced by the artists' impression of science rather than a scientist's impression of his own subject. Nevertheless this slightly unreal approach and several inadequacies in labelling and description do not seriously detract from the value of an exhibition which is so thoroughly in step with the times and which explains in simple ways such fundamental concepts.

Public Health

POTENCY OF VACCINE LYMPH

A. ANDERSON
M.D. Aberd., D.P.H., D.I.H.
DEPUTY CHIEF MEDICAL OFFICER, ANGLO-IRANIAN OIL COMPANY LTD, ABADAN, SOUTH PERSIA

THE calf lymph used in vaccination against smallpox quickly loses its potency under normal storage conditions, and in the tropics this loss is even quicker. The danger of using impotent vaccine is not only that the vaccination will not "take" but that it may produce an allergic papule indistinguishable from an immediate reaction.

At Abadan, a town of some 200,000 inhabitants near the head of the Persian gulf, about 30–60 cases of smallpox are recorded in non-epidemic years, and during the past nine years there have been two epidemic outbreaks—one in 1942–43 and the other in 1948. Despite every effort, a high level of immunisation cannot be maintained in the population because of the migration which goes on throughout most of the year. Thus when a major outbreak starts it is of the first importance to use vaccine of assured potency, and in the 1948 outbreak the method described below proved particularly effective.

The vaccine was sent by air from Great Britain, packed in ice in vacuum flasks. On arrival in Abadan it was taken immediately to a refrigeration room, where it was kept at a temperature of 14°F. (In winter the atmospheric temperature at Abadan may rise to about 120°F in the sun and 70°F in the shade.)

Small circular tins, about 10 in. in diameter and 5 in. deep were manufactured. In the centre of each tin was a circular compartment of the same depth with a diameter of about 1½ in. At the start of the working day the outer compartment was filled with a mixture of ice and salt, and into the central compartment were placed enough tubes of lymph for the number that the vaccinator could deal with in a single day. Strict instructions were issued that any vaccine which remained unused at the end of the day was to be destroyed, on no account was it to be used even on the following day.

With this technique some 85–90% of vaccinations "took." Judged by comparison with experience in the epidemic of 1942–43 when this method was not employed, it affords an improved hope of effective vaccination in tropical and subtropical countries.

The need for such a precaution is suggested by the following instances.

A driller, middle-aged, tough, and oft-vaccinated, said that he never "took", but the cold-stored vaccine, with which he was vaccinated as a routine after his three-yearly medical examination, produced an accelerated reaction which was as nearly primary as could be desired.

About the time of the 1942–43 outbreak, the American army set up a 500-bed hospital about twelve miles from Abadan and we formed a close liaison. One day we received an S.O.S., and found half of the hospital's professional staff suffering from modified smallpox. This unit had arrived a fortnight before, and coming from a northern State of the U.S.A. where smallpox is non-existent, its members had gathered round the first case of smallpox in the hospital. Anamnestic evidence made it clear that the *vaccinations of this unit before it embarked had not been successful*, although fortunately all its members had been successfully vaccinated in childhood. A seaman patient in the hospital and a paymaster, the former unvaccinated and the latter with an unsatisfactory vaccination history, both died of hæmorrhagic smallpox about the same time.

We know that repeated vaccination with *potent* vaccine is the means of preventing smallpox. Vaccination should be given the same publicity as the antidiphtheria campaign, and it should be pursued with vigour from infancy throughout the school years, otherwise there may soon exist in Great Britain a population continuously susceptible to outbreaks of a loathsome, disfiguring, and deadly disease, which can be prevented.

I wish to thank Dr. S. D. McClean, chief medical officer to the Anglo-Iranian Oil Company Ltd, for permission to publish this report.

Smallpox

Modified smallpox was diagnosed in a student from Calcutta who was disembarked at Marseilles from s.s. *Ranchi* on April 30. The *Ranchi* docked on May 8 in the Port of London. Warning letters are being sent to the medical officers of health for districts to which contacts are proceeding.

In an outbreak of smallpox at Tilburg, Holland, there had been altogether 29 cases up to the beginning of this week. There had also been 1 case at Utrecht and 1 case at Geldrop, which were contacts with the cases at Tilburg.

Statistics for Northern Ireland

In Northern Ireland during the year 1950 the infant and maternal mortality rates and the tuberculosis death-rate were the lowest ever recorded. The Registrar-General for Northern Ireland announces that the infant-mortality rate was 40 per 1000 live births, and the maternal mortality rate 1·2 per 1000 live births, compared with 45 and 1·4 in 1949. The death-rate from tuberculosis was 48 per 100,000 population.

Infectious Diseases in England and Wales

Disease	Week ended April			
	7	14	21	28*
Diphtheria	45	42	32	32
Dysentery	846	858	1002	871
Encephalitis				
Infective	4	1	1	3
Postinfectious	4	12	2	3
Food poisoning	69	142	44	71
Measles excluding rubella	28,829	22,656	19,025	18,008
Meningococcal infection	39	46	40	29
Ophthalmia neonatorum	34	44	41	45
Paratyphoid fever	27	13	12	4
Pneumonia, primary or influenzal	799	707	551	570
Poliomyelitis				
Paralytic	11	15	14	11
Non-paralytic	4	5	8	8
Puerperal pyrexia and fever	68	77	61	85
Scarlet fever	845	823	948	1034
Smallpox	—	—	—	—
Typhoid fever	8	6	4	4
Typhus fever	—	1†	—	—
Whooping-cough	4010	3335	3495	3643

* Not including late returns. † Not louse-borne. Imported case.

or highly specialised ones A daily average of 70 5 unsuccessful applications for admission suggests that enough extra beds to accommodate all the acute cases could be provided without laying an impossible burden on the hospitals

This may read like an attempt to explain away the winter's anxieties, but it was in fact a time of serious crisis, and the regional boards, whose agent the E B S is, took all the steps open to them to overcome it

THE FUTURE

Plans now being made on the basis of the winter's experience should go far to prevent the recurrence of such an emergency and enable the hospitals and their auxiliaries to deal with any unduly large number of applications for admission

It is clearly impracticable always to keep enough empty beds fully staffed and ready for the acute cases to meet major crises which only arise occasionally Even if it was possible, this would be an unjustifiable waste of personnel and material In an emergency, hospitals can usually increase their accommodation for acute cases by admitting fewer patients from their waiting lists and by other means

This winter, however, the position was complicated by the large number of nurses and other members of the hospitals' staffs who were incapacitated by influenza In future epidemics the same complication will almost certainly recur, and this must be taken into consideration when devising plans for the future

The scheme now being prepared is an adaptation of the air raid warning system of the late war The warning system will come into operation automatically when the pressure on the E B S mounts above a prearranged level When applications for admission reach the critical figure, a warning will be despatched to all the hospitals in the London area, this will be the signal for them to take whatever steps they consider necessary to clear beds for acute cases The scheme is intended to bring the full power of the hospitals to bear in a crisis, but there will be a corresponding system of all clear signals to ensure that the hospitals are not called on to continue their supreme effort when the immediate crisis is over

---

THE FESTIVAL EXHIBITIONS

MEDICAL SCIENCE DISPLAYED

ON May 3, the Festival of Britain was inaugurated by H M The King and on the following day the South Bank Exhibition opened its doors At last therefore there is an opportunity to judge this much criticised venture on its own merits, unclouded by controversy as to whether it ought ever to have been

THE SOUTH BANK

The first and most remarkable impression is the sense of space on this very restricted site Hemmed in by the River and York Road, by County Hall and Waterloo Bridge, the designers have achieved an astonishing amount of elbow room, and the great central concourse, with its flower beds, fountains, and trees is most unexpected The river terrace, on the inner bend of the river, commands the whole sweep from Westminster to St Paul's and is certainly a magnificent permanent accession to the beauties of London—a new "lung" of inestimable value from which the gay busy life of the river can be watched against a varied and fascinating skyline The architecture of the exhibition buildings is very modern, and of its kind excellent, with bold sweeping lines, clear bright colours, and skilful use of space Those who like such things will enjoy it, those who do not will hate it There are enough "modernistic" statues and frescoes to provide controversy for many a dinner table

The twenty pavilions set out to illustrate the contribution of Britain in many fields of science, engineering, and industry The way of life of the British people, their character and homes, their sport, recreations, and scenery, are all covered, and it is notable that the Official Guide lays much stress on the importance of all these to health Health however, has a pavilion to itself, under Waterloo Bridge, where the contributions of Britain to medical science and art are displayed and where the value of these contributions to the community and the individual are illustrated

At the entrance to the Health Pavilion is a section on "how the body works," illustrated by admirable working models of the circulation and respiration and of reflex action, and a less convincing one of the alimentary tract This leads on to nutrition and thus to "the preservation of health," the latter including public health, water, sewage, immunisation, and so on The contributions of medicine and surgery are next dealt with surgical instruments are well displayed and biological standards are also shown Blood transfusion is excellently handled, and then comes a section on anæsthesia A large wall painting of Florence Nightingale at Scutari, effective but somewhat imaginative, introduces a number of screens illustrating various aspects of nursing, and finally there is a remarkable section on plastic surgery This is likely to cause more controversy than all the rest of the pavilion put together Two excellent models demonstrating how burns and scalds can occur in children and old people lead on to a series of photographs, some in colour, illustrating the treatment of such burns—as well as the effects of inadequate treatment Punches are not pulled here, and it is questionable how far the propaganda effect in the preventing of burns will outweigh the protests of the squeamish Of the quality and sincerity of this section there can be no question—the photographs are brilliant —and it may well do much good

The Royal Festival Hall is perhaps the most exciting thing on the South Bank At the moment it looks rather incongruous—a huge solid mass among the flimsy exhibition structures—and it is too early to judge how its outside will look when completed and surrounded by parks and river walks But of its triumphant interior there can be only one opinion London once more has a concert hall where music can be properly heard in a comfort never previously experienced, and the planning of the promenades, restaurants, and foyers is spacious and dignified, giving really magnificent views of the river If nothing else had come out of the Festival of Britain this would have been worth while

SOUTH KENSINGTON

At the Festival Exhibition of Science, to be seen at the Science Museum, South Kensington, there is a sprinkling of medical demonstrations among the predominant ones illustrating the atomic age Indeed from the very entrance through a tortuous darkened tunnel, perhaps more suggestive of an approaching fun fair than a scientific exhibition, one is confronted with larger and larger scale models of the ultimate structure of graphite On emerging from the darkness the main exhibition hall is a dazzle of light coming from stereotyped structural formulæ constructed of electric bulbs, artificial lightning, and glowing cathode ray tubes This atomic approach merges easily with medicine in the description of the use of isotopes to measure the rate of replacement of plasma proteins and red cells and the use of isotopically labelled B_{12} for the study of its metabolism

Models illustrate the use of X ray diffraction in crystallography, and an imposing electronic brain consistently outwits mere human opponents in an arithmetical game called Nim. Genetics is generously represented with large scale translucent models of a unicellular organism in which movements of the chromosomes can be followed, and the ground is prepared for the introduction of the concept of mutations and their evolutionary significance. This theme is developed using drosophila as an illustration, but a much more striking example of a genetic variant is provided by a pair of waltzing mice who circle madly round their little arena while the normal mice next door doze peacefully. Genetics leads naturally to embryology, which lends itself well to explanation by models. In other corners are to be found exhibits to demonstrate the rôle of enzymes in the life cycle, the mechanism of the human and insect eye, and the appearance of common bacteria and viruses.

The descriptions of each exhibit are so worded as to be comprehensible to an uninitiated viewer, but simplification is surely overdone by such phrases as "The earthworm is simply a sac full of fluid." The display in general is influenced by the artists' impression of science rather than a scientist's impression of his own subject. Nevertheless this slightly unreal approach and several inadequacies in labelling and description do not seriously detract from the value of an exhibition which is so thoroughly in step with the times and which explains in simple ways such fundamental concepts.

Public Health

POTENCY OF VACCINE LYMPH

A. ANDERSON
M.D. Aberd., D.P.H., D.I.H.
DEPUTY CHIEF MEDICAL OFFICER, ANGLO IRANIAN OIL COMPANY LTD, ABADAN, SOUTH PERSIA

THE calf lymph used in vaccination against smallpox quickly loses its potency under normal storage conditions, and in the tropics this loss is even quicker. The danger of using impotent vaccine is not only that the vaccination will not "take" but that it may produce an allergic papule indistinguishable from an immediate reaction.

At Abadan, a town of some 200 000 inhabitants near the head of the Persian gulf, about 30–60 cases of smallpox are recorded in non epidemic years, and during the past nine years there have been two epidemic outbreaks—one in 1942–43 and the other in 1948. Despite every effort, a high level of immunisation cannot be maintained in the population because of the migration which goes on throughout most of the year. Thus when a major outbreak starts it is of the first importance to use vaccine of assured potency, and in the 1948 outbreak the method described below proved particularly effective.

The vaccine was sent by air from Great Britain, packed in ice in vacuum flasks. On arrival in Abadan it was taken immediately to a refrigeration room, where it was kept at a temperature of 14°F. (In winter the atmospheric temperature at Abadan may rise to about 120°F in the sun and 70°F in the shade.)

Small circular tins, about 10 in. in diameter and 5 in. deep were manufactured. In the centre of each tin was a circular compartment of the same depth with a diameter of about $1^1/_2$ in. At the start of the working day the outer compartment was filled with a mixture of ice and salt, and into the central compartment were placed enough tubes of lymph for the number that the vaccinator could deal with in a single day. Strict instructions were issued that any vaccine which remained unused at the end of the day was to be destroyed, on no account was it to be used even on the following day.

With this technique some 85–90% of vaccinations "took." Judged by comparison with experience in the epidemic of 1942–43, when this method was not employed, it affords an improved hope of effective vaccination in tropical and subtropical countries.

The need for such a precaution is suggested by the following instances.

A driller, middle aged, tough, and oft-vaccinated, said that he never "took", but the cold stored vaccine, with which he was vaccinated as a routine after his three yearly medical examination, produced an accelerated reaction which was as nearly primary as could be desired.

About the time of the 1942–43 outbreak, the American army set up a 500 bed hospital about twelve miles from Abadan, and we formed a close liaison. One day we received an S O S, and found half of the hospital's professional staff suffering from modified smallpox. This unit had arrived a fortnight before, and coming from a northern State of the U S A where smallpox is non existent, its members had gathered round the first case of smallpox in the hospital. Anamnestic evidence made it clear that the vaccinations of this unit before it embarked had not been successful although fortunately all its members had been successfully vaccinated in childhood. A seaman patient in the hospital and a paymaster the former unvaccinated and the latter with an unsatisfactory vaccination history, both died of hæmorrhagic smallpox about the same time.

We know that repeated vaccination with *potent* vaccine is the means of preventing smallpox. Vaccination should be given the same publicity as the antidiphtheria campaign, and it should be pursued with vigour from infancy throughout the school years, otherwise there may soon exist in Great Britain a population continuously susceptible to outbreaks of a loathsome, disfiguring, and deadly disease, which can be prevented.

I wish to thank Dr S D McClean, chief medical officer to the Anglo Iranian Oil Company Ltd, for permission to publish this report.

Smallpox

Modified smallpox was diagnosed in a student from Calcutta who was disembarked at Marseilles from s.s *Ranchi* on April 30. The *Ranchi* docked on May 8 in the Port of London. Warning letters are being sent to the medical officers of health for districts to which contacts are proceeding.

In an outbreak of smallpox at Tilburg, Holland, there had been altogether 29 cases up to the beginning of this week. There had also been 1 case at Utrecht and 1 case at Geldrop, which were contacts with the cases at Tilburg.

Statistics for Northern Ireland

In Northern Ireland during the year 1950 the infant and maternal mortality rates and the tuberculosis death-rate were the lowest ever recorded. The Registrar-General for Northern Ireland announces that the infant-mortality rate was 40 per 1000 live births, and the maternal mortality rate 1 2 per 1000 live births, compared with 45 and 1 4 in 1949. The death rate from tuberculosis was 48 per 100,000 population.

Infectious Diseases in England and Wales

Disease	Week ended April			
	7	14	21	28*
Diphtheria	48	42	32	32
Dysentery	846	858	1002	871
Encephalitis				
Infective	4	1	1	3
Postinfectious	4	12	2	3
Food poisoning	69	142	44	71
Measles excluding rubella	28 829	22 656	19 025	18 006
Meningococcal infection	39	46	40	29
Ophthalmia neonatorum	34	44	41	45
Paratyphoid fever	27	13	12	4
Pneumonia primary or influenzal	799	707	551	570
Poliomyelitis				
Paralytic	11	15	14	11
Non paralytic	4	5	8	8
Puerperal pyrexia and fever	68	77	61	85
Scarlet fever	845	823	948	1084
Smallpox	—	—	—	—
Typhoid fever	8	6	4	4
Typhus fever	—	1†	—	—
Whooping-cough	4010	3838	3498	3643

* Not including late returns † Not louse-borne imported case

In England Now

A Running Commentary by Peripatetic Correspondents

THE great physician patted my shoulder "My dear," he said kindly, "you are suffering from Housewife's Fatigue" Biting down a retort of "You're telling me!" or "Aren't we all!" and reminding myself once again that I would not be charged his usual fee, I thanked him prettily The examination had been very thorough He advised rest and massage I fancied he was going to suggest a folding of the hands in the South of France when he remembered my husband is a G P, so he offered me tea and biscuits instead

Massage gives one a lot of time to think, and I have occupied my sessions in wondering what research into this fatigue business would reveal The incidence in age-groups has been worked out at a local hospital, but I have seen no mention of the types of housewives afflicted or of how to recognise the onset What is the precipitating factor? Doctor's wives will, of course, realise something is wrong if they hear the telephone at dead of night when there has been no call or find themselves starting at bicycle-bells in the street, if even the most innocent of one's husband's victims in the waiting-room is seen to be a drug addict or potential suicide and the simplest message becomes fraught with shocking implications But what are the corresponding symptoms in other people's wives? Does the wife of a racehorse owner stand transfixed on meeting the milkman's horse and grip the railings with her jewelled fingers, yelling "Come on, Steve!" until she is led away by an understanding policeman? Does the engine driver's wife mistake an owl's hoot for the 9 15 drawing in and hastily prepare her good man's evening meal? I recommend this fascinating field of research to my husband's colleagues

Meanwhile, perhaps some medical M P would put this question to the Minister of Health

> "Is the Minister aware that the incidence of fatigue is increasing among housewives in Great Britain, and that unless something is done vast numbers of new housewives will have to be imported from Argentina at great national expense?"

This is Festival Year Wouldn't it be wonderful if for once we were spared the usual stilted reply and got this honest British retort

> "The Minister is well aware of the situation He couldn't care less"

I am afraid the Argentine housewife idea will appeal to husbands I can imagine her murmuring "Mañana" ever so sweetly into the phone

Anyone requiring further information should write to me I ought to know something about the subject, for I've got the disease Excuse me, there's another drug addict hammering on the door

* * *

When patients in sanatoria or mental hospitals take up their paint brushes and slap down their opinions of their surroundings or of life the results are exhilarating, and shows of pictures from such beginners lift the spirits in a remarkable way, but at the Royal Academy I found my spirits drooping Our professional artists paint much better, of course, but they also seem to have much less to say, and they say it so respectably no fulminations of rage against mother, no searching criticism of the hospital staff, no bursts of brilliant light or sulphurous darkness, matching a mood, no unlikely horses in the clouds or faces in the flowers, no meticulous windings of a thread, no birds or beasts fashioned of tiny coloured particles as though a coral insect had set out to paint a picture Just nice ordinary paintings which slide the onlooker back into his rut and turn on the rain A spark of rebellion comes from Richard Eurich in *A Judgment*, where the font end of a church is mysteriously full of tumbling instruments of music, flung down in such a headlong rush from the tower that the crimson curtains billow in the draught Otherwise I should put the psychological state of the exhibitors at about two glasses below par, except for one or two really bad depressions in purples, blues, and black, and an occasional euphoria in the reds *Les Jardins du Luxembourg*, by Derek Clarke, however, seemed jolly in its own right, and I would have gone off with James Fitton's *Woodland Path*, if that could have been arranged without unpleasantness Of professional interest were Prof T F Flower's wife and family, charmingly done by Dr Henry Lamb, and Dr Winifred Doherty had had the luck to be painted by Stanley Spencer Sir Alexander Fleming, in John Wheatley's clever drawing in chinese white, peers faintly out of green paper, looking like Beethoven—or a banshee

* * *

I can now disclose the menu and arrangements for the annual dinner dance shortly to be held by the Royal Society of Medicine (Section of General Practice) Having taken their seats at table members will read their morning papers for the five minutes needed for the preparation of the first course, an *Œuf Poché Interrompu*, "washed down" (as gourmets say) with *L'Eau Froide à Boire d'un Trait* When they have consumed about three quarters of this a telephone bell will give them the signal to withdraw and dance attendance during the half hour needed for the preparation of the last course, *Café Réchauffé à l'Anglaise* Dinner will be served in four sessions—late, later, latest, and extra—and members will be free to attend any of these, or all four if they're lucky

* * *

At interviews they always ask me why I went into psychiatry, and if I give them the real answer—because I could not make any headway in gynæcology—I do not get the appointment I am after Last time I was even refused the fare from Bootle to Skegness, where I had hoped to see the tail end of a particularly good aurora borealis Since then I have answered the question differently and in a poignant pregnant manner designed to hold the committee spellbound throughout the interview, as a result I have been appointed to no fewer than 31 full-time posts in the last fourteen days

I start my explanation of why I went into psychiatry by recalling my performance as a tenor tot in Turandot at the age of four Instead of this opera, applicants who adopt my method can mention touch typing, Milton's *Defensio Secunda*, their first conker championship, or any other evidence of prodigious ability, according to taste The age, however, is important, and only the very best raconteurs should attempt to raise it above five years or lower it below nine months The aim is to bring a nostalgic tear to the eye of even the dourest committee-man, reminding him of his own long passed childhood and of how bad he was at conkers, let alone opera I then sketch briefly the secondary events of my life that led to the Big Decision—Aunt Ada's Adie's syndrome, my early work on frogs' spawn, and whatever else, appropriate or not, that comes to mind, for by this time the battle is won

My more astute readers will see how, by slightly varying the theme, it is possible to answer such posers as why I went into orthodontics In this case it would be well if an early love for the Wheatstone bridge, or memories of the thrill enjoyed on first sighting the Leaning Tower of Pisa, could be cunningly woven into the fabric of the tale

* * *

The quality of the milk delivered at my home had obviously been deteriorating for some weeks, so I tackled the roundsman about it Was it, I asked, an effect of the shortage of new grass? "Well," he replied after thinking deeply for a minute or two, "it may be that, but to my mind it's because they get too much of this consecrated food" We left it at that

* * *

Any doubts about Medicine's contribution to the Festival pageantry should be set at rest by the vivid description in the *Observer* of May 6

> "In floodlit Trafalgar Square a nose to tail procession of vesicles crept slowly along"

On their way to the gathering at the Institute of Dermatology, of course

Letters to the Editor

OPPORTUNITIES FOR THE DOCTOR IN BRITAIN

SIR,—After two years in the United States we returned to Britain a few weeks ago for personal reasons and also to see what opportunities were open for medical graduates trained in internal medicine. We visited numerous hospitals and discussed the situation at length both with our contemporaries and with senior members of different university teaching staffs. While there were some obvious improvements in the hospital service, such as the upgrading of some hospitals by the provision of better consultant staffs, there were other developments which gave rise to misgivings as to their ultimate effect on the quality of British medicine.

Consultants in training are presented with a definite scheme of promotion which specifies certain periods in different grades. No provision appears to be made, or credit given, for a year or more spent in basic sciences such as pathology, which was previously regarded as a beneficial if not an essential part of the training of specialists. In the same manner a candidate who acquires training of an unusual but useful type, such as biochemistry, may find himself unable to return to the clinical field because his place on the promotion ladder has been filled.

Senior registrars with ten or more years' training find that they may be forced into general practice, for which they are no longer fitted by virtue of their specialisation. Interchange of specialists and general practitioners is no longer practicable. In one hospital that we visited six senior registrars, aged 35–40, nearing the end of their tenure of this grade, were trying without success to obtain posts as specialists. Some graded consultants did not have any hospital beds directly under their control, and were not expected to have them till after the age of 45.

Time spent on acquiring multiple or sometimes initial specialist degrees might be more profitably spent in a special interest such as research or further clinical experience. Some, but not all, such degrees are purely scholastic and do not require any apprenticeship in the subject. These degrees have been given a more important place in the new service than previously.

The ratio of consultants to beds and to general practitioners is low. Some consultants hold multiple appointments, thereby keeping the number down. Many people performing consultant duties are denied the name and prestige of consultant. The standard of general practice is necessarily dependent on the standard of consultant medicine, and economies in this service appear to be false. It is in the hospital mainly that new drugs are discovered and evaluated.

The main result of these difficulties is to cause a feeling of unrest and insecurity amongst those training as specialists. To some extent the direct relationship between effort and initiative and success is lost. The net result with overworked consultants and insecure registrars, must ultimately be a poorer service. The best-trained members of our profession should surely be the last to be dispensed with in the name of economy. Economies might be better made in the compensation now made to those with illness of short duration. We know that those working in hospitals are well aware of these conditions, but we wonder if doctors not engaged in hospital practice and also the general public realise the loss to the community when well trained men are forced to give up their specialty.

In conclusion we should like to thank our friends for their kindness on this visit.

J MACLEAN SMITH
JEANNE MONTGOMERY SMITH

Baltimore Maryland U.S.A.

POLIOMYELITIS

SIR,—I am stimulated to comment on one paragraph of Mr Le Vay's article in your issue of April 21. It is the one which begins "However troublesome pain and spasm may be, they must not be allowed to obstruct daily passive movements."

This practice has led to a great deal of unnecessary suffering in the acute stage of poliomyelitis. Whatever the cause of the pain there is nothing to suggest that the spasm is other than a protective mechanism. Passive (and active) movements within a range which does not produce pain are of value from the onset, but beyond this range they should be avoided.

Treatment in the bath and hot packs, which Mr Le Vay does not mention, are of considerable value in overcoming muscle spasm which persists after the acute stage.

Wingfield Morris Orthopædic Hospital Oxford.   J C SCOTT

SPECIALISATION IN TEACHING

SIR,—Despite increasing concern at specialisation the trend continues. It seems to be a deeply rooted feature of modern western civilisation; yet at the same time a need for people with wide knowledge and abilities is felt growingly in numerous fields. A leading article in *Science* about a year ago urged the education of general scientists, and a formidable curriculum was outlined for them. The preservation of sound general medical practice and the suitable training of new general practitioners is a more modest goal, yet one fraught with difficulties. It is a desirable goal for the extremely practical reason that the patient's body is indivisible.

Once past biology in the 1st M.B. examination our education is entirely by specialists—a procession of anatomists, physiologists, pathologists, assorted surgeons, obstetricians, metabolic physicians, and cardiologists—whose various teachings the student is expected to integrate for himself. Except for those few fortunate enough to participate in experiments at teaching general practice to undergraduates—notably those at Edinburgh[1] and Harvard[2]—at no time does the average student come under the influence of a teacher who would describe himself simply as a doctor, able to help him fit his specialised learning into its proper perspective. Many doctors have noted the prestige which specialists gain in the minds of their students by virtue of their position as teachers, but I have not read any comments on the allied, but none the less separate, problem that specialisation is made attractive because Medicine is being taught as a mere collection of specialties irrespective of by whom.

Miraculously most of us graduate with respect for something we call Medicine. Many of us feel that all specialisation entails some retreat from the central theme of Medicine. A few of us who are so persuaded also enjoy teaching and the stimulus of contact with other teachers and clinicians, but little outlet or encouragement is given to teachers who show no inclination to specialise. In both the clinical and the scientific departments of medical schools the selection of staff on their research ability has ensured that they are manned entirely by specialists.

Although the community supports universities primarily that they may teach, scientific departments are commonly organised on the polite myth that all faculty members are principally interested in something other than teaching (usually research) and are prepared to do their stint at teaching much as they are prepared to pay their income tax. It is of course essential that university teachers be able to refresh their teaching from some other activity, but need it necessarily be a specialty? Cannot some way be found whereby teachers can be general practitioners or vice versa?

---

[1] See Scott R *Lancet* 1950 ii 695

[2] See leading article *Ibid* p 659

Scientific, especially medical scientific, departments often carry one or two men regarded as "passengers" by their colleagues because they do no research or at least publish none I strongly suspect that a proportion of these men have got into academic medicine not realising in the first place how far away it would take them from the humanitarian side of their profession They are inactive in research because of a reluctance to specialise beyond a certain point which their general medical training disposes them to find the limit compatible with a humanitarian, as opposed to a scientific, outlook Only in their teaching can they feel sure that they are doing something of definite value to society

The more widespread teaching of general medicine to undergraduates would not only benefit the latter but might also provide an outlet for doctors with an urge to teach without having to make a pretence at embracing some specialty

Holbeach Lincolnshire A J RICHARDS

THEORY OF CEREBRAL LOCALISATION

SIR,—I agree with Dr Jefferson's thesis (April 28) that the results of hemispherectomy call only for a renewal of attention to already established, though recently unemphasised, clinical and experimental observations, rather than for any radical revision of theories of cerebral localisation , but the effects do not seem to me to argue against Jackson's view that destructive lesions cause negative symptoms

The clinical and electrical evidence suggests that the damaged hemisphere as a whole constitutes in Jacksonian terms a "discharging" quite as much as a "destructive" lesion The results of removal are essentially negative —namely, a reduction of abnormal discharge The beneficial effect on the remaining cerebral economy reflects the extent of the abnormal discharge removed Although, apart from the visual sphere, the evidence does not as yet reveal any clear loss of "normal" function, I would hazard a guess that further study will enable us to see something of that too though it may weigh very light in the balance of over all benefit to the patient

Oxford C W M WHITTY

SIZE OF MEDICAL SCHOOLS AND HOSPITALS

SIR,—I was interested in the letter from "Calculus" in your issue of April 21

I took my 1st M B work at Toronto University, in a class of 150 students Since then I have been at the Middlesex Hospital in London, where classes have averaged 45

At Toronto two shifts of 75 students were formed for practical classes These were each attended by the respective professors, assisted by three demonstrators In the physics and chemistry departments practical books were handed in for examination once weekly, and were verbally corrected at the next class In biology the last fifteen minutes of each three hour session was spent in a more or less informal viva from professor or demonstrator (working in rotation through the whole class), for which marks were assigned, these marks being considered when assessing the students' examination results in the first year final examinations Furthermore the chemistry professor within the first six weeks of the autumn term could accurately fit name to face of all of the 150 students This was achieved by assigning to each student a numbered seat in the lecture theatre, and the professor having on his desk a plan of the seats with the students' names entered on it Also, if any student missed a lecture in a subsequent practical period the professor saw to it that that student understood the substance of the lecture that he had missed

In physiology I had the good fortune to be taught by Prof Samson Wright and Dr (now Professor) D Slome Physiology, as taught by them, was not isolated studies of nervous system, circulation, digestion, &c Each field was discussed in relation to the others, and through all, by a rapid-fire question and answer technique, we were taught to think rationally and for ourselves

These experiences lead me to conclude that the complex graphs and statistics mentioned by "Calculus," of which I have even less understanding than he, are not the only factors in deciding how a big medical school ought to be Good teachers are essential, and come before problems of capital outlay, running costs, and so on It is not true that a personal relationship cannot be established in large classes or that two people cannot adequately teach physiology, when first class teachers willing to work at their job, can be found

London N W 3 ROY MOTTRAM

HYPERCALCÆMIC URÆMIA WITH NEPHROCALCINOSIS

SIR,—The interesting case recorded by Dr Fulton and Dr Paget (April 21) is surpassed by one described by Albright [1] This was of a man of 50 who had a single metastasis of the right ilium and sacrum from a "hypernephroma" of the kidney, associated with hypercalcæmia and hypercalcuria The interesting part of the story is that the serum and urinary calcium values went back to normal when the metastasis was irradiated, only to rise again when the condition relapsed

Dr Fulton and Dr Paget suggest that "the syndrome only develops in cases in which the bony secondaries are of sufficiently wide distribution or long duration" This cannot be, as in Albright's case they were not widely distributed , and their comparatively rapid response to irradiation with subsequent relapse shows that long duration is not important It is probably all a question of how quickly bone is being destroyed

Department of Pathology
University of Bristol OLIVER C LLOYD

FOOD AND ENERGY

SIR,—It is now some centuries since the scientific method of observation and experiment replaced authoritarianism, but I sometimes wonder whether the replacement was complete or whether the wheel is turning full circle For we continually meet with statements made, or uncritically quoted, by men of authority which, when subjected to scientific criticism, turn out to be no more than expressions of opinion When such statements of a technical nature are made by people not skilled in the relevant branch of technology there is at least the excuse of ignorance, but it ill becomes the expert to lend his authority by quotation which implies tacit approval

In his letter of March 10 Dr Franklin Bicknell, possibly with caution but certainly with subtle emphasis, quoted without comment from the report of the Productivity Team on Rigid Boxes and Cartons to the effect that diet plays an important part in enabling the American worker to work faster and to sustain the effort Dr Bicknell, with an accuracy which is unusual in such quotations, gave the entire relevant section of the report There is nothing in the report to substantiate this surprising claim, which turns out to be a statement of opinion, if not of prejudice, and not of fact

The only piece of what might purport to be evidence is that members of the productivity team were able to work all day without fatigue While the layman might be excused for putting this down to the first cause that comes to mind—namely, food—Dr Bicknell must surely agree that change of environment, change of working conditions, intellectual stimulus, new interests, to mention but a few might equally be responsible for the absence of fatigue

London W 13 A E BENDER

---

[1] Albright F Reifenstein E C *Parathyroid Glands and Metabolic Bone Disease* London 1948

THE PHYSIOLOGY OF SLEEP

SIR,—In my article of March 17 on Professor Hess's work I made some errors in describing the sleep producing area of the thalamus It would be more accurate if the relevant sentence read "This [sleep] only occurs after stimulating the hypnogenous zone, which is in the thalamus beside the massa intermedia and about 2 mm from the midline" In Hess's most detailed account of his sleep experiments[1] the area is defined as follows

> The upper and lower limits correspond to the lower half of the massa intermedia (which in cats is a constant landmark) The medial border is 2 mm from the midline The anterior and posterior limits are the tracts of Vicq d Azyr and of Meynert respectively The lateral border cannot be defined so certainly but is within the thalamus

More recent work in Zürich, which I have been privileged to see in the last few weeks, has modified this description slightly in two respects First, the zone extends dorsally to the upper limit of the massa intermedia Secondly, the most evocative zone is quite narrow and may be confined to the lamina medullaris interna

This is my interpretation of work that has only been published as a brief communication.[2] It shows that the sleep produced by stimulating the hypnogenic zone is not only normal by biological standards, but also produces the changes in the electro encephalogram that accompany natural sleep I hope that this important contribution to the study of sleep will be published in extenso and in English

St Bartholomew's Hospital London E C 1 **DONALD A MCDONALD**

POTASSIUM AND SODIUM BROMIDE

SIR,—The recent announcement, that sodium bromide may be dispensed by chemists in place of the potassium salt when supplies of the latter are not available to meet N H S prescriptions, should receive the widest publicity among doctors

Patients with congestive heart failure, hypertension, pre eclampsia, or obesity are commonly ordered a salt-restricted diet If, at the same time, the doctor should prescribe one of the several mixtures containing potassium bromide and the chemist supplies the sodium salt, the intake of sodium ion is likely to be sufficient to defeat the purpose of the diet In such circumstances doctors should endorse their prescriptions "not sodium bromide"

Woldingham Surrey **L M SPALTON**

A PATIENT'S VIEW OF RADIOGRAPHY

SIR,—Mr A, who has had disseminated sclerosis for nearly ten years and goes about in a wheeled chair, recently felt a pain, described by him as very slight, in the left hip and knee At once he began to hope that X ray examination of those joints might reveal the cause and lead to cure of all his symptoms

He applied to his general practitioner, who without discussion gave him a note for a consultant in the general medical outpatient department of the local hospital This second doctor observed that Mr A. had formerly attended the neurological clinic, and again without discussion referred him back there, where at a later date I saw him accompanied by his wife

After examining him I explained that there were no signs of disease of hip or knee, that the seat of the trouble, now as before, was the spinal cord and that unfortunately the proposed X-ray examination could not help

Mrs A —" I think he ought to have it to set his mind at rest "

I—" I'm sorry but I have a duty not to order X rays which I think unnecessary You must let me set his mind at rest "

Mrs A —" It's very hard on us with so little money coming in It s a shame "

I—" Your situation is hard and I sympathise, but have you thought who would pay for the X rays ? "

Mrs A (astonished at my ignorance)—" *Nobody* pays for them ! They come from the Government "

Mr A (getting down to brass tacks)—" I look at it this way Those X rays cost, say, fourpence each If I could have them and they got me back to work I could pay for them easy I d be glad to "

Have we no more economical means of ridding a patient of notions like these (which I believe I dispelled without ill feeling) than to book two appointments at a hospital for him, take him there and back twice by car, and give him interviews with *three doctors, including his own* ?

London W 1 **JOHN PENMAN**

CYANOSIS IN INFANTS FROM NITRATES IN DRINKING-WATER

SIR,—In their article of April 28 Dr Ewing and Dr Mayon White describe cyanosis in infants caused by nitrate in drinking water They suggest that some of the reported cases of familial idiopathic methæmoglobinæmia might really be due to the same cause, and they imply that the family we described,[1] living on a mountain farm and containing five affected members, all adults, might come into this category

Three of the affected members of this family had lived for considerable periods away from home (one as an employee in a large hospital), but no recovery from the symptoms had followed the change in water supply Moreover, Dr Ewing and Dr Mayon White are evidently unaware of further work on this family[2] in which it was shown that the methæmoglobinæmia was due to an enzyme deficiency in the erythrocytes The same enzyme deficiency was found in the affected brother and sister in a family we have just described in your columns[3] This family used the main water supply of a large town

We feel that on the present evidence there is no reason to depart from the generally held view that "well-water cyanosis" is an environmental disease of infancy Familial idiopathic methæmoglobinæmia, on the other hand, is due to an inborn biochemical error, the symptoms of which usually, though not invariably, appear in infancy and persist, unless treatment is instituted, into adult life

Department of Biochemistry Queen s University Belfast. **D C HARRISON** **Q H GIBSON**

SIR,—The interesting article by Dr Ewing and Dr Mayon White prompts me to record briefly a similar case The condition is probably not rare in rural areas.

In November 1950 a 3 week old male infant was referred to hospital by Dr A. H Cheshire, of Brewood, South Staffs The infant was the fifth child, and all the others had been reared in the same cottage, which was in a country lane some distance from the nearest dwelling

He was born about 2 weeks prematurely, and at birth weighed 6 lb 2 oz At 10 days of age he was taken off the breast and put on to a dried milk mixture He was described as lusty, but had been jaundiced from a few days after birth Soon after being put on the bottle his skin became dusky, and discoloration increased up to the time of his admission to hospital

On admission he showed a peculiar slaty cyanosis tinged with faint jaundice and he appeared pale weight 6 lb 15 oz *Physical examination* was negative apart from a soft systolic murmur

Investigations —Urine normal Radiograph of chest normal Blood Hb 55%, red cells 2,940 000 per c.mm white cells 12,700 per c.mm (polymorphs 41%, lymphocytes 57%, monocytes 2%) Blood group A, rhesus positive, Coombs test negative - *Considerable amount of methæmoglobin* present (absorption band at 630 mμ abolished by sodium hydrosulphite) Serum bilirubin 1 8 mg per 100 ml

---

[1] Hess W R *Helv physiol acta* 1944 2, 305
[2] Hess R jun Akert K Koella W *Ibid* 1950 8 60

[1] Gibson Q H Harrison D C *Lancet* 1947 ii 941
[2] Gibson Q H *Biochem. J* 1948 42 13
[3] Breakey V K St G Gibson Q H Harrison D C *Lancet*, April 28 1951 p 935

Progress—The infant's condition was good, and he took his feeds readily, so ascorbic acid 150 mg daily was given By the next day the cyanosis was less marked, and it disappeared in 3 days By the time of discharge from hospital, after 6 days, he appeared normal and weighed 7 lb 1 oz His hæmoglobin was 85%

Now, at the age of 6 months, he has developed normally and cyanosis has not recurred

The water supply to the cottage came from a shallow well, the water from which was found to contain nearly 400 parts of nitrate per 1,000,000 The probable reason why the other children had not suffered similarly was that they were breast fed for a considerably longer period

Wolverhampton H EVERLEY JONES

HEARTBURN

SIR,—Heartburn is a troublesome symptom in some patients, so it may perhaps be worth recording that it usually responds to the administration of ferric ammonium citrate (I give ferri et ammon cit gr 5, in plenty of water, p.r n) Bismuth carbonate is also frequently effective These observations suggest that heartburn may be caused by the presence of sulphides in the upper bowel Ferric salts oxidise sulphides, and bismuth salts form an insoluble precipitate of bismuth sulphide The *National Formulary* "white mixtures," containing no bismuth, are ineffective in the treatment of heartburn

Lowestoft N B EASTWOOD

AN IMMUNOLOGICAL PROTEST

SIR,—It is with regret that I have to point out certain unwarranted conclusions in recent publications by Mr L B Holt He has made important contributions to immunology by introducing P T A P, by establishing the importance of the amount of carrier in this preparation, and by demonstrating phagocytosis of some of the injected material His reputation, based upon this work, may lead many readers to accept and sometimes repeat statements in his writings without checking the original papers upon which they were based and without examining critically his experimental data

For example, writing of "a final baseline level of immunity," he [1] states that "Glenny and Barr 1947" [2] "have reported a similar phenomenon in horses in which tetanus titres were observed over a period of five years following a single inoculation of tetanus toxoid" Tetanus antitoxic titres were not followed in any horse over a period of 5 years nor was there any reference to a horse receiving a single injection of toxoid There was, however, a horse mentioned that had been *hyperimmunised* with tetanus *toxin* for a period of $5^1/_2$ years which lost very little antitoxin during the first 13 months after injections had ceased It would also be unfortunate if other writers repeated another statement about tetanus toxoid made by Holt [3] that "we know that no corresponding advantage is gained in preparing an Alum Precipitated Tetanus Toxoid" (p 144) It is true that two injections of tetanus toxoid at suitable intervals confer good immunity, but the antigenic efficiency of many batches of tetanus A P T is far in advance of that of the original plain toxoid Glenny, Hamp, and Stevens [4] showed that the addition of 1% potash alum to tetanus toxoid greatly increased the antitoxic responses in guineapigs and horses

In *Developments in Diphtheria Prophylaxis* [3] Holt has a section entitled "A Critical Review of Glenny's Work", this "work" consists of a single paper by Glenny, Buttle, and Stevens published in 1931 [5] Those who read this review side by side with the original paper will realise how completely Holt failed to understand the work he criticised and how unjustified he was in saying that "results and comments do not appear to tally or agree with the remarks in the preamble to the paper" or "the same explanation was presented to account for a completely opposite result"

Holt's objection to the use of horse serum in the first experiment shows that he was not aware of the work of Glenny, Hopkins, and Waddington [6] in 1925 nor of that of Glenny and Waddington in 1928 [7] Again his suggestion that guineapig serum should have been used must have been made without any thought of the task of collecting from guineapigs twenty years ago the 2000 units of antitoxin needed for the experiment In addition, he must have overlooked the statement by Glenny, Barr, Ross, and Stevens [8] that "non avid antitoxin is constantly met with in the serum of guineapigs immunised with diphtheria prophylactics" Such non avid antitoxin would have been most unsuitable for the work described by Glenny, Buttle, and Stevens There are many more criticisms in the review, all of which can equally be shown to be unjustified Holt's criticism appears to be directed against the statement "that the improved response due to the addition of alum to toxoid can be attributed to the antigen remaining in the body sufficiently long to continue its action after the tissues have acquired the power of rapid response" (the so called depot theory) Holt himself appears to show that this is true some 17 pages later in his book

As one of the two authors who first described the primary and secondary response phenomenon, I must protest against the use of the expressions "second" and "tertiary" response It is inconsistent to speak of primary, second, and tertiary responses and shows a misunderstanding of the *two essential types* of responses.

Wellcome Research Laboratories,
Beckenham Kent A T GLENNY

*** We have shown this letter to Mr L B Holt, who replies

"Mr Glenny's first point is that I misquoted him in an article I wrote in 1949 Just after the article appeared, Mr Glenny wrote drawing my attention to the inaccuracy I replied acknowledging the error and apologised Since that time I have not had a suitable occasion to rectify the error publicly, and am pleased to take this opportunity to do so now

"My words 'We know that no corresponding advantage is gained in preparing an Alum Precipitated Tetanus Toxoid' are part of a statement concerned with the discovery by Glenny et al of the greatly enhanced potency of alum-precipitated diphtheria toxoid over its parent formol toxoid I wrote

> 'From a purely physiological aspect this phenomenon is probably best put into perspective as one emphasising the low degree of physiological activity of diphtheria formol toxoid as a primary stimulus We know that no corresponding advantage is gained in preparing an Alum Precipitated Tetanus Toxoid, and that Tetanus Formol Toxoid, per se, is an excellent antigen'

"The full heading of the section of my book which Mr Glenny mentions is 'A Critical Review of Glenny's Work and His Explanation for the Enhanced Potency of A P T' The subject matter of this section is the enhanced antigenic activity of A P T compared with formol-toxoid This section is introduced by four relevant references to Glenny's work and deals in detail with a fifth,[5] the only one (to my knowledge) in which he and his co workers describe experimental work on this subject and in which an explanation of the findings is given The alleged unjustness of my remarks concerning some of the explanations given in this paper by Glenny, Buttle, and Stevens should perhaps be left to others to assess

"Regarding the use of horse antitoxic serum, my criticism was

> 'It is thought highly probable that the use of foreign protein antitoxin itself must have considerably modified

---

1 Holt L B *Brit J exp Path.* 1949 30, 289
2 Barr, M Glenny A T *Lancet* 1947 ii 647.
3 Holt L B Developments in Diphtheria Prophylaxis London 1950 p 144
4 Glenny, A T, Hamp A G Stevens M F *Vet J* 1932 88 90
5 Glenny A T Buttle G A H, Stevens M F *J Path Bact* 1931 34 267
6 Glenny A T Hopkins B E Waddington H *Ibid* 1925, 28 305
7 Glenny A T Waddington H *Ibid* 1928 31 403
8 Glenny A T Barr M Ross H E Stevens M F *Ibid* 1932 35 495

> the response of guinea pigs to the initially injected toxoid quite apart from its being the specific antibody to the primary antigen used — it follows that guinea pig antitoxin should have been employed in order to avoid the use of foreign protein antitoxin (Ref. 3, p. 74.)

That the criticism seemed valid, but was unfounded, is shown in the fact that Inga Scheibel repeated the experiment, using homologous antitoxin, and obtained the same results as Glenny et al. who used heterologous antitoxin. This is referred to on p. 163 in my book. The fact that Mrs. Scheibel repeated the experiment with homologous antitoxin would seem to answer the point about the low avidity of guineapig antitoxin.

> “Concerning the ‘depot theory,’ although on p. 90 of my book it is shown that a single *large* inoculation of P.T.A.P. does result in a (superimposed) secondary response—i.e., the inoculum operates over a long enough period to produce a secondary response—it is also shown that the secondary response makes little contribution to the far more important ‘base line’ titre. The further observation that the amount of toxoid (*provided the very small essential minimum is used*) associated with the optimal amount of $AlPO_4$ carrier makes no material difference to the 12 week antitoxin level argues even more strongly against the suggestion ‘that the improved response due to the addition of alum to toxoid can be attributed to the antigen remaining in the body sufficiently long to continue its action after the tissues have acquired the power of rapid response.’ Even so, this suggestion has been exhaustively analysed and an alternative offered which has a basis expressed in physiological terms (p. 67 et seq.)

“Immunologists are all aware of the classical paper of Glenny and Südmersen,[9] describing the ‘primary and secondary response’ phenomena—an observation of fundamental importance. Mr. Glenny has also described other types of response. I too have described another —that following a third inoculation of potent material —which was different from the typical primary or secondary response, and I quite simply labelled it “tertiary” response (Ref. 3, p. 160). No doubt other types of response will be described in the future. The expression ‘second response’ was used to denote the response to the second injection only—to distinguish it from *any* secondary response. The term seemed valid, because ‘secondary response’ has come to mean the response to any injection subsequent to an efficient primary stimulus, and not all such secondary responses have exactly the same character. The greater part of my work has been and is, an attempt to gain an insight into the physiological basis of these phenomena; my observations lead me to suspect that they are more complex than would be implied in ‘two essential types of responses.’”—ED. L.

MUNCHAUSEN'S SYNDROME

SIR,—You may like to learn that Munchausen's syndrome is not confined to Great Britain. In Sweden similar frauds are headlined as “Köpenickiades” after the German town of Köpenick—the scene of a famous hoax in 1906. However, I gladly accept Dr. R. A. J. Asher's term, though, like Dr. Paul Wingate, I feel that the noble baron would not have approved of the company; and I should like to describe two examples of the syndrome that I have seen.

CASE 1.—This patient belongs to the subspecies laparotomophilia, with possible motives 2 and 5. He is known to most of the doctors in central Sweden as ‘X-son with the ship,’ because, unfortunately for him, he has a large ship tattooed on his chest. In 1924 he was operated on for a perforated duodenal ulcer, and since then he has been admitted innumerable times to all the hospitals in and around Stockholm with the symptoms of an acute perforation. If recognised he would promptly drop the pretence and say ‘I see there's nothing doing this time”, and he would then dress and leave quietly. Often he deceived the doctors and got free board and lodging for the night. Although he managed to avoid an operation he was not afraid of one, but usually he was discharged in a few days or discharged himself, taking the hospital soap with him. I first heard of him in 1933 when I was a student, and later met him several times and saw his name on all the hospital black lists in Stockholm. I had almost forgotten him when he arrived at this hospital (70 miles from Stockholm). On two occasions he attended with a fake coronary thrombosis. The second time I had the honour of dealing with him, and I do not think he will return again.

There is a story concerned with this case which illustrates the dangers of a too hasty conclusion.

A patient who gave the name of “X-son” entered a hospital in Stockholm and complained of the symptoms of a perforated duodenal ulcer. He was seen by an inexperienced medical student, who telephoned the doctor in charge for advice. He was told to look for a tattooed ship on the patient's chest, and when this was found the patient was discharged. A few hours later he returned, and this time there was no doubt about the diagnosis. Unfortunately the wrong “X-son” with the wrong ship had been thrown out.

CASE 2.—Fifteen years ago a patient was admitted to a Stockholm hospital with pyrexia of unknown origin. He was a pleasant youngish man who gave his name as Ondonte van der Tockayennie, and said that he was a Spanish nobleman of an old family which had returned to Spain with the Duke of Alba after the liberation of the Netherlands. After admission to hospital he continued to run a high continuous fever, which was attributed to infected lower teeth. These were extracted without effect on the fever. Then osteitis was suspected, and the jugular vein was ligated (this was before the sulphonamide era), but he continued to run a temperature. Finally half the mandible was removed, but the fever continued. The patient remained unperturbed and pleasant. By the time he was caught manipulating the thermometer the police had discovered that he was a wanted criminal with a common Swedish name and several aliases.

The remarkable thing about this patient was that he could not reasonably have believed that it was possible to carry on the fraud to his advantage.

Centrallasarettet, Eskilstuna,
Sweden.

SVEN GÖSTA SJÖBERG.

EXPERIMENTS ON FAT ABSORPTION

SIR,—I read with interest last week's paper by Dr. Auld and Dr. Needham. Perhaps they and readers would be interested in two experiments I performed 5–6 years ago when I was surgical chief assistant and resident surgical officer at the Christie Hospital and Holt Radium Institute, Manchester.

At the completion of two left block dissections of the neck I introduced a fine rubber tube into the distal end of the bisected thoracic duct. I did this because I was interested in the total daily flow of chyle and to find out what happened when these patients were given a fatty meal. So far as I can recall the total chyle drained in 24 hours after operation was 350 ml. in one patient and 400 ml. in the other. When fatty meals were given the rate of flow increased from 350 to 500 ml. and from 400 to 550 ml. per day; specimens became more ‘milky,’ and the amount of fat in each case doubled. In the fasting specimens fatty acids were present, but their amount increased after a fatty meal. Unfortunately, after the second day the tube came out during change of dressings, but the opening sealed off almost immediately, and neither patient suffered or was delayed in hospital. At that time I did not have the opportunity to continue further research in this line, and I have misplaced the detailed analyses of the specimens I collected.

I see no objection to placing a cannula in the thoracic duct in patients undergoing, say, a cervical sympathectomy or a block dissection of the neck. The patients appear to suffer no inconvenience, and specimens for analyses can be collected from the duct after the ingestion of fats. The chyle collected may or may not represent the total flow through the thoracic duct, which will depend on how freely the duct communicates with the venous and lymphatic systems and the ease of flow through these anastomotic channels.

The above two patients were admitted to hospital under the care of my chief, Mr. W. R. Douglas.

Royal Hospital, Sheffield.

DAVID AIKEN.

---

[9] Glenny, A. T., Südmersen, H. J. *J. Hyg., Camb.* 1921, 20, 176.

PARAFFIN IN SYRINGES

Sir,—In his letter last week, Dr Woodmansey presses concern that syringes supplied ready for use e lightly lubricated with liquid paraffin, as suggested the M R C memorandum quoted by Dr McCartney arch 3)

Although some centres claim that no lubricant what er is required we have found that the loss of syringes jamming is less when a lubricant is used, and that uid paraffin is an efficient lubricant provided that only very slight trace is applied to the piston of the syringe us may be done easily and routinely by dipping the d of the piston into a solution of liquid paraffin (1 ml) trichlorethylene (1 lb) The piston is then inserted to the barrel and worked up and down for a second or o until the trichlorethylene evaporates The film of uid paraffin remaining is infinitesimal so that the risks umerated by Dr Woodmansey are obviated

W Trillwood
Director of Pharmaceutical Services,
United Oxford Hospitals
Churchill Hospital Headington, Oxford

ACTION OF DIPHENYLHYDANTOIN SODIUM ON THE ADRENAL GLAND

Sir,—Six epileptics under treatment with diphenyl dantoin sodium ('Dilantin Sodium') have been idied They received the drug in doses of 2 6–6 5 g per kg body weight per day In addition most of em were receiving phenobarbitone daily With 1 ception these drugs had been given for more than a ar before the investigation started

All 6 patients (2 men and 4 women, aged 17–37 years) d gingival hypertrophy which has continued to ogress Tissue biopsies showed that the hypertrophy iefly involved the connective tissue and that the tivity of alkaline phosphatase present there was eater, especially in capillaries, than in similar tissue tained from control subjects who were not epileptics d who received no therapy Skin reactions were also served, and there was some evidence that diphenyl dantoin sodium caused a relative lymphocytosis

In view of these findings, and of the evidence that caline phosphatase activity and collagen formation are luenced by hormones of the pituitary adrenal complex,[1] was decided to study the effect of diphenylhydantoin lium on mice, and to examine particularly the adrenal nds It has already been shown that diphenylhydan n sodium can produce slight adrenal hypertrophy in e guineapig[2]

In a preliminary series of experiments 15 mg per kg body ight per day was given to the animals by intraperitoneal ection over a period of 120–125 days, at the end of which animals were killed Controls received an equal volume 0 9% sodium chloride solution (The daily supplement Na^+ received by controls was always greater than that en as diphenylhydantoin) All the treated animals showed tensive pathological changes in the adrenal glands In e animal there was hypertrophy only in the others, sides hypertrophy, asymmetrical degenerative changes were served, chiefly in the fascicular zone but also in the merular zone and the medulla The adrenals of the ntrols did not show these changes In these mice there s no hypertrophy of the gingival tissues

If the reactions observed do not result merely from e application of a non specific "stressor," then the estion arises whether the action of diphenylhydantoin dium and perhaps other anticonvulsants may not be cribed to some interference with the pituitary adrenal mplex either by action on the central nervous system at some intermediate point In addition, diphenylhydantoin sodium may inactivate circulating hormones of the pituitary adrenal complex or potentiate their action on tissues by some hitherto unsuspected peripheral action, perhaps on capillaries It may be noted that in rats deoxycortone acetate has already been shown to reduce the excitability of the central nervous system, excitability can be restored to normal by simultaneous administration of A C T H or whole extract of the adrenal cortex[3]

Diphenylhydantoin sodium, then, would appear to have some use as a physiological tool to study the pituitary adrenal complex Finally, these results may throw some light on the mechanism responsible for clinical epilepsy Further work is in progress

Department of Zoology,
King's College
University of London

P H Staple
Nuffield Dental Research Fellow

PUBLICITY IN CANCER

Sir,—As Mr Patey points out in his letter last week, the word "early" as applied to malignant disease is ambiguous

The only criterion of an early case, in my opinion, is that the malignant state is still confined to its site of origin Any clinical manifestation is, for the most part, an indication that the disease is established and its extent doubtful In cases of a lump in the breast, however, suitable publicity might well be helpful in pointing out that absence of pain does not mean freedom from danger

London W 1

F D Saner

CATION-EXCHANGE RESINS

Sir,—May I reply to the comments of Dr MacIntyre and Dr Jordan (April 28) on my article of April 14 on the cation exchange resin 'Zeo Karb 225'

In the first place I must point out that I avoided any discussion of the physicochemical aspects of cation exchange, since I considered the subject too specialised for your journal The data and my observations were presented in the simplest possible manner with the object of providing clinicians and others with some practical quantitative information on the resin, particularly in view of the somewhat scanty literature on the subject as a whole in medical journals

As Dr MacIntyre and Dr Jordan remark, the data for the sodium hydrogen exchange system show that the reaction obeys the law of mass action, the values for the equilibrium constant KH/Na for the range of concentrations studied varying between the limits 3 18–3 38 From the theoretical point of view, saturation of the resin with sodium would never reach completion under the conditions of my experiments Consequently the suggested conditions for full saturation and 100% efficiency of sodium exchange were intended only as an approximation, and were indeed deduced by extrapolation of curves based on only a few experiments

As regards the exchange in sodium calcium systems, one can determine the equilibrium conditions from the relevant physicochemical constants But in some of my experimental systems as many as four cations were in competition for the absorptive seats on the resin, under which circumstance direct observation of the equilibrium conditions is probably simpler to perform than the corresponding mathematical analysis Further, in systems of univalent bivalent cation exchange the exchange isotherm is not independent of the absolute concentration of the two ions in the aqueous phase as it is in univalent univalent systems—a property which leads to mathematical complications in systems involving calcium

Finally, I would like to point out that removal of hydrogen ions from the exchanger solution as they are

---

Baker B L Whitaker W L *Endocrinol* 1950 46 541 Pirani C Stepto, R C Sutherland, K *J exp Med* 1951 93 217 Spain, D M, Molomut N Haber A *Science* 1950 112 335 Watson E M *Endocrinol* 1940 27, 521 Williams H L Watson E M *Ibid* 1942, 29 250

Emmett A D Hartzler E R, Brown R A *J Pharmacol* 1943 78 215

[3] Woodbury, D M Chi Ping Cheng Sayers, G, Goodman L S *Amer J Physiol* 1950 160 217

released from the resin, apart from being desirable from the physiological point of view, should lead to greater exchange efficiency of the resin by exclusion of their competitive effect in the reaction As I have reported, magnesium trisilicate has proved unsuitable for this purpose, but other possibilities in this direction are being considered

Selly Oak Hospital Birmingham F MORTON

Parliament

National Health Service Bill

IN the House of Commons on May 2 this Bill was considered in committee On clause 1, Mr J ENOCH POWELL moved an amendment to lay the duty of assessing the charge for appliances according to the means of the patient on the regional hospital boards or the local executive councils, instead of the National Assistance Board Mr FRED MESSER also disliked the assessment being undertaken by the N.A.B , but thought that Mr Powell's proposal would add to the existing inconsistencies of the National Health Service What would happen, for instance, to patients who entered teaching hospitals ? He foresaw that the regional boards would have to do the work through their management committees, which he deprecated Dr CHARLES HILL was filled with dismay at the suggestion of adding still further to the functions of the local executive councils Mr ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, believed Mr Powell's proposal to be impracticable The only way which was administratively feasible, and which would avoid waste, was to use the staff and offices already available The N.A.B , for instance, already dealt with claims for refund of N H S travelling allowances and were in closer contact with the public than the regional boards or local executive councils. The amendment was by leave withdrawn

THE STRANGER WITHIN OUR GATES

Mr E H KEELING moved an amendment providing that visitors, whether of British or foreign nationality, should pay in full both for spectacles and false teeth Two years ago it was estimated that the cost of providing health services to visitors was £200,000 The patient's national registration number was given on every application for teeth or spectacles Surely it would not be any hardship to ask him actually to produce his identity card, when the optician or dentist could tell at a glance whether the patient was a visitor

Mr HILARY MARQUAND said he already possessed statutory powers to recover charges for dentures and spectacles from non-residents The powers had not been used because there were grave administrative difficulties in the way The optician or dentist had no power to insist on the disclosure of a patient's national registration number If a practical method could be devised he would be willing to consider whether charges for medical treatment might be made to foreigners About 700,000 foreigners visited this country in 1950, and it was calculated that possibly about 55,000 obtained treatment under the service

Mr ANEURIN BEVAN said that the estimate of the cost of treatment to foreign visitors was wholly surmise, and the figure of £200,000 could be assumed to be higher than the actual figure The amendment was mean in spirit and intention. The Minister would be going far beyond the original intention if he exercised his ingenuity to make regulations to put charges on foreigners who used the health service There was much pressure behind the amendment, it was that certain elements of the medical profession would be able to charge fees. (Cries of " Oh ! ") If he were asked to put his finger on where abuses in the health service took place, Mr Bevan said, he would single out the manipulation of fee-paying beds by specialists in hospitals There was more abuse from that than in any other part of the service Abuses also took place often among the dentists and opticians in the National Health Service, which had not yet existed long enough to eradicate commercialism from the medical profession. One of the results of having a good health service and good nutritional standards was that we had not a large experience of some epidemic diseases on which to train our doctors It might therefore become necessary, and indeed before he left the Ministry of Health he had discussed this with his medical advisers, for us to bring patients from different parts of the Colonial Empire to be treated in Britain

Dr HILL thought this was much ado about nothing He did not think that the visitor to this country regarded it as necessary, reasonable, or sensible that part of the hospitality we provided should be free dentures and spectacles The amendment was negatived by 285 votes to 254

Mr MESSER moved an amendment to provide that free spectacles and dentures should be supplied not only to hospital patients but to anyone " under medical treatment in any institution or in his own home " Mr BLENKINSOP agreed that there were real anomalies between one category and another Mr Messer's proposed exemption would be too wide, but Mr Blenkinsop agreed to consider sympathetically, though not very hopefully, whether any easement in the position could be made The amendment was withdrawn

A TRIAL RUN

Dr BARNETT STROSS moved an amendment to put a term to the contemplated charges They should, he proposed, only continue in force until March 31, 1952, unless Parliament otherwise determined Mr MARQUAND found it difficult to see how the nation's economic situation could change sufficiently in one year to enable us to withdraw the charges But he sympathised with the view that there should be a review after a reasonable period to see whether the need still existed One year's experience would be too short, and they would require two full years' working of the charges to measure their effects Then they could see, for instance, whether there had been any improvement in the school dental service, and how hospital expenditure was moving He would introduce a new clause on the report stage to bring the charges to an end in April, 1954

The clause was ordered to stand part of the Bill by 262 votes to 3

On clause 2 Mr BLENKINSOP accepted an amendment, moved by Mr MESSER, to ensure that no increase could be made in the charges laid down in the Bill without legislation, though reductions could still be made by order in council

TREATMENT ABROAD FOR THE TUBERCULOUS

On the question that clause 3 stand part of the Bill Mr MESSER said it ought to be understood that Switzerland had nothing to offer this country in the way of positive treatment So far as surgical work was concerned, for instance, we had not merely as good but better surgeons But there was a type of tuberculosis which could be better treated in Switzerland, and he hoped that the Government would give consideration to that aspect He feared many would be disappointed at the number of cases they would be able to send to Switzerland, and it would be wrong to delude tuberculosis patients with the hope that they would be able to get immediate treatment more quickly now Regional hospital boards, he understood, would select the type of case to be sent and it would be difficult to say who should have priority

Lieut -Colonel WALTER ELLIOT said that although this provision might be small it was something To choose patients was not so difficult as not being able to make a choice at all It was true that Switzerland was not a better country for the treatment of tuberculosis than our own, but it had staff and beds and that was the essential thing " Let us bring the two together as rapidly and as extensively as possible " Miss MARGARET HERBISON, joint under-secretary of State for Scotland, said that though the number of beds available at present was small the clause was evidence of the Government's determination to conquer a grave social problem They had chosen respiratory cases in an attempt to bring down the incidence, because these were the cases where there was a fear of infection This clause and the remaining clauses were ordered to stand part of the Bill.

On there committal of the Bill on May 7 Mr MARQUAND, in fulfilment of his promise to Mr Messer to reconsider the wording of the provision exempting hospital inpatients

PARAFFIN IN SYRINGES

SIR,—In his letter last week, Dr Woodmansey expresses concern that syringes supplied ready for use are lightly lubricated with liquid paraffin, as suggested in the M R C memorandum quoted by Dr McCartney (March 3)

Although some centres claim that no lubricant whatever is required we have found that the loss of syringes by jamming is less when a lubricant is used, and that liquid paraffin is an efficient lubricant provided that only a very slight trace is applied to the piston of the syringe This may be done easily and routinely by dipping the end of the piston into a solution of liquid paraffin (1 ml) in trichlorethylene (1 lb) The piston is then inserted into the barrel and worked up and down for a second or two until the trichlorethylene evaporates The film of liquid paraffin remaining is infinitesimal so that the risks enumerated by Dr Woodmansey are obviated

W TRILLWOOD
Director of Pharmaceutical Services,
United Oxford Hospitals
Churchill Hospital Headington, Oxford

ACTION OF DIPHENYLHYDANTOIN SODIUM ON THE ADRENAL GLAND

SIR,—Six epileptics under treatment with diphenyl hydantoin sodium ('Dilantin Sodium') have been studied They received the drug in doses of 2 6–6 5 mg per kg body weight per day In addition most of them were receiving phenobarbitone daily With 1 exception these drugs had been given for more than a year before the investigation started

All 6 patients (2 men and 4 women, aged 17–37 years) had gingival hypertrophy which has continued to progress Tissue biopsies showed that the hypertrophy chiefly involved the connective tissue and that the activity of alkaline phosphatase present there was greater, especially in capillaries, than in similar tissue obtained from control subjects who were not epileptics and who received no therapy Skin reactions were also observed, and there was some evidence that diphenyl hydantoin sodium caused a relative lymphocytosis

In view of these findings, and of the evidence that alkaline phosphatase activity and collagen formation are influenced by hormones of the pituitary adrenal complex,[1] it was decided to study the effect of diphenylhydantoin sodium on mice, and to examine particularly the adrenal glands It has already been shown that diphenylhydantoin sodium can produce slight adrenal hypertrophy in the guineapig [2]

In a preliminary series of experiments 15 mg per kg bodyweight per day was given to the animals by intraperitoneal injection over a period of 120–125 days, at the end of which the animals were killed Controls received an equal volume of 0 9% sodium chloride solution (The daily supplement of Na^+ received by controls was always greater than that given as diphenylhydantoin) All the treated animals showed extensive pathological changes in the adrenal glands In one animal there was hypertrophy only, in the others, besides hypertrophy, asymmetrical degenerative changes were observed, chiefly in the fascicular zone but also in the glomerular zone and the medulla The adrenals of the controls did not show these changes In these mice there was no hypertrophy of the gingival tissues

If the reactions observed do not result merely from the application of a non specific "stressor," then the question arises whether the action of diphenylhydantoin sodium and perhaps other anticonvulsants may not be ascribed to some interference with the pituitary adrenal complex either by action on the central nervous system or at some intermediate point In addition, diphenylhydantoin sodium may inactivate circulating hormone of the pituitary adrenal complex or potentiate thei action on tissues by some hitherto unsuspected periphera action, perhaps on capillaries It may be noted that i rats deoxycortone acetate has already been shown t reduce the excitability of the central nervous system excitability can be restored to normal by simultaneou administration of A C T H or whole extract of the adrena cortex [3]

Diphenylhydantoin sodium, then, would appear t have some use as a physiological tool to study th pituitary adrenal complex Finally, these results ma throw some light on the mechanism responsible fo clinical epilepsy Further work is in progress

Department of Zoology,
King's College,
University of London.

P H STAPLE
Nuffield Dental Research Fellow

PUBLICITY IN CANCER

SIR,—As Mr Patey points out in his letter last week the word "early" as applied to malignant disease i ambiguous

The only criterion of an early case, in my opinion, i that the malignant state is still confined to its site o origin Any clinical manifestation is, for the most part an indication that the disease is established and it extent doubtful In cases of a lump in the breast, however, suitable publicity might well be helpful in pointing out that absence of pain does not mean freedom from danger

London W 1

F D SANER

CATION-EXCHANGE RESINS

SIR,—May I reply to the comments of Dr MacIntyre and Dr Jordan (April 28) on my article of April 14 on the cation exchange resin 'Zeo Karb 225'

In the first place I must point out that I avoided any discussion of the physicochemical aspects of cation exchange, since I considered the subject too specialised for your journal The data and my observations were presented in the simplest possible manner with the object of providing clinicians and others with some practical quantitative information on the resin, particularly in view of the somewhat scanty literature on the subject as a whole in medical journals

As Dr MacIntyre and Dr Jordan remark, the data for the sodium hydrogen exchange system show that the reaction obeys the law of mass action, the values for the equilibrium constant KH/Na for the range of concentrations studied varying between the limits 3 18–3 38 From the theoretical point of view, saturation of the resin with sodium would never reach completion under the conditions of my experiments Consequently the suggested conditions for full saturation and 100% efficiency of sodium exchange were intended only as an approximation, and were indeed deduced by extrapolation of curves based on only a few experiments

As regards the exchange in sodium calcium systems, one can determine the equilibrium conditions from the relevant physicochemical constants But in some of my experimental systems as many as four cations were in competition for the absorptive seats on the resin, under which circumstance direct observation of the equilibrium conditions is probably simpler to perform than the corresponding mathematical analysis Further, in systems of univalent bivalent cation exchange the exchange isotherm is not independent of the absolute concentration of the two ions in the aqueous phase as it is in univalent univalent systems—a property which leads to mathematical complications in systems involving calcium

Finally, I would like to point out that removal of hydrogen ions from the exchanger solution as they are released from the resin, apart from being desirable from the physiological point of view, should lead to greater exchange efficiency of the resin by exclusion of their competitive effect in the reaction As I have reported, magnesium trisilicate has proved unsuitable for this purpose, but other possibilities in this direction are being considered

---

[1] Baker B L Whitaker W L *Endocrinol* 1950 46 544 Pirani C Stepto R C Sutherland, K *J exp Med* 1951 93 217 Spain D M, Molomut N Haber A *Science* 1950 112 335 Watson, E M *Endocrinol* 1940, 27 521 Williams H L Watson E M *Ibid* 1942, 29 250

[2] Emmett A D Hartzler E R Brown R A *J Pharmacol* 1943 78 215

[3] Woodbury D M, Chi Ping Cheng Sayers G Goodman, L S *Amer J Physiol* 1950 160 217

Selly Oak Hospital Birmingham F MORTON

Parliament

National Health Service Bill

IN the House of Commons on May 2 this Bill was considered in committee On clause 1, Mr J ENOCH POWELL moved an amendment to lay the duty of assessing the charge for appliances according to the means of the patient on the regional hospital boards or the local executive councils, instead of the National Assistance Board Mr FRED MESSER also disliked the assessment being undertaken by the N A.B , but thought that Mr Powell's proposal would add to the existing inconsistencies of the National Health Service What would happen, for instance, to patients who entered teaching hospitals ? He foresaw that the regional boards would have to do the work through their management committees, which he deprecated Dr CHARLES HILL was filled with dismay at the suggestion of adding still further to the functions of the local executive councils Mr ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, believed Mr Powell's proposal to be impracticable The only way which was administratively feasible, and which would avoid waste, was to use the staff and offices already available The N.A.B , for instance, already dealt with claims for refund of N H S travelling allowances and were in closer contact with the public than the regional boards or local executive councils The amendment was by leave withdrawn

THE STRANGER WITHIN OUR GATES

Mr E H KEELING moved an amendment providing that visitors, whether of British or foreign nationality, should pay in full both for spectacles and false teeth Two years ago it was estimated that the cost of providing health services to visitors was £200,000 The patient's national registration number was given on every application for teeth or spectacles Surely it would not be any hardship to ask him actually to produce his identity card, when the optician or dentist could tell at a glance whether the patient was a visitor

Mr HILARY MARQUAND said he already possessed statutory powers to recover charges for dentures and spectacles from non-residents The powers had not been used because there were grave administrative difficulties in the way The optician or dentist had no power to insist on the disclosure of a patient's national registration number If a practical method could be devised he would be willing to consider whether charges for medical treatment might be made to foreigners About 700,000 foreigners visited this country in 1950, and it was calculated that possibly about 55,000 obtained treatment under the service

Mr ANEURIN BEVAN said that the estimate of the cost of treatment to foreign visitors was wholly surmise, and the figure of £200,000 could be assumed to be higher than the actual figure The amendment was mean in spirit and intention. The Minister would be going far beyond the original intention if he exercised his ingenuity to make regulations to put charges on foreigners who used the health service There was much pressure behind the amendment, it was that certain elements of the medical profession would be able to charge fees (Cries of "Oh!") If he were asked to put his finger on where abuses in the health service took place, Mr Bevan said, he would single out the manipulation of fee-paying beds by specialists in hospitals There was more abuse from that than in any other part of the service Abuses also took place often among the dentists and opticians in the National Health Service, which had not yet existed long enough to eradicate commercialism from the medical profession. One of the results of having a good health service and good nutritional standards was that we had not a large experience of some epidemic diseases on which to train our doctors It might therefore become necessary, and indeed before he left the Ministry of Health he had discussed this with his medical advisers, for us to bring patients from different parts of the Colonial Empire to be treated in Britain

Dr HILL thought this was much ado about nothing He did not think that the visitor to this country regarded it as necessary, reasonable, or sensible that part of the hospitality we provided should be free dentures and spectacles The amendment was negatived by 285 votes to 254

Mr MESSER moved an amendment to provide that free spectacles and dentures should be supplied not only to hospital patients but to anyone "under medical treatment in any institution or in his own home" Mr BLENKINSOP agreed that there were real anomalies between one category and another Mr Messer's proposed exemption would be too wide, but Mr Blenkinsop agreed to consider sympathetically, though not very hopefully, whether any easement in the position could be made The amendment was withdrawn

A TRIAL RUN

Dr BARNETT STROSS moved an amendment to put a term to the contemplated charges. They should, he proposed, only continue in force until March 31, 1952, unless Parliament otherwise determined Mr MARQUAND found it difficult to see how the nation's economic situation could change sufficiently in one year to enable us to withdraw the charges But he sympathised with the view that there should be a review after a reasonable period to see whether the need still existed One year's experience would be too short, and they would require two full years' working of the charges to measure their effects Then they could see, for instance, whether there had been any improvement in the school dental service, and how hospital expenditure was moving He would introduce a new clause on the report stage to bring the charges to an end in April, 1954

The clause was ordered to stand part of the Bill by 262 votes to 3

On clause 2 Mr BLENKINSOP accepted an amendment, moved by Mr MESSER, to ensure that no increase could be made in the charges laid down in the Bill without legislation, though reductions could still be made by order in council

TREATMENT ABROAD FOR THE TUBERCULOUS

On the question that clause 3 stand part of the Bill Mr MESSER said it ought to be understood that Switzerland had nothing to offer this country in the way of positive treatment So far as surgical work was concerned, for instance, we had not merely as good but better surgeons But there was a type of tuberculosis which could be better treated in Switzerland, and he hoped that the Government would give consideration to that aspect He feared many would be disappointed at the number of cases they would be able to send to Switzerland, and it would be wrong to delude tuberculosis patients with the hope that they would be able to get immediate treatment more quickly now Regional hospital boards, he understood, would select the type of case to be sent and it would be difficult to say who should have priority

Lieut -Colonel WALTER ELLIOT said that although this provision might be small it was something To choose patients was not so difficult as not being able to make a choice at all It was true that Switzerland was not a better country for the treatment of tuberculosis than our own, but it had staff and beds and that was the essential thing "Let us bring the two together as rapidly and as extensively as possible"

Miss MARGARET HERBISON, joint under-secretary of State for Scotland, said that though the number of beds available at present was small the clause was evidence of the Government's determination to conquer a grave social problem They had chosen respiratory cases in an attempt to bring down the incidence, because these were the cases where there was a fear of infection This clause and the remaining clauses were ordered to stand part of the Bill.

On the recommittal of the Bill on May 7 Mr MARQUAND, in fulfilment of his promise to Mr Messer to reconsider the wording of the provision exempting hospital inpatients from the charges, moved an amendment defining those eligible for exemption as a patient

> "who is resident in a hospital at the time when the appliance is supplied and has been continuously so resident since the examination or testing of sight

Mr Marquand stressed that those who were in pay-beds or in disclaimed hospitals were not exempt from the charges The two groups whom the Government wished to exempt were those for whom the provision of spectacles or dentures was a natural part of treatment in hospitals, and those who were long stay or chronic hospital patients But Members were very dissatisfied with his proposal Dr **Hill** thought it involved the innocent patient in a gamble as to whether the appliance arrived during his stay in hospital Mr **Leslie Hale** suggested that a man with a broken leg could get false teeth while in hospital, while people were often not long in hospital for an ophthalmic operation Mr **Messer** himself could only see difficulties arising from the amendment, and he admitted he preferred the Bill in its original form The amendment was formally negatived

Mr **Marquand** moved a new clause fixing April 1, 1954, for the date of expiry of the Act, unless the House expressly resolved otherwise

MAINLY FINANCIAL

In the debate on the third reading Mr **Hugh Linstead** described the charges as a recognition by the Cabinet that the health service had had more than a proper share of our resources and that it was right that the excess should now be met by the user and not by the taxpayer He regretted, however, that the charges fell so heavily on two sections only The charges, in his view, were the inevitable result of the policy which had been pursued since the introduction of the service Dr **Barnett Stross** pointed out that the cost of the service worked out at about £8 per head per annum He could not agree that that was too large a share of our national resources Mr **Messer** thought the Bill undermined the principle of a completely free service He faced the future with foreboding, and he believed the sooner we could take the service out of the hands of the Treasury and finance it by other means the better He thought there was a possibility of this being done We should then be able to organise the service without always being faced with the fact that here was a ready pool, from which the Chancellor could draw

Dr A D D **Broughton** said everyone disliked the charges made in the Bill, but he thought they had been made necessary by the rapid development of the service He confessed that if he were edentulous, myopic, and tuberculous he would regard the eradication of tuberculosis as of more importance than the provision of dentures and spectacles

Colonel **Elliot** said that if we accepted that a ceiling must be put on the health service he did not see how we could escape from the logic that something must be done to implement that view It might well be possible to tackle the matter in another way, but at least the Bill got away from the idea that the service was sacrosanct and must not be touched

Mr **Marquand** thought the Bill provided distasteful machinery to accomplish a useful purpose But if these charges were not made, before long we should have to close hospital beds He could not agree with Dr Hill that the charges had been made in a slapdash manner The charges chosen would inflict less hardship than others consistent with making sufficiently large savings So far as possible they had tried to shield the sick, and to protect the poor they had empowered the National Assistance Board for the first time to give help to people in full-time employment He looked forward with some confidence to the possibility of a more peaceful world at the end of three years when our burdens would be lessened and we would be able to go forward to an improvement and expansion of our great National Health Service

QUESTION TIME

Hospital Group Management Committees

Lieut Commander **Richard Thompson** asked the Minister of Health how many persons had resigned from, or for other reasons ceased to serve on, hospital group management committees during 1950—Mr **Marquand** replied 751 members of hospital management committees in England and Wales

In answer to a further question he added that the number of seats on hospital management committees in England and Wales filled on March 31, 1951, was 6370, but the actual number of serving members was somewhat less, as many were members of more than one committee

Mr **Harold Sutcliffe** In view of these figures is not the number of resignations very high ? Mr **Marquand** The members are appointed normally for three years, 751 out of 6370 is not a high number

Hospital Waiting-lists

In answer to a question Mr **Marquand** stated that the number of people on hospital waiting lists in England and Wales on Dec 31, 1950, was 553,577

Hospital Service Reserve

In reply to Mr **Messer**, Mr **Blenkinsop** said that the number of recruits enrolled in the National Hospital Service Reserve was now 14,675 Since in the event of war the hospital and first aid services would need about 80,000 additional nurses he could not regard the present rate of progress as satisfactory

Sheffield Health Centre

Mr **Somerville Hastings** asked the Minister why the comprehensive health centre which the Sheffield Health Committee decided to inaugurate in 1948 by conversion of the Frith Park maternity and child welfare centre was not yet in operation , and what was holding up the anticipated progress —Mr **Marquand** replied I understand that the doctors concerned are now unwilling to coöperate

Mr **Hastings** Can the Minister use his good offices with these difficult doctors, so that at any rate we may have one health centre in operation as an experiment before long ? —Mr **Marquand** Nothing would please me better than that the doctors should coöperate, because approval for the centre was given quite a long time ago Mr **Hastings** Would the Minister consider calling a meeting of the difficult doctors ? It is not all the doctors in the neighbourhood who are involved Could he not arrange for a meeting of such doctors and put the case to them ?—Mr **Marquand** I would be very glad to look into that possibility

University of St Andrews

Replying to a question the Prime Minister announced that a royal commission has been set up

> 'To inquire into the organisation of University education in Dundee and its relationship with St Andrews University, and to recommend what changes, if any, should be made in the constitution, functions, and powers of the University of St Andrews of University College Dundee or of any other body or institution concerned"

Prof Dugald Baird, F R C O G , is the only doctor among the eight members named by Mr Attlee

Thames Pollution and Public Health

Mr J A **Boyd Carpenter** asked the Minister of Health whether he was aware of the pollution of the River Thames, and whether, in view of the opening of the bathing season, he had any statement to make as to dangers to health involved in bathing in this river —Mr **Marquand** I am advised that above Teddington the risks to bathers are not great I understand from the Minister of Local Government and Planning that to purify the Thames completely would cost more money, materials, and labour than we can afford at present

Mr **Lionel Heald** In view of the very large number of people who bathe in the Thames, at places like Runnymede, for example, does not the Minister think that the expression he has used, that the danger is 'not great, might be put a little more specifically ?—Mr **Marquand** It is impossible to measure accurately the risk to health One can only give a general opinion based on that of my medical advisors

Sir **Ralph Glyn** asked the Minister of Health whether his attention had been drawn to the statement by the chairman of the Thames Conservancy that no instance had ever been reported, so far as the Thames was concerned, by any medical authority to the effect that the spread of poliomyelitis had been due to bathing in that river , and if he would consider the advisability of recommending the Medical Research Council, in conjunction with the Catchment and River Board Association, to go into the whole question of bacteriological pollution of rivers and lakes in the United Kingdom and the supposed effect bathing had in promoting this disease —Mr **Marquand** replied My medical advisors are in agreement with the statement mentioned The Medical Research Council are already engaged in an extensive investigation of poliomyelitis, in which I am assured that no field of inquiry as to possible causes will escape attention.

Sanitary Facilities in Prisons

Mr ANTHONY GREENWOOD asked the Home Secretary whether it was his intention to modernise the inadequate sanitation of the prisons —Mr CHUTER EDE replied Although the prisons in England and Wales are overcrowded, I do not accept the implication that the sanitary facilities in the prisons are in general inadequate for health and hygiene The existing facilities are being steadily brought up to modern standards, where necessary, but no radical change in the type of facilities provided is contemplated

Replying to a further question Mr EDE said the ablution facilities in the prisons in England and Wales were not ideal, but could hardly be described as inadequate Each prisoner had a water jug and wash basin in his cell with soap, brush, and towel he was allowed to have a hot bath, weekly, and the arrangements for washing in the workshops were being steadily improved.

Medicine and the Law

"Continuously under Care and Treatment"

WHEN the Herbert Act allowed a husband or wife to petition for divorce in England on the ground of incurable insanity, and again when in the following year a like remedy was given by the Divorce (Scotland) Act, it was emphasised that there would be grave difficulty in obtaining medical evidence that in a particular case the insanity was incurable The two statutes required the petitioner to show that the respondent spouse had been "continuously under care and treatment" for at least five years, the "care and treatment" being detention in accordance with an order made under the appropriate law governing mental treatment

In the recent case of F *v* F, reported in the *Times* (April 28), the probate Divorce and Admiralty Division has held that the word "continuously" means what it says The wife had been admitted to a mental hospital in England under a reception order in October, 1945 In December, 1946, the order was discharged and she was taken under escort to a mental hospital in Scotland where a sheriff's order was issued under the Lunacy (Scotland) Acts In March, 1948, she was brought back from Scotland to another mental hospital in England Though there might be little doubt that her condition was continuous, there had been the brief interval in December, 1946, before she was certified in Scotland, during that short space of time there was no certificate in existence There was also the similar break in March, 1948 The Commissioner accepted and applied the dictionary meaning of "continuous" as "uninterrupted," 'conjoined without intervening space of time" He dismissed the petition on the ground that there were periods of time when the statute was not complied with.

The decision seems inevitable In Safford *v* Safford (1944), where the patient had been granted a total of 43 days' absence on trial for health under section 55 of the Lunacy Act, 1890 and a total of 59 days' absence on trial under section 275, it was held that there had been no interruption of the detention period Earlier in Benson *v* Benson (1941), where the wife had been discharged and was immediately transferred to another mental hospital as a voluntary patient, it was also held that there had been no interruption When the Herbert Act was passed, it unfortunately omitted to provide that detention in a Scottish mental hospital should count towards the five-year period In 1938 the Scottish Act expressly allowed detention in an English mental hospital to be so reckoned in Scotland And by the Law Reform (Miscellaneous Provisions) Act, 1949, it was enacted that detention under the appropriate statute in Scotland, Northern Ireland, the Isle of Man, or the Channel Islands might be taken into account in a petition in an English court But, as the recent decision shows, there must be no break in the ' continuous" care and treatment

Notes and News

GENERAL MEDICAL COUNCIL

THE results of the voting in the recent election of eleven members of the council under the Medical Acts, 1886 and 1950, were as follows The names of the successful candidates are shown in capitals

ENGLAND	
JOHN THORNTON INGRAM M.D	16 253
REGINALD HUGH BALFOUR BARROW M.D	15 601
HARRY GUY DAIN M D	15 554
OCTAVIUS CYRIL CARTER, M.B	15 300
EDWARD ANDREW GREGG M.D	15 221
NOEL EVERARD WATERFIELD O B.E. F R.C.S	14 851
JAMES ALEXANDER BROWN M.D	14 669
Thomas Beaton O B.E M D	8884
WALES	
WILFRED VIVIAN HOWELL, M.B.	unopposed
SCOTLAND	
ROBERT WILLIAM CRAIG O B.E M.D	unopposed
IAN DINGWALL GRANT M.B.	unopposed
IRELAND	
FRANK KANE M.D	unopposed

The term of office of these members of the council is five years from April 30, 1951

TWO OF QUEEN ELIZABETH'S PHYSICIANS

Two physicians in ordinary to Queen Elizabeth were Walter Baily or Bayley (c 1529–92), F.R.C.P (c 1581) fellow of New College regius professor of medicine in the University of Oxford, and later physician to the Queen, and his son in law Anthony Aylworth (c 1547–1619), also fellow of New College, who succeeded Bayley first as regius professor (1582–97) and later as royal physician They were both buried in the antechapel of New College, where the brasses on their graves are still remarkably well preserved, each including a portrait of the subject In 1904 exceptionally fine rubbings of these brasses were made for Mr L G H. Horton Smith, and he had photographs of these rubbings, endorsed with relevant details mounted and framed He has now presented the rubbings and photographs to the Royal College of Physicians

SOCIETY OF CHIROPODISTS

THE annual convention of the Society of Chiropodists was marked this year by the fulfilment of a long-cherished ambition. Opening the three-day convention at Friends House, London on April 26 Sir Henry Cohen, president of the British Medical Association said that the report of the Committee on Medical Auxiliaries had assured the chiropodists of professional status, the goal for which they had long striven. It must have given the society especial satisfaction to learn that it was the only organisation whose examinations the committee recognised as adequate for chiropodists wishing to work in the National Health Service He was glad, he said that the president of the B.M.A. had been invited to open the convention because it was the B.M.A. which had been instrumental in setting up the Board of Registration of Medical Auxiliaries and this had been the first formal step in the emergence of chiropody as a profession in its own right

Later that day, at a dinner held at the Park Lane Hotel London, Mr H Osmond Clarke, proposing the health of the society congratulated the chiropodists on attaining the dignity of a profession. It was well deserved he said, for chiropody was an important part of the medical service and no orthopædic unit was complete without a chiropodist The new advance added Mr Osmond Clarke, was of particular pleasure to him, for he had been associated with the society for many years and on occasions had been privileged to lecture at the Manchester School of Chiropody Replying to the toast Mr J H Hanby, the president, said that the society had every reason to be happy at this time, for the Cope report could be described as a judgment on its struggle for recognition. From its earliest days the society had tried to adopt a high standard of ethics and education taking the medical profession as its example It had been helped to reach this standard by the wisdom and guidance of eminent doctors many of whom were present The society, he said, realised the great responsibilities that accrued from the report but it would not flinch from them. The health of The Medical Profession was proposed by the Dean of St. Paul s, and Lord Webb-Johnson replied

HISTORY OF PHARMACY EXHIBITION

As a contribution to the Festival of Britain, the Wellcome Research Institution (183–193, Euston Road, N W 1) has arranged an exhibition to illustrate the history of pharmacy from the earliest times to the birth of chemotherapy The exhibition, which was opened by Sir Howard Florey, F.R S, on May 8, includes many rare books, prints, containers, and appliances The printed works on show include the earliest books on materia medica by Greek writers, an 11½ ft mediæval scroll bearing a pictorial recipe for the Philosopher's Stone, the early herbals, and the first edition of the *Pharmacopœia Londinensis*, and trace the evolution of alchemy to pharmacy and chemistry Drug containers range from the kohl jar of Queen Hatshepsut (1500 B C) to the medicine chests of Lord Nelson and George Washington, and include some outstanding examples of the ceramic art Other sections illustrate the fundamental discoveries of chemistry and chemotherapy, the early apparatus used in anæsthesia, and the development of drug manufacture The exhibition is beautifully arranged and many of the exhibits, apart from their historical interest, are notable as works of art

THE HANDICAPPED CHILD

THE two month team training course on the reablement of physically handicapped children, which we announced on March 3, was attended by 49 fellows from seven European countries Planned to let experts from war devastated countries see something of modern technique in this particular field, it was financed by the World Health Organisation, the United Nations Department of Social Affairs, and UNICEF, organised by the Ministries of Health and Education, and administered by the British Council The syllabus was prepared by Dr Harold Balme, joint consultant on rehabilitation to the three sponsoring organisations and the Ministry of Health, who presided at most of the joint sessions, and the medical lecturers included Sir Allen Daley, Dr Wilfrid Sheldon Dr C D S Agassiz, Dr F S Cooksey, and Dr Evelyn Lucas

In the first fortnight an attempt was made, by lectures, visits and demonstrations, to present the complete picture of the modern treatment, reablement, education, vocational training, and employment of physically handicapped children Four weeks were devoted to intensive technical training, the teams being broken up into groups according to their various specialties and planted out in appropriate institutions During this period the detailed arrangements were undertaken for the orthopædic surgeons by Sir Harry Platt, for the physiotherapists by Dr Cooksey, and for occupational therapists, teachers, and social workers by Miss Lindsay and Miss Hope Murray, while representatives of the Ministry of Labour helped to plan the programmes for the vocational training instructors A tour by motor coach in the seventh week enabled the visitors to see something of the larger industrial centres, and to go to institutions in Leeds, Wakefield, Manchester, Oswestry, Malmesbury, and Oxford The final week was given to reports from the fellows themselves, who discussed the problems of their own countries and the points that had impressed them in the British approach

The success of the course should encourage similar undertakings in the future

"THE SNAKE PIT" AND THE PENDULUM

FOR those with friends or kin in mental hospitals *The Snake Pit* was doubtless a terrifying film, heightening the dread of mental illness, giving colour to stories of rough handling and callous methods of treatment, and doing nothing to lift the dark shadow which has for so long hung over hospitals for the insane It had many important qualities it showed that the mentally sick are capable of recovery, and that they can be successfully treated, and it was very good cinema, holding the attention by fine acting, clever photography, and skilful presentation But many have felt that the picture it gave of some kinds of American institution—whether accurate or not—could only serve to prejudice the work of our own mental hospitals, which are very different

In *Out of True*, described as 'the answer to *The Snake Pit*," British mental hospital care is presented in the familiar manner of the documentary, and it would be pleasant to be able to say that the results are therefore more convincing Unfortunately the pendulum has been allowed to swing too far the other way True the film opens well with the sick wife dreaming she has murdered her mother in law, and waking up to throw herself off Hammersmith Bridge, but once she is inside the hospital no painful episode of any kind is allowed to ruffle the peace of the onlooker All the other patients seem to be on the eve of discharge, treatment is so various and thorough that it is positively non stop, and doctors and nurses have a saintly wisdom which all of us may envy but few of us achieve

It would be unfair to say that the picture is false on the contrary, every incident, every scene, every bit of equipment is accurate, the photography is good, the dialogue sparing But so much is left out that the result is far from lively Good acting might have breathed a little life into it, but though Jane Hylton looks nice, and even worried at times, her hair remains curly and shining throughout, and she is too well bred for her circumstances—among which are two pleasantly cockney little boys It is doubtful whether this valiant effort on the part of the Crown Film Unit will erase from the minds of the public the impression made by *The Snake Pit*

University of Oxford

In a congregation held on April 26 the following degrees were conferred

D M—Q J G Hobson, P C Reynell
B M—Mario L S Beesley D L Hadley

Dr R A Chambers has been elected to a Radcliffe travelling fellowship at University College

University of Cambridge

Prof J D Boyd has been appointed to the chair of anatomy in succession to Prof H A Harris, who retires on Oct 1

Dr Boyd who is 43 years of age was educated at the Royal Belfast Academical Institution and at Queen's University, Belfast, where he graduated B SC in 1927 with first-class honours and M B with honours three years later After holding a Rockefeller fellowship at Johns Hopkins Hospital he was appointed lecturer in anatomy at Cambridge in 1935, and he held this post till he took up his present chair at the London Hospital His published work includes papers on the development of the upper lip and the carotid body

Prof R A Peters, F R S, has been elected to an honorary fellowship of Gonville and Caius College

On April 28 the following degrees were conferred

M D—D A W Edwards M E Moore C N *Pulvertaft* O L Wade I G Wickes
M Chir—J F R Withycombe
M B B Chir—* G S Brindley *P E Huddy

* By proxy

University of Edinburgh

The Cameron prize for 1951 has been awarded to Prof Tadeus Reichstein and Prof E C Kendall in recognition of their researches leading to the discovery of 'Cortisone'

University of Glasgow

On April 28, 1951, the degree of M D was conferred on Robert Paul (with commendation), D C Watt, and T S Wilson

University of New Zealand

Dr Gerald Smyth, consulting gynæcological surgeon to Johannesburg Hospital, has been appointed to the postgraduate chair of obstetrics and gynæcology at Auckland University College He will also be medical director of the obstetrics and gynæcology unit at Cornwall Hospital in Auckland, as well as director of the new Auckland women's hospital when it is built

Dr Smyth, who is 47 graduated M B at Trinity College Dublin. He was elected F R C P I in 1931 and F R.C O G in 1947

Rheumatism Research Fellowship

The University of Leeds in association with the Leeds Regional Hospital Board invite applications for a research fellowship in the surgery of rheumatism at a nominal salary of £1000 to £1300 Further particulars will be found in our advertisement columns

Royal Cancer Hospital Centenary

The hospital will be open between Tuesday and Friday, May 15 and 18, for visitors to outpatient clinics, operations, and radiotherapy sessions and the Chester Beatty Research Institute will be open to visitors on Wednesday, May 16, from 7 P M to 9 P M, and on Thursday, May 17, from 10 A.M to 6 P M when a series of demonstrations will be presented Further details may be had from the house governor of the hospital, Fulham Road London S W 3

International Scientific Film Congress

The fourth of these congresses is to be held in the Municipal Museum, the Hague, from Sept 15 to 22 Further information may be had from the secretary of the Scientific Film Association, 4, Great Russell Street London, W C 1

London County Medical Society

A clinical meeting of this society will be held at St Ebba's Hospital Epsom, on Tuesday, June 5, at 3 P.M. Further information may be had from Dr A. Kahan, the hon. secretary, St James Hospital Ouseley Road, Balham, S W 12

Casualties in Korea

Recent casualty lists contain the names of the following R.A.M.C officers

Wounded —Captain THOMAS DUNGAVEL, M.B. Glasg
Missing —Captain R P HICKEY M.B. Lond. Captain D R. PATCHETT, M.R.C.S.

Hospital Mattresses

The British Standards Institution has published two draft standards for hospital mattresses as follows (1) bordered mattresses (CS[M]572), and (2) spring interior mattresses (CS[M]571) Comments should reach the institution, 24/28, Victoria Street, London, S W 1 before June 19

Toxic Chemicals in Agriculture

Under this title the working party set up by the Minister of Agriculture and Fisheries under the chairmanship of Prof S Zuckerman, M.D F.R.S , has issued its report (H.M. Stationery Office Pp 16 1*s*) We referred to this committee s work in our issue of March 31 (p 728)

Scottish Society of Anæsthetists

This society held its annual meeting at Dunblane Perthshire between April 27 and 29 Dr H. H Pinkerton (Glasgow) the president delivered an address on General Anæsthesia for Collapse Therapy in Pulmonary Tuberculosis Dr T J C MacDonald (Aberdeen) was elected vice president. Dr W W Mushin (Cardiff) was a guest of the society, and gave a short talk which he entitled the Null Hypothesis. The prize which the society is awarding annually for the best paper submitted from a registrar was won this year by Dr J G Robson (Glasgow)

Sickness Benefit for Contacts

Under National Insurance regulations a person who has been in contact with an infectious disease can be treated as incapable of work for the purposes of claiming sickness benefit only if he is excluded from work on the certificate of a medical officer of health The Ministry of National Insurance states that such a patient who asks his doctor for a certificate should be advised to apply at once to the M.O.H. If under these circumstances, a patient claims sickness benefit on a certificate signed by his own doctor the local National Insurance office will in order to avoid delay send the relevant particulars to the M.O.H. asking him whether he will consider issuing the necessary certificate The patient s own doctor and the patient himself will be informed

New Maternity Wing at Hackney

On May 2 the Duchess of Gloucester opened a new maternity wing at Hackney Hospital, London. This wing was originally planned in 1937 but work was suspended in 1940 after the main structure had been completed. When building was resumed in 1949 the original plan for 86 beds was superseded by one for 109 beds. The building is constructed of brickwork on a steel frame with reinforced concrete floors The ground floor contains 3 single 1 two bed and 6 four bed rooms nursery room, lecture-room, waiting room, and office the first floor 7 single, 1 two-bed, and 6 four bed rooms, and nursery room the second floor 4 single 1 two-bed, and 6 four bed rooms, premature babies unit and nursery room the third floor (west wing) delivery section of 4 delivery rooms delivery and operating room, 3 first-stage rooms (2 single and 1 three-bed) and 1 single bed room for eclampsia cases, and the third floor (south wing) 4 four bed rooms for antenatal cases 1 day room with balcony solarium, examination room and doctors room. The staircase and lift are centrally placed and there is an external staircase at the end of each wing Each floor has a solarium, provided with radiant heat. The building is heated by steam and hot water with automatic temperature control in those rooms where a constant temperature is important

Fatal Shock from Television Set

At an inquest on a boy of 4 years, who died while watching television at his home in Leicestershire on May 3, the jury returned a verdict of accidental death, with a rider that there might have been more insulation on the set (*Times*, May 8) The boy, who was lying on the hearthrug with his older sister, appeared to have put his face against the metal loud speaker grille when his foot was on the fender , a radio expert found that owing to a defect in the loud speaker securing bolts the grille was in direct contact with the mains

British Society for Research on Ageing

The annual conference of this society will be held on June 2 at 3 P.M., at the medical school of the Middlesex Hospital, London, W 1 The following are to speak Dr Lester M. Morrison, of Los Angeles, on the Dietary and Medicinal Treatment of Atherosclerosis Prof R E Tunbridge, F.R.C.P , Process of Ageing in Connective Tissues Mr V Korenchevsky D.SC , Rôle of Deficiency of Sex Hormones in the Processes of Ageing, and Hormonal Treatment of Senescence in Male Rats Mr D C Hardwick B.SC , Histamine Metabolism and Ageing Dr E Geiringer Mechanism of Coronary Thrombosis

Police Surgeons Association of Great Britain

Police surgeons from all over Great Britain met on May 2 at New Scotland Yard to form a new association to be known as the Police Surgeons Association of Great Britain. The meeting was convened by the Metropolitan Police Surgeons Association, which was wound up on forming the new body Dr W G Johnston, president of the Metropolitan association, said that already 250 of the 1000 police surgeons in the country had applied for membership of the new organisation, a response which exceeded all expectations. The Metropolitan association had been of great value in improving conditions and amenities for its members and the new organisation would be even more successful for it would provide effective representation of all the police surgeons in the country Its aims would be first to improve and standardise conditions and rates of remuneration, and later to press for the establishment of a postgraduate diploma in forensic medicine for those engaged in police work. The need for this diploma was becoming greater since forensic medicine as a subject was slowly disappearing from the student s curriculum and from the final examinations

Dr W G Johnston was elected president of the new association, Dr R D Summers secretary, and Dr C J Berkeley Way treasurer

Fourth World Health Assembly

Seventy six member nations and territories were invited to send representatives to W.H.O s fourth World Health Assembly which opened in Geneva last Monday Three further nations—Japan, Spain, and the West German Federal Republic—whose claim for full membership will be examined by the assembly are also represented. Among the agenda are the adoption of international sanitary regulations which are intended to replace the existing sanitary conventions technical discussions on the education and training of medical and public health personnel and consideration of the director general s proposal for a 1952 budget of $8,700 000 (about $2 million more than the current budget) Prof René Sand, of Brussels is to receive the Leon Bernard prize

The United Kingdom delegates and advisers are

Ministry of Health.—Sir John Charles, F.R.C.P Dr Melville Mackenzie Mr W H Boucher Miss E Cockayne S.R.N and Mr F A. Mells
Department of Health for Scotland.—Sir Andrew Davidson M.D
Colonial Office.—Dr Wilson Rae.
General Register Office —Mr George North LL.D Dr W P D Logan, and Mr A E Joll

Dr Melville Mackenzie will also attend a meeting of the executive board of the World Health Organisation which will follow the World Health Assembly

---

The Dentists Register 1951, published at 18*s* by Constable & Co Ltd. 10, Orange Street Leicester Square, London W C 2 for the Dental Board, contains 15 327 names of dentists (including 122 dentists from the Dominions and Colonies and 277 foreign dentists) as against 15,052 (including 72 dentists from the Dominions and Colonies and 268 foreign dentists) in 1950

Diary of the Week

MAY 13 TO 19

Tuesday, 15th

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St Mary's Hospital Medical School, W 2

5 P M Prof Wilson Smith F R S Problem of Protection Against Staphylococcal Infections (Almroth Wright lecture)

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W C 2

5 P M Dr E J Moynahan Bonds and Blisters the Physics and Chemistry of Blister Formations

Wednesday, 16th

ROYAL COLLEGE OF PHYSICIANS Pall Mall East S W 1

5 P.M Dr T F Fox Professional Freedom (Last Croonian lecture)

UNIVERSITY OF LONDON

5 30 P.M (University College, Gower Street W C 1) Prof A Fessard (Paris) Comparative Electrophysiology (First of three lectures)

INSTITUTE OF DERMATOLOGY

5 P.M Dr J O Oliver Chronic Inflammation

INSTITUTE OF OPHTHALMOLOGY, Judd Street W C 1

5 30 P.M Dr C J Gavey How far do Fundus Appearances Reflect Cardiovascular Diseases ?

NORTH EAST LONDON MEDICAL SOCIETY

3 30 P M (Prince of Wales's Hospital Tottenham N 15) Clinical meeting

OXFORD UNIVERSITY

5 P M (Radcliffe Infirmary, Oxford) Mr V E Negus Defences of the Air Passages, with Relation to Ciliary Action (Litchfield lecture)

Thursday, 17th

UNIVERSITY COLLEGE, Gower Street W C 1

4 45 P M Prof H A Krebs F.R.S Energy Transformations in Living Matter (Last of four lectures)

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Corner, S W 1

4 30 P M Dr Desmond Curran Psychiatry lecture demonstration

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE 26 Portland Place W 1

7 30 P M Prof Brian Maegraith Dr E Sherwood Jones Dr W H H Andrews Pathological Processes in Malaria—Progress Report

BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1

8 45 P M Sir Stanford Cade The Influence of Radiology on the Diagnosis and Treatment of Intrinsic Carcinoma of the Larynx (Mackenzie Davidson lecture)

MIDDLESEX COUNTY MEDICAL SOCIETY

3 P.M (Napsbury Hospital St Albans) Demonstrations and coloured film on Transorbital Leucotomy

OXFORD UNIVERSITY

4 15 P M (Radcliffe Infirmary) Prof T N A Jeffcoate Incoördinate Uterine Action (Litchfield lecture)

HONYMAN GILLESPIE LECTURE

5 P.M (University New Buildings Teviot Place Edinburgh) Mr John Gillingham Arteriovenous Malformations of the Head

UNIVERSITY OF ST ANDREWS

5 P M (Medical School Small's Wynd Dundee) Prof J H Burn, F R.S Physiological and Clinical Importance of Noradrenaline

Friday, 18th

UNIVERSITY OF LONDON

5 30 P M (University College W C 1) Prof D Bovet (Rome) Natural and Synthetic Sympatholytic Drugs and their Structural Relationship with Sympathomimetic Substances

FACULTY OF RADIOLOGISTS

2 15 P M (Royal College of Surgeons Lincoln's Inn Fields W C 2) Sir Geoffrey Jefferson F R.S The Meningiomas (Skinner lecture)

ROYAL EYE HOSPITAL, St George's Circus Southwark, S E 1

5 P.M Miss M Savory Ophthalmic Injuries

INSTITUTE OF DERMATOLOGY

5 30 P.M Dr G B Dowling Clinical demonstration

INSTITUTE OF OPHTHALMOLOGY

5 30 P M Mr H E Hobbs Gonioscopy after Glaucoma Operations

Saturday, 19th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY

10 30 P M (Preston Hall Sanatorium near Maidstone Kent) Dr H. V Morlock In my Opinion

---

Dr S Leonard Simpson is to give a paper to the New York Academy of Medicine on May 15 on the Adrenal Gland He will also give an address to the Los Angeles Medical Association on Pituitary adrenal Hyperfunction

Dr J F Brailsford is to lecture in Lisbon and Madrid under the auspices of the British Council

Mr Albert Sharman is sailing for the United States, where he is addressing the American Society for the Study of Sterility and the American Medical Association

Appointments

BROWN, C P M B Manc, D A asst anæsthetist West Manchester hospital group

BRUETON N F W M B Brist deputy director South Western Regional Blood Transfusion Service

BUSH FREDERIC M A M B Camb D.M R.E consultant radiologist St Margaret's Hospital Epping

CROWLEY NORA, M B N U I asst M O maternity and child welfare and school medical inspection Northants

DARKE, G H M B Lond F R C.S E consultant surgeon, South Somerset clinical area.

DOHERTY J F, M B M RAD Lpool asst radiologist Lancaster hospitals group

DUNN, D M, M B Durh F R C.S consultant orthopædic surgeon Colchester group of hospitals

EARLE B V, M D Dubl, M.R.C.P senior psychiatric registrar, Bristol mental hospitals

EDGE J R, M D Leeds M R C P senior asst M O Red Cross sanatoria of Scotland

ELLISON, D J M.B Edin M R C.P.E senior medical registrar Bath clinical area

FERGUSON CHRISTINA, M B St And asst M O H Ross and Cromarty

HUMPHRIES, BARRYMORE M B Sheff, D OBST asst M O maternity and child welfare, Birmingham

JENKINS, MARY, M B Wales D P H asst M O H Newport Mon

LESLIE W I, M B Edin consultant area pathologist Prince of Wales's Hospital London

MARTIN MARGARET, M B Edin temporary M O maternity and child welfare Birmingham

MITCHELL J B M D Lond M R C P consultant physician, Bolton hospitals centre

NERI L E M B Madras registrar in thoracic surgery, Hawkmoor Sanatorium Bovey Tracey Devon

PORTER K R D M B E, M R.C.S L.D S D P H asst. senior M.O, Oxford Regional Hospital Board

RAEBURN CYRIL, M R C.S consultant pathologist Leytonstone group of hospitals

RAINS KATHLEEN M.R C.S, D A asst anæsthetist South Manchester area

RENTON P H M D Manc deputy director, Manchester Regional Blood Transfusion Service

SINTON, J R M D Lond M R C P resident asst physician Baguley Sanatorium Cheshire

SPENCER J G C M A, M D Camb F R C.S asst. pathologist Frenchay Hospital Bristol

STEWART, ROBERTA, M B Manc, D OBST asst M O maternity and child welfare, Manchester

WARRINGTON, H C, M B Manc D.M R T asst radiotherapist Christie Hospital and Holt Radium Institute Manchester

WILMOT, T J, M.S Lond F R C.S consultant ear nose and throat surgeon, West Tyrone group of hospitals, Northern Ireland

Colonial Service

CATTELL M L, M.B Wales M O, Nigeria

KUCHARSKI J W, M B Polish School of Medicine M O, Tanganyika

KUCZYNSKI K, M B M O, General Hospital Barbados

MASON K D, M B Lond M O (temporary) Nigeria.

SUBRAMANI A S M B Rangoon M R C O G M O, special grade (temporary), Nigeria

SUTOROWSKI, Z MED DIP Warsaw M O (temporary) Gold Coast

SWEETNAM J T M B Dubl M O Nigeria

Births, Marriages, and Deaths

BIRTHS

BARKWORTH —On April 28, the wife of Dr F B S Barkworth —a son

DALRYMPLE —On April 25 in London the wife of Mr Kenneth Dalrymple, F R C S —a daughter

FRIEDLANDER —On May 2 in Manchester to Dr Jean L Broughton wife of Dr H A Friedlander—a daughter

HALL SMITH —On April 30 at Hove the wife of Dr Patrick Hall-Smith—a daughter

HEBBERT —On April 26 the wife of Dr John Hebbert—a daughter

HILL —On May 1 in Edinburgh the wife of Dr A G S Hill —a son

PRINGLE —On April 29, the wife of Dr Edward Pringle—a son

MARRIAGES

BOSC—COSSLETT —On May 2, in Manchester François Victor Augustin Bosc M B to Nancy May Cosslett

RITCHIE—WARING —On May 1, in Manchester Robert Wilkie Ritchie M B to Kathleen Waring

WALLEY—WINTERBOTHAM —On April 28, at Beaconsfield Bucks Ronald Victor Walley, M B to Betty Margaret Winterbotham M B

DEATHS

LIVINGSTONE-LEARMONTH —On April 28 in Edinburgh Basil Lockhart Livingstone Learmonth M B Edin aged 84

STEPHEN —On May 2 in London, George Mackie Stephen M A, M B Aberd

THEOBALDS —On May 1 in London Owen le Marc Theobalds M R.C.S aged 90

TRAPNELL.—On April 28 at Beckenham Kent Francis Cyril Trapnell M D Camb

WAYTE.—On May 4 at Croydon, John Wayte M A B.M. Oxfd aged 89

DISTURBANCE OF THE PUPILLARY REACTIONS*

J H DOGGART
M.A., M.D Camb , F.R C S
SURGEON, MOORFIELDS, WESTMINSTER, AND CENTRAL EYE HOSPITAL LONDON

NOT only in the realm of pharmacological experiment, but also in everyday clinical practice, there has assuredly been a great change in our conception of the pupillary reactions. Reference to the textbooks of forty or fifty years ago will confirm something vividly remembered by many a clinician alive today—i e , the dogmatic interpretation of pupillary phenomena, contrasted with the diffident attitude of modern teachers. A man exhibiting loss of the light reflex in one or both pupils stood less chance of being accepted for life assurance without “ loading ” of his policy than he would stand nowadays, when most candidates for medical diplomas can reel off a list of non syphilitic reasons for that abnormality.

The semeiology of the pupil in the realm of head injury was almost as cogent as were the *sortes biblicæ* in ethical problems. Such-and-such manifestations in the pupil were the signal for trepanning, because their meaning was all too clear. The situation is different now. Modern developments in cranial surgery, linked with knowledge derived from necropsy findings, pathological histology, radiography, and other technical advances, have shown that many of the old clinical rules were fallacious through over simplification. “The exception proves the rule,” says the old proverb. “Yes,” one might reply, “ and so does a *pinch* of salt improve a plate of soup, but *too many* exceptions will wreck the rule, just as too many cooks *or* a surfeit of salt will spoil the broth.”

CLINICAL EXAMINATION

Let it not be supposed, however, that pupillary signs have lost their importance. When we consider the extent of the nerve paths dealing with modifications in the size of the pupil, and if we also bear in mind the number and variety of important structures with which those nerve paths enter into relation, the absurdity of neglecting pupillary changes must be self evident; but their significance cannot be properly assessed if it is expressed as a set of rigid rules. Abnormal pupillary reactions, if they are to help in building up diagnosis and prognosis, must be considered in relation to (*a*) the associated ocular signs, and (*b*) the remainder of the clinical evidence.

Routine examination of the eye will in a large proportion of cases supply the explanation for unilateral and bilateral abnormality of the pupil. Thus we may find that the iris sphincter has been ruptured by trauma, or that adhesions have been established between the iris and the cornea or lens. Ophthalmoscopy may reveal optic atrophy, or macular disease or other important lesions of the fundi and media. Instances could easily be multiplied, but the essential thing to remember is that ingenious but mistaken neurological reasons for a given pupillary disturbance have often been adduced when the real cause lay open to inspection in the eye itself.

In assembling the remainder of the clinical evidence we should pay special attention to the history, and try to ascertain what parts of the pupillary pathways have suffered. Impulses may be abolished altogether, or intensified, or in some cases may show wider fluctuation than is consistent with health. The relevant nerve paths may be severed, irritated, or stretched, or perhaps subjected to pressure by extravasated fluid, neoplastic masses, or displaced bone. Horner's syndrome, which results from abolition of the impulses from the right or left cervical sympathetic nerve, is an excellent instance of variety in causation. These associated signs of miosis, slight ptosis, and enophthalmia can be occasioned by birth injury, intracranial lesions, retropharyngeal abscess, cervical rib, or apical tuberculosis—to mention only a few of the possible causes. Claude Bernard's syndrome, which is the converse of Horner's, is a well known feature of thyrotoxicosis, but can also arise from a multitude of different lesions in the thorax, neck, or elsewhere.

CHANGES WITH AGE

Some of the pupillary reflexes are known to exist in the sixth month of fœtal life. The psychosensory reflex is absent at birth but appears within a few days, by which time the reactions of maturity are already evident. External stimuli—e g , light, near objects, and sensory impressions on the eyelids or the cornea—nearly always impel constriction, whereas internal changes—e.g , fear, pain, and nausea—tend to dilate the pupil. Thus we may say that miosis in sleep is attributable to a dearth of psychological activity.

In old age the average size and activity of the pupil are alike diminished by reason of atrophic changes in the iris musculature, hyaline degeneration of the stroma, and perhaps partial calcification of the iris vessels. The moment of death is marked by sudden opening of the pupil, and people used to regard this as the window through which the soul was wafted away from the body. Progressive contraction occurs with the onset of rigor mortis, but it has been observed that eserine, atropine, and various other drugs continue to act on the pupil until an hour or more after death.

PUPILLARY MECHANISM

Mention of the part played by local vascular changes in the production of senile miosis recalls that Langworthy and Ortega (1943) look on the so-called dilator muscle as a negligible factor in pupillary reaction. According to them, sympathetic mydriasis can only be achieved through the medium of the iris vessels. These workers also criticise the former conception of two antagonistic systems governing the pupillary movements. The sympathetic fibres, they say, act in harmony with those of the parasympathetic system, the latter holding the main power but able to exert more sensitive regulation by reason of the permanent tonic background created by the dilator impulses.

Lowenstein (1940, 1946) has made detailed investigations into the pupillary mechanism with the aid of cinematographic apparatus. In this way he has been able to secure motion pictures in darkness as well as in light. The “ dark ” pictures were taken with infra-red filters whereby records could continue to be made without maintaining retinal stimulation. Analysis of his results indicates that a latent period of rather more than a fifth of a second follows the impingement of light upon the retina. The pupil's contraction can be resolved into a rapid primary phase succeeded by two slower phases. Cessation of stimulation by light ushers in another latent period of just over a fifth of a second, and then come the three phases of dilatation.

The main practical significance of Lowenstein's work lies in the hope of gaining detailed facts about the separate responsibility of the sympathetic and parasympathetic systems for a given pupillary abnormality. In some cases of anisocoria, for instance, the ordinary methods of clinical examination may fail to show which is the abnormal eye, and whether the sympathetic or the parasympathetic system is at fault; but Lowenstein claims that the rapid primary phase of contraction to light is entirely a parasympathetic phenomenon, whereas the secondary and tertiary phases depend on sympathetic activity. If stimulation by light is followed by an abnormally long latent period, and then by a contraction

---

*Based on a talk given at Christchurch to the Ophthalmological Society of New Zealand

Diary of the Week

MAY 13 TO 19

Tuesday, 15th

Wright Fleming Institute of Microbiology St Mary's Hospital Medical School, W 2

5 P M Prof Wilson Smith F R.S Problem of Protection Against Staphylococcal Infections (Almroth Wright lecture)

Institute of Dermatology, St Johns Hospital Lisle Street W C 2

5 P M Dr E J Moynahan Bonds and Blisters the Physics and Chemistry of Blister Formations

Wednesday, 16th

Royal College of Physicians Pall Mall East S W 1

5 P.M Dr T F Fox Professional Freedom (Last Croonian lecture)

University of London

5 30 P M (University College Gower Street W C 1) Prof A Fessard (Paris) Comparative Electrophysiology (First of three lectures)

Institute of Dermatology

5 P M Dr J O Oliver Chronic Inflammation

Institute of Ophthalmology, Judd Street, W C 1

5 30 P.M Dr C J Gavey *How far do Fundus Appearances* Reflect Cardiovascular Diseases ?

North East London Medical Society

3 30 P M (Prince of Wales s Hospital, Tottenham, N 15) Clinical meeting

Oxford University

5 P M (Radcliffe Infirmary Oxford) Mr V E Negus Defences of the Air Passages, with Relation to Ciliary Action (Litchfield lecture)

Thursday, 17th

University College Gower Street W C 1

4 45 P M Prof H A Krebs F R S Energy Transformations in Living Matter (Last of four lectures)

St. George s Hospital Medical School, Hyde Park Corner S W 1

4 30 P M Dr Desmond Curran Psychiatry lecture-demonstration

Royal Society of Tropical Medicine and Hygiene, 26 Portland Place W 1

7 30 P M Prof Brian Maegraith Dr E Sherwood Jones Dr W H H Andrews Pathological Processes in Malaria —Progress Report

British Institute of Radiology 32 Welbeck Street W 1

8 45 P M Sir Stanford Cade The Influence of Radiology on the Diagnosis and Treatment of Intrinsic Carcinoma of the Larynx (Mackenzie Davidson lecture)

Middlesex County Medical Society

3 P M (Napsbury Hospital St Albans) *Demonstrations and* coloured film on Transorbital Leucotomy

Oxford University

4 15 P M (Radcliffe Infirmary) Prof T N A Jeffcoate Incoördinate Uterine Action (Litchfield lecture)

Honyman Gillespie Lecture

5 P M (University New Buildings Teviot Place Edinburgh) Mr John Gillingham Arteriovenous Malformations of the Head

University of St Andrews

5 P M (Medical School Small s Wynd Dundee) Prof J H Burn, F R.S Physiological and Clinical Importance of Noradrenaline

Friday, 18th

University of London

5 30 P M (University College, W C 1) Prof D Bovet (Rome) Natural and Synthetic Sympatholytic Drugs and their Structural Relationship with Sympathomimetic Substances

Faculty of Radiologists

2 15 P M (Royal College of Surgeons Lincoln s Inn Fields W C 2) Sir Geoffrey Jefferson F R.S The Meningiomas (Skinner lecture)

Royal Eye Hospital, St George s Circus Southwark S E 1

5 P.M Miss M Savory Ophthalmic Injuries

Institute of Dermatology

5 30 P.M Dr G B Dowling Clinical demonstration

Institute of Ophthalmology

5 30 P M Mr H E Hobbs Gonioscopy after Glaucoma Operations

Saturday, 19th

South East Metropolitan Regional Tuberculosis Society

10 30 P M (Preston Hall Sanatorium near Maidstone Kent) Dr H. V Morlock In my Opinion

---

Dr S Leonard Simpson is to give a paper to the New York Academy of Medicine on May 15 on the Adrenal Gland He will also give an address to the Los Angeles Medical Association on Pituitary adrenal Hyperfunction.

Dr J F Brailsford is to lecture in Lisbon and Madrid under the auspices of the British Council

Mr Albert Sharman is sailing for the United States, where he is addressing the American Society for the Study of Sterility and the American Medical Association

Appointments

Brown C P , M B Manc , D A asst anæsthetist, West Manchester hospital group

Brueton, N F W M B Brist deputy director, South Western Regional Blood Transfusion Service

Bush Frederic M A , M B Camb D M R.E consultant radiologist St Margaret s Hospital Epping

Crowley Nora M B N U I asst M O maternity and child welfare and school medical inspection Northants

Darke, G H , M B Lond F R C S E consultant surgeon South Somerset clinical area

Doherty J F , M B , M RAD Lpool asst radiologist Lancaster hospitals group

Dunn D M , M B Durh , F R C S consultant orthopædic surgeon Colchester group of hospitals

Earle B V M D Dubl , M R C P senior psychiatric registrar, Bristol mental hospitals

Edge J R , M D Leeds M R C P senior asst M O Red Cross sanatoria of Scotland

Ellison, D J M B Edin M R C P E senior medical registrar Bath clinical area

Ferguson Christina M.B St And asst M O H Ross and Cromarty

Humphries, Barrymore M B Sheff , D OBST asst M O maternity and child welfare Birmingham

Jenkins Mary, M B Wales D P H asst M O H. Newport, Mon

Leslie, W I , M B Edin consultant area pathologist, Prince of Wales s Hospital London

Martin Margaret, M B Edin *temporary* M O *maternity* and child welfare Birmingham

Mitchell J B M D Lond M R C P consultant physician, Bolton hospitals centre

Neri L E , M B Madras registrar in thoracic surgery Hawkmoor Sanatorium Bovey Tracey Devon

Porter K R D M B E , M R C.S L.D.S D P H asst. senior M O Oxford Regional Hospital Board

Raeburn Cyril M R C.S consultant pathologist Leytonstone group of hospitals

Rains Kathleen M R C.S , D A asst anæsthetist South Manchester area

Renton P H M D Manc deputy director Manchester Regional Blood Transfusion Service

Sinton, J R M D Lond M R C P resident asst physician Baguley Sanatorium, Cheshire

Spencer, J G C M A M D Camb , F R C S asst pathologist, Frenchay Hospital Bristol

Stewart Roberta M B Manc D OBST asst M O maternity and child welfare, Manchester

Warrington H C , M B Manc D M R T asst radiotherapist Christie Hospital and Holt Radium Institute Manchester

Wilmot, T J M.S Lond F R C S consultant ear nose and throat surgeon, West Tyrone group of hospitals Northern Ireland

Colonial Service

Cattell M L M B Wales M O , Nigeria

Kucharski J W , M B Polish School of Medicine M O , Tanganyika

Kuczynski K , M B M O , General Hospital Barbados

Mason K D M B Lond M O (temporary) Nigeria

Subramani A S , M B Rangoon M R C O G M O special grade (temporary), Nigeria

Sutorowski Z MED DIP Warsaw M O (temporary) Gold Coast

Sweetnam J T M B Dubl M O Nigeria

Births, Marriages, and Deaths

BIRTHS

Barkworth —On April 28 the wife of Dr F B S Barkworth —a son.

Dalrymple —On April 25 in London the wife of Mr Kenneth Dalrymple F R C S —a daughter

Friedlander —On May 2 in Manchester to Dr Jean L Broughton wife of Dr H A Friedlander—a daughter

Hall-Smith —On April 30 at Hove the wife of Dr Patrick Hall Smith—a daughter

Hebbert —On April 26 the wife of Dr John Hebbert—a daughter

Hill —On May 1 in Edinburgh the wife of Dr A G S Hill —a son

Pringle —On April 29 the wife of Dr Edward Pringle—a son

MARRIAGES

Bosc—Cosslett —On May 2, in Manchester, François Victor Augustin Bosc M B to Nancy May Cosslett

Ritchie—Waring —On May 1, in Manchester Robert Wilkie Ritchie M B to Kathleen Waring

Walley—Winterbotham —On April 28, at Beaconsfield Bucks Ronald Victor Walley M B to Betty Margaret Winterbotham M B

DEATHS

Livingstone-Learmonth —On April 28 in Edinburgh Basil Lockhart Livingstone Learmonth M B Edin aged 84

Stephen —On May 2 in London George Mackie Stephen M A M B Aberd

Theobalds —On May 1 in London Owen le Mare Theobalds M R C.S aged 90

Trapnell —On April 28 at Beckenham Kent, Francis Cyril Trapnell M D Camb

Wayte —On May 4 at Croydon, John Wayte M.A B.M. Oxfd aged 89 sign is of grave import Supragenicuiate lesions do not *directly* interfere with the pupillary reactions but may exert an indirect influence from hæmorrhage The question of multiple injury must always be considered before we venture to interpret the signs Thus, for instance, radiographic evidence and exact localisation of an intracranial foreign body cannot alone enable us to explain the signs, because the main havoc may be due to destruction along the path pursued by the missile on the way to its final lodgement

GENERAL ANÆSTHESIA

Psychosensory impulses are responsible for the wide-open pupils commonly seen during induction of anæsthesia, but soon the pupillary diameter reverts to normal, and the response to light is retained until narcosis has gone deeper than is usually safe in surgical operations Some patients are more susceptible than normal to the preoperative injection of atropine, hence a disproportionate degree of mydriasis may become evident Even so, the reaction to light is a valuable guide to the anæsthetist and is far preferable to the corneal reflex. The so-called " anæsthetic eye " is seldom due to the action of vapour, but rather to abrasion of the epithelium by fingers or gauze.

SPECIAL ABNORMALITIES

Argyll Robertson Pupil —The mistaken application of an Argyll Robertson label to every pupil which does not react to light but reacts to convergence is nowadays less common than it used to be, because the existence of a similar phenomenon in the tonic pupil has so often been emphasised of recent years The genuine Argyll Robertson pupil is small and does not dilate under the influence of atropine, though painful stimuli can still produce mydriasis The outline is seldom a regular circle, and is sometimes quadrilateral or elliptical. Another criterion laid down by Argyll Robertson purists is that the optic tracts must be healthy In other words they would withhold the Argyll Robertson label from all patients afflicted with serious defect of vision Loss of light reflex with retention of the reaction to convergence has been recorded in different diseases of the central nervous system—e g, disseminated sclerosis—and in injury to the base of the brain. The lesion responsible for an Argyll Robertson pupil is probably in the upper half of the mid brain near the aqueduct of Sylvius

Tonic pupils are commoner in women than in men, and often arise suddenly The third decade is the most likely time of onset, and the abnormality is unilateral in most cases Diminished tendon-jerks, especially of the ankle and knee, have often been noted, but this association is by no means invariable The affected pupil is usually larger than normal, and its variability in size contrasts strongly with the rigid miosis of an Argyll Robertson pupil. Irregularity of circumference is another typical feature, and the light reaction, direct and consensual, is absent or impaired Another point of difference from the Argyll Robertson pupil is the ready response to mydriatics but perhaps the most striking feature of all is the slowly progressive contraction of a tonic pupil on convergence, followed by even slower relaxation when the effort has been relinquished.

Paradoxical pupillary reactions offer a fascinating field for speculation It will be recalled that one of the cardinal elements of Horner's syndrome is miosis In some cases, however interruption of the cervical sympathetic has been followed by temporary mydriasis during mental excitement No certain explanation is known but it has been suggested that the dilator muscle is more susceptible to the action of adrenaline after deprivation of its nerve supply Reflex mydriasis under stimulation by light, and a similar response to convergence, have also been described.

Rare abnormalities of the pupil occur in endless variety Thus cases are on record in which rhythmical contraction and dilatation occurred synchronously with the excursions of *nystagmus* Well-marked *ectopia*, especially in an upward and inward direction, has more than once been noted in association with neoplasms of the pineal gland or of the third ventricle The gift of *voluntary mydriasis* must be at least as common as voluntary nystagmus, and I used to know a Belgian lady whose chief device of allurement was deliberate *hippus* When she gazed at you, with her pupils collapsing and expanding like a pair of concertinas, it was time to think of other things. One last abnormality can be mentioned In *cog-wheel pupil* the diameter waxes and wanes in a series of jerks instead of describing a continuous sweep

GENERAL CONCLUSIONS

Pupillary reactions in health and disease provide rich material for the anatomist, pharmacologist, and clinician alike Subject to innumerable congenital malformations as well as daily fluctuations in size, liable to be modified by age, and susceptible to the effect of drugs, injury, and disease, the pupils may be likened to a pair of mirrors in which strange events can be viewed with varying shades of distinctness, so long as they are considered in relation to the images emanating from other sources, but mirrors artificially isolated will cloud the issue and lead us into distortion, like the mirrors that adorn the walls of a fun fair

REFERENCES

Langworthy O R Ortega L (1943) *Medicine* 22 287
Lowenstein O (1940) *Arch Neurol Psychiat Chicago* 44 227
— (1946) *Ibid* 55, 652

THE USE OF THE PHONOCARDIOGRAPH IN CLINICAL MEDICINE*

William Evans
M.D, D.Sc Lond, F.R C.P
PHYSICIAN TO THE CARDIAC DEPARTMENT OF THE LONDON HOSPITAL, AND TO THE NATIONAL HEART HOSPITAL, CONSULTING CARDIOLOGIST TO THE ROYAL NAVY

Recording the heart sounds and murmurs is not a new science, the practice is as old as electrocardiography The characteristic electrocardiographic patterns in the several forms of heart disease are familiar to us, and it is timely to examine in what manner the phonocardiogram helps in the diagnosis of cardiovascular disorders Mention should be made of a handicap which no longer applies to the electrocardiogram—i.e, that standardisation of the sound record has not yet been wholly achieved, but this drawback has not hindered materially the contribution already made by the test to the interpretation of auscultatory signs, nor is the advent of this desirable standardisation of records to be long delayed.

I intend here to recount the ways in which the phonocardiograph has already helped, to name the circumstances in which the tracing is a necessary test, and to suggest what part it can play in the solution of outstanding problems

WHAT PHONOCARDIOGRAPHY HAS ALREADY ACCOMPLISHED

It should never be the purpose of phonocardiography to bring to light heart sounds or murmurs which do not yield to auscultation, its function is to show where these lie in relation to the separate phases of the cardiac cycle, and their exact incidence in the different parts of systole or diastole In this work of precise allocation of heart sounds and murmurs the test has enabled the clinician exclusively effected by the primary phase, Lowenstein concludes that the sympathetic system is disturbed He calls this type of response the tonohaptic reaction, and has noted its association with catatonia, postencephalitic parkinsonism, Frohlich's syndrome, and other disorders

---

* Based on a communication made to the International Congress of Physicians in London, 1947

PHARMACODYNAMIC TESTS

Without attempting any detailed review of Lowenstein's work, we can hope that it will facilitate differential diagnosis in many obscure disorders of the central nervous system, especially if the apparatus of investigation can be simplified Meanwhile a cruder method of differentiating sympathetic from parasympathetic abnormality exists in the pharmacodynamic tests, which depend on the fact that some drugs stimulate, and some depress, the parasympathetic-system, whereas its rival is stimulated by other drugs—e g , cocaine By noting the responses made to different drugs, we can, for instance, usually differentiate spastic from paralytic mydriasis

MODIFICATIONS IN DISEASE

Pupillary abnormality can be classified in different ways, and no attempt will here be made to set up a comprehensive system One of the obvious plans is to separate anomalies into static and dynamic, and that distinction is in some respects convenient , but of course the healthy pupil, and many types of unhealthy pupil, may show considerable fluctuation throughout our examination Moreover there will be numerous instances of static abnormality in which the reactions are also abnormal To take the simplest possible example, a pupil anchored by ring posterior synechia might be smaller than normal, but would also betray dynamic abnormality in the negative sense of failing to respond to stimuli

Experienced clinicians can observe at a glance whether the diameter of a pupil departs unduly from the average of about 3 5 mm , and whether there is any *important* difference between the two sides The word " important " is emphasised because chance congenital discrepancy between the innervation, musculature, or stromal architecture of the two irides is the likeliest explanation in many cases of *small* difference—say, not more than 0 5 mm

Other features to be surveyed in each pupil are the shape and degree of regularity of its circumference Any associated atrophy or irregularity of the iris stroma should also be noted, and there are various other items more interesting to the ophthalmologist than to the physician Obvious examples are the pigment frill at the rim of the pupil, the presence of persistent pupillary membrane or epicapsular stars, and the state of the lens fibres, in so far as the latter can be ascertained on preliminary scrutiny with the aid of a loupe

Simple routine inspection without an array of pupillometric devices will often supply not only facts of importance but also guidance as to what other special items of information should be sought The response of each pupil to light, direct and consensual, and to convergence must also be ascertained It has now been shown that the efferent nervous pathway for constriction of the pupil on convergence is not necessarily the same as that which subserves the response to stimulation by light We know that the innervation of the eye and its adnexa is subject to considerable variations, as indeed may happen elsewhere in the body , and it may well be that in many people the two pathways coincide throughout In some people, however, it has been possible to prove that the constrictor impulses derived from convergence are relayed by cells other than those of the ciliary ganglion

Here it seems appropriate to mention that universal agreement has not yet been reached about the relative efficacy of accommodation and convergence in provoking miosis It will be remembered that, where the older clinicians spoke of the pupils reacting to accommodation, their successors tend to speak of a convergence reaction, and indeed it seems clear that convergence is at any rate the major force Those who insist on attributing to accommodation *at least a share* in the pupillary constriction are apt to enlarge on instances in which focusing still provokes miosis after abolition of the power to converge , but their opponents retort that, even after manifest convergence has been rendered impossible, it is necessary to allow for *latent* convergence, in the nervous impulses which would otherwise have approximated the two eyes, and that these impulses, not those of accommodation, are the effective constrictors

ANATOMICAL CONSIDERATIONS

All interpretations of the pupillary signs should be made in the light of up to date anatomical facts The Edinger Westphal nucleus, from which emerge the pupillo constrictor fibres, receives excitatory stimuli from the occipital and frontal regions of the cortex, but recent researches have shown that the frontal cortex also sends out inhibitory impulses In other words, mydriasis formerly regarded as mediated by stimuli travelling from the frontal cortex to the sympathetic centre in the hypothalamus is really attributable to cortical inhibition exerted on the Edinger Westphal nucleus

Another important anatomical feature is the existence of an inhibitory sympathetic pathway from the hypothalamus to the constrictor centre , and it is abundantly proved that mydriasis accompanying powerful emotions is achieved not so much by stimulation of the sympathetic fibres as by inhibition of parasympathetic constricting nerves

One more anatomical fact should be emphasised The old teaching that the afferent pathway of the light reflex relayed in the superior colliculi had to be abandoned some years ago It is now generally agreed that, in man, the pupillary fibres leave the optic tracts before the lateral geniculate body is reached They pass by way of the brachium of the superior colliculus to reach the pretectal nucleus at the junction of the diencephalon and the tectum of the mid brain Most of the fibres cross in the posterior commissure, but some remain on the same side, with the result that fibres from each optic tract enter both Edinger Westphal nuclei Thus stimulation of the pretectal area induces bilateral pupillary constriction

PUPILLARY CHANGES IN HEAD INJURY

Routine inspection of the pupils will enable us in many cases to identify, and in others to suspect, lesions of the visual apparatus, and it may incidentally furnish early evidence about disease of the central nervous system In cases of head injury examination of the pupils may similarly convey information about the situation and extent of the damage, but a still more important reason for watching the pupil in such circumstances is to seek guidance about the need for operation Thus unilateral dilatation and immobility of one pupil rapidly supervening in a case which had at first displayed no pupillary abnormality should suggest ipsilateral intracranial hæmorrhage, and similar signs are likely to become manifest in the opposite pupil unless the flow is staunched The mechanism of this phenomenon is not known for certain, but pressure upon the parasympathetic centre in the mid brain is often blamed Others postulate traction on the nerve trunk by the tectorial pressure cone

Pontine hæmorrhage may provoke bilateral miosis, and severance of one optic nerve abolishes the direct response to light but leaves the consensual reaction unimpaired Bilateral mydriasis and inactivity is of no localising or prognostic value when it is noted in the immediate post traumatic stage, but persistence of this

Pulmonary Stenosis

When the systolic murmur of pulmonary stenosis is confined to the pulmonary area and is accompanied by a thrill, and the second heart sound is attenuated in the same area, the clinical diagnosis usually presents no difficulty, and the electrocardiogram of right heart preponderance is expected.

When a thrill is absent, the murmur not loud, and cyanosis present, Fallot's syndrome is the usual explanation.

When both thrill and cyanosis are absent, the differential diagnosis of an innocent murmur in this area from the murmur of slight pulmonary stenosis becomes difficult. It is here that a phonocardiogram may give valuable help. If the tracing shows a pansystolic murmur continuing almost up to, and even embracing the aortic moiety of the second heart sound, leaving a short silent gap in front of an attenuated pulmonary second sound, the presence of pulmonary stenosis is confirmed, but if the murmur is confined to mid systole it is innocent.

To substantiate these inferences made from a study of the phonocardiogram in patients in whom clinical examination was implemented by the electrocardiographic and radiological examination, observations need to be made in patients where cardiac and pulmonary artery catheterisation has been an additional test. Should this specific phonocardiogram be confirmed for the murmur of pulmonary stenosis and for the innocent murmur in the pulmonary area, investigation of such murmurs by cardiac catheterisation need not afterwards take place.

Ventricular Septal Defect

The innocent parasternal systolic murmur has already been described, and the phonocardiogram shows it to be a short high frequency murmur in mid systole. On the other hand, the murmur of ventricular septal defect, usually accompanied by a thrill, is a pansystolic murmur and is continued in strength up to the second heart sound. In this differential diagnosis, therefore, the phonocardiogram has become a valuable test, but it has yet to determine the relationship between the termination of the murmur and the aortic and pulmonary components of the second heart sound.

Splitting of Second Heart Sound

Splitting of the second heart sound in the pulmonary area is a common finding in health. If its threshold of audibility is high enough to allow it to be heard along a line joining the mitral area to the xiphisternum, bundle branch block or constrictive pericarditis is the usual cause, and rarely cardiac infarction.

CLINICAL PROBLEMS WHICH WILL YIELD TO PHONOCARDIOGRAPHY

Although opinion may be expressed even now on some of the problems discussed under this head, further investigation is needed before our knowledge of them is complete.

Since phonocardiography has been applied more often to test clinical auscultation in *hypertensive heart failure*, it has become clear that the triple rhythm is usually created by the addition of the third heart sound. When moderate tachycardia is present, as is often the case, the coincidence of the natural or intensified auricular sound with the added third heart sound will accentuate it (summation triple rhythm).

Mention has already been made of some cases of *hypertension without heart failure* where the auricular portion of the first heart sound is seen as a prominent wave in the phonocardiogram and when this is joined by the natural third heart sound on account of tachycardia a triple rhythm is initiated (innocent summation triple rhythm). Future work may give the reason for this accentuated auricular sound, which is a feature of only a few patients with hypertension. The two kinds of triple rhythm can be distinguished on clinical grounds, because the kind associated with hypertensive heart failure arises in a patient in whom a past history of nocturnal breathlessness (cardiac asthma) is always present.

When the phonocardiogram is recorded in patients with *mitral valve disease* (mitral stenosis) it will show one or more of three murmurs—presystolic, pansystolic, or mid diastolic. It is for future investigation to show how often these are found together or separately, and the circumstances that decide their presence. In the meantime it may be said that, since a mid diastolic murmur is a common finding in the phonocardiogram of mitral disease, it should encourage a careful search for this murmur during auscultation in a patient where a diagnosis of mitral disease is suspected on other grounds. It is also necessary to decide whether hearing a clear third heart sound is inimical to the diagnosis of mitral valve disease, and whether the sound in that event is invariably impure from an associated mid diastolic murmur.

So far the *innocence* or otherwise of a murmur on phonocardiographic grounds has been decided from its place in the cardiac cycle, but a determination of the frequency of the separate murmurs may also contribute to a readier recognition of the innocent ones from among others.

There are more problems which may yield to phonocardiography, and only allusion to some of them have been made. When most is known of its interpretation phonocardiography will come into common use, and it will have as its chief function the according of greater precision to the art of auscultation, and rendering unnecessary other more elaborate tests which impose unwarranted discomfort on a sick patient.

REFERENCES

Leatham A. (1947) Personal communication.

Levine S A Harvey W P (1949) Clinical Auscultation of the Heart Philadelphia

ACTION OF ASCORBIC ACID ON TUBERCULIN-SENSITIVITY IN GUINEAPIGS

AND ITS MODIFICATION BY DIETARY AND HORMONAL FACTORS

D A Long, M.D Lond   A A Miles, M.A. Camb, F R C P   W L M. Perry, M.D St And.

From the National Institute for Medical Research Mill Hill, London

In a previous paper (Long and Miles 1950), it was shown that adrenocorticotrophic hormone (A C T H) or 'Cortisone' given to a guineapig infected with B C G would diminish its sensitivity to tuberculin by a significant though limited, amount. In this paper we show that in the guineapig neither cortisone nor A C T.H has any direct effect on tuberculin allergy, their desensitising action depends on dietary factors.

As a routine, our sensitised guineapigs were maintained on a pelleted diet (Bruce and Parkes 1947). This diet is grossly deficient in ascorbic acid, which was provided in a supplement of unlimited raw cabbage. It was on such animals that we demonstrated the desensitisation by cortisone and A C T.H. In a subsequent attempt to determine the role of vitamin C in allergic hypersensitivity, we substituted in one experiment ascorbic acid, 20 mg by mouth three times a week, for the cabbage, and found that guineapigs maintained on this diet were apparently not desensitised by cortisone. In another experiment, sensitised guineapigs fed on pellets alone to tell the various forms of triple heart rhythm, enlisting this sign to help significantly in diagnosis, and has made easier the clinical recognition of an innocent heart murmur.

Clinical Classification of Triple Heart Rhythm

Since triple rhythm denominates the cadence produced when three heart sounds recur in successive cardiac cycles, the designation should not apply, for instance, to most cases of mitral stenosis, where the added noise is the mid diastolic murmur which begins at the third heart sound and converts it into a murmur. Cautious auscultation should distinguish splitting of heart sounds from triple rhythm, because split sounds are never separated sufficiently to produce the cadence so obvious when three separate sounds create a triple heart rhythm. The phonocardiogram has shown that there are only three kinds of triple rhythm, and the first is the only important one, the other two having most weight in differential diagnosis.

Triple Rhythm from Addition of Third Heart Sound.—This may be met with in healthy people, when it is common up to the age of 20 years, uncommon after 30, and not found after 40. It can be told from that met with in heart disease on clinical grounds, and among the distinguishing features the one needing greatest emphasis is the patient's age; for if triple rhythm from addition of the third heart sound is found after the age of 40, one of the following conditions should be sought in turn to account for it: hypertensive heart failure; cardiac infarction; pulmonary heart disease, including pulmonary embolism, emphysema, and primary pulmonary hypertension; heart failure from aortic stenosis or aortic incompetence; constrictive pericarditis; auricular septal defect; and familial cardiomegaly. In the case of the last three, splitting of the second sound is often the explanation of a casual auscultation which at first may have interpreted it as triple rhythm.

Triple Rhythm from Audible Auricular Sound.—Appreciable separation of the auricular and ventricular parts of the first heart sound as a result of delayed auriculoventricular conduction, with prolongation of the P–R period in the electrocardiogram to 0·25 sec. or longer, is the common cause of this kind of triple rhythm.

Occasionally in hypertension a special feature of the phonocardiogram is a conspicuous auricular portion of the first heart sound. In such cases the addition of tachycardia, either induced or occurring fortuitously, causes a coincidence of the accentuated auricular sound with the natural third heart sound and creates a triple heart rhythm (innocent summation triple rhythm).

Triple Rhythm from Added Sound in Late Systole.—Here the adventitious sound is placed nearer to the second than the first heart sound. It may be so close to the second as to simulate splitting of this sound, but it is seldom confused with triple rhythm caused by the addition of the third heart sound. This auscultatory sign is not common and it has no significance except in differential diagnosis.

Phonocardiogram of Innocent Heart Murmurs

When the examination of subjects exhibiting a murmur but no evidence of heart disease included a phonocardiogram, it was possible to assemble physical signs which permitted a clinical recognition of three common types of innocent heart murmurs audible in or near the mitral area. In all three kinds the tracing was distinctive, showing a relatively silent gap between the murmur and the first heart sound which precedes it and another between the murmur and the second heart sound which succeeds it.

Innocent Murmur of Reclining Posture.—This is blowing in character and is not loud; hence, it often disappears on deep inbreathing. It is louder in the reclining posture, when the mitral murmur is joined by one in the pulmonary area. It is common in young people and is never met with after the age of 40. The phonocardiogram shows the murmur in mid systole.

Innocent Murmur in Late Systole.—This murmur too, is blowing in character; it is loud and short, persisting on deep inbreathing; it is found at all ages. It occupies late systole and is nearer to the second than the first heart sound, and this feature is easily made out by auscultation; graphically the murmur ends short of the second sound. Rarely, a murmur apparently in late systole has been shown to arise from mitral valve disease, but in this event the phonocardiogram shows that, although the bulk of the murmur may occupy late systole, it starts as a less intense murmur as far back as the first heart sound, and therefore is not a murmur confined to late systole, as is the case with the innocent variety.

Innocent Parasternal Murmur.—This murmur is blowing in character and is loud enough to persist during deep inspiration. It is loudest in the fourth intercostal space at the left border of the sternum, but is never accompanied by a thrill. Although commoner in young people it is often found in older adults. The murmur occupies mid systole, and the phonocardiogram may be a valuable test in diagnosis, differentiating it from the pansystolic murmur of ventricular septal defect.

CLINICAL STATES REQUIRING A PHONOCARDIOGRAM FOR DIAGNOSIS

Mitral Valve Disease

When a thrill is found in the mitral area, or when presystolic or mid diastolic murmurs are audible, the diagnosis of mitral stenosis is not in doubt, but if a systolic murmur is the only outward sign, the clinical diagnosis of mitral valve disease gives rise to difficulties, which may include equivocal appearances on radiological examination. It is in this circumstance that a phonocardiogram is an indispensable test. If the murmur is the outcome of mitral valve disease, the tracing will show the murmur filling systole (pansystolic), and a mid diastolic murmur may also be evident.

Aortic Stenosis

Among newer information that has come to us about aortic stenosis is the appreciation that its systolic murmur, often without a thrill, is frequently louder to the left than to the right of the sternum. Thus is added another systolic murmur to the many found in the mitral area, and the phonocardiogram has proved valuable in distinguishing it from the others. Leatham (1947) and Levine and Harvey (1949) have described a distinctive pattern for it, where the main bulk of the murmur is in mid systole, sometimes starting a little late, and especially showing a silent gap between the murmur and the second heart sound.

Patent Ductus Arteriosus

Since the operation of ligature of a persistent ductus arteriosus has become commonplace, the clinician's responsibility in its diagnosis has increased. A characteristic continuous murmur must be demanded as well as a physiological electrocardiogram, but experience dictates that no patient should proceed to operation without a preliminary phonocardiogram which not only displays the continuity of the murmur throughout systole and diastole, but also shows accentuation of the murmur in late systole and particularly at the second heart sound in early diastole. Attention to the sound tracing will diminish the instances where an open ductus cannot be found at operation, and the test should become routine practice, especially where the murmur is not accompanied by a thrill.

ascorbic acid found in the full factorial analysis. All but one combination of more than two factors, as would be expected, approach the significant level. The single exception—i.e., cortisone + A.C.T.H. + ascorbic acid—is not significant, owing to the exceptionally high variation between the responses of the five animals in this particular group. It should be noted also that, when all four factors were given together, the sensitivity was diminished fourfold, and that this is a significantly greater change than that produced by ascorbic acid alone.

The figure shows the mean responses to these isolated treatments. The fitted slope of the common regression line has been made to pass through the mean of each treatment group. This is permissible because the factorial analysis showed that there were no significant departures from a common regression and that the treatment dose interaction was not significant—i.e., the slopes of all the lines may be considered to be linear and parallel. To simplify the interpretation, those groups in which A.C.T.H. was given have been omitted from the graph because it is evident that A.C.T.H. behaves in this respect like cortisone.

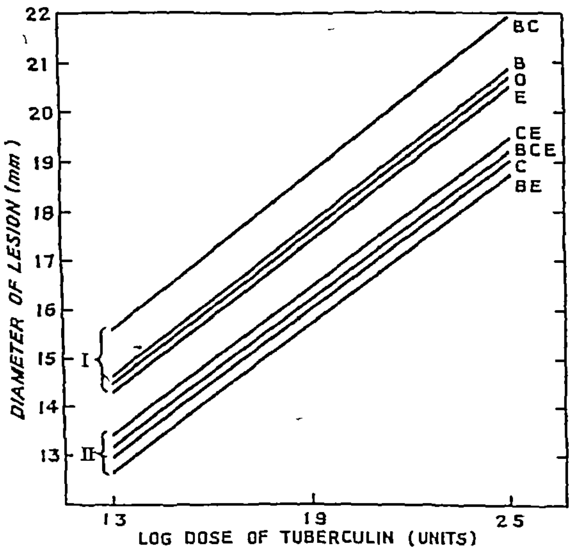
Summarised Conclusions from the Analysis

The effects shown graphically in the figure are summarised in table III, experiment 1. Sensitivity is cited simply as high and low according to the position of the response line in group I or group II (see figure). From the results we infer that:

1. Ascorbic acid diminishes tuberculin sensitivity, or, rather, maintains sensitivity at the low level (group *c*).
2. Cortisone and A.C.T.H. have no action on the sensitivity of guineapigs fed on a diet deficient in ascorbic acid (group *b*).
3. Neither cortisone nor A.C.T.H. separately increases the desensitising action of ascorbic acid (group *d*).
4. Cabbage, which contains ascorbic acid, does not diminish sensitivity (group *e*).
5. Cabbage inhibits the desensitising effect of excess ascorbic acid added to the diet (group *f*).
6. Both cortisone and A.C.T.H. antagonise the anti-ascorbic acid effect of cabbage (groups *g* and *h*).

Cabbage Factor

We must therefore postulate in cabbage a factor which directly affects the metabolism of ascorbic acid, modifying its desensitising action, and, if we regard desensitisation as a natural function of tissue ascorbic acid, then cortisone and A.C.T.H. affect sensitisation only by modifying this dietary derangement of ascorbic acid metabolism.



Dose-responses to 20, 80, and 320 i.u. of tuberculin in sensitive guineapigs with parallel regression lines fitted to mean diameters of lesions: B, cabbage; C, ascorbic acid; E, cortisone; O, controls.

TABLE III—EFFECT OF ASCORBIC ACID AND CABBAGE SUPPLEMENTS TO A BASAL DIET AND OF SINGLE INJECTIONS OF CORTISONE 2 MG. AND GLUTATHIONE 100 MG. ON TUBERCULIN HYPERSENSITIVITY OF B.C.G.-INFECTED GUINEAPIGS

Expt.	Group	Treatment	Tuberculin sensitivity
1	(*a*)	Basal diet	High*
	(*b*)	+ cortisone	High
	(*c*)	+ ascorbic acid†	Low*
	(*d*)	+ ascorbic acid and cortisone	Low
	(*e*)	+ cabbage†	High
	(*f*)	+ cabbage and ascorbic acid	High
	(*g*)	+ cabbage and cortisone	Low
	(*h*)	+ cabbage and ascorbic acid and cortisone	Low
2		Basal diet	
	(*k*)	+ ascorbic acid‡	Low
	(*l*)	+ ascorbic acid and glutathione‡	High
	(*m*)	+ cabbage and cortisone	Low
	(*n*)	+ cabbage and cortisone and glutathione	High

* For definition see text.　† In the diet.
‡ A single intraperitoneal injection.

The nature of the cabbage factor must be determined by direct fractionation of active extracts. But in this connection it is worth noting the observation of Schultze et al. (1938) that acid-insoluble SH compounds, as well as glutathione, inhibited the oxidation of ascorbic acid by a preparation of liver cells. An SH compound is found in the seeds and roots of certain vegetable foods, including the brassicæ (Astwood et al. 1949), and it is probable that similar substances are present in extracts of cabbage leaves (Greer and Astwood 1948), because both have antithyroid activity. Such substances, if absorbed from the alimentary tract, might diminish the tissue reactions of ascorbic acid associated with desensitisation. We found (table III, experiment 2) that, in guineapigs fed on a diet deficient in ascorbic acid, 100 mg. of glutathione in the reduced state, given intraperitoneally 6 hours before the tuberculin injections, inhibited the desensitising action of 100 mg. of ascorbic acid injected intraperitoneally (table III, *k* and *l*), and a similar dose of glutathione had the same effect in cabbage-fed guineapigs in which the cabbage factor was antagonised by cortisone (table III, *m* and *n*).

DISCUSSION

The relation we have found between ascorbic acid, a cabbage factor, and cortisone or A.C.T.H. may of course be peculiar to the allergic guineapig. Other animals may react differently. For example, in rabbits on the same pelleted diet but receiving no cabbage, our colleague Dr. J. H. Humphrey (personal communication) finds that the Arthus reactivity is greatly diminished by a single injection of cortisone. In these rabbits, which do not depend on diet for their ascorbic acid, the vitamin was presumably present in tissues, and could not have been antagonised by a cabbage factor. Nevertheless, the guineapig resembles man in needing dietary ascorbic acid, and may also be closely analogous in allergic reactivity.

Since we were able to modify the allergic state only between two well-defined limits, embracing at the most a four- to five-fold change in hypersensitivity, the extrapolation of our findings to cover the whole range of hypersensitivity in the guineapig is probably not justifiable. We might have effected a greater change had we used a basal diet free from ascorbic acid. Nevertheless within these limits we are confident that the changes from high to low, and from low to high, sensitivity are real. We are less certain that the guineapigs under various treatments assigned to either the high or the low groups had essentially the same sensitivity. The variability of the responses in five guineapigs is relatively large, and with more guinea-until they became moderately deficient in ascorbic acid (cf Long 1950) were more sensitive than those fed on pellets and ascorbic acid It is difficult to correlate the results obtained in different experiments, because of the great variation in the mean responses of different groups of sensitised guineapigs to tuberculin We accordingly devised a factorial experiment with guineapigs maintained on pellet diet alone, to explore the relations of cortisone, A C T H, cabbage, and ascorbic acid in their action on tuberculin sensitivity

METHODS

The design of the experiment is evident in the first column of table I, where the 15 combinations of treatment with the four substances are listed Five albino guineapigs, weighing about 350 g, were used for each combination, and a 16th group of five served as a control All the animals were given 2 mg wet weight of B C G in the right adductor muscles, and were tuberculin tested 28 days later by the multiple dose method (Long and Miles 1950) During this 4 week period unlimited cabbage, and 20 mg of ascorbic acid by mouth three times a week, were given to the appropriate groups In cabbage fed animals desensitisation with cortisone was greatest when a single dose was given subcutaneously 6 hours before the tuberculin injections, given at this time its effect was maximal with 5 mg per kg of body weight and scarcely detectable with 0 2 mg per kg In the experiments, therefore, we used a dose of 2 mg in the 350 g guineapigs 6 hours before the tuberculin One international unit of A C T H (equivalent to 1 mg of Messrs Armour's La 1 A standard) was given subcutaneously $2^1/_2$ hours before the tuberculin injection

As in our previous work, the diameter of the 24 hour tuberculin lesions was proportional to the logarithm of the dose of tuberculin, and the degree of sensitivity could be estimated by the relative positions of the dose response lines fitted to mean lesion diameters plotted against log dose, as in the accompanying figure

RESULTS

Full Analysis

It is clear from the figure that the response lines tend to cluster into two groups In group I, exemplified by the animals on pellet diet alone (control), the sensitivity is relatively high, in group II it is relatively low Moreover, although within each group there are differences in response, yet only one of these differences on analysis proved to be significant On the other hand, all the responses in group II differed significantly from those in group I That is, we were unable to diminish the sensitivity of the controls by more than a limited amount, corresponding to a three- to four fold change in tuberculin reactivity, and this maximum effect was produced, in guineapigs on a diet deficient in ascorbic acid, by treatment with ascorbic acid alone

TABLE I—COMPLETE ANALYSIS OF VARIANCE OF EXPERIMENT WITH COMBINATIONS OF FOUR DIETARY OR HORMONAL FACTORS

Source of variation	Sum of squares	D F	Mean square	Variance ratio	P*
Between treatments	249 5644	15	16 6376	2 545	<0 01
A	15 2763	1	15 2763	2 327	
C	26 3013	1	26 3013	4 006	<0 05
B	18 1775	1	18 1775	2 760	
E	45 5446	1	45 5446	6 937	<0 05
AC	8 2696	1	8 2696	1 260	
AB	33 7126	1	33 7125	5 135	<0 05
BC	27 9825	1	27 9825	4 262	<0 05
CE	0 0825	1	0 0825		
BE	58 9546	1	58 9546	8 9797	<0 01
AE	2 7200	1	2 7200		
ACE	0 0001	1	0 0010		
ABE	1 4963	1	1 4963		
ABC	6 9871	1	6 9871	1 0642	
BCE	3 9913	1	3 9913		
ABCE	0 0683	1	0 0683		
Between doses	1544 6946	2	772 3473	117 641	<0 001
Linearity	1542 2535	1	1542 2535	235 282	<0 001
Departure from linearity	2 4410	1	2 4410		
Between animals	407 0190	62†	6 5653	(Error)	
Treatment dose interaction	21 2904	30	0 7097		
Residual	203 2167	124	2 3647		
Total	2515 8151	233			

A C T H = A Ascorbic acid = C
Cabbage = B Cortisone = E

* Values for probability are given only for effects that are significant

† 2 animals died during the experiment so 2 degrees of freedom have been omitted from the error

TABLE II—COMPARISON OF INDIVIDUAL TREATMENT EFFECTS WITH THE EFFECT IN CONTROLS

Treatment compared	Potency ratio	Variance ratio	P
C	2 054	4 615	0 05–0 10†
B	0 977		
E	1 104		
A	0 901		
AC	1 893	3 919	0 05–0 10†
EC	1 794	2 597	0 10–0 20†
AB	1 443	1 069	0 20–0 40
EB	2 869	5 353	<0 05*
AE	0 957		
BC	0 656	2 371	0 10–0 20†
ABC	1 751	13 251	<0 01*
EBC	1 843	3 559	0 05–0 10†
AEC	1 501	1 040	0 20–0 40
AEB	2 616	6 332	<0 05*
ABCE	4 417	50 982	<0 001*
(Controls)	(1 000)		

Each figure in column 2 represents the dose of tuberculin required to produce a lesion of a given diameter in the treatment group, the corresponding dose in the control group being taken as unity Thus in the first group listed, about twice as much tuberculin was required—i e the animals were half as allergic as the controls.

* Significant effect † Effect approaching significance

Complete analysis of the experiment (table I) leads to the following conclusions

(1) Ascorbic acid produces a significant effect

(2) Cortisone produces a significant effect

(3) Ascorbic acid, since it produces an effect alone, has no significant interaction with cortisone or with A C T H, but the interaction between cabbage and ascorbic acid is significant

(4) Cabbage, which alone has no effect, has a significant interaction with both A C T H. and cortisone

It is apparent, therefore, that there is a complex relationship between cortisone and A C T H on the one hand, and cabbage and ascorbic acid on the other, further information about the nature of this relationship is obtained by comparison of the direct effects of the individual treatments with those in the controls These direct comparisons are shown in table II Since they are made with groups of five animals only, the advantage of the factorial design, which enables the comparisons of the effects to be made on groups of forty animals, is lost Nevertheless the information obtained in both ways can be pooled with great advantage Of the four factors only ascorbic acid has an effect that approaches significance, it has decreased sensitivity twofold Cortisone alone has not altered the sensitivity, and we must attribute the significant change produced by cortisone, found in the full factorial analysis, to the fact that the synergism of cortisone with the other factors outweighs the absence of any effect of cortisone alone This is clear from the figure Moreover, the effect of combining cortisone with cabbage and the effect of combining cortisone with ascorbic acid both approach significance, and this is true, to a lesser extent, of similar combinations with A C T H No effect is produced by a combination of cortisone and A C T.H in the absence of both cabbage and ascorbic acid Cabbage, given with ascorbic acid, both prevents the action of ascorbic acid and actually diminishes its effect—i e, increases sensitivity—by an amount which is almost significant This explains the significant interaction of cabbage and are ready to go home within about a fortnight from the operation.

Shortly after starting to employ this new procedure I found that the operation could be completed without haste in twenty to thirty minutes, involved a minimal blood loss, allowed of a complete "adenomectomy," and was generally followed by early ambulation with an easy and quick convalescence. The operation in fact gave such satisfaction that it soon became my routine method of prostatectomy, and now five years later continues to be so. I reserve perurethral resection for the fibrous glands, the sclerotic bladder necks, and the malignant obstructions. The suprapubic transvesical approach may be utilised when some additional bladder lesion, such as a new growth, a diverticulum, or a massive stone, is present, though my tendency now is to do a retropubic prostatectomy even when some concomitant bladder disorder necessitates a separate transvesical incision.

My first retropubic prostatectomy was done in December, 1945, and by November, 1950, I had personally performed the operation on 500 patients. During these five years my operations in hospital and private practice for the relief of prostatic obstruction numbered 704. The methods used were as follow:

Method	*No of cases*
Retropubic prostatectomy	500
Suprapubic transvesical prostatectomy	64
Perurethral prostatic resection	123
Suprapubic cystostomy	17

ALTERNATIVE METHODS

The suprapubic transvesical prostatectomies listed include a series of 53 operations by the Wilson Hey (1945) technique, which in the earlier stages of this work I was simultaneously assessing. Since the retropubic operation became my method of choice, the suprapubic transvesical route has been used on 7 occasions only. The perurethral resections include 52 malignant cases where obstructive symptoms were unaffected or inadequately relieved by stilbœstrol. Suprapubic cystostomy as the sole procedure for relieving prostatic obstruction was used only when urinary retention supervened in patients with some other coexisting mortal disease or who had reached a stage of terminal senile physical or mental dissolution and were therefore unlikely to survive for long. The last 5 consecutive patients dealt with in this way were as follow: (*a*) aged 87, uræmic and diabetic, lived four weeks, (*b*) aged 82, physically active but senile, resumed normal micturition and dispensed with suprapubic tube, continues well after six months, (*c*) aged 82, gross hypertension, myocarditis and bronchitis, lived eight weeks, (*d*) aged 85, mental disorientation continues after ten months, and (*e*) aged 88, retention developed while under medical care for acute bronchitis and congestive heart-failure, lived 5 months.

SELECTION OF PATIENTS FOR RETROPUBIC PROSTATECTOMY

It will be apparent from the foregoing paragraphs that no patient seeking relief from a prostatic obstruction was denied operation by the retropubic method unless his prostate was diagnosed as of the fibrous or malignant variety and therefore best dealt with by perurethral resection or unless he was so enfeebled that his short expectation of life rendered anything beyond palliative relief futile. Advanced age, though naturally associated with an increased risk, was not deemed a contra-indication. Thus 80 (16%) of the 500 patients in this series were aged 75 or more: 29 were aged 75, 16 were aged 76, 11 were aged 77, 9 were aged 78, 5 were aged 79, and 10 were aged 80 or more.

If the prostatism is complicated by some other serious constitutional disease—e.g., a coronary lesion with severe myocardial changes—operation is not advised if the obstructive symptoms are not too severe and the patient can get along in reasonable comfort. If, on the other hand, a patient with a similar cardiovascular lesion has retention, or an obstruction which causes difficult micturition, retropubic prostatectomy is carried out. He is not condemned to a permanent cystostomy and the distressing conditions of living generally associated with that expedient. Everything possible is done to improve the cardiac weakness and vascular circulation. If weeks are needed for this purpose, or to permit adequate improvement of severe kidney damage resulting from long standing back pressure or to correct a profound secondary anæmia, a cystostomy tube is inserted under local anæsthesia. Riches's (1943) method of suprapubic catheterisation is favoured for this preliminary procedure. If the optimum improvement is likely to be obtained within a week or two, the bladder is drained through an indwelling urethral catheter. This method of preparation is applicable to most cases. Two stage retropubic operations have been carried out on only 16 of the series, and in 5 of them suprapubic tubes had been in place from four weeks to four years before the patients came under my care. In 2 other patients who were referred with suprapubic tubes it was found impossible to open up the retropubic space and the transvesical approach had to be used. The low insertion of the tubes and the considerable perivesical inflammation which had followed had obliterated the space from dense fibrosis.

MORTALITY

The over all mortality for the 500 retropubic prostatectomies was 6%. The mortality in the 80 patients aged 75–87 was 8·7%, including 2 of the octogenarians. In the last 100 consecutive operations on patients aged less than 75 the mortality was 3%.

(1) A known sufferer from coronary sclerosis, aged 69 who had lost a leg in the first world war died on the tenth day from a sudden cardiac attack after helping to adjust his artificial limb.

(2) A diabetic, aged 68, who weighed 18 st., stood the operation well but on the third day developed an acute ileus with gastric dilatation to which he quickly succumbed.

(3) A man, aged 70, admitted with chronic retention and uræmia showed considerable improvement after suprapubic catheter drainage, but relapsed into uræmia after a second stage operation and died on the third day.

POSTOPERATIVE COMPLICATIONS

The average patient running a smooth postoperative course has an aperient administered on the second evening, is allowed up to the commode the following morning, and has the catheter removed later that day. From then on he is encouraged to be up and about for a longer period each day until he is ready to go home. In my last 50 consecutive hospital cases, excepting one who remained in hospital for more than three months until he died of ventricular heart failure, and another who, because of a complicating mucous colitis, did not leave until the forty-seventh day, the average postoperative day of dismissal was the sixteenth.

An uncomplicated and speedy recovery is aided if during the first twelve hours after operation judicious supportive treatment is given. The transfusion of a pint of blood, begun during the operation and slowly completed on the patient's return to bed, is a great help to the aged prostatic, even when the blood-loss at operation has not exceeded a few ounces. During the immediate postoperative period the drainage from the urethral catheter must be carefully supervised and any blockage from clots prevented by squirting an ounce or two of sterile water through the catheter, suction by syringe is used to evacuate clots if necessary. A copious fluid intake is maintained and ensured, if required, by intravenous infusions. Urinary antiseptics, usually a sulphonamide with penicillin or streptomycin, are routine. In spite of these measures complications may arise.

pigs in each treatment group we might have demonstrated significant differences of tuberculin reactivity between groups that we have considered as similar, but such differences would probably be small and would not affect the general conclusions we have drawn from the gross mean differences observed between batches of five animals

As regards the nature of the hypothetical cabbage factor, the inhibition of ascorbic acid desensitisation by administered glutathione does not necessarily imply that the cabbage factor is an SH compound But it at least supplies a model for the action of the factor If ascorbic acid is protected from irreversible oxidation in the animal by tissue glutathione, as suggested by the in vitro studies of Borsook et al (1937), the maintenance of sensitivity at the high level by a cabbage diet and the change from low to high by injected glutathione, may both be due to interference with reactions involving the oxidation of ascorbic acid But whether the cabbage factor merely increases the concentration of glutathione like substances in the tissues or catalyses the reduction of ascorbic acid by such substances, in a manner analogous to the in vitro action of substances extracted from cauliflower by Hopkins and Morgan (1936), Crook and Hopkins (1938), and Crook (1941), cannot be determined until we know more of the quantitative aspect of the metabolism of ascorbic acid in relation to other tissue constituents of a particular piece of allergic tissue —e g, skin An interpretation of the tissue reactions in terms of in vitro biochemistry may then prove to be invalid

We have no evidence of how the cortisone cabbage factor antagonism is related to the ascorbic acid effect But, if the interaction of cabbage factor and ascorbic acid involves glutathione or is due to substances with some of the properties of glutathione, the reported diminution of the glutathione in human blood by administered A C T H (Conn 1950), or in rat blood by cortisone (Lazarow and Berman 1950), suggests that these hormones may act on metabolic systems in close relation with ascorbic acid In this connection it should be noted that the reducing capacity of the skin of our guineapigs, as judged by the intradermal injection of the oxidation reduction indicator dye 2 6 dichloro phenolindophenol (Rotter 1938), was greatly diminished for several hours after a single injection of A C T H or of cortisone

But the relation of all these phenomena is at present highly speculative

SUMMARY AND CONCLUSIONS

Using the response to intradermal tuberculin as a measure of allergic hypersensitivity in albino guineapigs infected with B C G, we find that

1 Guineapigs on a diet grossly but not completely deficient in ascorbic acid have a relatively high sensitivity This sensitivity is diminished by adding ascorbic acid to the diet, but not by providing ascorbic acid in raw cabbage

2 The factor in cabbage which leads to the inhibition of the desensitising action of ascorbic acid contained in the cabbage also inhibits the desensitising action of excess of ascorbic acid added to the diet

3 Single injections of cortisone or of A C T H diminish the sensitivity of guineapigs on a cabbage diet

4 Single injections of cortisone or of A C T H do not alter the sensitivity of guineapigs either on a basal diet deficient in ascorbic acid, or on this diet augmented by ascorbic acid.

5 The effect of a cabbage diet on ascorbic acid desensitisation is imitated by a single injection of glutathione

We conclude that there is in cabbage a factor which on ingestion leads to the inhibition of the desensitisation produced by the metabolism of ascorbic acid in the tissues of the allergic guineapig, and that the desensitising action of cortisone or of A C T H in cabbage fed animals is indirect, depending on the reversal of the cabbage effect by the hormones The cabbage factor may possibly be an SH compound

We are indebted to Dr Knud Tolderlund, of the State Serum Institute, Copenhagen, for the B C G, and to Dr F Bergel, of Roche Products Ltd, for the glutathione

REFERENCES

Astwood, E B, Greer, M A, Ettlinger M G (1949) *J biol Chem* 181, 121
Borsook, H Davenport H W Jeffreys, C E P, Warner R C (1937) *Ibid*, 117, 237
Bruce H M Parkes, A S (1947) *J Hyg Camb* 45 70
Conn J W (1950) Proceedings of the First Clinical A C T H Conference, Chicago 1949 Philadelphia and London, p. 86.
Crook E M (1941) *Biochem J* 35 226
— Hopkins F G (1938) *Ibid* 32 1356
Greer, M A Astwood E B (1948) *Endocrinology* 43 105
Hopkins F G Morgan E J (1936) *Biochem J* 30, 1446
Lazarow, A, Berman J (1950) *Anat Rec* 106 215
Long D A (1950) *Brit J exp Path* 31 183
— Miles A A (1950) *Lancet*, I 492
Rötter, H (1938) *Wien klin Wschr* 51 205
Schultze M O Stotz E, King C G (1938) *J biol. Chem.* 122 395

RETROPUBIC PROSTATECTOMY

REVIEW OF 500 CASES

Arthur Jacobs
F R F P S

SURGEON IN CHARGE, UROLOGICAL DEPARTMENT, GLASGOW ROYAL INFIRMARY

FIVE years have passed since THE LANCET published Millin's (1945) first paper on his new method of prostatectomy by the retropubic extravesical approach The technique he advocated caused a considerable stir among urologists, who but some fifteen years earlier had begun to use the then comparatively new perurethral operations with increasing enthusiasm Millin, himself a former keen advocate and skilled exponent of perurethral prostatic resection, claimed that his operation represented a great advance not only over the loop and punch perurethral methods but also over the older suprapubic and perineal operations Because the prostate is essentially an extravesical structure, he was convinced that it should be extirpated by an extravesical approach. Although this can be done by perineal prostatectomy, he considered that method far from ideal, because of the possibility of sequelæ such as incontinence and urethro rectal or perineal fistulæ He therefore devised an alternative extravesical attack, the fundamental steps of which are as follow

The retropubic space behind the symphysis is exposed through a low abdominal incision, either transverse or vertical The prostate gland within its capsular coverings is defined below the bladder and cleared of overlying fat The capsule is then opened by a transverse incision 1 cm below the bladder neck The lower extremities of the lateral lobes are freed with scissors, and the separation is continued with the finger, working from below upwards until both lateral lobes and the middle lobe, when present, are delivered The complete adenomatous mass is then detached A wedge from the posterior lip of the vesical neck is now excised, this being an essential step in the operation to obviate subsequent contracture at the vesico urethral outlet The cavity is carefully inspected, spurting vessels are caught in forceps and coagulated with the diathermy, and any small residual adenomata or loose tags are removed with scissors so that a smooth surface remains A catheter is now passed along the urethra into the bladder, and the prostatic capsule is closed with a continuous catgut suture The wound is closed, a drain of corrugated rubber being delivered through a stab incision in the lower skin flap when a transverse incision has been used, and through the lower end of the wound when the incision has been a vertical one The drainage from the catheter must be carefully watched after operation to ensure that there is no blockage from clots The patient can generally get up on the second day, and void urine with ease when the catheter is removed on the third day Most patients

ERYTHEMA MULTIFORME EXUDATIVUM MAJOR (STEVENS-JOHNSON SYNDROME)

D W Ashby
M.D Lond, M.R C.P
LATE SENIOR MEDICAL REGISTRAR

Theresa Lazar
M.B, M.R C.P
LATE MEDICAL REGISTRAR

QUEEN ELIZABETH HOSPITAL BIRMINGHAM

Stevens and Johnson in 1922 described a "new eruptive fever" characterised by pleomorphous rash, ulceration of the mouth, purulent conjunctivitis, and severe constitutional symptoms

As many workers have since pointed out, cases closely resembling those of Stevens and Johnson had been described long before Most of them had been regarded as examples of "erythema multiforme exsudativum" (Hebra) In his original account in 1860 Hebra described erythema multiforme as a simple skin disease with no mucosal or systemic manifestations, in 1866 he referred to a case with pneumonia At the turn of the 19th century several authors described erythema multiforme with buccal, conjunctival, penile, and vulvovaginal lesions, and urethral discharge (Quinquaud 1882, Kaposi 1893, Hanke 1901, Mracek 1902) Duhring (1896) reviewed 122 cases of erythema multiforme seen in Turkey, these were often accompanied by fever, a high proportion by mouth lesions, and a quarter by eye lesions, the disease was mostly mild Other names under which cases indistinguishable from Stevens Johnson syndrome have been published are "ectodermosis erosiva pluri orificalis" (Rendu 1916) and "dermato stomatitis" (Baader 1925) More recently it has been shown that the skin need not necessarily be affected (Gilbert and Hing 1946), and that abacterial pneumonia may be a feature (Commission on Acute Respiratory Diseases 1946, Finland et al. 1948) Interest in the condition in this country has been aroused by Murray (1947) and Nellen (1947) Several writers have reviewed the literature Some have tabulated a few features of published cases —e g, Wentz and Seiple (1947), Soll (1947), and Fletcher and Harris (1945) Soll recorded the largest series of personal cases since Dühring, 20 being tabulated

The present paper is an analysis of 77 previously reported cases and 4 of our own.

CASE RECORDS

Case 1 —A man, aged 22, was admitted under Dr E Bulmer on Feb 28, 1949

History —On Feb 17 he felt hot, as if he were going to have a cold, and next day he had a sore throat, headache, and cough. He was seen by his doctor on Feb 21 and found to have pyrexia On Feb 23 his mouth looked red and inflamed, and he was given penicillin lozenges and sulphathiazole tablets A patch of consolidation was detected clinically at the right lung base By Feb 27 he had ulceration of the lips, difficulty in breathing and swallowing, and a sore on his penis

On admission his temperature was 100°F, and respirations 24 per minute He looked ill and cyanosed His conjunctivæ were injected His lips were swollen and ulcerated, with black crusts on the lower lip (fig 1) His tongue was swollen and red The inside of his mouth showed extensive redness, ulceration, and bleeding, and a patchy formation of membrane There was no membrane on the tonsils The left tonsillar gland was enlarged The percussion note was impaired at the right lung base, where the breathing was bronchial The penis showed a meatitis, with a circular ulcer 1 cm in diameter but no urethral discharge The spleen was not palpable There was no rash

Investigations —The Wassermann reaction of the serum was doubtfully positive A white cell count showed 11,000 per c.mm, with polymorphs 83 7% (9207 per c.mm) and eosinophils 1 7% (187 per c.mm) There were a few pus cells in the urine There was a cold agglutinin titre of 1 in 16, with a trace of 1 in 32 A swab from the mouth grew a mixed culture, with monilia predominating Radiography of the chest showed consolidation of the right lower lobe

Diagnosis and Treatment —Stevens-Johnson syndrome was diagnosed, and no treatment was given other than boric lotion and 'Protargol' drops to the eyes

Progress —On March 3 a maculopapular rash developed on the chest, back, and extremities, it had gone by March 10 On March 3 also a blister developed on the left conjunctiva, near the inner canthus This had ruptured on March 4 and was only just visible by March 16 The patient's temperature remitted to 102°F until March 1, and subsequently there were evening peaks to 100°F until March 5, thereafter it became normal He was discharged symptom free on March 16

Case 2 —A boy, aged 18, was admitted under Prof W Melville Arnott on Dec 21, 1949, with rash and ulcerated mouth (figs 2 and 3)

History —He had a similar bout in 1943, with severely ulcerated mouth swollen crusted lips, and ulcerated foreskin. He returned to school within 4–6 weeks He also gave a history of angioneurotic œdema whenever he took aspirin, but he had not taken any before the present illness or before his attack in 1943

On Dec 8, 1949, he developed a cold and malaise and was given sulphapyridine 1 g four hourly from Dec 15 His temperature ranged between 99° and 102°F, and on Dec 17 he developed a swollen mouth, a rash, painful micturition, a urethral discharge, and an ulcer beneath the foreskin. The rash appeared first on the arms and spread to the legs, with sparse involvement of the trunk. The sulphonamide tablets were discontinued on Dec 17 and intramuscular penicillin started.

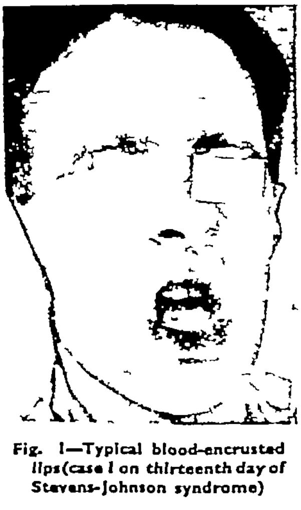


Fig. 1—Typical blood-encrusted lips (case 1 on thirteenth day of Stevens-Johnson syndrome)

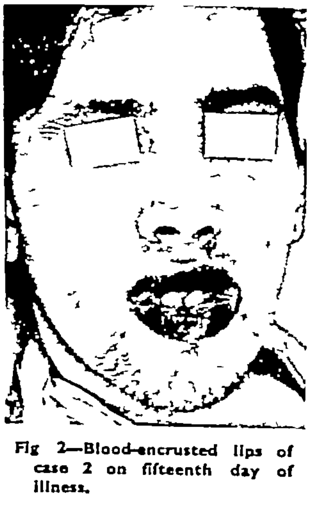


Fig 2—Blood-encrusted lips of case 2 on fifteenth day of illness.

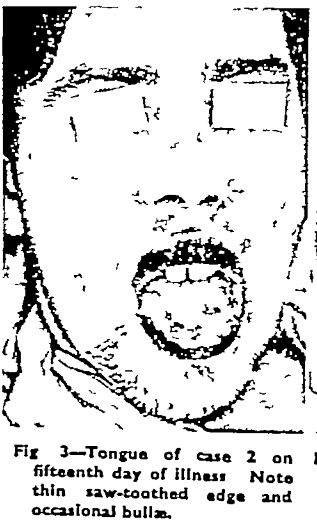


Fig 3—Tongue of case 2 on fifteenth day of illness Note thin saw-toothed edge and occasional bullæ.

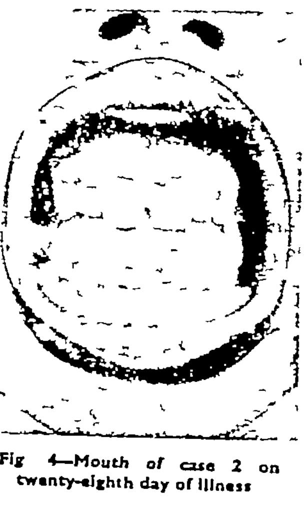


Fig 4—Mouth of case 2 on twenty-eighth day of illness

Hæmorrhage, more severe than the frank hæmaturia normally expected during the first one or two days, may necessitate aspiration for clots On 2 occasions this reactionary bleeding was severe enough to necessitate a cystostomy In about 6–8% of cases a secondary hæmorrhage occurs, usually three or four days after removal of the catheter and severe enough to necessitate its reinsertion Usually all that is necessary is to aspirate clots through the catheter and leave it in place for one or two days, but sometimes the bleedings recur after clear urine has been voided In 1 such case only, after a third bleeding on the ninth day had followed two previous attacks, did I deem a cystostomy necessary The patient nevertheless went home eighteen days later with the suprapubic sinus completely closed

Leakage of urine through the wound is rare In the last 50 consecutive cases it has been a minor transient incident with 2 patients only Closure of the capsule with a continuous suture which takes an adequate bite of both flaps and secures the extreme ends of the opening is the surest way of avoiding it There have been 3 instances of prolonged leakage

In 1 it was a sequel to the cystostomy necessitated on 1 of the 2 patients who had had a severe reactionary hæmorrhage

In another it was a sequel to suprapubic drainage which was established at the time of operation because of profuse sanguinous oozing after the enucleation of a large septic prostate This patient had had a cystostomy with subsequent resection of the prostate eight years previously The suprapubic leakage in both instances persisted for three months until excision of the fistula and closure of the bladder proved completely successful

The third instance was in a man, aged 76, with overflow incontinence, gross urinary infection, alcoholic cirrhosis, and uræmia, the blood urea level being 125 mg per 100 ml Only slight improvement followed drainage with a suprapubic catheter Prostatectomy was performed in preference to leaving him with a permanent cystostomy The wound became infected and persistently leaked urine while he lingered in a suburæmic state He died sixty six days after operation

Osteitis pubis is a serious though fortunately rare complication It may follow any operation on the bladder or the prostate, cases having been reported after suprapubic cystostomy and perurethral resection On one occasion with me it was a sequel to a vesico urethral suspension for stress incontinence in a female There has been an incidence of 3 cases following the retropubic operations

One, early in the series, developed into an osteomyelitis This was a sequel to infection, probably due to trauma caused by the extraction of a large calculus through the bladder neck A sequestrum had subsequently to be removed

The other two examples were sequelæ to apparently normal postoperative courses In neither was the complication diagnosed until after the patients had returned home, when they experienced increasingly severe pain in the pelvic region, especially on attempting to stand Rest in bed for several months was required, and 1 patient took nearly a year before becoming entirely free from discomfort

In the last case in which I have seen osteitis pubis, the acute phase was apparently aborted by large doses of vitamin B combined with short-wave diathermy, as suggested by Lavalle and Hamm (1949) The patient, a woman, was up and about within four weeks of starting this treatment

Postoperative contracture of the bladder neck was a sequel in about 6% of cases before excision of a wedge from the posterior lip of the neck was recognised as a necessary step in the operation These contractures, when severe, were satisfactorily corrected by endoscopic resection, but the complication is now seldom encountered

LATE POSTOPERATIVE FOLLOW UP

The objective in any method of prostatectomy, apart from minimal mortality and morbidity, is a normally functioning bladder which permits the patient to retain urine for adequate periods and to empty the bladder with ease, a condition which should be permanent In the course of routine follow up dozens of patients have been tested for residual urine, and many of these have had cystoscopic or cysto urethroscopic examinations. Except for some previously mentioned instances in the earlier stages of this work, when a wedge was not excised from the posterior lip of the bladder neck, the excellence of the functional results, as judged by ease of micturition, a clear urine, complete control, absence of residual urine, and little nocturnal disturbance, has been striking To ascertain the long term results of the operation, a questionnaire was sent to 50 of 51 consecutive patients operated on from June to October, 1948, there having been 1 postoperative death in this group It was considered that an interval of not less than two years and three months after operation was adequate to permit the assumption that the functional status of the bladder then obtaining was likely to be permanent The patients within this group could be regarded as a fair average of the whole series, 22 of them being aged 70 or more 12 were aged 70–74, 8 were aged 75–79, 1 was aged 80, and 1 was aged 82 Malignant disease of the prostate had been proved in 5 cases An analysis of the information obtained from the replies to the questionnaire is as follows

Retropubic prostatectomies from June to October 1948, reviewed in January, 1951	50
Died since operation	10
From intercurrent disease, 7 2 aged 77 and 72 from cerebral arteriosclerosis, after 4 and 5 weeks 1 aged 62 from a general 'break up' after 7 months, 2 aged 62 and 78 from coronary thrombosis after 10 and 11 months, 1 aged 63 from malignant pancreas after 1 year 6 months and 1 aged 72, from pneumonia after 1 year 9 months	
From prostatic malignancy, 3 1 aged 60 at three months, 1 aged 82 at six months, and 1, aged 65 at 1 year 1 month.	
Untraced	1*
Available for report	39
Voiding urine with good force	*Yes* 35 *No* 4†
Complete control of bladder	*Yes*, 35, *No* 4‡
Nocturnal frequency	*None* 11, *Once*, 19 *Twice*, 5, *Every 2 or 3 hours* 4

---

* Left home town well a year after operation

† In 2 of the 4 without good force this is better than before operation, in 1 the same, and in 1 worse Two (1 better 1 same) had urethral strictures, sequelæ to former prostatic resections.

‡ In 2 of the 4 without complete control there is merely dribbling at the end of micturition and in 1 there is precipitancy The 4th who is one of the 2 surviving malignant cases, has incontinence which developed eighteen months after operation

CONCLUSIONS

My purpose here has been to assess retropubic prostatectomy, and I have tried not to suppress any difficulties or complications encountered In dealing with large numbers of prostatic patients, and the constitutional ailments which so often accompany their advancing years, complete freedom from troubles cannot be expected, whatever procedure is used The prostatectomist must develop that method which he finds most suitable and successful, and I can say without hesitation that no method I formerly used has proved so consistently satisfactory I consider my experiences confirm the claims of Millin et al (1949) that this operation is associated with a relatively low mortality, is generally followed by an easy speedy convalescence and a minimum of morbidity, with an excellent functional result, and that of all the available techniques it "conforms most nearly to the modern surgical ideal"

REFERENCES

Hey W H (1945) *Brit. J Surg* 33 41
Lavalle, L L Hamm F C (1949) *J Urol.* 61 83
Millin T (1945) *Lancet* ii 693
— Macalister, C L O Kelly P M. (1949) *Ibid* i 381
Riches, E W (1943) *Brit J Surg* 31 135

Knowledge of the distribution of the molecular weights in a given polymer can most readily be obtained by its separation into fractions of different molecular weight, but in the case of P V.P no satisfactory method of fractionation has been found Alternatively, a weight average molecular weight * (M_w) can be determined, and then the ratio of number to weight average molecular weights for any sample gives some indication of the distribution of molecular weights, since number average molecular weights are more sensitive to the low molecular weight molecules present, and the weight average is more sensitive to the high molecular weight molecules At least approximately, the intrinsic viscosity * $[\eta]$ is proportional to the weight average molecular weight Intrinsic viscosities and ratios $M_w/[\eta]$ are given in table I. There are variations in number average molecular weight and in molecular distribution between all samples examined Sample 3 appears to be particularly abnormal and would not be passed for clinical use, but the variation between the other samples is probably the normal variation to be expected between different batches of P V P

The osmotic pressure exerted by the P V P component in aqueous or saline solutions depends on its concentration, its number average molecular weight, and, in more concentrated solution, on interactions between different polymer molecules, and not on the presence of any other components The normal variations between batches of P V P are such that the osmotic pressure of a 3 5% solution (as in plasmosan) is 0 033–0 040 atmospheres, comparable in range to the normal values for the colloidal osmotic pressure of blood

P V.P is slightly surface active, a 0 025% solution in a neutral M/150 phosphate buffer lowering the surface tension by 5 dyne per cm Experiments involving the injection of P V P beneath films of albumin, globin, and fibrinogen at the air water interface indicate that any interaction between the protein and P V.P involves very weak forces of interaction

TOXICITY

Immediate Toxicity

From the pharmacological point of view P V.P, the important ingredient of plasmosan, is not toxic even when given in high dosage, the lethal dose for laboratory animals being 8 g per kg of body-weight, death being due to cardiovascular insufficiency attributable to hyperviscosity of the blood (Combined Intelligence Objectives Subcommittee 1945) Therapeutic doses are well tolerated

In the original clinical experiments done in Germany with P V.P preparations pyrogenic reactions, albuminuria, and hæmaturia developed in some instances, but there is no evidence that any late harmful effects were seen. Follow up of the patients in this country, to whom plasmosan containing the new preparation of P V P was given, some as long as three years ago, has revealed no late side effects from its use

No ill effects follow the subcutaneous and intramuscular injections of 25% aqueous solutions of P V.P, in which form it is extensively used in France as a retarding agent for penicillin, insulin, and certain hormones

Remote Toxicity

The most likely late toxic effect of injecting foreign colloid substances into the circulation is the risk of deposition in fixed tissue cells of the body, although this is unlikely with the present preparation, which is so highly soluble and shows so little interaction with other materials Rabbits of average body weight 2 5 kg were bled 5 ml per kg of body weight and transfused with different quantities of plasmosan in deliberate overdosage, in amounts of 10–40 ml. of plasmosan per kg of body-weight The dose commonly used in man is about 8 ml of plasmosan per kg of body-weight The rabbits were killed after 14 and 28 days Apart from a small, probably agonal, hæmorrhage seen in one rabbit no macroscopic changes were visible post mortem. Dr William Whitelaw, consultant pathologist, Birmingham, examined and reported on various sections from these animals The lung, kidney, and liver of rabbits killed on the 28th day showed no change on any of the doses used The livers showed no evidence that storage had taken place In the kidneys from rabbits killed on the 14th day after a dose of 40 ml per kg of body-weight some swelling of the cells of the convoluted tubules was seen These changes were not seen, however, in similar specimens taken at 28 days, suggesting that, if present earlier in these particular rabbits, they had later cleared If these changes had had any relationship to the dosage of P V P used they were transitory

Four patients in our series, to whom 500–1500 ml of plasmosan had been given, who later died from their injuries or disease, showed at necropsy no macroscopic or microscopic changes which could in any way be ascribed to plasmosan

FATE IN THE BODY

When any foreign substance is introduced into the blood stream it is most desirable to know what becomes of it—whether it is excreted unchanged or undergoes modification in body fluids and tissues This is particularly important when a considerable quantity of the substance is used, as with a plasma substitute In metabolic studies of this kind it is most satisfactory if the fate of a given dose can be followed in the body by estimating blood levels at regular intervals and quantitative recovery of the original or breakdown products from body excretions Investigations of the blood alone may not account for all the foreign substances in the body at any one time, because there may be selective distribution between the blood and the fixed tissue cells So far it has not been possible in the case of P V.P to make quantitative studies to elucidate this point, but from many histological and biochemical studies it seems likely that the *P V.P fraction of plasmosan in therapeutic doses* does not become attached to fixed tissue cells but remains in the blood stream until it is finally excreted

Until recently not more than 50% of a given dose of P V.P could be recovered quantitatively from the urine, by tests which have later been developed on the lines discussed below The question arose whether the balance unaccounted for was retained in the body or excreted as an unidentified compound It seemed unlikely, however, that significant quantities were retained in the body, because there was no clinical evidence of retention An improvement in the technique of estimation shows that in ordinary circumstances 75% of the *P V P content of plasmosan may* be recovered from the urine, a figure as high as 90% was obtained on a single occasion With suitable adjustments this method can be used to determine blood levels

Plasmosan exerts no ill effects on kidney function, and a typical fluid balance chart from a healthy person to whom 500 ml. of plasmosan was given is shown in fig 1 Concurrent blood urea and urea clearance

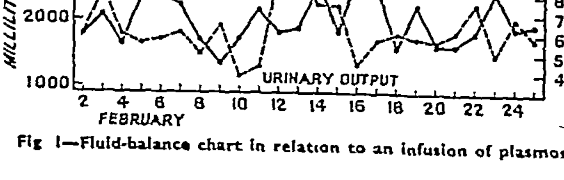


Fig 1—Fluid-balance chart in relation to an infusion of plasmosan.

PLASMOSAN

A SYNTHETIC SUBSTITUTE FOR PLASMA

W R Thrower
M.D Lond , M R C P
CLINICAL ADVISER

H Campbell
M A., Ph D Camb
PHYSICAL CHEMIST

RESEARCH LABORATORIES, MAY & BAKER LTD

For patients who have lost much blood, transfusion with appropriate amounts of whole blood is the treatment of choice The aim of the immediate treatment of shock is to restore the volume of circulating blood by improving the venous return, the cardiac output, and consequently the blood pressure Bayliss (1919) showed that the addition of 6% gum arabic to physiological saline solution could extend the period during which saline solutions restore the volume of circulating fluid by retarding the rate of excretion of fluids Unfortunately, inconsistencies in gums, and side effects due to long retention in the body, particularly in the liver, hindered general clinical use of this fluid

Various alternatives to gum have since been examined Infusion of natural plasma, or substitutes for it, does not of course restore the oxygen carrying power of the blood except in so far as all available erythrocytes are brought into use Attempts to improve the oxygen carrying power of artificially prepared solutions for infusion have been made by adding various hæmoglobin preparations to saline solutions, but these have proved unreliable and dangerous, principally because of renal complications due to free hæmoglobin in the blood stream (Holmes and Thrower 1924) But despite this lack of oxygen carrying power the prompt infusion of plasma and plasma substitutes can be life saving

Among several colloid substances suggested as agents to retard the excretion of saline solutions by the kidneys, polyvinylpyrrolidone (P V P) seemed promising (Hecht and Weese 1943) A saline solution incorporating a P V P compound was prepared and used in Germany with some success as a plasma substitute during the 1939–45 war, but side effects due to that particular preparation restricted its use elsewhere, particularly in countries where there were adequate supplies of natural blood products Improved methods of preparing P V P have permitted the development of a solution known as ‘Plasmosan,’ which is free from the objections to the German product and has proved safe and effective in clinical practice The composition of plasmosan is as follows

Polyvinylpyrrolidone	3 5 g	per 100 ml
Sodium (Na^+)	301 mg	,, ,,
Potassium (K^+)	22 ,,	,, ,,
Calcium (Ca^{++})	9 ,,	
Magnesium (Mg^{++})	0 06	
Chloride (Cl^-)	582 ,,	
Bicarbonate (HCO_3^-)	17	
Dissolved carbon dioxide (CO_2)	75	

The concentration of P V P is one which gives a colloidal osmotic pressure approximating to that of whole blood The total electrolytes make the solution isotonic The proportion of the various ions is similar to that in human plasma Early experience suggested that the solutions were more stable in the presence of a trace of free dissolved carbon dioxide The adjustment of any electrolyte imbalance is recognised as of increasing importance in transfusion practice Work is contemplated which may permit the development of a plasmosan capable of simple adjustment to the needs of particular cases on the lines suggested by Young (1951)

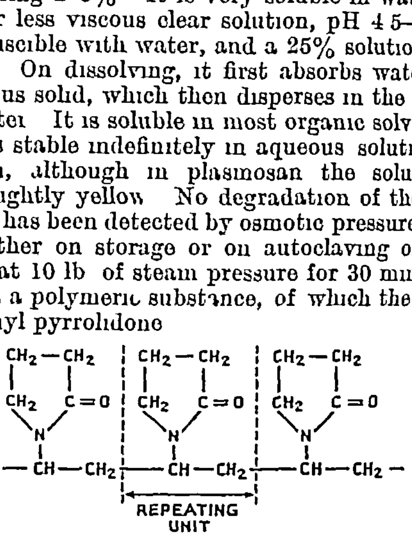
Before any plasma substitute can be considered suitable for clinical use, certain basic requirements must be satisfied It must have a high margin of safety Its viscosity, colloidal osmotic pressure, and tonicity must approximate to those of the recipient's blood. It should be retained in the body sufficiently long to be effective, and its fate should be known Blood grouping reactions should not be disturbed, or the erythrocyte sedimentation rate (E S R) unduly increased Kidney function must not be disturbed And no antigenic reaction must be excited

CHEMISTRY AND PHYSICAL CHARACTERISTICS

P V P , as used in plasmosan, is a white solid which is slightly hygroscopic, the normal water content of the powder being 2–3% It is very soluble in water, giving a more or less viscous clear solution, pH 4 5–7 0 It is readily miscible with water, and a 25% solution is easily obtained On dissolving, it first absorbs water to give a gelatinous solid, which then disperses in the remainder of the water It is soluble in most organic solvents

P V P is stable indefinitely in aqueous solution and in plasmosan, although in plasmosan the solution may become slightly yellow No degradation of the polymer molecules has been detected by osmotic pressure measurements, either on storage or on autoclaving of aqueous solutions at 10 lb of steam pressure for 30 minutes.

P V P is a polymeric substance, of which the repeating unit is vinyl pyrrolidone



POLYVINYLPYRROLIDONE

The possibility of small departures from this structure has still to be investigated From a consideration of its method of preparation, no sample of this polymer seems likely to contain molecules of a unique molecular weight (as found with the serum-proteins) but there will be molecules of a range of different molecular weights, as found with most synthetic polymers. The limits of the molecular weight range depend on the exact method of preparation of the polymer (see below) In aqueous solution the P V P molecule is believed to be more extended than the globular serum proteins Some evidence for this is obtained from the greater increase in specific viscosity and osmotic pressure with concentration in the case of aqueous solutions of P V.P than of serum albumin

TABLE I—AVERAGE MOLECULAR WEIGHTS AND INTRINSIC VISCOSITY OF P V P

Sample no	M_N	$[\eta]$	$\frac{M_N}{[\eta]}$
2	29 000	0 213	$1\ 4 \times 10^5$
3	140 000*	0 190	$7\ 4 \times 10^5$
4	49 000	0 196	$2\ 5 \times 10^5$
5	56 000	0 220	$2\ 5 \times 10^5$
6	56 000	0 196	$2\ 9 \times 10^5$

* Sample 3 is particularly abnormal and would not be passed for clinical use

Number average molecular weights * (M_N) have been calculated from osmotic pressure measurements on aqueous solutions, and typical values are given in table I

---

* Number average molecular weight (M_N) and weight average molecular weight (M_W) are defined by

$$M_N = \frac{\sum M \times N_M}{\sum N_M}$$

$$M_W = \frac{\sum M^2 \times N_M}{\sum M \times N_M}$$

where N_M molecules of actual molecular weight M are present in the sample
Intrinsic viscosity $[\eta]$ is defined by $[\eta] = \underset{c \to 0}{\mathrm{Lt}}\ \eta_{sp}/c$
where η_{sp} is the specific viscosity of a solution of concentration c g per 100 ml solution.

A healthy man, aged 31, sustained three major open fractures in an accident and suffered severe shock Two hours after the accident, before an infusion of plasmosan 500 ml., the E.S.R. was 3 mm. in 1 hour (Westergren) Three days later the E.S.R. was 30 mm. in 1 hour

Other patients have shown a similar rise in the E.S.R. after plasmosan infusions

Since the introduction of many substances to whole blood induces hæmolysis, it was important to determine whether plasmosan had this effect In-vitro blood samples with and without the addition of solid P.V.P were prepared After storage for four days spectrophotometry failed to distinguish between the concentration of free hæmoglobin in the plasmas from the two samples To observe whether any hæmolysis was caused in vivo, serum bilirubin estimations were made on patients to whom plasmosan had been given For example, in a man, aged 58, with hæmatemesis, the serum bilirubin level was 0 2 mg per 100 ml (4 units) before, and 0 2 mg per 100 ml. 48 hours after, an infusion of 500 ml. of plasmosan

In the composition of the saline solution in which P.V.P is presented 0 05% $CaCl_2$ is present In the intact animal and in man the concentration of calcium salts in the circulation does not influence the risk of intravascular clotting Difficulties might, however, arise at the time of a change from plasmosan to citrated whole blood administered through the same giving set, owing to clots formed by the interaction of the Ca ion in plasmosan on citrated blood In practice we have encountered no difficulties from this theoretical possibility with blood to which 3% trisodium citrate and 15% glucose had been added Magendie et al. (1947), using 10% citrated blood in vitro, drew attention to the possibility of clotting, and recommended that the giving set should be washed through with normal saline solution before making the change

CLINICAL USE

Plasmosan has been given for various conditions in adults and infants for whom the use of fresh or reconstituted plasma would normally be indicated, and it seems to be interchangeable with plasma and to have no contra indications Arden et al. (1951) have used it in 37 cases The rate of administration should conform to that commonly used for plasma infusions, one or more bottles of 500 ml. being given as required. No side-effects from plasmosan infusions have been seen The largest amount given to any patient in our experience was 3500 ml. in a week. Because of its saline content excessive quantities of plasmosan may cause waterlogging, but before such a situation might develop alternative infusions would normally be considered In some instances no further infusions are necessary, but, if whole blood is needed, appropriate amounts can be given, when it becomes available, through the same apparatus

Since P.V.P does not occur in nature, previous contact is unlikely under ordinary conditions, and no antigenic reaction need be expected after a primary administration of plasmosan Though the possibility of sensitisation cannot be entirely ruled out, the chemical nature of P.V.P makes such a reaction unlikely Attempts to sensitise guineapigs have failed

The results of some simple routine clinical pathological tests may be modified at times by the presence in body fluids of the large P.V.P molecule, which has reducing properties In the blood this may be manifest in a measurable deviation from the true blood sugar level of the patient Again, reducing substances may be identified in the urine without sugar being actually present because of the properties of P.V.P A false positive test for albumin with the trichloracetic acid reagent or Esbach's quantitative method may be met Tests involving the use of cold nitric acid and heat tests are unaffected

Plasmosan keeps perfectly well and requires no special conditions for storage Thus it can always be at hand for the prompt treatment of any circulatory emergency in which transfusion is indicated and it may provide the sole treatment necessary

Our thanks are due to Mr W H George, Mr V S Hughes Davis and Mr E B Whittingham for collaborating, and to Dr Clara Cross for much help during this long investigation. We are indebted to Mr B Bell, Mr P O Kane, and Dr H G Kaul for some of the physicochemical measurements

REFERENCES

Arden G P Mandow G A. Stoneham F J R. (1951) *Lancet* i 1099

Bayliss W M. (1919) see *Spec Rep Ser med Res Coun Lond* no 25

Combined Intelligence Objectives Subcommittee (1945) item 24 file XXV–54

Hecht G Weese H (1943) *Münch med Wschr* 90 11

Holmes R. C Thrower W R (1924) unpublished data

Magendie Servantie Duplan Poulinier (1948) *Pr méd* 56 200

Young W (1951) *Proc R Soc Med* 44 12

PLASMOSAN IN THE PREVENTION AND TREATMENT OF SHOCK

G P ARDEN
M.B Lond., F.R C S
ACCIDENT AND ORTHOPÆDIC SURGEON

G A MANDOW
M.B Camb, D.A.
ANÆSTHETIST

F J R STONEHAM
M.R C S
ANÆSTHETIST

WINDSOR GROUP OF HOSPITALS

AN efficient substitute for blood is needed because of the increasing number of transfusions given, the danger of plasma jaundice, and the threat of another war

Obviously blood is and must remain the most efficient fluid for combating shock. Plasma is second best and often very effective, but it occasionally causes toxic reactions or infective hepatitis Dextran seems to be as effective as plasma in the treatment of shock and is nontoxic, but it upsets blood grouping and is rather expensive and difficult to produce

MATERIAL

We have used 'Plasmosan' as a plasma substitute in 37 cases, either because of acute injury or during major operations

Accident or operation	No *of cases*
McKee or Smith Petersen pinning	9
Gastrectomy	6
Cup arthroplasty	5
Multiple fractures	4
Spinal fusion	2
Burns	2
Osteotomy of femur	1
Arthrodesis of hip	1
Partial colectomy	1
Amputation of leg below knee	1
Salpingo-oöphorectomy	1
Shortening of leg	1
Abortion	1
Laminectomy	1
Nephrectomy	1
Total	37

Most of the cases were major orthopædic cases which in our opinion would have required intravenous therapy either during or after the operation The average age was 54, the youngest patient was aged 7, and the oldest 84 Of the 37 patients 17 were male and 20 female

METHOD

Plasmosan was given at the start of each operation and was followed in many cases by blood The mixing of plasmosan with blood seems to be harmless Procaine 2 g in plasmosan 500 ml. was also used in several cases tests showed no alteration in renal efficiency due to the treatment

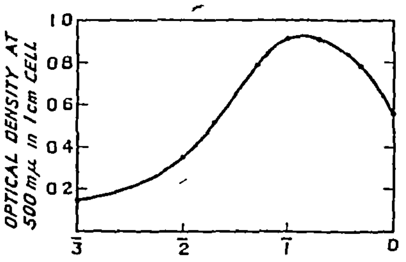


Fig 2—Variation of optical density at 500 mμ with concentration of P V P in solution

METHODS OF ESTIMATION

Early reports on P V P indicated that it could be estimated colorimetrically after the addition of iodine Methods have now been developed which allow of its estimation in urine and in serum

The addition of an aqueous solution of iodine in potassium iodide turns an aqueous solution of P V P red brown owing to a broad absorption band at 500 mμ The structure of the coloured compound has not been established, but it is believed to be due to the interaction of the I_3^- ion with the P V P molecule, since an alcoholic solution of iodide does not yield any coloured compound The intensity of the colour depends on the concentration of iodine and potassium iodide in the reagent The optimum concentrations are used in the methods outlined below The colour intensity depends on the P V P concentrations, as in fig 2, hence, to get reliable results, it is necessary to ensure, by dilution, that the concentration of P V P in the solution tested is less than 0 1 g per 100 ml The interference in the development of the colour by compounds in urine and serum can be eliminated by diluting the urine and by treating the serum with calcium chloride solution

The influence of certain drugs on the estimation of P V P in plasma has been determined (table II) All the drugs were present in the plasma at a concentration of about 5 mg per 100 ml Only 'Flaxedil' introduced a large error

The colorimetric measurements were made at 500 mμ with a 'Unicam' SP 500 spectrophotometer and cells of optical length 1 cm Any photo electric colorimeter with a filter with maximal transmission at about 500 mμ —e g, Ilford 603—can, however, be used with little loss of sensitivity

In Urine (Concentration range 0 05–10 g per 100 ml)

(1) Dilute the urine 100 times with distilled water

(2) To 5 ml of this solution add 1 ml of 0 006 *N* iodine in *N*/1 aqueous potassium iodide

(3) The optical density of solution (2) is measured against water at 500 mμ

(4) The concentration of P V P present in the original urine is found by using calibration curves determined experimentally with urine solutions of known concentrations of P V P

In Plasma and Serum (Concentration range 0 02–0 8 g per 100 ml)

(1) 1 ml of plasma or serum and 10 ml of aqueous *N*/10 calcium chloride are gently boiled for $^1/_2$–1 minute Loss of liquid is prevented by placing a funnel in the mouth of the boiling tube The solution was filtered through a Whatman no 42 paper which has been proved not to adsorb P V P

(2) 5 ml of the filtrate and 1 ml of 0 006 *N* iodine in *N*/1 aqueous potassium iodide are mixed, and the optical density against water is measured at 500 mμ

(3) The concentration of P V P is found by using a calibration curve determined experimentally with plasma or serum solutions of known concentrations of P V P

TABLE II—EFFECT OF DRUGS ON ESTIMATION OF P V P

Drug	Effect on P V P concentration estimated by iodine method
Morphine tartrate	No effect
Thiopentone	No effect
Atropine	No effect
Sodium penicillin	6 % reduction
Procaine hydrochloride	4 % reduction
Soluthiazole	3 % reduction
Sulphamerazine	2 % increase
Sulphadiazine	5 % increase
Sulphathiazole	6 % increase
Flaxedil	16 % reduction

Fig 3, which is a composite curve, shows the excretion of P V P in the urine normally to be expected after the infusion of 500–1000 ml of plasmosan into patients with circulatory failure due to major surgical operations or to accidental trauma The rate of excretion increases with the improvement of the circulation and greater urinary output The plasma P V P level decreases steadily after the infusion, but its detailed correlation with the urinary excretion is difficult, since the plasma volume and its change on restoration of the circulatory volume are unknown When plasmosan 500 ml. was injected, initial plasma P V P levels of about 0 35 g per 100 ml were obtained, which at the end of about 50 hours decreased to about 0 2 g per 100 ml It has yet to be ascertained whether the high output of P V P during the first 48 hours is due to the excretion of P V P in the smaller range of molecular size, the larger molecular fraction coming later The small fraction not accounted for in fig 3 may be explained partly by experimental errors and partly by delay in the excretion of large molecular particles Possibly the large molecular particles may in the body be slowly degraded to smaller molecules, which are then excreted Whether any P V P is lost in the fæces is unknown

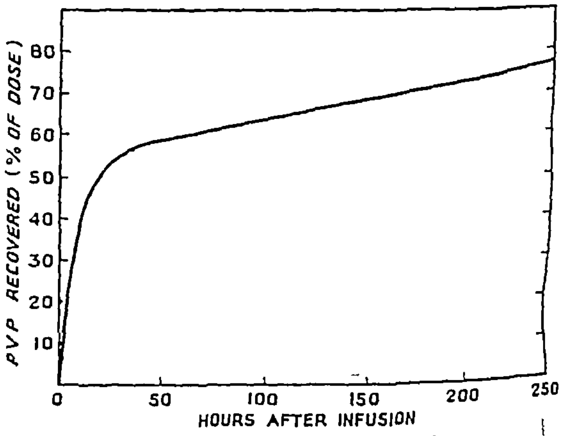


Fig 3—Recovery of P V P from urine

EFFECTS OF PLASMOSAN ON WHOLE BLOOD

In vitro different quantities of plasmosan and whole or citrated blood mix readily, and the same applies under clinical conditions With the plasma P V P levels likely to be met in practice (<0 5%) microscopy of erythrocytes reveals no significant changes If excessive (10%) plasma P V P levels are used, the red cells become crenated The clotting time and bleeding time of patients recently given infusions of plasmosan are unaffected, and blood grouping reactions are not disturbed Erythrocytes do not absorb any measurable quantity of P V P at normal plasma P V P levels

It has long been recognised that the addition to blood of colloid substances of high molecular weight raises the E S.R, and it was expected that the addition of plasmosan would do the same In in vitro experiments the E S R increased with increasing concentrations of P V P In clinical practice it is difficult to obtain accurate records, because often the patient's disease also raises the E S.R The following case, however, illustrates what can happen

TABLE II—RESULTS OF AGGLUTINATION TESTS

Strain of leptospira	Agglutination titres	
	On 7th day	On 11th day
L icterohæmorrhagiæ A	1 100	1 3000
L icterohæmorrhagiæ AB	1 100	1 3000
L canicola	1 30	1 3000
L grippotyphosa	0	0
L pomona	0	0
L ballum	0	1 300
L sejroe	0	0

Necropsy Findings—The body was well-developed, well-nourished, and icteric, with crural and preputial œdema There was a slight fibrinous pericarditis The pericardial and pleural surfaces showed petechial hæmorrhages The lungs were œdematous and, microscopically, contained small foci of bronchopneumonia The kidneys, which were equal in size, together weighed 420 g and showed a few cysts, the largest of which was 2 cm in diameter Both ureters were duplicated, and the renal pelves were slightly dilated On section of the kidneys there was eversion of the cut edges, and the yellowish cortices were friable Microscopy revealed a few scarred glomeruli Nearly all the glomeruli were normal, without fibrous thickening of Bowman's capsules The proximal convoluted tubules showed swelling of the epithelium, some mitoses, a few necrotic and calcified cells, and a narrow lumen. The distal tubules had a wide lumen often filled with granular brown casts. The epithelium was flattened, disintegrated, and often filled with brown granular pigment Throughout the interstitial tissues there were scattered collections of lymphocytes, plasma cells, clasmatocytes (macrophages), and a moderate number of polymorphs, especially in the cortico medullary area

The liver showed, histologically, dissociation of liver cells, but this phenomenon was entirely lacking in a formalin fixed specimen obtained by liver puncture immediately after death The cell dissociation therefore was a post-mortem artefact The liver cells were swollen and the nuclei unstable with many mitoses Some cells were necrotic The biliary capillaries were often filled with bile Disse's spaces were wide and œdematous Sections from the suprarenals, heart, pancreas, and testes showed small interstitial inflammatory foci similar to those in the kidneys Calf muscle showed microscopically necrosis, inflammation, and regeneration with giant muscle cells

Laboratory Investigations—Samples of blood serum for leptospiral examinations were obtained on the 7th and 11th days of illness The results of agglutination tests are given in table II

TABLE III—RESULTS OF CROSS ABSORPTION TEST

Titre against	Unabsorbed	After absorption with		
		L ictero hæmorrhagiæ		*L canicola*
		A	AB	
L icterohæmorrhagiæ A	1 3000	0	1 30	0
L icterohæmorrhagiæ AB	1 3000	0	0	0
L canicola	1 3000	1 100	1 300	0

Since equally high titres were attained with both *L icterohæmorrhagiæ* and *L canicola* in the last sample of serum and no test was possible at a later date owing to the patient's death, a cross absorption test was done with the last serum sample, which clearly showed that the infecting organism must have been *L canicola* (see table III)

Examination of Dogs—The patient had owned three dogs which had not shown any symptom of illness before or during the patient's illness In two of these dogs leptospiræ were found in the urine on microscopy by dark ground illumination (table IV) and leptospiral agglutinins were detected in the serum Urine from dogs 2 and 3, which had leptospiræ in their urine, was inoculated into white mice and guineapigs All the mice remained negative, but from one of the guineapigs, inoculated with urine from dog 3, a strain of leptospira was isolated which agglutination tests proved to be *L canicola*

Examination of Patient's Wife—A search for agglutinins in the blood serum of the patient's wife also gave positive results

Strain	*Titre*
L icterohæmorrhagiæ A	1 300
L icterohæmorrhagiæ AB	1 100
L canicola	1 3000

Although a significant titre for *L canicola* was observed, the canicola infection of the patient's wife must have been very mild, since she did not remember feeling ill recently

DISCUSSION

Diagnosis—Leptospirosis was diagnosed when the results of the agglutination tests were known, but the species of leptospira responsible was not clear, because in the last sample of serum equally high titres for both icterohæmorrhagic and canicola strains were found It is in such cases that cross absorption tests may be very valuable and in the present case they proved what was supported by results of the examination of the patient's wife and dogs, that the leptospira responsible was *L canicola*

Necropsy revealed that the primary kidney disease which caused death was a lower nephron nephrosis The histological picture was exactly like that described in fatal cases of leptospirosis icterohæmorrhagica Jeghers et al (1935) and Ashe et al (1941) give the same description as Beitzke (1917) "There are swelling and more or less marked necrosis of the epithelium of the convoluted tubules and interstitial infiltrations of lymphocytes, and to a lesser degree polymorphonuclear leucocytes and eosinophils Granular and bile containing casts are common The glomeruli are unchanged in most cases The damage is thus predominantly in the tubules" There is some evidence from published accurate case records that in most instances the interstitial infiltration is conspicuous, especially in the cortico medullary area The cysts present in the kidney probably had nothing to do with the cause of death, contrary to what was thought at one time by one of us (J W W), whose opinion, mentioned by Weetch et al (1949), must therefore be withdrawn According to recent published reports lower nephron nephrosis seems to be nearly always the cause of the renal affection accompanying leptospiral infections

TABLE IV—RESULTS OF TESTS ON DOGS

—	Dog 1	Dog 2	Dog 3
Leptospira in urine	−	+	+
Agglutination titre with strain			
L icterohæmorrhagiæ A	0	1 1000	1 300
L icterohæmorrhagiæ AB	0	1 1000	1 300
L canicola	0	1 3000	1 3000

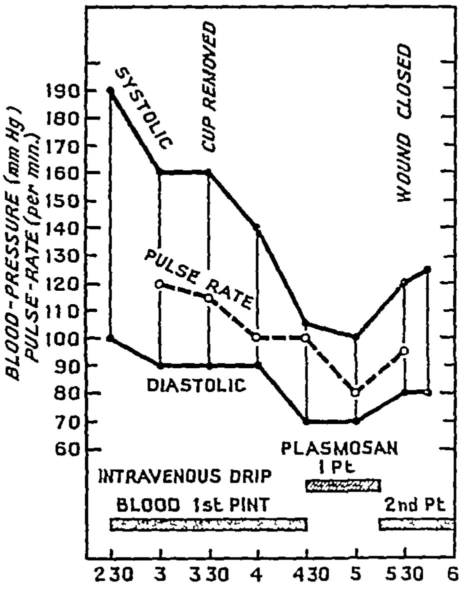
In the light of present experience, the treatment, though possibly preventing a further steep rise of the blood urea level after Nov 17 by restricting protein katabolism and increasing body fluids, must have been deleterious in many respects At that time (1946) there was some evidence, not confirmed since, that an increase of plasma sodium promoted the transfer of serum-potassium to the cells The normal figures of chloride and bicarbonate on Nov 19 do not mean that the sodium level (which was not determined) was normal too, it is even highly probable that it was far in excess, to judge from the œdema, meteorism, and frothy diarrhœa Part of the carbohydrate was given as lactose, since this was less disagreeable than cane sugar to the patient Probably the lactose had given rise to fermentation, and, since the patient was taking sodium carbonate, carbon dioxide was formed in the acid intestinal contents The same effect has since been seen in another patient taking large amounts of lactose and sodium carbonate

The average amount of plasmosan infused per patient was 600 ml, the smallest infusion being 500 ml, and the largest 2000 ml Plasmosan alone was given to 18 patients, and plasmosan and blood to 19 During the transfusions serial blood-pressure recordings were taken and charted with the pulse rate (see figure)

Plasmosan flows readily, and it has not been necessary to discard any, although some bottles have been stored for months

RESULTS

One patient died who had sustained burns There were no febrile reactions or urticaria which could be attributed to the plasmosan Any plasmosan that leaked into the subcutaneous tissues at the site of venepuncture seemed to cause no reaction In most cases plasmosan maintained the blood pressure satisfactorily, and in a few cases the blood pressure rose One pint was usually given in 45 minutes Increasing the rate helped to maintain the blood pressure if it was falling In operations which lasted more than $1^{1}/_{2}$ hours, or when there was considerable blood loss, the use of blood became necessary to maintain the blood pressure and to replace the hæmoglobin After the infusion of plasmosan blood grouping was repeated in several cases and no difficulty was experienced Hæmodilution and anisocytosis were noted in a few cases from 2 to 4 days after the transfusion



Pulse and blood-pressure during revision cup arthroplasty under thiopentone (1 g), Flaxedil (80 mg) and cyclopropane and oxygen

There was no interference with wound healing, except for the presence of a hæmatoma in a few cases

The 4 patients with multiple injuries (2 bilateral compound fractures of tibia and fibula, 1 fracture of pelvis and wrist, and 1 fracture of humerus and femur) were treated with plasmosan alone None of these patients, however, were really shocked on admission, and the patients were operated on without a significant drop in the patient's blood pressure

In 2 major operations plasmosan alone was given, and, although the blood loss in each cases was significant, the blood pressure was well maintained during the operation

Case 1 —A girl aged 19, had a right subtrochanteric femoral shortening of 2 in performed, and the fragments fixed with a nail plate The operation lasted $2^{1}/_{2}$ hours An infusion of plasmosan 1000 ml maintained a satisfactory blood pressure throughout The estimated blood loss was $1^{1}/_{2}$ pints

Case 2 —A man, aged 58, with non union of a subtrochanteric osteotomy, had a bone graft and plate applied to the site of non union The operation lasted $1^{3}/_{4}$ hours An infusion of plasmosan 1000 ml kept the blood pressure satisfactory throughout The estimated blood loss was 1 pint

CONCLUSIONS

When a supply of whole blood is not to hand we advocate the immediate use of plasmosan as a sound and effective measure for maintaining the blood pressure

In most cases of shock plasmosan will restore blood pressure to normal for a time, and this has enabled us to economise in the use of blood

Plasmosan, in the quantities we used, seems to be an inert non-toxic fluid which will satisfactorily maintain the blood pressure during major operations with significant blood loss It keeps well, it is relatively cheap, and we are informed that it can be produced in unlimited quantities

We are grateful to our colleagues for information and data concerning their cases Messrs May & Baker Ltd supplied the plasmosan

---

THE FIRST KNOWN FATAL CASE OF CANICOLA FEVER

J W WOLFF
M D Amsterdam
CHIEF OF BACTERIOLOGICAL DEPARTMENT, INSTITUTE FOR TROPICAL HYGIENE AND GEOGRAPHICAL PATHOLOGY

R VAN DAM
M D Amsterdam
PATHOLOGIST,
BINNENGASTHUIS

J E MINKENHOF
HEAD OF DEPARTMENT OF
INFECTIOUS DISEASES,
WILHELMINA HOSPITAL

AMSTERDAM

REPORTING a fatal case of canicola fever in Sheffield in 1949, Weetch et al mentioned that up till then there had been only one death from this disease (Ruys 1947) Since no details of that case have been published, and death from canicola fever is still rare, we obtained the case record from Prof J G G Borst and present it here

CASE RECORD

A man, aged 55, was admitted on Nov 14, 1946, to the department of medicine of the University of Amsterdam, with five days' history of severe pain in the lumbar region and calves and a temperature of 104°F

On examination he was severely ill, with conjunctival injection, some small ecchymotic spots on the extremities, and a consolidation of the right lower lobe of the lungs No sputum was produced Pulse rate 110 per min, blood pressure 100/70 mm Hg Urine urobilin + + +, bilirubin negative, but after two days strongly positive, protein 0 1 part per thousand Blood urea 379 mg per 100 ml, chlorides 92 m eq, and bicarbonate 14 m.eq per litre Diagnosis bronchopneumonia and uræmia, probably due to Weil's disease

Treatment —Penicillin, 30,000 units eight times a day, protein free diet providing 2000–2800 calories daily, and containing 110 g of sodium bicarbonate, 52 g of sodium chloride, and 14 litres of water in five days

Course —The amounts of urine passed in the next four days were 485, 500, 380, and 360 ml Blood and plasma findings are set out in table I After death the bladder contained 715 ml of urine Severe œdema developed, and massive meteorism greatly hampered respiration and circulation and made peritoneal dialysis impossible There was also diarrhœa with frothy stools The blood pressure fell to 80/50, and the patient died on Nov 20 with symptoms of peripheral circulatory failure No signs of pulmonary œdema had been noted during life

TABLE I—BLOOD AND PLASMA FINDINGS

Date	Hæmatocrit (%)	Chlorides (m eq per litre)	Bicarbonate (m eq per litre)	Urea (mg per 100 ml)
Nov 16	35	92	14 5	379
Nov 17	36	82	16	476
Nov 18	34	79	18	486
Nov 19	32	81	13	535
Nov 20	34	94	27 2	530

TABLE III—COAGULATION TIMES (SEC) OF IRRADIATED FIBRINOGEN

Time of irradiation of fibrinogen (min)	Coagulation time of thrombin 0 2 ml (6 5 units per ml) + fibrinogen 1 0 ml	Appearance of clot
0	13 8	Firm
1	14 0	Firm
2	14 8	Less firm
4	15 8	Thread like
8	23 0	Floccular

To provide further evidence on this point, a sample of purified fibrinogen prepared from citrated human plasma by ether precipitation (Kekwick et al 1946) was subjected to ultraviolet irradiation in a quartz cell 4 8×4 8×1 cm, uniform irradiation being ensured by continuous stirring

Irradiation at room-temperature of a 1% solution of fibrinogen in citrate saline solution for 1 hour led to the appearance of a floccular precipitate, the protein remaining in solution falling to 0 5% The rise in temperature during the irradiation was less than 5°C

A 0 2% solution was irradiated for various periods, and the coagulation time measured on the addition of thrombin The results are summarised in table III As the duration of exposure is increased, the coagulation-time becomes longer, and the clotting becomes more indefinite This parallels the behaviour of plasma given increasing exposures in the irradiator

SUMMARY

Though irradiation of plasma at 2537 Å increases the coagulation time and changes the clot, it does not increase the antithrombic activity

The addition of purified fibrinogen to irradiated plasma brings back the coagulation time towards its original value, and the irradiation of pure fibrinogen prolongs the coagulation time as in plasma

The principal effect of irradiation on the coagulability of plasma is due to modification of its fibrinogen

Our thanks are due to Dr R A Kekwick for valuable discussion and criticism

REFERENCES

Cutler S S Burbank, B Marzullo E R (1950) *J Amer med Ass* 143 1057
Habel K Sockrider B T (1946) *J Immunol* 56 273
Kekwick R A Mackay M E Record B R (1946) *Nature Lond* 157 629

DEFLATION OF DISTENDED BOWEL AT OPERATION

A G R Lowdon
O B.E M.A., M.B Edin., F.R C S.E
ASSISTANT SURGEON, EDINBURGH ROYAL INFIRMARY, LECTURER IN SURGERY, UNIVERSITY OF EDINBURGH

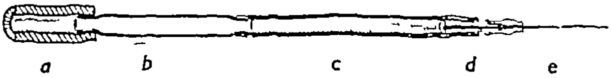
DISTENDED bowel is often an impediment to the surgeon at operation and a postoperative embarrassment, if not worse to the patient It has been taught that only exceptional circumstances will justify the surgeon in taking any measures during the operation to reduce this distension, and, because the content of the intestine is potentially infective, any measure which carries a risk of contaminating the field of operation from this source is inadmissible unless it is essential to the operation On the other hand, most operations on the alimentary tract involve controlled exposure of mucosa at some stage, and with proper technique this can be made safe The careful oblique insertion of a small needle into the lumen of the bowel and its equally careful withdrawal need be no more dangerous than the insertion of seromuscular sutures into distended colon (as in making the spur of a proximal colostomy for obstruction) If the needle is hollow and the bowel content passing through it can be removed completely from the operation field through a closed system, the procedure should not be a breach of aseptic technique It should in this way be possible to remove the gaseous content of distended bowel without infecting the peritoneum

A trial has been made of deflation of distended bowel with a hollow needle connected to the suction apparatus In the last four years this technique has been used in more than 50 operations of various kinds, its benefits have often been obvious and gratifying, and there has been no reason to suppose that it was responsible for any undesirable complications At first the measure was reserved for cases of severe distension where considerable benefit was to be expected from its relief, but more recently it has been used with advantage for less imperative indications

Deflation of the bowel at operation may be practised more commonly than I am aware of, but I find that most surgeons in training, encountering it for the first time, regard it as heterodox and dangerous

TECHNIQUE

The aspiration is done through a hollow needle with a diameter of 0 7–0 9 mm The needle is connected to a metal fitting attached to a sterile suction tube It is often advisable to aspirate at more than one point, and a fresh sterile needle is used for each puncture, it is then necessary to treat the fitting as septic and to hold a needle which is being removed from it or attached to it by grasping the hilt of the needle with a pair of forceps After the final aspiration the suction tube is discarded



Apparatus for deflation of distended bowel : *a* suction tubing *b* glass connection *c* compressible tubing *d* metal fitting for needle *e*, needle diam 0·7–0·9 mm

The needle is inserted through the bowel wall obliquely or, better still, so that its track passes for about 0 5 cm through the muscular layers before penetrating the sub mucosa and mucosa As the needle is withdrawn, the wall of the bowel is compressed on the shaft with a swab moistened in dilute 'Dettol' lotion The swab and needle are then discarded In the colon the puncture should be made through a tænial band It has not been found necessary or considered desirable to close the puncture point with a suture

Only gaseous contents can be profitably removed in this way Even fluid in the small intestine blocks the needle so readily that no useful reduction of distension can be obtained by attempts to remove it It is easy to tell by inspection and palpation of the distended loops if the distension is largely gaseous In very distended small intestine fluid levels can be seen, and care must be taken to keep the point of the needle out of fluid

When small intestine is being deflated, not more than three loops—about 60 cm of gut—can be reduced by one puncture, and several punctures are often necessary to reduce widespread distension In the colon the result is more dramatic, and experience has shown that almost complete deflation can be obtained by two punctures, one at the mid point of the transverse colon and one at the apex of the pelvic colon To obtain the best results the suction must not be strong and the operator should be able to stop and start it at will This can be achieved by having a short length of compressible tubing between the suction tubing and the metal fitting for the needle (see figure), the surgeon has merely to compress this tubing

SUMMARY

A fatal case of canicola fever is described

The cause of death was uræmia due to lower nephron nephrosis, with terminal bronchopneumonia

There is some evidence from published reports that the renal disease in leptospirosis is nearly always a lower nephron nephrosis

We wish to thank Professor Borst for his kind permission to publish the clinical data

REFERENCES

Ashe W F Pratt Thomas, H R , Kumpe, C W (1941) *Medicine, Baltimore* 20 145
Beitzke H (1917) *Berl klin Wschr* 64, 1572
Jeghers, H J , Houghton, J D Foley, J A (1935) *Arch Path* 20 447
Ruys, A C (1947) cited by van Thiel, P H (1948) The Leptospiroses Leyden p 139
Weetch, R S Colquhoun J , Broom, J C (1949) *Lancet*, i, 906

COAGULABILITY OF IRRADIATED PLASMA

J W LYTTLETON
M.Sc N Z , Ph D Lond
BEIT MEMORIAL RESEARCH FELLOW

L VALLET
B A Camb
OF M R C BLOOD PRODUCTS RESEARCH UNIT

LISTER INSTITUTE, CHELSEA

Cutler et al (1950) have shown that human plasma irradiated with ultraviolet light is less readily coagulable on the addition of thrombin They interpreted this fact as indicating an enhancement of the antithrombic activity of plasma

Experiments made by us on human plasma suggest that the main reason for the delay in coagulation after irradiation lies in a modification of the fibrinogen rather than an activation of the antithrombin

EXPERIMENTAL

In the apparatus used for irradiation (Habel and Sockrider 1946) plasma is allowed to form a thin film on the inside surface of a metal cylinder, 71 cm long and 5 1 cm in diameter, rotating at 1000 r p m at 8° to the horizontal The source of radiation, which is mounted axially within the cylinder, is a Hanovia 24 in low-pressure mercury vapour lamp from which more than 90% of the energy radiated is in the 2537 Å band The length of exposure is inversely related to the rate of flow of the plasma The average film thickness was calculated to be 0 11 mm and 0 085 mm at 3 1 and 1 7 litres per hr respectively

TABLE I—COAGULATION TIME (SEC) OF PLASMA ON ADDITION OF HUMAN THROMBIN

Treatment of plasma	Thrombin 0 2 ml (24 units per ml) added to plasma 1 0 ml	Thrombin 0 2 ml (12 units per ml) added to		
		Plasma 0 8 ml , citrate saline 0 2 ml	Plasma 0 8 ml cit saline 0 1 ml fibrinogen 1 % 0 1 ml	Plasma 0 8 ml fibrinogen 1 % 0 2 ml.
Agitation	7 6	15 0	15 0	17 0
Agitation and ozonisation	10 6	20 8	17 0	17 6
Agitation ozonisation and irradiation (flow 1 7 litres per hr)	21 4	44 0	21 2	21 0
Agitation ozonisation and irradiation (flow 3 1 litres per hr)	14 2	27 0	20 2	20 4
Untreated controls	8 0	16 2	16 0	17 6

During treatment the plasma is subjected to three influences the mechanical agitation and extreme extension of surface resulting from the rapid spinning , the presence of ozone produced in the tube by the ultraviolet radiation acting on atmospheric oxygen , and the ultraviolet radiation itself

Samples of citrated human plasma (nine days old) were subjected to the following treatments

(1) Mechanical agitation of passing through the spinning tube

(2) Mechanical agitation and ozonisation with ozone passing from another source over the spinning plasma

(3) Mechanical agitation, ozonisation, and ultraviolet irradiation (as in normal irradiation treatment), rate of plasma flow 1 7 litres per hr

(4) As in (3) but rate of flow 3 1 lites per hr

(5) Left untreated, as controls

RESULTS

Table I gives the coagulation times of these samples on the introduction of thrombin, with and without the addition of fibrinogen The effect on coagulability of adding different quantities of thrombin to the samples is also shown

In table II the antithrombic activity of the samples is given This has been expressed in terms of the rate of inactivation of thrombin when incubated with samples of each treated plasma at 37°C During incubation, samples of the mixture were removed and used to coagulate a purified fibrinogen The coagulation times thus observed were converted to thrombin units by previous calibration, and the percentage of the thrombin inactivated in the first ten minutes' incubation was used to express the relative antithrombic activities of the plasma

TABLE II—ANTITHROMBIC ACTIVITY * OF TREATED PLASMA

Treatment of plasma	Thrombin inactivated by plasma (%)	
	Before defibrination	After defibrination with a trace of thrombin
Agitation	40	41
Agitation and ozonisation	36 5	33
Agitation ozonisation and irradiation (flow 1 7 litres per hr)	33	30 5
Agitation ozonisation and irradiation (flow 3 1 litres per hr)	33	30 5
Untreated controls	37 5	35

* Expressed as % thrombin inactivated in 10 min at 37°C when 4 75 ml of thrombin (12 units/ml) is incubated with 0 25 ml. of plasma

These results show that the antithrombic activity of plasma is not increased by irradiation , on the contrary it seems slightly reduced It is apparently increased by the mechanical treatment alone, but the increase is slight

The delay in coagulation of plasma by thrombin as a result of irradiation seems to be primarily due to an effect on the fibrinogen, and not to an increase in the normal antithrombic activity or to a heparin like substance causing thrombin inhibition This is suggested by two facts (1) the addition of fibrinogen to the system restores the coagulation time to a value near that of the control , and (2) the clot formed in irradiated plasma is abnormal Whereas in normal plasma the fibrin gel appears abruptly from a completely liquid condition, the treated plasma becomes progressively more and more viscous, with the result that the fibrin gel develops gradually

The fact that the coagulation times of treated plasmas are not restored completely to the value given by the controls is presumably due to the distribution of the added thrombin between the normal and modified fibrinogen molecules

The reduction in coagulability of plasma fibrinogen seems to be due both to the ozonisation and to the ultraviolet irradiation Mechanical treatment alone promotes coagulation to a slight extent abnormality—no free fluid was present, and only occasional explosions of bowel sounds in the right iliac fossa were heard on auscultation The rectum was loaded with fæces which were removed with an enema without relief to the pain, and there was no local tenderness or abdominal tenderness on rectal examination At this stage the blood pressure was 90/60 mm. Hg The patient's condition did not improve, and he was diagnosed as having intestinal strangulation, but with no obvious explanation for the absence of bowel sounds A plasma drip was started The systolic blood pressure was 80 mm Hg, but at times it was not recordable

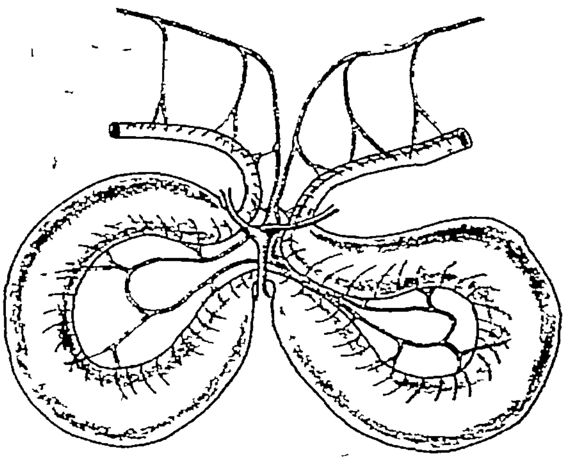
Operation at 2 15 P.M under gas-oxygen and ether (Dr N G Johnson) without any relaxant When the abdomen was opened through a right paramedian incision, the first loop of gut to present was completely collapsed This was followed proximally and, except for two stretches of about 5 in which were about normally distended it was completely collapsed up to the duodenojejunal flexure Duodenum and stomach were normal, and there was no evidence of perforation or fluid Traced downwards from the original presenting loop, the gut remained collapsed until about 2 ft from the ileocæcal valve, where it was collected into a sort of rosette (see figure) by three short string like adhesions One of the adhesions completely, and the other two partially, occluded the gut After the adhesions had been divided, the affected portion of gut was about 15 in. long Where the occlusion was complete, the gut wall was congested and appeared slightly bruised, this section of gut was dilated to nearly twice the normal size Distal to the adhesions the cæcum and the whole of the colon were completely collapsed. There were a few moderately enlarged mesenteric glands but nothing else abnormal At the end of operation the systolic blood pressure had steadied to 80–90

Postoperative Course—Apart from the pint of plasma the patient was given no intravenous fluid By next day he was much better, and he had no postoperative abdominal distension His resting blood pressure was 112/70 mm Hg He was discharged from hospital on his tenth postoperative day with his wound healed and having been walking about the ward since his fourth postoperative day Seen at the end of October he was fit and itching to return to playing rugby football. His bowels had moved daily without medicine since his discharge from hospital

Follow up—He was last seen on Aug 3, 1950, when his weight was $7^{1}/_{2}$ st, his appetite excellent, and his bowels opened daily without medicine

DISCUSSION

Ogilvie (1948), Dunlop (1949), Handley (1949), and Macfarlane and Kay (1949) have reported cases of colonic obstruction for which no cause was found at operation, and this condition has been called Ogilvie's syndrome There is however, no fundamental clinical difference between such cases and those of spastic ileus reviewed by Aird (1949a)



One complete and two partial occlusions of gut caused by three short string-like adhesions six months after appendicectomy

In the present case there was complete occlusion of small intestine by an adhesion, and dilatation of gut proximal and distal to the site of complete obstruction Two further adhesions, one proximal and one distal to the main adhesion, partially occluded bowel about 7 or 8 in from the complete obstruction The clinical picture was that of collapse, low blood pressure, scaphoid abdomen, few bowel sounds, and continuous retching, with little if any vomit In view of these signs and symptoms, the findings at operation were surprising Aird (1949b) has suggested that a widespread spastic ileus would be the most logical interpretation of the collapsed gut proximal to the adhesions

SUMMARY

An unusual case of intestinal obstruction is presented in which there was complete mechanical occlusion of gut but in which the gut proximal to the obstruction was collapsed The clinical picture was one of severe shock

REFERENCES

Aird I (1949a) A Companion in Surgical Studies Edinburgh
— (1949b) Personal communication
Dunlop J A (1949) *Brit med J* i 890
Handley R S (1949) *Ibid* p 891
Macfarlane J A Kay S K (1949) *Ibid* ii 1267
Ogilvie W H (1948) *Ibid* ii 671

THE ANGINOSE TYPE OF GLANDULAR FEVER

REPORT OF A CASE REQUIRING TRACHEOTOMY

I M LIBRACH
M B Belf, D.P.H, D C H
RESIDENT MEDICAL OFFICER, ILFORD ISOLATION HOSPITAL, ESSEX

GLANDULAR fever is now being diagnosed more often and is no longer regarded as rare Its relatively protean manifestations have been described by Bernstein (1940), Smeall (1942), Halcrow et al (1943), Contratto (1944), Tidy (1950b), and others

The commonest manifestations, in my experience, are generalised splenic and lymph gland enlargement and the anginose form Owing to the decreasing incidence of faucial diphtheria the anginose form of glandular fever has become more important in differential diagnosis, yet it is diagnosed with reluctance—possibly because it is natural to think of the more serious condition of diphtheria

It is unwise, however, to consider that glandular fever is wholly benign Deaths have been reported as due to neurological complications, hepatitis, ruptured spleen, and respiratory obstruction (Custer and Smith 1948, Ainley 1949, Lemierre et al 1948) The reason why so few cases of respiratory obstruction have been published is probably that, in the absence of a Paul Bunnell test most of them have been labelled as swab negative diphtheria None of the reviews cited above mentions this complication, nor does Joyce (1946) in a paper on the complications of glandular fever Wintrobe (1946) even asserts that "in the anginose form laryngeal obstruction is unknown"

The earliest case and the youngest patient (aged 11 months) that I could find were reported by Chen and Teng (1941) Tracheotomy immediately relieved the symptoms

Story and McCabe (1946) report a case in which emergency tracheotomy was successful in relieving complete respiratory obstruction in a man aged 20

Lemierre et al (1948) describe two further cases a man aged 21 died from faucial obstruction in hospital but in the second case a boy of 18 was probably saved by tracheotomy partially or completely as desired During the aspirations the assistant manipulates the bowel gently to bring the gas content of neighbouring loops up to the needle, in the colon this may be done by compression of the flanks

ILLUSTRATIVE CASES

Peritonitis and Ileus

A man, aged 64, was seen 24 hours after the onset of acute abdominal pain, he was very ill, with gross distension of the abdomen, loss of liver dullness, and signs of peritonitis Perforated peptic ulcer was diagnosed At laparotomy it was found that the loss of liver dullness was due not to pneumoperitoneum but to distended coils of small intestine between liver and diaphragm There was a perforation of an anterior duodenal ulcer, but it was found to have sealed spontaneously The perforation, reopened by the dissection, was sutured, and discharges were sucked out of the peritoneal cavity It was then appreciated that the bowel was so distended that closure of the abdominal wound would be difficult if not hazardous The distension was largely gaseous, and the bowel was deflated by aspiration so completely that the abdomen after closure was scaphoid In this case six punctures were made five in the small intestine, and one in the transverse colon In the postoperative period distension did not recur, intestinal sounds were heard twenty four hours after operation, the patient had a spontaneous bowel motion on the third day, and his recovery was uneventful

Subsequent experience has confirmed the impression that deflation is sometimes valuable in paralytic distension, but if it is to be as effective as in the case described above operation must be early In later cases the bowel content tends to be more fluid than gaseous I have considered, but have not yet attempted, the treatment of paralytic ileus by laparotomy for deflation with a needle and aspiration This measure would be justified only if percussion and X rays showed that the distension was largely gaseous

Intestinal Obstruction

The commonest indication for deflation of the gut by needle and suction is intestinal obstruction In obstruction of the distal colon distension is easily relieved by puncture and aspiration of the transverse colon It is often found that most of the cæcal gas can be removed by manipulating it gently to the needle I have not found it necessary to aspirate directly the cæcum or the ascending colon, puncture of the cæcum might involve additional risk because of the low vitality of the cæcal wall

If the obstruction is distal to the iliac colon, aspiration of the distended part of the pelvic colon is also desirable The colon should be aspirated at the highest point of a loop of transverse or pelvic colon which has been delivered from the wound, because the gases will then tend to rise to the needle

In colonic obstruction with gross distension it is advisable to make the first intra abdominal manœuvre a gentle exposure of distended transverse colon and insertion of a needle As deflation proceeds, further manual exploration becomes easier and safer I believe that this practice makes laparotomy and exploration practicable in some patients who might otherwise be better treated by blind cæcostomy

When the distended colon has been deflated, a proximal colostomy can be made at the site of election with much greater ease and safety Sutures to construct a colostomy spur are easily inserted, the deflated bowel is more mobile and more easily delivered, and the opening of the colostomy can be delayed without adding to the patient's discomfort

In cases of colonic obstruction it is seldom necessary to aspirate the small intestine, but in some late cases this has been done with added advantage

When the obstruction is due to volvulus of the sigmoid colon, deflation with a rectal tube passed by an assistant and manipulated by the surgeon is preferable if practicable However, if the twist is so tight that a rectal tube cannot be made to pass, initial aspiration of the distended loop with a needle makes its delivery and manipulation comparatively easy and safe

Two of the patients on whom I have deflated the colon by aspiration died of cardiovascular and respiratory complications within a week of operation Necropsy in both cases revealed no peritoneal infection due to the procedure

When the small intestine is obstructed, the distended coils are easily deflated if their content is gaseous, but in such cases the content is sometimes fluid and punctures should not be made unless it is obvious that the distension can be materially reduced A puncture in a loop of bowel which has to be left distended should be valvular and safe, but there may be some increased risk if an ineffective puncture has been made

Other Conditions

Gaseous distension of the colon may be encountered in any major abdominal operation When this is considerable it may interfere with closure of the abdominal wound and it usually leads to an uncomfortable immediate postoperative period for the patient On two occasions I have deflated the colon in the course of partial gastrectomy for peptic ulcer In each case the operations were facilitated and the patient had a smooth postoperative course

Deflation has also proved helpful in patients being treated for carcinoma of the pelvic colon by exteriorisation resection with clamps The reduction of distension of the proximal colon by removal of its gas permits the proximal clamp to be left on the bowel for three days or more Experience has shown that the gas does not reaccumulate rapidly and that postoperative discomfort is reduced

WARNING

Deflation of the bowel by aspiration should not be attempted without due indication With the muscular relaxation which modern anæsthesia can provide, its use simply to facilitate closure of the abdomen will rarely be justified When it is done in cases of paralysis or obstruction the minimal number of punctures should be made

SPASTIC ILEUS IN THE PRESENCE OF MECHANICAL OBSTRUCTION OF SMALL INTESTINE

J Grieve

B Sc, M B St And, F R C S E

LECTURER IN SURGERY IN THE UNIVERSITY OF ST ANDREWS

Prolonged spasmodic contraction of gut has many causes (Aird 1949a), but it is seldom due to mechanical obstruction of the bowel, as in the case described here

CASE RECORD

A boy aged 14, had his appendix removed through a right gridiron incision in March, 1949 He was well thereafter until the early hours of Sept 23, 1949, when he woke between 4 and 5 A M with agonising central abdominal pain The pain was spasmodic but did not pass off completely at any time Between 6 and 7 A M he was seen by his doctor, who thought he might have a perforated ulcer At that time the boy's temperature was 97°F and his pulse rate 90

On admission to hospital about 10 A M his pulse was 108 and his temperature 96°F He was collapsed and greyish white He kept retching but brought up only a very small amount of watery material with little evidence of bile staining His tongue was clean and his abdomen concave There was no guarding or rigidity and apart from some tenderness just to the right of the umbilicus there was little

Hospital, Romford, for the pathological findings, and Dr G Laing Brown, medical superintendent, for permission to publish.

REFERENCES

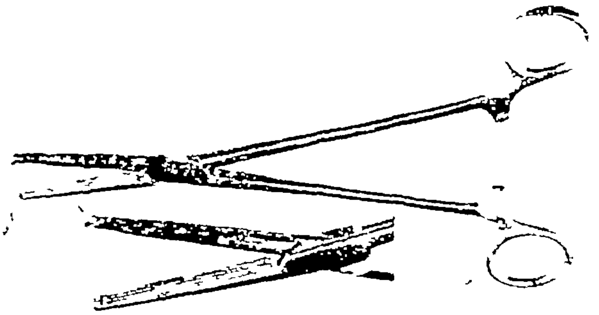
Ainley N J (1949) *Ulster med J* 2 219
Bernstein A (1940) *Medicine Baltimore*, 19 85
Bower, A G Affeldt J E West H (1949) *J Pediat.* 35 58
Chen, K. C Teng C T (1941) *Chin med J* 59 116
Contratto A W (1944) *Arch intern Med* 73 449
Custer R P Smith E. B (1948) *Blood* 3 830
Halcrow J P A Owen L M Rodger N O (1943) *Brit med J* ii 443
Johnson R D (1944) *J Amer med Ass* 124 1254
Jones G P Jones E (1949) *Brit med J* ii 1212
Joyce F T (1946) *Arch intern Med* 78 49
Lemierre A Morin M Allison M. (1948) *Bull. Soc Méd Hôp Paris* 64 51
Mitman M (1950) Personal communication
Ravenna, P Snyder J (1948) *Ann intern Med* 28 861
Smeall J T (1942) *Edinb med J* 49 291
Story, G B T MacCabe A F (1946) *Brit med J* ii 652
Stroebel, C F Hallberg O E Stevens J E (1948) *Arch intern Med* 57 1102
Tidy H L (1950a) Personal communication
— (1950b) *Postgrad med. J* 26 9
Wintrobe M. M. (1946) Clinical Hematology 2nd ed. Philadelphia

New Inventions

CLAMPS FOR HYSTERECTOMY

After trying many patterns of hysterectomy clamp, I have evolved the following hybrid from what I consider to be the best features of several other clamps. No originality is claimed, and graceful acknowledgment is made to Maingot, Mayo Ochsner, Kocher, and Sir Heneage Ogilvie.

The clamp is rather heavily built but is light in the hand because of its good balance; it has a box joint and a rat toothed point. The main feature is the longitudinal grooving of the jaws. The clamp is 8½ in. long, and the jaw is 2½ in long.



The virtue of this clamp is that, in grasping a thick vascular pedicle, such as the ovariopelvic or the uterine, no part of the pedicle can escape from the grip of the jaw. With transversely grooved clamps this happens all too often. The loss of the uterine artery once or twice in those circumstances prompted the design of this clamp, which is made by Hawkins and has been tried and has found favour in the eyes of my colleagues. It is equally suitable for abdominal and vaginal hysterectomy, and even general surgeons might perhaps find it of value on occasion.

I should like to acknowledge the kind coöperation of Miss Bartlett (theatre sister), Mr A. E Embray (curator of instruments), and Mr N K. Harrison (of the photographic department)—all of St Bartholomew's Hospital.

St Bartholomew's Hospital
London

J HOWKINS, M D, M.S, F R C.S, F R C O G

. . . it can be regarded as certain that . . . the great bulk of the members of any modern community ought to be able over the whole of a full life span, to continue to contribute to the productive skills which are essential in such a community and to do so without undue fatigue or strain, but to their own happiness and satisfaction. —SIR FREDERIC BARTLETT F.R.S in a foreword to *Skill and Age* by A T Welford and others (London, 1951)

Reviews of Books

Malignant Disease of the Female Genital Tract

STANLEY WAY, M.R.C.O.G, gynæcologist to the Newcastle Regional Cancer Organisation Royal Victoria Infirmary Newcastle. London *J & A Churchill* 1951. *Pp* 279 *24s*

WRITTEN primarily for the practising gynæcologist, this is not only a textbook but also, in large part, a statement of the author's views and experience, supported by liberal use of case-histories. The chapter on cancer of the cervix, for example, provides a fair summary of much that has been published in recent years together with much first-hand information.

Mr Way's approach is based on his acceptance of the reliability of the biopsy cell count, associated with the names of Spear and Glucksmann, to distinguish between radioresistant and radiosensitive tumours of the cervix. He claims that by comparing a biopsy of cervix before irradiation with subsequent biopsies taken during irradiation, the response of the tumour to irradiation can often be foretold, and he believes that in the case which responds favourably to radium irradiation can do more and with a lower mortality than surgery. In the case which responds unfavourably—the so called radioresistant case—the prognosis is bad but surgery holds out the best hope. This view is contrary to that of Heyman, of Stockholm, who holds that in radioresistant cases surgery is dangerous and should be restricted to those in which at laparotomy, no extension of the growth beyond the uterus is found.

What Mr Way says on cancer of the ovary tends to confirm current ideas; the treatment of choice is surgery, in spite of an operative mortality-rate of 10–15%, and the value of postoperative X-radiation remains debatable. Most will agree, too, that the treatment of cancer of the vulva is essentially surgical and that the results of radium and X rays have been very disappointing. In the chapter on this condition, as indeed throughout the book, emphasis is laid on the importance of the lymphatic system in relation to the spread of malignant disease and its treatment. For cancer of the vulva the author has adopted a method of extended radical operation, which he has completed in 75 cases with an operative mortality-rate of 14.6%. Of the cases treated, 21 were operated on more than five years ago with an absolute survival-rate of 90%. The most important steps in the operation are the widespread removal of vulva, and the resection of the lymphatic glands at least as far as Cloquet's gland. The high survival-rate has been made possible by wide experience in the past ten years, by an agreement with his colleagues to submit to him all the cases they see, Mr Way has examined 127 patients with cancer of the vulva. It is to be hoped that his plea for concentration of such cases in a few selected centres will succeed.

Visual Anatomy

Head and Neck. SYDNEY M FRIEDMAN, M.D, PH D, professor of anatomy University of British Columbia Vancouver. Springfield, Ill *Charles C Thomas*. Oxford *Blackwell Scientific Publications*. 1950. *Pp* 217 *47s 6d*

LIKE so many of his colleagues, Professor Friedman has been depressed to find how little anatomy students remember a year or two after they have completed their dissection course. He has therefore planned a series of books dealing with regional anatomy, designed as revision texts, both for undergraduates and postgraduates, and presenting only that material which is essential for the practice of medicine.

The first volume of this series deals with the head and neck and consists of 93 illustrations each with a short facing descriptive text, the aim being a visual rather than a textual presentation. These illustrations are distinctive line drawings by the author rather resembling woodcuts which omit details and concentrate on the main features; they are sufficiently striking to compel close study. The approach is synthetic: the bones are gradually clothed with successive layers of muscle which in turn envelop vessels and nerves and are eventually covered by the enclosing deep fascia. In each diagram the new facts are presented against the background of the preceding one, and there is some deliberate repetition.

Bower et al (1949) record a case in which tracheotomy was done and the patient, a boy aged 2, recovered

Jones and Jones (1949) report a case in a man of 22 in which tracheotomy became urgent and was done with relief of symptoms

Tidy (1950a) has known of tracheotomy being required in the severe anginose form, but he has had no personal cases

In the following case tracheotomy was successful

CASE RECORD

A schoolboy, aged 11, was admitted to hospital on April 15, 1950, as a suspected case of faucial diphtheria A throat swab taken at home had been negative for diphtheria, but had grown hæmolytic streptococci in profusion. The boy had been ill with sore throat since April 8, but he had recently developed difficulty in breathing He had been treated at home with penicillin and sulphamerazine His past history was uneventful He had not been immunised against diphtheria, but three years previously he had been found to be Schick negative

On admission he was acutely ill His temperature was 103 8°F, pulse rate 118, respirations 30 a minute His neck was much swollen, and his fauces were œdematous, as were his tonsils, which met in the midline and were covered with an extensive exudate Other systems were normal

Treatment and Progress —Faucial diphtheria was diagnosed, and the patient was given antiserum 200,000 units intramuscularly, penicillin 500,000 units six hourly, and oxygen by B L B mask Three hours after admission he was worse, his breathing being more difficult He was slightly cyanosed Five hours later he was very restless, and sedation with 'Sodium amytal' had little effect Ten hours later his restlessness had increased He was dyspnœic and cyanotic, and there was recession of the soft parts of the neck and chest The local throat condition, though difficult to see, was much as on admission In view of the respiratory distress Mr William Ibbotson did a high tracheotomy, which almost immediately relieved all distress The operation proved difficult because of bleeding and because of œdema of the muscles and fascial planes

Postoperative Course —Next morning (April 16, 1950) the patient was comfortable, and the faucial area was less œdematous, but the tonsils were covered with thick white membrane indistinguishable from that of diphtheria The blood pressure was 110/70 mm Hg A piece of membrane was removed from the inner tracheotomy tube, and forty eight hours later some more was coughed up through it On April 19, 1950, a maculo papular rash appeared on the face, trunk and limbs, but the local membrane was separating, and two days later the temperature settled and remained so until the patient s discharge On April 26, eleven days after the operation, the tracheotomy tube was removed On May 2, the throat was clean and all the swollen glands had subsided Tonsillectomy, done on May 22, proved difficult because of multiple capsular adhesions and excessive hæmorrhage from the left tonsil bed The patient was discharged free from all signs and symptoms on June 22

Bacteriology —Three examinations of throat and nose swabs (on admission, and two days and four days later) were all negative for diphtheria bacilli and hæmolytic streptococci (direct and culture) Throat membrane (coughed up) was also negative for diphtheria bacilli and hæmloytic streptococci (direct and culture) Post tonsillectomy throat and nose swabs were also negative for diphtheria and hæmolytic streptococci (direct and culture)

Serology —Wassermann and Kahn reactions were negative A Paul Bunnell test done on April 23 (eight days after admission) was positive to a titre of 1 in 512 after absorption with guineapig kidney Repeated on May 25, 1950 (forty days after admission) it was positive to 1 in 80, and after absorption with guineapig kidney 1 in 40

White-cell Counts —On April 23, 1950, there were 6200 white cells per c mm (polymorphs 44%, lymphocytes 51%, monocytes 4%, eosinophils 1%) On May 3, 1950, there were 7200 per c.mm (polymorphs 21%, lymphocytes 67%, monocytes 12%) The appearance of the mononuclear cells suggested glandular fever

Other Investigations —Radiography of the chest was normal on April 19, 1950 Electrocardiography was normal. The blood urea level on April 27, 1950, was 37 mg per 100 ml

DISCUSSION

Mitman (1950) regards glandular fever primarily as an infection of the hæmopoietic system As in other affections of this system there is a liability to faucial and gingival trouble, which is probably secondary Perhaps one could go further and call it an affection chiefly of the reticulo endothelial system—i e, infective reticulosis Tidy (1950b) says that all the blood forming tissues are affected, but the myeloid system less severely and for a shorter period than the other elements

Though glandular fever is primarily an affection of the first two decades of life, most of the published cases of respiratory obstruction have been in adolescents and young adults rather than in infants

In all the published cases the obstruction developed three to nine days after the onset of the illness The degree of obstruction has varied from complete obstruction requiring emergency tracheotomy to minor obstruction manifested by hoarseness and stridor In some cases there has been doubt whether to perform tracheotomy or not—e g, Johnson (1944) and Stroebel et al (1948)

The obstruction may be pharyngeal or laryngeal, or both, and it may be due to œdema or to membrane, or both. Ravenna and Snyder (1948) describe what they regard as the characteristic appearance of the œdema of the pharynx and larynx in this disease In more than half their cases the fauces were a brilliant red There was faucial œdema, the uvula at times resembling "a pear shaped bag filled with water" Usually no exudate was present The typical picture of follicular tonsillitis, Vincent's angina, and even diphtheria was also seen However, I cannot help feeling that there is no characteristic faucial picture in glandular fever, for, if we hold the ultimate site of the disease to be the hæmopoietic system, leukæmia and agranulocytosis as well as the common infections, are likely to produce similar appearances

Ravenna and Snyder describe a case of respiratory obstruction in a boy aged 3 years Laryngoscopy showed much œdema of the arytenoids, but the vocal cords were clear Next day whitish membrane covered the right arytenoid, and this condition continued for a week, after which the œdema spread to the epiglottis Extensive ulceration extended from the arytenoids into the glottis and down the trachea On the other hand, in the second case published by Lemierre et al (1948) laryngoscopy revealed neither œdema nor false membrane in the larynx, but there was enormous œdema of both tonsils and pharynx, which were covered with exudate Laryngoscopy was impracticable in the present case, but at tracheotomy gross œdema of the muscles and fascial planes was found, and pieces of membrane were extracted later through the tracheotomy tube This suggests that the larynx and the trachea were affected as well as the fauces

The obstruction seems to be due to inflammation The membrane represents devitalised and necrotic mucosa indistinguishable from that of diphtheria (Tidy 1950b, Smeall 1942) Œdema of the neck rivals that of diphtheria, but suppuration is very rare The faucial œdema causes anxiety, even obstruction, but despite this the patient does not look toxic

SUMMARY

A case of glandular fever in a schoolboy aged 11 years requiring tracheotomy is described The pathology of the condition is briefly discussed

I wish to thank Dr K M Hickey for his help in the treatment of this case Mr W Ibbotson for his surgical assistance Dr E Atkinson, of the department of pathology, Oldchurch

Hospital, Romford, for the pathological findings, and Dr G Laing Brown, medical superintendent, for permission to publish

REFERENCES

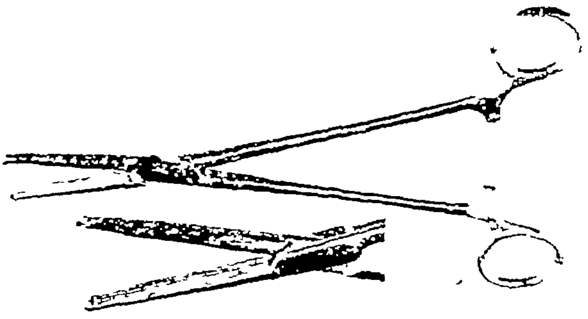
Ainley N J (1949) *Ulster med J* 2 219
Bernstein A (1940) *Medicine Baltimore* 19 85
Bower A. G Affeldt J E West H (1949) *J Pediat* 35 58
Chen K. C Teng C T (1941) Chin med J 59 116
Contratto A W (1944) *Arch intern. Med* 73 449
Custer, R P Smith E B (1948) *Blood* 3 830
Halcrow J P A Owen L M Rodger N O (1943) *Brit med J* ii 443
Johnson R D (1944) *J Amer med Ass* 124 1254
Jones G P Jones E (1949) *Brit med J* ii 1212
Joyce F T (1946) *Arch intern Med* 78 49
Lemierre A Morin, M Allison M. (1948) *Bull Soc Med Hôp Paris* 64 51
Mitman M. (1950) Personal communication
Ravenna, P Snyder, J (1948) *Ann intern Med* 28 861
Smeall J T (1942) *Edinb med. J* 49 291
Story, G B T MacCabe A F (1946) *Brit med J* ii 652
Stroebel C F Hallberg O E Stevens J E (1948) *Arch intern Med* 57 1102
Tidy, H L (1950a) Personal communication
— (1950b) *Postgrad med J* 26 9
Wintrobe M M. (1946) Clinical Hematology 2nd ed Philadelphia.

New Inventions

CLAMPS FOR HYSTERECTOMY

AFTER trying many patterns of hysterectomy clamp, I have evolved the following hybrid from what I consider to be the best features of several other clamps No originality is claimed, and graceful acknowledgment is made to Maingot, Mayo-Ochsner, Kocher, and Sir Heneage Ogilvie

The clamp is rather heavily built but is light in the hand because of its good balance, it has a box joint and a rat-toothed point The main feature is the longitudinal grooving of the jaw The clamp is $8^1/_2$ in. long, and the jaw is $2^1/_2$ in long



The virtue of this clamp is that, in grasping a thick vascular pedicle, such as the ovariopelvic or the uterine, no part of the pedicle can escape from the grip of the jaw With transversely grooved clamps this happens all too often The loss of the uterine artery once or twice in those circumstances prompted the design of this clamp, which is made by Hawkins and has been tried and has found favour in the eyes of my colleagues It is equally suitable for abdominal and vaginal hysterectomy, and even general surgeons might perhaps find it of value on occasion

I should like to acknowledge the kind coöperation of Miss Bartlett (theatre sister) Mr A. E Embray (*curator of* instruments) and Mr N K Harrison (of the photographic department)—all of St Bartholomew's Hospital

St Bartholomew's Hospital
London

J HOWKINS, M D, M.S,
F R C.S, F R C O G

---

it can be regarded as certain that the great bulk of the members of any modern community ought to be able over the whole of a full life span to continue to contribute to the productive skills which are essential in such a community and to do so without undue fatigue or strain, but to their own happiness and satisfaction. —SIR FREDERIC BARTLETT F.R.S in a foreword to *Skill and Age* by A T Welford and others (London, 1951)

Reviews of Books

Malignant Disease of the Female Genital Tract

STANLEY WAY, M.R.C O G, gynæcologist to the Newcastle Regional Cancer Organisation, Royal Victoria Infirmary, Newcastle London J & A. Churchill 1951 Pp 279 *24s*

WRITTEN primarily for the practising gynæcologist, this is not only a textbook but also, in large part, a statement of the author's views and experience, supported by liberal use of case-histories. The chapter on cancer of the cervix, for example, provides a fair summary of much that has been published in recent years together with much first-hand information

Mr Way's approach is based on his acceptance of the reliability of the biopsy cell count, associated with the names of Spear and Glucksmann to distinguish between radio resistant and radiosensitive tumours of the cervix He claims that by comparing a biopsy of cervix before irradiation with subsequent biopsies taken during irradiation, the response of the tumour to irradiation can often be foretold, and he believes that in the case which responds favourably to radium, irradiation can do more and with a lower mortality than surgery In the case which responds unfavourably—the so called radioresistant case—the prognosis is bad but surgery holds out the best hope This view is contrary to that of Heyman, of Stockholm who holds that in radioresistant cases surgery is dangerous and should be restricted to those in which, at laparotomy, no extension of the growth beyond the uterus is found

What Mr Way says on cancer of the ovary tends to confirm current ideas, the treatment of choice is surgery, in spite of an operative mortality-rate of 10–15%, and the value of postoperative X-radiation remains debatable Most will agree, too, that the treatment of cancer of the vulva is essentially surgical and that the results of radium and X rays have been very disappointing In the chapter on this condition, as indeed throughout the book, emphasis is laid on the importance of the lymphatic system in relation to the spread of malignant disease and its treatment For cancer of the vulva the author has adopted a method of extended radical operation, which he has completed in 75 cases with an operative mortality-rate of 14 6% Of the cases treated, 21 were operated on more than five years ago with an absolute survival-rate of 90% The most important steps in the operation are the widespread removal of vulva, and the resection of the lymphatic glands at least as far as Cloquet's gland The high survival-rate has been made possible by wide experience in the past ten years, by an agreement with his colleagues to submit to him all the cases they see, Mr Way has examined 127 patients with cancer of the vulva It is to be hoped that his plea for concentration of such cases in a few selected centres will succeed.

Visual Anatomy

Head and Neck SYDNEY M FRIEDMAN M D PH D professor of anatomy, University of British Columbia Vancouver Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 217 *47s 6d*

LIKE so many of his colleagues, Professor Friedman has been depressed to find how little anatomy students remember a year or two after they have completed their dissection course He has therefore planned a series of books dealing with regional anatomy, designed as revision texts, both for undergraduates and postgraduates, and presenting only that material which is essential for the practice of medicine

The first volume of this series deals with the head and neck and consists of 93 illustrations, each with a short facing descriptive text the aim being a visual rather than a textual presentation. These illustrations are distinctive line drawings by the author rather resembling woodcuts which omit details and concentrate on the main features they are sufficiently striking to compel close study The approach is synthetic the bones are gradually clothed with successive layers of muscle which in turn envelop vessels and nerves and are eventually covered by the enclosing deep fascia In each diagram the new facts are presented against the background of the preceding one and there is some deliberate repetition to drive home important points The figures are perhaps least happy when dealing with the interior of the skull, but elsewhere they are most clear and helpful

The accompanying text has the simplicity, force, and economy which we have learned to associate with Canadian anatomical texts There are one or two slips, such as the statement that stimulation of the cervical sympathetic causes flushing of the face, and no doubt, as the author anticipates, many will quarrel with the selection of material and the varying stress laid upon it It is clearly impossible to draw a hard and fast line between what is necessary for medical practice and what is not, but Professor Friedman has succeeded in producing a good and unusual book which will undoubtedly smooth the path of those revising the anatomy of the head and neck

Encyclopedia of the Eye

Diagnosis and Treatment CONRAD BERENS, M D, F A C S executive eye surgeon, New York Eye and Ear Infirmary professor of clinical ophthalmology, Post Graduate Medical School, New York University, EDWARD SIEGEL, M D, attending ophthalmologist, Champlain Valley Hospital, Plattsburg, New York Philadelphia and London J B Lippincott 1950 Pp 272 40*s*

THE authors present this introduction to ophthalmology in the form of an encyclopædia, subject matter being arranged under the letters of the alphabet instead of following the usual anatomical system The text is sound accepted teaching, but it is difficult to see what precise advantage this form of presentation has over the more usual style In some cases the required information may be obtained a little more quickly, but there are also disadvantages, for adequate illustration is hardly possible, and indeed the colour reproductions are not up to standard and would have been better omitted

A Text Book of Venereal Diseases

R R WILLCOX, M D, consultant in venereal diseases, St Mary s Hospital, London London Heinemann Medical Books 1950 Pp 439 32*s* 6*d*

THERE is always a demand for a sound textbook on the diagnosis and treatment of venereal diseases, and particularly now, when so many new methods of treatment have been introduced within a few years This book is up to date, and covers the field reasonably well, some of the chapters, notably that dealing with congenital syphilis, are very good indeed But Dr Willcox's ideas about the pathology of the venereal diseases seem to be a little uncertain, and though his exposition is lucid, his style is careless and of a raciness perhaps out of place in this setting, Some obvious mistakes suggest undue haste in writing thus it would hardly be possible to reduce paraphimosis with the patient in the prone position The illustrations are a mixture of good and bad, and it is unfortunate from the point of view of students in this country that so many lesions are shown on coloured skins When photomicrographs are included the magnification is not given These small things cause unnecessary irritation, but fundamentally the book is sound

Animal Evolution

G S CARTER, fellow of Corpus Christi College and lecturer in zoology in the University of Cambridge London Sidgwick & Jackson 1951 Pp 368 30*s*

A DISCUSSION of the theory of evolution of animals should be based, as the author says, on all the facts of animal biology But that is naturally impossible in a book of this size, so a selection of the more important facts is made before the theory is discussed Those facts are set out in five chapters palæontological data, genetics, the species in zoology, infraspecific categories, and competition, isolation, and natural selection The chapter on genetics, perhaps because it is a selection of facts that bear on evolution, is probably one of the best and most interesting of its kind By contrast the chapter on species is disappointing In the rest of the book too much space is given to discussing " pre adaptation " one can only adapt to a change, one cannot " preadapt " or " postadapt " The author tells us that " the object of the book is to discuss whether a theory can be put forward at the present time that will explain the means by which evolutionary change has been brought about " Evolution itself is taken for granted, but is rather artificially divided into micro-, macro-, and me evolution The argument of the book describes a circ the first part narrating the facts of evolution in ter of the theory, and the second part announcing t theory in terms of the facts Nevertheless it is full interesting information

Enterobacteriaceae

F KAUFFMANN, M D, chief, International Salmonel and Escherichia Centre, Copenhagen Copenhagen Munksgaard 1951 Pp 338 50*s*

THE writer of this expensive monograph has a international reputation as an authority on its subject It is difficult to find any modern work on the bacteriolog of the enterobacteriaceæ to which he has not accorde critical appreciation, and to those who concern themselve with the identification and taxonomy of this group hi book will be indispensable It is full of useful and well designed tables, and, if the language seems stilted a times, the meaning is always clear Yet one must regre that so much earlier work is disregarded Some of it i certainly difficult to fit into our newer conceptions, bu it records the experience of serious scholars and we ca still learn from it The author's attitude is strictly tha of a laboratory worker, and he carries it to the point o omitting any note of the origin of the species of salmonella Those whose chief interests are in the pathology o epidemiology of this group of organisms will not fin his book very rewarding

Renal Function

Transactions of the First Conference, October 20–21, 1949 Editor STANLEY E BRADLEY, Department of Medicine Columbia University, New York New York Josia Macy, Jr, Foundation 1950 Pp 172 $2 50

THE Macy Foundation reports are difficult for th general reader, and even for the specialised research worker what is under discussion is not always exactly defined In this volume the section by Jean Oliver on histochemical studies of tubule function became finally bogged down by a semi-philosophical argument on the meaning of " secretion " But F Binkley discusses well the rôle of glutaminase, a kidney constituent which may act like an ion-exchange resin, R W Berliner deals with tubular secretion of potassium and acid, and L G Wesson with water absorption by the tubules The book gives much insight into American research and is valuable for the advanced investigator

---

An Eighteenth Century Lectureship in Chemistry (Glasgow Jackson Son & Co 1950 Pp 220 21*s*)—*This* well documented history, edited by Mr Andrew Kent, PH.D, tells of the life work of William Cullen, who did much to rescue chemistry from the toils of alchemy The extracts from some of Cullen s lectures make most attractive reading, andthe account of Dr Joseph Black and his experimental work is equally good The foundation of the first lectureship finally established the status of chemistry as a special science, and a regius chair of chemistry at Glasgow resulted in 1818 For though the University of Edinburgh took an early practical share in the development of chemistry, Glasgow University has the honour of first encouraging the new science

N A P T Handbook of Tuberculosis Activities in Great Britain and the Commonwealth (13th ed London National Association for the Prevention of Tuberculosis. 1951 Pp 370 30*s*)—Dr Harley Williams, with the assistance of Mr H F Hughes and Miss Elizabeth Harrison, has brought up to date this complete and invaluable directory of hospitals, sanatoria, and clinics of regional hospital boards and hospital management committees, and of tuberculosis services in the British Commonwealth This new edition begins appropriately with an account of the old tuberculosis service in Great Britain and of the changes in its structure and in the legislation affecting it since July, 1948 The information relating to this country which follows is comprehensive, and set out clearly under the headings of the different regional boards The editor regrets that he has not, in this arrangement, been able to group local authority services together with those provided by the boards for, as he points out, one local authority may be in two, or even three, such regions More than a quarter of the book deals with tuberculosis services in other parts of the Commonwealth, Dr Williams has been disappointed only in his hope of including information about Pakistan

THE LANCET

LONDON SATURDAY, MAY 19, 1951

Acute Tubular Necrosis

A NEW and effective treatment often leads to striking advances in our knowledge of underlying pathology In 1949, BULL and his colleagues,[1] at the Hammersmith Hospital described a conservative method of treating anuria It will be recalled that, after the introduction of the artificial kidney by KOLFF, an instrument was set up at Hammersmith. This was used for many cases of anuria, and study of these cases led to the introduction of the new method, which was based on three simple principles (1) to avoid overburdening the body with fluid, (2) to reduce protein katabolism (and urea formation) to a minimum by means of a high-calorie, protein free diet, and (3) to maintain a rough electrolyte balance by giving no added electrolytes and returning any lost by vomiting With these principles in mind the Hammersmith group devised a mixture of peanut oil, glucose, and water (now often termed the Hammersmith Cocktail) which, when given by intragastric drip, has proved both simple and effective, and in uncomplicated anuric uræmia it has replaced both the artificial kidney and peritoneal dialysis The prognosis in cases of anuria due to tubular damage, such as may follow a mismatched transfusion, shock, abortion, concealed accidental hæmorrhage, surgical operation, or poisoning, has thus been remarkably improved, for the patient is kept maintained in good condition until the kidneys recover spontaneously

BULL and his associates have now reported investigations on renal function in cases of anuria treated by this new method[2] They point out that anatomically in such cases there is necrosis followed by regeneration of the renal tubular epithelium, and they suggest that the term " acute tubular necrosis " should replace the unsatisfactory title " lower nephron nephrosis " coined by LUCKE in 1946[3]—a suggestion which will certainly be applauded on this side of the Atlantic BULL and his colleagues recognise three functional phases in acute tubular necrosis (1) the phase of anuria or severe oliguria, (2) the early diuretic phase, when the daily urine volume first reaches a litre, and (3) the late diuretic phase, when tubular function is returning to normal. Little is known about renal function during anuria, it has been suggested that any glomerular filtrate that forms leaks back, through the necrotic tubular cells, into the venous plexuses, but this is speculation. BULL's observation that with anuria the total renal plasma flow is low and there is a considerable arteriovenous oxygen difference offers no support for the view that the disorder ensues from a " shunt " During the early diuretic phase tubular function is severely impaired, for the tubules cannot concentrate urea or creatinine, nor can they conserve electrolytes, so that sodium, potassium, and chloride are poured out in the urine, and the renal tubular extraction of *para*-aminohippurate is also reduced In this phase the maximal rate of tubular reabsorption of glucose was below normal in the two patients in whom it was measured, and the rarity of glycosuria in this condition and in the terminal stages of chronic renal failure requires further investigation. Study of the reabsorption of other " threshold substances," such as phosphate, calcium, and the amino-acids, during this period of tubular dysfunction may show that the loss of function is maximal in the distal tubule

The onset of diuresis after many days of anuria is a source of delight to the patient, the doctor, and the nursing staff, but BULL and his colleagues remark that, even when diuresis has set in, tubular dysfunction persists, and that the outpouring of electrolytes during this period may lead to serious symptoms and even death In the treatment of anuria, therefore, it is not sufficient to tide the patient over the anuric phase by means of the peanut-oil/glucose drip, maintaining equilibrium until the tubules regenerate in the early diuretic phase any dangerous loss of electrolytes must be made good. Why can the newly formed or regenerated tubular cell not concentrate the glomerular filtrate, and how does the kidney regain its remarkable power of maintaining electrolyte and water balance ? Study of the action of pituitary and suprarenal hormones during the early diuretic phase may throw some light on these problems

Two Ways of Grant-giving

" THIS demi-paradise," the dying John of Gaunt remarked with satisfaction, enumerating the advantages of living on a small island. It is possible nowadays to pick holes in his argument, but broadly speaking the blessings of our rough island life still make up for the drawbacks It is, for example, a blessing—or at all events a convenience—that the University Grants Committee (only some 18 persons strong) are able " to cultivate an intimate and in many respects informal relationship with those responsible for formulating and executing university policy "[1], " to survey the various fields of academic study with the objects both of securing that there are no unfilled gaps and also of avoiding unnecessary overlapping ", and to encourage the dual purpose of our universities, as centres of teaching and research, by means of block grants which the universities themselves apportion out among their undertakings The method is simple, friendly, and effective, but perhaps only suited to a country which is reasonably compact In the United States the Public Health Service has a similar duty of distributing grants from national funds—though to medical schools only, and almost entirely to subsidise research A committee appointed by the Surgeon General of the service, to study research and educational grants, fellowship programmes, and the costs of medical education, reports[2] that, to review applications and

---

[1] Bull G M. Joekes A M. Lowe K G *Lancet* 1949 ii 229

[2] Bull, G M. Joekes A M. Lowe K. G *Clin Sci.* 1950 9 379

[3] Lucke B *Milit. Surg* 1946 99 371

---

[1] University Developments from 1935 to 1947 Report of the University Grants Committee London H.M. Stationery Office, 1948

[2] Medical School Grants and Finances Report by the Surgeon General's Committee on Medical School Grants and Finances In three parts Federal Security Agency Public Health Service Publication no 53 Washington United States Government Printing Office 1951

select the investigators and investigations to be supported, the service has set up 19 technical advisory groups (called “ study sections ”), each composed of about 10 members, most of whom are “affiliated with medical schools, hospitals or universities,” and who serve for an average of five years The recommendations of the study sections are reviewed by one of five National Advisory Councils—the Health, Cancer, Heart, Mental Health, and Dental Research Councils —and the projects which the councils recommend are referred to the Surgeon General of the Public Health Service for final decision The amount of work entailed for the members of the study sections—who include “ a large proportion of the Nation’s most productive investigators ”—“ eats heavily into the time that they can spend on their own work ” This has caused the committee serious concern, and they suggest that the time consumed in this way could be substantially reduced

At first glance it is not easy to see why the work of allocating grants should be so arduous American four year medical schools number only 72 (29 public, 43 private)—not much more than double our own 30 odd schools, though they are of course larger and more widely separated The chief difficulty seems to lie in the fact that applications for grants are made not by the medical schools and universities but by individual investigators or groups of investigators The study sections have therefore to keep a sound balance between the support of established investigators and the encouragement of promising newcomers—which, as the report says, calls for the most discriminating judgment It seems probable that a central body, receiving most of its evidence on paper, must sometimes get the answers wrong , but the committee are confident that this is rarely so they assure the medical schools that “ with some rare exceptions that would occur no matter who picked the investigators to be supported, the grantees are selected objectively and a relatively incompetent man will seldom be supported while the application of a relatively competent investigator is turned down ”

The sums to be distributed are very large, and have risen greatly in the last ten years In 1941, medical schools were spending $4 million a year on research, and Public Health Service grants were in the region of only $83,000, all of which was allocated to research on cancer During the war support for research in the medical schools came from the Office of Scientific Research and Development, and reached as much as $7 million in one year After the war grants from this source were replaced by other Federal funds, and the medical schools, of course, had other sources of research funds as well Thus by 1948 they were spending $17 million on research, half of which came from Federal sources , and half the Federal funds were distributed by the Public Health Service The committee are satisfied that such diversity of support assures “ diversity of interest, philosophy, purpose and viewpoint,” and effectively expands the range of intellectual inquiry

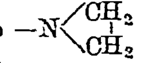
Funds for the maintenance of the schools themselves have not increased on anything like the same scale “ basic operating costs,” which in 1941 were $27 million, were $53 5 million by 1948—less than double, though in the same period research funds had increased more than fourfold This has led to some curious situations thus while research projects grow and flourish, and are allocated sums for new buildings, equipment, and staff, the teaching side of medicine is seriously hampered in its work , though students are increasing, 33 schools have recently had to curtail one or more aspects of teaching Moreover, buildings and equipment are in many cases inadequate for proper teaching The committee estimate that the schools need an additional $40 million a year immediately —$10 million for the public schools and $30 million for the private schools Where it is to come from they are not at all clear They do not believe that existing sources of funds will produce an additional $30 million a year for private schools in the foreseeable future, and think it unlikely (unless there is a sharp change in the outlook of State and city legislative bodies) that the $10 million needed by the public schools will be available either For us, who see teaching and research as the inseparable duties of a university or medical school, the obvious answer seems to be the conversion of research funds into block grants for both purposes But though the committee declare that “ research and teaching in medical schools should not and cannot be considered apart from one another,” and that research “ cannot flourish where other functions of the school are starving,” they are emphatically opposed to any sharing of research funds. The general financial problem, they say, would not be solved, and the one function of the schools now approaching a reasonable standard would be disrupted

They may well be right it is unlikely that sources of additional income for American medical schools have as yet been fully tapped But until adequate funds are found various people will experience some hardship Foremost perhaps must be put the students who are losing important opportunities 5 of the medical schools have curtailed or eliminated their courses in public health and preventive medicine, and 10 have retrenched on preclinical training The seasoned research-worker faces a much graver situation Grants are given to support the projects of individual investigators, or groups of allied projects constituting a programme Some large programmes have been supported for many years, but even so the support is for work described in advance by the investigators, and not for disposal at the discretion of the institution When the grant is made, the senior investigator is told, as a matter of courtesy, the number of years for which he will receive support , but there is no assurance of indefinitely continued support, nor do the committee favour any legislation to ensure it The schools, understandably, hesitate to establish too many senior faculty appointments with security of tenure, when these are supported by grants for research projects , for the grant may be withdrawn, and the schools are not in a position to accept financial responsibility for investigators thus left high and dry As a result there is a growing body of “ extremely well-qualified investigators who live from hand to mouth without the security provided by firm attachment to a teaching institution ” It might be thought that these are young men who are well justified in taking the risk for a few years in order to complete work in which they are keenly interested , but other passages in the report suggest that this is not so America cherishes the young, and the committee warn the study sections that “ undue reliance upon past performance may lead to support of people who have passed the peak of scientific productivity and to inadequate support of those who are developing into leaders in their fields " They fear that too much stress is being laid on projects of long standing compared with new projects

The University Grants Committee strike a more tranquil note While they believe that, in this country, " the obligation of research stands in no present danger of being overlooked," they hint that " the notion of research, both for its own sake, and for the results that may follow from it, has acquired in some minds a disproportionate value " They confess that we have " no universities in which the provision of teaching blocks is not a necessity," and that both teaching and research are seriously hampered by lack of space , but where it is in their power to relieve these necessities they favour neither function, but impartially offer grants where they can do most good They admit that, since in research, they back institutions, not individuals, there is some tendency for the largest grants to go to the old established places with a long record of successful work , but lest this should lead to concentration of the best men in the universities which could pay the highest salaries, they have suggested a plan to reduce inequalities of salary , and in practice this has worked out well. The relationship of the State with the universities may fairly be described, they think, as a partnership, in which neither is out to get the better of the other While the U G C and the American Public Health Service evidently do not see eye to eye about policy, we feel that the grant-distributing methods of the British body may fairly be commended for study to the American one

Substitute for Nitrogen Mustards

THE "nitrogen mustard" group of β chloroethylamine compounds have proved a valuable addition to the means of treating chronic leukæmias, Hodgkin's disease, and some cases of mycosis fungoides But these compounds have disadvantages they must be given intravenously, and in a saline drip without which thrombosis of the vein is almost inevitable , they are powerful vesicants, and so must be handled with the utmost care , and they may cause a really unpleasant, if short-lived, attack of nausea and vomiting a few hours after administration These disadvantages have limited the use of nitrogen mustards to special centres , this is just as well because they are also powerful depressors of hæmopoiesis, and repeated blood counts are essential for safety Many attempts have been made to prepare a drug with similar action that could be given orally and would not cause so many unpleasant reactions So far the only compound of any value has been β naphthyl di 2-chloroethylamine , this was prepared by HADDOW and his co workers, whose code name for it is ' R48 ' R48 has been tested extensively in this country under the ægis of the Medical Research Council , and reports on its use have come from MATTHEWS[1] at Oxford and from GARDIKAS and WILKINSON[2] at Manchester Neither of these reports was enthusiastic R48 did produce a good therapeutic effect in some cases of chronic leukæmia—especially chronic myeloid leukæmia—and in Hodgkin's disease , but the general estimate was that the results were inferior to those from intravenous chloroethylamines

A new compound acting like the nitrogen mustards has now been introduced by KARNOFSKY and co-workers[3] in New York This substance is known as triethylene melamine (T E M), but it is not so different from the chloroethylamines as its name suggests The effect of the nitrogen mustards depends on a reversible chemical rearrangement that takes place when they are dissolved in water, and the important part of this change is the formation of very reactive cyclic ethyleniminonium compounds containing the group  $-N\langle{}^{CH_2}_{CH_2}$, triethylene melamine contains three of these groups attached to a triazine ring T E M was originally introduced in the textile industry for improving the finish of rayon fabrics , it is readily soluble in water, and solutions are prepared only in water or saline, since T E M reacts with many substances , it is relatively stable in alkaline mediums, but reacts rapidly in acid solutions T E M was first tested experimentally by PHILIPS and THIERSCH,[4] who found that it acted much like the nitrogen mustards but was notably less toxic On transplantable mouse leukæmia the effect of T E M was similar to that of the nitrogen mustards, and cells from treated animals could not be successfully transplanted in other susceptible animals Trials of similar compounds showed that at least two ethyleniminonium rings were necessary for activity

T E M has now been tested in man by KARNOFSKY and his colleagues, who gave the drug both intravenously and orally to patients with chronic leukæmias, Hodgkin's disease, lymphosarcoma, and neoplasms For intravenous use a 0 5% solution in isotonic saline is prepared, and this can be injected directly into a vein without a running drip , but, as with nitrogen mustards, great care must be taken to avoid any leak outside the vein, for otherwise a severe local reaction ensues The dose given in one injection was 2–3 mg , larger doses were liable to cause nausea and even vomiting As with nitrogen mustard, the effect of repeated doses is cumulative, and the maximum effect is reached one to three weeks after the last dose , T E M depresses the hæmopoietic marrow, but unless the dose is lethal recovery sets in within three weeks and regeneration is usually complete A safe total dose seems to be between 8 and 12 mg (0 12 to 0 20 mg per kg body-weight) in a single course Intravenous T E M treatment produced responses in a reasonable proportion of patients with chronic myeloid or lymphatic leukæmia or with Hodgkin's disease, and two out of seven patients with lymphosarcoma obtained some benefit , the response of five patients with reticulosarcoma was regarded as unsatisfactory Patients with any of these conditions whose lesions were refractory to irradiation or nitrogen mustard were also refractory to T E M The drug was tried on some patients with various tumours, but the results were negative On the whole, it was not thought that intravenous T E M had much advantage over nitrogen mustards Orally T E M tablets were given in doses of 2 5–10 mg daily The drug has to be taken on an empty stomach, because it reacts readily with many organic substances, so usually it was given one hour before breakfast Since T E M is inactivated more rapidly in acid media, varying gastric acidity causes differences in the amounts needed by different patients to produce an effect, one way out of this difficulty would be to give it with sodium bicarbonate, but results with this technique are not yet known There is no doubt that T E M by mouth depresses hæmopoietic tissue, in fact the depression may be more severe than that with intravenous administration, so dosage has to be controlled very carefully Most patients tolerate 5 mg a day, but those in poor health can often manage only 2 5 mg, while some of the more robust can take 10 mg, unpleasant reactions usually take the form of nausea or vomiting The initial dose is 2 5–5 mg daily for two days only, at the end of a week the blood-count is checked, particularly the white-cell count, and if this is satisfactory a second course is given, further treatment is decided by the results of weekly checks The maximum effect appears in two to three weeks, and then further treatment is decided by the patient's blood level, his general condition, and the effect on the lesion KARNOFSKY and his co-workers state that if improvement has not occurred in 3–4 weeks, and moderate leucopenia and anæmia have been produced, further T E M treatment is unlikely to be of any benefit Treatment with oral T E M is a highly individual affair, for each patient's dose must be adjusted according to his reactions, but the results in the chronic leukæmias and in Hodgkin's disease are quite as good as those with intravenous nitrogen mustard and much better than those with oral chloroethylamines such as R48 Two patients with mycosis fungoides were given oral T E M, and one responded Results with a miscellaneous group of carcinomas have been very poor

---

[1] Matthews W B *Lancet* 1950 i 896

[2] Gardikas C Wilkinson, J F *Ibid* Jan. 20, 1951 p 137

[3] Karnofsky D A Burchenal J H Armistead G C jun Southam C M. Bernstein J L Craver L F Rhoads C P *Arch intern Med* 1951 87 477

[4] Philips F S Thiersch J B *J Pharmacol* 1950 100 398

Triethylene melamine may thus enable us to treat the relatively slowly progressive cases of leukæmia and Hodgkin's disease by oral administration instead of by repeated intravenous infusions This would be a welcome improvement, at the same time, however, T E M is a highly active and potentially dangerous substance that must be used only with all the precautions that apply to nitrogen mustards Meanwhile it should certainly be given a wider trial, and the fact that a substance of this structure produces the same effects as the nitrogen mustards will suggest the synthesis of allied compounds, some of which may be safer to handle

Annotations

A NEW SYNTHETIC STEROID

IN his centenary lecture to the Chemical Society in London on April 26, Prof R B Woodward described the complete chemical synthesis of a new steroid compound by a method developed in his laboratory at Harvard Steroids have, of course, been synthesised before—the hormones œstrone and equilenin by several different methods—but this is the first process which might be extended or adapted to produce 'Cortisone' or other corticoid compounds The characteristic feature of the corticoids is their reactive functions in ring C of the steroid system (fig 1), and it is the presence of reactive functions at positions 11 and 17 which make the new steroid potentially convertible into compounds of that type

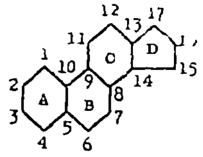
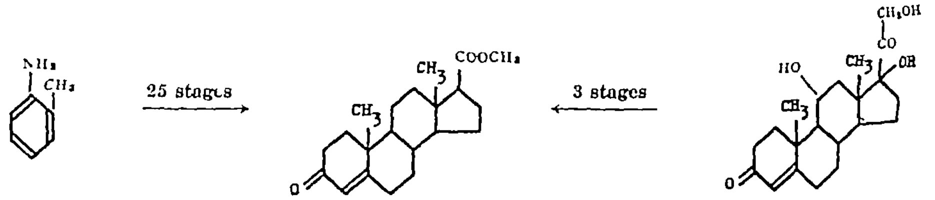


Fig 1 Ring-system of steroid compounds



(I) o Toluidine

(II) Woodward's Steroid

(III) Natural Compound F

Double bonds at 9–11 and 16–17 are not shown

Fig 2. I–II: 25-stage synthesis of Professor Woodward's new compound III–II 3-stage production of identical compound from natural 17 hydroxy-corticosterone

Professor Woodward's synthesis (fig 2) starts from *o* toluidine, an aromatic compound readily obtainable from coal tar distillates and much more plentiful than deoxycholic acid, the present source of cortisone The *o* toluidine (I in fig 2) becomes ring C of the structure, to this a four carbon chain is attached to form a six membered ring, and, when rings B and A have successively been added, this ring is opened and re closed in the final stages to form the five membered ring D At each stage the chances of side reactions or ring closures on wrong positions are reduced to a minimum by means of protecting groups, and by using reactions whose stereo chemical effects are well established Professor Woodward and his colleagues ensure that the final product will have the configuration of the natural steroids, though it is not known to occur in nature The compound is still racemic, but its resolution into optically active isomers is likely to be completed shortly The structure of the new steroid has been confirmed by forming it, by a simple three stage transformation, from natural 17 hydroxy corticosterone (Compound F, III in fig 2) and showing that the resulting compound and the purely synthetic version are identical, with infra red spectra that can be superimposed

It would be premature to hail this technique as a source of cheap synthetic cortisone in the near future Even if extending the 25 stage synthesis to produce cortisone turns out to be unexpectedly simple, it is by no means certain that the product will be cheaper than the cortisone derived from bile acids Professor Woodward gave no indication of the steroid yield obtained, but it is probably very small Time will show how far his work can be applied to the large scale manufacture of steroid hormones and their analogues Meanwhile, there can be no two opinions about its great scientific value

PLASMA SUBSTITUTES

THE interest shown in plasma substitutes during the late war, particularly in countries which had no organised transfusion services, has been revived by the unsettled state of the world and by a fear that the violent weapons now being developed may cause so many casualties that ordinary treatment by blood transfusion will become impossible

The many substances used as substitutes include gelatin dextran and polyvinylpyrrolidone (P V P)

Experience of gelatin is confined almost entirely to the United States: apart from its relatively brief effect, and the need to convert it from a gel to a sol by warming before use, it seems satisfactory. Dextran is used in many hospitals here and in Scandinavia and Holland: it restores blood volume satisfactorily, and remains in the circulation long enough to sustain it until the amount of circulating plasma protein is again sufficient for this purpose. The third substance mentioned, P.V.P., is a newcomer to this country, though as 'Periston' it has been used in Germany during and since the war, and as 'Subtosan' it enjoys a vogue in France. Two reports on P.V.P. made here under a British proprietary name 'Plasmosan' appear in our present issue. It seems to be easy and cheap to make; it is apparently non-antigenic and non-toxic; and it does not need special conditions of storage. Urinary excretion accounts for some 50–55% in twenty-four hours; and the question arises whether a substance to be used for restoring blood-volume could not with advantage be retained longer in the blood stream—a result that might be attained by adjusting the relative proportions of the smaller and larger molecular fractions. The fate of the P.V.P. which does not appear in the urine is not known with certainty. German reports state that none is excreted in the bile. Examination of the tissues of animals given large doses of P.V.P. has revealed no morphological changes, but it would be instructive to have reports on chemical analyses of tissues. The performance of certain clinicopathological tests is said to be affected.

The preliminary report of the clinical results suggests that P.V.P. can be used with advantage, particularly during surgical operations in which "shock" occurs; but its blood-volume restoring properties—in other words, its value as a plasma substitute—cannot properly be assessed until its effects on the circulation are known in more detail. Observations in burns patients and those who have suffered blood loss or trauma will be needed to permit a full evaluation: in particular we shall want serial records of blood-pressure and pulse-rate, of plasma protein, hæmoglobin, and hæmatocrit levels, and if possible of cardiac output and right auricle pressure. The main function of any plasma substitute is to restore and maintain the circulating blood-volume until the patient's own plasma protein returns to the circulation, and success in doing this is the main criterion by which such substances must ultimately be judged.

ILLEGITIMATE CHILDREN

THOSE who undertake to help unmarried mothers need to know a great deal about the law, especially the statutes relating to custody and maintenance of illegitimate children, legitimation, adoption, paternity and blood-tests, affiliation, inheritance, and nationality—as well as the benefits to which the mothers are entitled, and the arrangements for fostering and boarding out the children. In a new booklet,[1] decoratively bound and nicely printed, Miss Lena M. Jeger, on behalf of the National Council for the Unmarried Mother and her Child, sets out all this necessary information and more. Her clear well-written paragraphs are like an arc lamp in the dark thicket of legal terminology; and a good contents page, well-chosen headings, and an index help to make the way still plainer.

As Prof. Alan Moncrieff says in an introduction, illegitimate babies start their lives under grave disadvantages. Since 1918 there have never been less than 40 illegitimate infants for every 1000 children born alive. The peak was reached in 1945, but even in 1949 the rate was 50.7 per 1000 live births. Miss Jeger reminds us in a foreword that in 1918 the death-rate during the first year of life was 91 per 1000 liveborn legitimate children, and 185—more than double—per 1000 liveborn illegitimate children. In 1949 the comparable figures were 32 and 45—the rates, in fact, are drawing nearer to each other, but even so are grossly different. The neonatal death-rates have always been closer: in 1918 they were 34.5 per 1000 legitimate live births and 66.4 per 1000 illegitimate live births; in 1948 the comparable figures were 19.3 and 27.4. This bears out the common experience of social workers that it is not in the first month of life but later in the first year that the illegitimate infant is exposed to specially unfavourable influences. His chief trouble, of course, is that his mother has to go out to work, and she may not earn enough to get him well looked after. But it is not only on the physical side that he suffers; lacking his mother for a great part of the day, he may become backward in his emotional development; and moreover, as Miss Jeger points out, "he is going to miss a father in the same way that any child who loses his father early, through death or separation, misses him." The baby whom the young mother was courageously determined to keep may grow into "a difficult, naughty and exhausting child"; and both he and his mother will then need help.

The National Council, founded in 1918, has always worked for legislative reform to help the illegitimate child. Much progress has been made, as this little book bears witness. But, as Miss Jeger puts it, "no legislation can compel anybody to give the unmarried mother what she usually most needs—friendship, understanding, and companionship in what is almost inevitably a lonely and deeply traumatic experience." Armed with this guide to the statutory provisions, the social worker—or even the untrained well-wisher—should be able to deal fairly easily with the material problems and turn her attention to the more fundamental needs of the pair she is anxious to help.

DETECTION OF SPINAL BLOCK

THE Queckenstedt test is well known for its value in demonstrating spinal block; but in some cases of partial block the findings are equivocal, and occasionally there may be a normal rise of cerebrospinal fluid pressure even though myelography or operation discloses compression of the spinal cord. Kaplan and Foster Kennedy[1] have investigated the effect of different positions of the cervical spine on the response to bilateral jugular compression (usually the test is carried out with the cervical spine straight or very slightly flexed). Of 294 patients with various neurological disorders, 12 showed an abnormal response to jugular compression with the cervical spine in either full flexion or full extension while there was a normal rise of pressure with the neck in the neutral position. In 8 of these 12 patients exploratory laminectomy was performed; none had a spinal neoplasm, but in 4 there was a "compressing exostosis of the cervical spine," due either to arthritis or to a calcified disc protrusion at C5–6 level; in 2 a disc protrusion at C5–6 or C6–7 level; and in 2 adhesive arachnoiditis around the mid or lower cervical cord. The whole series included 31 cases in which cervical cord compression was diagnosed clinically; these comprised the 12 cases already referred to, 3 in which there was a complete Queckenstedt block with the neck in any position, and 16 with normal responses to jugular compression even with full flexion or full extension of the neck. Exploration was performed in 7 of this last group: no demonstrable compressing lesion was found in 6, while in the 7th there was a slight filmy arachnoiditis.

Kaplan and Foster Kennedy regard this modification of the Queckenstedt test as helpful in the diagnosis of spinal compression at C5–6 level, which is the pivotal point for movement of the cervical spine on an immobile thoracic spine In their cases no removable cause of spinal compression was demonstrated by the manœuvre, but it entails no especial inconvenience to the patient and would be worth carrying out in patients with cervical cord lesions before deciding about the need for myelography

---

[1] Illegitimate Children and their Parents. London: National Council for the Unmarried Mother and her Child, 21, Coram Street, London, W.C.1. 1951. Pp. 72. 3s. 6d.

[1] Kaplan, A., Kennedy, F. *Brain*, 1950, 73, 337.

OUR MENTAL HOSPITALS

As our population grows, so do the numbers of our mentally sick For years now our mental hospitals have been getting more and more crowded, and—as the Board of Control note in their latest report [1]—the overcrowding on Jan 1, 1950, amounted to 14%, as against 12 2% on Jan 1, 1949 The results, as they point out, are not to be measured only in terms of actual overcrowding (though that is bad enough) the pressure on beds also obliges the hospitals to limit the number of voluntary admissions This means that preventive work and early treatment are both gravely hindered, which can only bring a greater load on the hospitals in the future

Three factors, the board find, have contributed to this serious situation In 1949 some 3034 mental hospital beds were still being used for other purposes, and though by 1950 the number had fallen to 2753, even these could be spared very ill At the end of 1949 there were 146,228 people under mental hospital care—an increase of over 1500 on the preceding year The board comment that the return of borrowed beds is not proceeding as rapidly as necessary, moreover, of the beds so far returned, over 2600 are still awaiting reconditioning and re equipment In the course of the year 1949–50 only 87 of these returned beds had been refitted, and the number of new beds provided for mental patients by the regional hospital boards was only 92—a total increase of 179 beds in a service treating an additional 1500 people This can only mean the setting up of extra beds in wards already full The situation would be eased if all the beds now available could be fully staffed, but at the end of the year a further 2279 beds were out of commission merely because staff could not be found for them Staffing, however, had improved on the whole since the previous year there had been an addition of 303 full time and 618 part time women nurses, and of 517 full time male nurses, with a fall in the ratio of patients to nurses from 7 6 to 7 4 for women and 5 5 to 5 4 for men This ratio is much too high Loss of trained and experienced staff, moreover, has been progressive, and " continuance of the service even at its present level is only possible by the use of less trained persons and by the very substantial use of part time nurses " Part timers, indeed, have proved invaluable, but their number cannot be increased indefinitely, and their employment brings its own administrative problems

Short handed, cramped, and housed, in the main, in inconvenient buildings, the mental service is yet giving an unflagging long term demonstration of how to make the best of things The incidence and death rate from tuberculosis in mental hospital patients is being steadily if slowly reduced, the death rate from gastro intestinal infections has fallen to less than 1 per 1000 patients The death rate per cent of the average number of residents, though, in 1949, it was 1 17 above the rate of the previous year, is nevertheless below the mean percentage for the past ten years—which means that very good work has been done during a time when overcrowding has been steadily increasing

Social and cultural activities—as well no doubt as occupational therapy—are everywhere gaining ground In 1949 the Council for Music in Hospitals was giving concerts in 44 mental hospitals, while the Picture Library Scheme organised by the British Red Cross Society was already supported by 30 hospitals The report does not mention the progress made in establishing therapeutic social clubs or in the setting up of art classes, but many hospitals are now interesting themselves in these forms of therapy In 56 hospitals the Women's Voluntary Services continue to give help and are now undertaking follow up visits to patients—a piece of service which may do something to replace the community care formerly given throughout the country by the National Association for Mental Health

Methods of collecting statistics from mental hospitals have been revised, and an index card has been adopted for individual returns on patients admitted to mental hospitals in England and Wales The completed cards are sent to the General Register Office, and punched cards are prepared from them, from which statistics can be produced mechanically The system came into operation at the beginning of 1949, and is working smoothly, and at the same time regulations for the keeping of hospital registers were brought up to date A scheme is being prepared to deal with patients' earnings Sometimes convalescent or stable patients go out to work for local employers and earn several pounds a week The hospital is entitled to recover from them such part of the cost of their maintenance and incidental costs as seems reasonable Part of the remainder is to be kept by the patient as pocket money, and the rest will be banked on his behalf This means that on discharge he has a sum of ready money Moreover, since his capacity to earn is well established, his status usually rises with his relatives and friends

BREAST CANCER IN MOUSE AND MAN

THE discovery in mice of Bittner's milk factor, a virus like agent transmitting heritable mammary tumours to young sucklings, naturally led to attempts to identify a similar factor in human milk It may cause surprise that, though Bittner discovered the milk factor about 1936, only in the last couple of years have similar reports about human milk come to hand This is because in man identification of such a factor depends on a different method The mouse agent can be found by experimental transmission to other susceptible mice Even these experiments take nearly two years of the life of a mouse, and during this time the young test mouse is growing up, maturing, and herself becoming a cancer prone breeder Along those lines—and there is no other direct biological test, for a human agent would not be transferable to mice—it will take a very long time, the collaboration of several generations of observers, and much careful well planned work to obtain similar information in man about the relation between breast cancer in mothers, breast feeding, and breast cancer in daughters and grand daughters Nevertheless such records are being undertaken

Meanwhile some very small particles, varying in diameter from 200 to 1200 Ångstrom, have been seen with the electron microscope in preparations of mouse mammary tumours and mouse milk both at Leeds [1] and in the U S A The precise relation of these particles to Bittner's milk factor is not yet decided, but it is significant that when the factor is known to be absent the particles can be found only very rarely The Leeds workers have now reported some findings in human milk [2] These are tantalisingly equivocal, for although particles were found in 11 out of 11 breast tumours and in 4 out of 4 samples of milk from patients with breast cancer, they were also found in 11 out of 12 samples of normal milk, 1 of which contained a large number of particles It may be that some of the producers of these

---

[1] H.M Stationery Office 1951 Pp 9 6d

[1] Passey R D Dmochowski L Astbury W T Reed R *Nature Lond* 1947 160 565

[2] Passey R D, Dmochowski L Astbury, W T Reed R Eaves G *Ibid* 1951 167 643

11 positive samples will in the future develop breast cancer, but it is improbable that all will do so These findings, which accord with others in the U S.A ,[3] make it necessary to interpret the results with caution In the realm of electron microscopy, which is now making such small particles visible, we are still in the stage of exploration

This work, however tedious and apparently unrewarding, must be done, because the milk factor is one of the few clues we have to a continuing cause of cancer One of the rewards of the work is, perhaps, to set others thinking and wondering about the chances that the somewhat peculiar multiple hereditary tumours of mice are, in their natural history and behaviour, really comparable with human breast tumours, which more often than not are single The mouse also develops solitary mammary tumours, but these are found in oldish breeders of strains from which Bittner's milk factor is known to be absent, nor can the factor be recovered from these tumours Are these not more comparable with the human disease than the multiple heritable tumours? Possibly both types occur in man as in the mouse Descriptive pathology may have overlooked multiple origins or confused them with regional neoplasia, still, it is not very likely that the appearance of seeding, seen in mice, with a great many adenomas together with two or more frank tumours at separate sites, would have escaped attention The seeding itself is a most odd feature, which suggests that packets of particles or milk factor have settled out of the blood stream from time to time in some favourable nidus We still do not know what conditions encourage this focal infection followed by cell proliferation, except that it requires a special susceptibility that is inherited as a mendelian dominant, and an adequate amount of ovarian hormone The purely focal contribution is unknown

PSYCHOSOMATIC MEDICINE AND PSYCHOTHERAPY

Psychosomatic medicine commands widespread attention in contemporary medical thought—even in 1943 Dunbar[4] listed 2400 references—but it remains a term vaguely understood and loosely employed It was therefore an important occasion when, on May 8, Prof Ernst Kretschmer, of Tubingen, probably the greatest living pioneer in the study of inter relations between constitutional types and their mental and physical disorders, addressed the psychiatric section of the Royal Society of Medicine

Professor Kretschmer, whose paper was translated by Dr E B Strauss (who is also the translator of his *Textbook of Medical Psychology*), declared that there was a need to define the concept of psychosomatic medicine Physicians tended either to think of disease processes in terms of organic changes, or else to go to the opposite extreme and ascribe them all to psychogenic factors Psychosomatic diseases should be regarded, not as discrete entities, but as cycles or sequences Emotional causes produced autonomic and endocrine reactions, and this increased somatic activity had a boomerang effect on the affective state, producing emotionally over determined imagery and behaviour patterns In the human organism there was a constant autonomic irradiation, and whether this produced a psychosomatic illness depended not only on the nature and intensity of the stimuli but also on the state of the organism itself The basic constitutional types that he had described[5] differed in their liability to develop illness in reponse-to stress, the athletics tended to have specific vasomotor reactions and they suffered from cerebral arteriosclerosis about three times as commonly as did the pyknics, in whom the incidence of hyperpiesia was above average A multidimensional approach was necessary, one must consider the meaning of an organic disease and seek to understand the symbolism behind a symptom Psychotherapy was applicable in syndromes that were complex-determined, and in syndromes in which a definite complex could not be discovered but which were accompanied by generalised intrapsychic tension Morbid syndromes not of psychogenic origin were also benefited by the easing of tension from psychotherapy

Professor Kretschmer remarked that at his clinic the methods were based largely on the work of Schultz[6] and Jacobson[7] and Yoga The therapist acted as instructor or trainer, and the patient was encouraged to take an active part in his treatment "Fractional hypnosis" was employed to aid in the regulation of tonus by a series of conditioned reflexes This was accompanied, in the purely psychological sphere, by an analysis of the patient's current problems, the resulting insight could be employed didactically in the form of "maxims" during the hypnoid state, or else pure suggestion could be used to overcome symptoms which persisted after their dynamic causes had been removed The aim of the induced tonus regulation was to loosen up the patient in every sphere This could relieve or cure numerous organic diseases that were associated with autonomic or endocrine disequilibrium Therapeutic nihilism resulted from regarding morbid pathology as an accurate reflection of the pathological process in the living individual, by relieving vasomotor spasm, for instance, psychotherapy might not only relieve functional disorder but liberate healing impulses that could modify structural changes In bodily illness, then, should psychotherapy or general methods first be tried? The answer was whichever was thought more likely to cure that particular case Where there was doubt the organic methods should usually be tried first since these were less time consuming, but in some cases the converse applied The too organically minded physician and the too psychogenically minded psychotherapist should each reconsider his position

Dr W Sargant also spoke of the necessity for carefully selecting the cases for a particular method of treatment, if a treatment was extended to cases outside its scope it became discredited He himself was asking the neurosurgeons to perform a very anterior leucotomy for certain psychosomatic or organic disorders, and was getting some promising results, for in certain cases of rheumatism, skin disease, cardiac neurosis, and cardiovascular disease, relief of the mental tension often improved not only the patient's affective state but the actual symptom itself

Describing his system of "autogenic training," Prof J H Schultz, of Berlin, said that this derived directly from hypnosis and auto hypnosis and from Yoga Basically it consisted of six series of exercises, first, progressive relaxation of the voluntary musculature, beginning with one arm ("weight exercises"), secondly, progressive relaxation of the blood vessels, which are brought under voluntary control ("warmth exercises"), then training in voluntary control of the nervous regulation of the heart, of respiration, of the abdominal viscera, and of certain cerebral functions not normally under voluntary control The results of training could be demonstrated thermometrically and by alterations in chronaxie His methods had been used in Germany and North West Europe for the past twenty years, and it had been estimated that 50% of all functional dystonias responded to this training

Sir Horace Evans, F R C P, and Sir James Paterson Ross, F R C S will be in attendance on the King during his Australian tour next year

---

[3] Gross, L, Gessler A E McCarty K. S *Proc Soc. exp Biol., N Y* 1950 75 270
[4] Dunbar F Psychosomatic Diagnosis New York, 1943
[5] Kretschmer E Physique and Character London 1925
[6] Schultz J H Seelische Krankenbehandlung Jena 1919
[7] Jacobson, E Progressive Relaxation Chicago 1938

Public Health

THE PREVENTION OF TUBERCULOSIS IN YOUNG PEOPLE

A W Anderson
M D Lond
CHEST REGISTRAR, HARROW

R Grenville-Mathers
M A , M.D Camb , M R C.P , F R F P S
CHEST PHYSICIAN, HARROW

H J Trenchard
M B Birm , M R C P , D M R (D)
CHEST PHYSICIAN, EDGWARE , FORMERLY CHEST PHYSICIAN, HARROW

The decision of the Ministry of Health to allow B C G vaccination to be used in this country has been hailed as a great step forward in the drive to prevent tuberculosis So far we have not yet implemented a scheme for B C G vaccination, and the opportunity has been taken to review the efficacy of the preventive measures at present in force, so that some idea may be obtained of the benefits likely to result from the use of the vaccine in the area served by the Harrow clinic The figures here cited are derived from an area which is residential and densely populated—a typical dormitory The vital statistics are favourable compared with national rates

The general measures used for the prevention of tuberculosis have comprised education of the patient, rehousing, and supervision of contacts, especially children The first two measures are well known as potent methods of reducing the spread of tuberculosis Education of the patients is undertaken mainly by the chest clinics' health visitors Instruction is given in the patient's own home, so that all adult members of the family are aware of what should be done As regards housing, one out of every six new houses is allocated to the medical officer of health for the rehousing of tuberculous families on medical grounds

TABLE I—TUBERCULIN STATE OF 818 CHILD CONTACTS WHEN FIRST SEEN AND OF 783 NON CONTACTS

Age (yr)	Index case bacteriologically positive		Index case bacteriologically negative		Non contacts	
	No tested	No positive	No tested	No positive	No tested	No positive
Less than 1	67	4 (6%)	45	1 (2%)	10	0
1 +	47	7 (15%)	33	1 (3%)	7	0
2 +	43	15 (35%)	31	2 (6%)	9	0
3 +	51	15 (29%)	28	5 (18%)	14	0
4 +	45	18 (40%)	23	1 (4%)	12	0
5 +	39	16 (41%)	16	4 (25%)	41	0
6 +	30	15 (50%)	21	5 (24%)	25	2 (8%)
7 +	38	17 (45%)	20	4 (20%)	27	0
8 +	39	14 (36%)	13	3 (23%)	13	0
9 +	30	16 (53%)	15	3 (20%)	13	0
10–15	89	51 (57%)	55	5 (9%)	612	89 (14%)
Total	518	188 (36%)	300	34 (11%)	783	91 (11%)

CONTACT EXAMINATION

The examination of contacts is a time consuming procedure, and a considerable part of the health visitors' time is spent in persuading contacts to attend for their follow up examinations After the first two years the attendances of contacts seen previously drop sharply

For each case notified an average of four contacts, adults and children, have been examined in a search for sources of infection and for any damage done by the notified case We here present the results of examining 818 child contacts (under the age of fifteen when first seen) who have been tuberculin tested and followed up for various periods

TUBERCULIN TEST

The tuberculin test generally used has been the application of tuberculin diagnostic jelly (A & H) after rubbing vigorously with acetone until the skin is erythematous A large number of those over the age of ten have had a negative jelly test checked by an intradermal injection of 1 mg of Old Tuberculin The jelly test is accepted by us as being equivalent to the Mantoux test 0 1 mg in these age groups Of 255 children tested with both the diagnostic jelly and the intradermal tuberculin 0 1 mg , the results agreed in 232 In 10 the intradermal test was positive and the jelly test negative, while in 13 the intradermal test was negative and the jelly test positive These results are in agreement with Paterson (1944) and Dick (1950)

TABLE II—RELATIONSHIP OF CONTACTS TO THEIR INDEX CASE

Relationship	Mother	Father	Uncle	Aunt	Brother	Sister	Grandfather	Grandmother	Cousin
No tested	266	302	24	16	42	43	18	4	2
No positive	80 (30%)	103 (34%)	2 (8%)	3 (19%)	11 (26%)	15 (35%)	7 (39%)	1 (25%)	0

TUBERCULIN STATE ON FIRST EXAMINATION

Table I gives the reactions to tuberculin of the 818 contacts at this first examination according to whether the index case was positive or not to Ziehl Neelsen sputum smear or laryngeal swab culture Altogether 36% of the children in contact with a bacteriologically positive case were tuberculin positive when first seen, usually one to two weeks after diagnosis of the index case, whereas only 11% of those children in contact with bacteriologically negative cases were tuberculin positive This is identical with the percentage obtained on examining 783 non contacts in the same age groups

All the contacts included in this series were both domiciliary and familial contacts of the index case The relationship to the index case is shown in table II The risk of developing a positive tuberculin reaction from a parent was high, but there were no grounds for concluding that infection from either father or mother was more likely for a child of the same or the opposite sex Although the numbers were small, the great risk run by children in the same house as a grandparent with tuberculosis was apparent

Of the 222 children who were tuberculin positive when first examined 23 had definite tuberculous lesions—in the great majority of cases a Parrot Ghon focus

Of all the 818 children 3% (and 10% of those who were tuberculin positive) had a definite lesion The great

TABLE III—TUBERCULOUS LESIONS DISCOVERED AMONG 222 CONTACTS TUBERCULIN POSITIVE WHEN FIRST SEEN

—	Index case bacteriologically positive	Index case bacteriologically negative
Parrot Ghon focus	11	1
Collapsed lobe	3	—
Pleural effusion	4	—
Meningitis (fatal)	1	—
Miliary tuberculosis	1	—
Perihilar flare	0	2
Total	20	3

TABLE IV—PERIOD OF FOLLOW UP OF TUBERCULIN POSITIVE CHILDREN

Time of observation (yr)	½	1	2	3	4	5	More than 5
Index case positive	16	25	30	17	6	5	2
Index case converted	9	28	13	7	4	1	5
Index case negative	6	5	9	2	4	2	3
Total	31	58	52	26	14	8	10

majority of cases, as was to be expected, came from the children in contact with sputum-positive cases (table III)

FOLLOW UP

All the 818 children have been followed for various periods. For follow up purposes they have been divided according to whether the index case was persistently bacteriologically positive, bacteriologically negative, or bacteriologically converted—i e, the sputum and laryngeal swab became negative as a result of treatment The average period of follow-up for these groups was as follows

Index case negative		
Children tuberculin negative	476 child years	(average 1 8 yr)
Children tuberculin positive	85	2 7
Index case converted		
Children tuberculin negative	365	2 3
Children tuberculin positive	145	2 1
Index case persistently positive		
Children tuberculin negative	372	1 8
Children tuberculin positive	280	2 7

POSITIVE REACTORS

Table IV shows in more detail the number in each group of tuberculin positive contacts who have been followed up The period of observation starts from the date of first examination and ends on the date last seen for those remaining normal throughout, but on the date of the first abnormal film for others The time is given in completed years, hence a child observed for two years and nine months is recorded as having been observed for two years

Altogether 4 children who were tuberculin-positive when first seen have developed lesions (one was in contact with a sputum negative case, and the others with cases which were persistently sputum positive)

TABLE V—FOLLOW UP OF TUBERCULIN NEGATIVE CHILDREN SHOWING THE NUMBER WHO UNDERWENT TUBERCULIN CONVERSION

Time of observation (yr)	½		1		2		3		4		5		More than 5	
Index case positive														
Total	46		54		27		14		13		9		7	
No converted		21		13		7		4		6		5		1
Index case converted														
Total	16		52		39		22		12		9		9	
No converted		2		9		2		–		2		4		–
Index case negative														
Total	54		85		64		37		14		9		3	
No converted		12		3		6		2		1		1		–
Total	116	35	191	25	130	15	73	6	39	9	27	10	19	1

(1) Male aged 2 years, developed a temporary collapse of the left upper lobe two years later

(2) Male aged 10 developed bilateral pleural effusion six months later

(3) Female aged 1, developed meningitis a year later and recovered. No lesion had been detected previously

(4) Male aged 6 developed a transient collapse of the right middle lobe after two years observation.

Thus of the group of children tuberculin positive on first examination, by far the greater number (98%) did not develop a lesion even when in continued contact with a case of pulmonary tuberculosis whose sputum was persistently positive

NEGATIVE REACTORS

The 596 children who were tuberculin-negative on first examination have all been followed up for at least six months Table V shows in more detail the number of tuberculin-negative children who have been followed up and the interval before tuberculin conversion took place. The intervals stated are in completed years of observation, as for the tuberculin positive children, the period of observation being here regarded as terminating as soon as tuberculin conversion took place Altogether 101 tuberculin conversions were observed The largest number were in children in contact with persistently positive index cases, as would be expected However, the number of conversions among the contacts of apparently negative cases shows how poor are our methods of detecting tubercle bacilli in the sputum of patients

It is surprising how long children can remain in contact with a persistently sputum-positive relative without tuberculin conversion occurring There were 23 children, under one year of age on first examination, in contact with a persistently sputum positive parent, and yet after six months there had been only 4 conversions (table VI)

TABLE VI—TUBERCULIN NEGATIVE CHILDREN UNDER ONE YEAR OF AGE WHEN FIRST SEEN IN CONTACT WITH POSITIVE INDEX CASE

Period observed (yr)	½	1	2	3	4
Number of children	23	16	11	2	2
Number of conversions	4	2	3	0	1

The relation to the index case was as follows mother 10, father 9, uncle 2, aunt 1, and sister 1

The social conditions in the homes of these 23 children were analysed by the appropriate health visitors as follows

Good	15 cases,	2 conversions
Fair	4 „	1 „
Poor	4 „	1 „

This avoidance of infection in the home is paralleled in experiments on animals Calmette (1936) showed how difficult it is to infect even the guineapig experimentally by inhalation Very rarely did infection occur even when the guineapigs were kept in the same room as a tuberculous patient expectorating up to 7000 million bacilli a day Calmette ascribed this to the large diameter (100–500 μ) of the droplets expectorated, this made them fall quickly to the ground He postulated that infection only takes place by coughing directly in front of a child

The lesions associated with tuberculin conversion were analysed All these cases were followed up by X ray films and screening for at least six months after conversion, and any lesion found in that period was counted as a lesion accompanying tuberculin conversion Occasionally a primary focus was not visible at first but became visible during the following months

INDEX CASE PERSISTENTLY POSITIVE

57 conversions occurred among the 170 children in this group, the time interval for this being given in table VII

The lesions found on tuberculin conversion or within six months of its occurrence were as follows

None	42 children
Parrot-Ghon focus	8 „
Hilar enlargement	4 „
Meningitis	1 „
Collapsed lobe with cavity	1 „

Thus 14 children, during the period of observation, developed lesions, 1 child who had no lesion on conversion, developed tuberculosis of the adult type four years later, 1 with a Parrot Ghon focus developed a tuberculous hip six months later, and 2 with hilar enlargement developed a collapsed lobe later

INDEX CASE BACTERIOLOGICALLY CONVERTED

There were 19 conversions in this group (table VII), 3 of these children developed a Parrot Ghon focus, and in the remaining 16 children no lesion was detected

INDEX CASE BACTERIOLOGICALLY NEGATIVE

There were 25 conversions followed up in this group (table VII), 1 child developed meningitis on conversion, and in the remaining 24 children no lesion developed

TABLE VII—FOLLOW UP OF CONTACTS AFTER TUBERCULIN CONVERSION

Period followed after conversion (yr)	½	1	2	More than 2
Index case positive	8	29	9	11
Index case converted	8	5	5	1
Index case negative	13	7	5	—

As would be expected, the greatest number of lesions found when tuberculin conversion took place was in those children in contact with patients with a persistently positive sputum

The number of children who developed lesions while under continued observation was 19, whereas a lesion was already present in 23 on first examination Thus the greatest damage had been done among the child contacts by the time the index case was diagnosed

B C G VACCINATION

It is important to remember that among 101 tuberculin conversions only 18 lesions were discovered, and most of these were radiological findings of no very serious significance, requiring observation and supervision but seldom treatment Only 1 death occurred It is true that tuberculous infection in children can become a tragedy, and that about half the deaths in childhood are due to tuberculosis, but this high incidence is largely due to the small total number of deaths in this age group The danger of a natural infection is likely to be due to the uncontrolled dose of bacilli so received, B C G is alleged to be a method of causing infection with a controlled dose of innocuous organisms If all the 596 children who were tuberculin negative on first examination had been vaccinated with B C G, and if this vaccine is fully effective, only 18 cases of disease would have been prevented, and these cases were spread over five years It can therefore be seen that the use of B C G in child contacts is not likely to reduce the incidence of tuberculosis very much

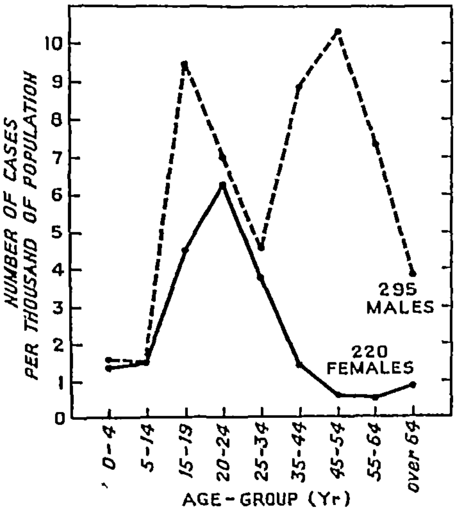


Fig 1—Age-distribution of 295 male and 220 female notifications of tuberculosis

It must also be borne in mind that vaccination with B C G is likely to lead to a sense of security in the patient's family, with a consequent reduction in the care taken over the general measures of prevention of infection

If B C G vaccination is to be used most effectively it must be used in other ways than only among nurses, medical students, and contacts of known cases The work of the mass miniature radiography units has shown us that there is at least one sputum positive ambulant undiagnosed case per thousand of population The damage done by these undiagnosed cases has been assessed by analysing 104 consecutive notifications of children received by the medical officer of health

No contact with a known case, and no source for the infection found	66 (63%)
No contact with a known case, but source found on examining contacts	10 (10%)
Diagnosed at first attendance as a contact	16 (15%)
Disease developed after contact broken by removal of the infectious case	9 (9%)
Children in continual contact with a known case	3 (3%)
Total	104

It can be seen that in 63% of cases no source for the infection was found in domiciliary or familial contacts

Fig 1 shows the age distribution of 295 males and 220 females notified during the eighteen months from January, 1949, to June, 1950, in the urban district of Harrow, given as the incidence per thousand of population It will be seen that there is a big jump in the number of cases in the age group 15–25 Fig 2 shows the percentage of 933 non contacts who were found to be tuberculin positive Most of the non contacts between the ages of 11 and 18 were obtained from examining the pupils in a grammar school There is a great jump in the percentage of positive reactors to tuberculin immediately on leaving school, and this recent infection in this group is probably the cause of the large number of cases of tuberculosis found in the 15–25 age group (Wallgren 1948) and results from infection from unknown sputum positive cases of tuberculosis in our midst A reduction in incidence of tuberculosis is only to be hoped for if the effect of infection in this group can be minimised, and it seems that the best use of B C G is to vaccinate all school leavers

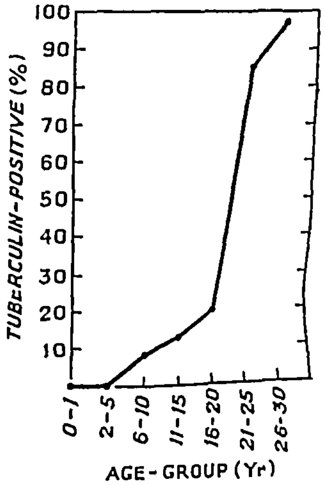


Fig 2—Percentage of non-contacts tuberculin-positive in various age-groups

SUMMARY

The findings are given of routine tuberculin testing of 818 child contacts, of whom 222 were positive when first seen

The results of 101 tuberculin conversions are analysed In the whole series there was only 1 death

Arguments are produced favouring the use of B C G in school leavers as most likely to reduce the present high incidence of tuberculosis

We are most grateful for the invaluable assistance given by Miss E M Jewell

REFERENCES

Calmette A (1936) L'infection bacillaire et la tuberculose chez l'homme et chez les animaux Paris chapter 15
Dick W I (1950) *Brit med J* ii 111
Paterson D (1944) *Ibid* i 531
Wallgren A (1948) *Tubercle* 29 245

Special Articles

OFFICE MANNERS *

G P HARDY ROBERTS
C B , C B E
SECRETARY SUPERINTENDENT THE MIDDLESEX HOSPITAL

VERY few things can be done well without taking thought and trouble That is my excuse for speaking to you about matters which may seem too elementary to deserve attention

A hospital administrator has to do much of his work his office, and his time there is mainly taken up with iterviews, correspondence, telephone conversations, and onferences , and yet how little is said about these things the average course of instruction in administration

The importance of this side of his work is the greater you accept my view that the chief administrative fficer should delegate all routine duties to his colleagues nd so leave himself free to deal with the so called minor roblems, which are numerous, and the matters of major olicy, which are few If his office is the place to which enior administrative officers can come for advice about heir work, junior officers for help over personal problems, patients with complaints, medical staff with requests of various kinds , if every inquiry by letter or telephone which does not "belong" to any department is brought to him—you may agree that skill and care over interviews and letters call for some consideration

Before we go any further let me say that it is easy to talk about these things and to suggest the right line to take For my part, I should not like to confess how often I fail to observe the following simple code

INTERVIEWS

It is a good plan to be accessible to everyone Don't let your secretary become your gaoler , insist that she arranges an interview for everyone who wants to see you You will find that few people will abuse the privilege , those who do can be dealt with appropriately

A small amount of "stage management" is worth while, especially when you are to see someone from outside the hospital Your secretary should put ready such papers as may be needed , and if it seems likely that you will have to consult any of your colleagues, while the interview is in progress, she should see that they are "on call" Let your desk be clear of all other papers and files

Decide, before your visitor comes in, how long you can spare for the interview , and have a small clock on your desk in line with your visitor's chair so that you can keep it in view without it being obvious to him Remember that almost any interview will be a failure if you give the impression of being short of time The purpose of the average caller is to get something off his chest , so, unless he wanders from the point, it is best to let him have his say, before you begin Avoid any appearance of hurrying him, give him your entire attention, and let nothing seem to distract you The telephone should be switched through to your secretary, so that she can take the calls (There are few things more irritating than trying to talk to someone who is forever turning away to speak on the telephone) If there is an urgent message for you, she should write it down and bring it in unobtrusively, so that you can glance at it, when it is your turn to speak, and not while your visitor is leading up to his peroration

I suggest that the more timid and diffident your visitor, the more important it is to observe these rules Whatever the outcome of the interview may be, there is a good chance that he will leave your office feeling that he has had "his money's worth," even if he has not had his way

CORRESPONDENCE

The chief complaint of people who write letters to public bodies, Government departments, and so forth, is that they have to wait a long time for an answer, and that, when it comes, it is often hard to understand

Where possible all letters should be answered the day they arrive This is not so difficult to achieve if you take care never to have a "pending" tray in your office Letters from members of the public, if the required answer cannot be given at once, should be acknowledged politely (and that does not mean sending a printed card) within forty eight hours of receiving them

Things go wrong, even in the best hospitals , so from time to time you will get letters of complaint Some of these letters may be couched in abusive terms, and you will be tempted to write a biting rejoinder By all means do so (if it relieves your feelings) but consign it to the waste paper basket, and send in its place a courteous reply If the hospital is at fault, admit it and apologise , if the allegation is false, deny it, as firmly as you like, but as politely as possible It is always a mistake to have a row on paper We all know a few fortunate people whose charm of manner allows them to get away with quite outrageous remarks in the course of conversation But no-one can do that in a letter The letters which go out from your office should be dignified, without being pompous or unfriendly , they should be clear, concise, and to the point

Don't be intimidated by your secretary Very few people can dictate a perfect letter straight off, if the subject is a difficult one Dictate a draft to begin with , then work on the draft, taking out long words and turning complicated sentences into simple ones Never sign a badly written letter to save your secretary trouble , it is much better that she should be inconvenienced than that your letter should give offence or be misunderstood If she is the right kind of secretary, she will agree with this

TELEPHONES

The Hollywood version of the high powered executive, barking orders into a battery of telephones, is not one that I commend to you In my view, the telephone is a rather dangerous instrument, useful mainly in emergencies, or for getting the answer to a simple question When it is a matter of enlisting people's help, or of giving them detailed instructions, it is nearly always more satisfactory to see them personally When it is necessary to give a rebuke to a junior officer, it is nearly always unwise to use the telephone, because you won't know whether he is grinning impenitently or in floods of tears Above all, do not tell the switch board to put you through to someone and then keep him waiting on the line before you pick up your receiver Hardly anyone can avoid feeling cross when this is done to him

CONFERENCES

You cannot draw a line through a hospital and say that all on this side is medical, and all on that, administrative , there is a measure of integration at most levels Consequently, many of the problems that will confront you will consist in the need to provide the administrative requirements of experts in technical matters, which are beyond the range of the ordinary layman's knowledge

This is quite good for the soul of the administrator, and gives him a proper sense of humility But it need not depress you to the extent of feeling that you will be so blinded by science as to be unable to serve the expert in an administrative capacity If you show yourself to be a willing and interested listener, he can usually be persuaded to explain his problem to you in simple

---

* An address given to trainees in hospital administration

language I have used the word "expert" instead of "specialist" or "clinician," because these technical matters will derive not only from the medical departments, they will relate to engineering, nursing, finance, catering, and so on

There is no need to have an intimate knowledge of these subjects, but to be prepared to examine them from a common sense administrative angle To do this it is necessary to confer with the people who have first hand knowledge of the subject, be they professors or plumbers, ward sisters or consultants, architects or cooks Never be too busy in your office, or outside it, to listen to and question the men and women who are experts in their own line The administrator who "thinks he knows," and acts without advice, is a danger to any organisation The wise administrator will not try to conceal his ignorance, he will have the good manners and the good sense to confer with the experts, and to ask them to "vet" his plans and instructions before he puts them into effect

Lose no opportunity for conferring with the matron At a teaching hospital, in particular, she has a large command and a great responsibility, and it is essential that she and the chief administrator should march in step This cannot happen if you exclude her from all administrative matters, except those directly concerned with nursing It is better to bring her in on every problem in which she is likely to be interested, and you will find that there are many in which it is valuable to you to have her advice and help

Remember, too, that the man at the Ministry who signs himself "your obedient servant," and seems such an alarming bureaucrat, will usually prove to be a human and helpful colleague, when you have had an off the record talk with him in your office, over lunch or a cup of tea In my view, this sort of conference is often of greater value than the more formal kind in big committee rooms, and can save an amount of official letters

There is a type of senior executive who seeks to emphasise his own importance by keeping as much information as possible "under his hat" You will find that very little of your work is confidential For the rest, you will make the task of your colleagues and principal subordinates easier and more interesting if you keep them in the picture about your actions and plans Let your office be an information bureau rather than a miniature Kremlin

LOOKING FOR TROUBLE

One of the best things to do with your office is to leave it—for an hour or two every day However much work you may have on hand, however deeply submerged you may be in official memoranda and circulars, you should get out and about the hospital, and see things for yourself It is a mistake to get office bound

I am not suggesting that you should be a "snooper" On the contrary, I think it is better to make your visits to wards and departments at regular intervals, accompanied by the matron or the head of the department concerned Ward sisters and others will then know the day on which you come to see them, and will get the habit of producing their problems and difficulties to discuss with you It is no good persuading yourself that these things will be brought to your notice in your office, that will only happen with the more important ones, and usually too late If you want trouble (and you should be a glutton for trouble) you must go and look for it Having found it, you must do something about it, otherwise people will decide that it is not worth their while to tell you things

THE RÔLE OF THE ADMINISTRATOR

My last bit of advice is to avoid the mortal sin of administration—the belief that the tail can wag the dog In these days, finance comes into everything, and management has become very complicated In these things, it is our duty to advise the board of governors and to give effect to their decisions Many of their more important decisions relate to medical matters, and it is very easy for the chief administrative officer to misuse his influence with the board, and to obstruct the projects of the medical committee Where this happens, or even seems to happen, the seed is sown of dissension between doctor and administrator, and the plight of the hospital is like that of an army whose commander is dominated by his quartermaster general

If we are wise, we shall remember that, in the war against disease, we are not front line troops Our role, and we can be proud of it, is to be of service to the medical and nursing staff More often than not, we can help only in small ways, by taking on the dull jobs, by being enthusiastic about other people's plans, by being heedless of our own rights and anxious about the needs and privileges of others The English saint of long ago might have been thinking of modern hospital administrators when she said

> "to yield is to command, to be unknown is to be celebrated, and work that seems of little use comes nearest to the working of miracles"

A MENTAL HOSPITAL IN BRITISH COLUMBIA

JOHN MOSS

C.B.E

WHEN I was in Canada last year, I visited the Provincial Mental Hospital at Essondale, British Columbia, which has accommodation for 3600 patients. This is in all respects a modern hospital with excellent facilities for clinical investigation, diagnosis, and treatment of all mental and neurological conditions In addition to medical and surgical facilities it provides all accepted forms of psychiatric therapy

EQUIPMENT AND ADMINISTRATION

The occupational therapy department, run on the lines of well developed units of the kind in our own mental hospitals, offers the choice of a wide range of interesting crafts Recreation and play are organised by a recreational director, for it is argued that if recreation is necessary for a well balanced life in the case of normal persons, it is even more necessary for mental patients A golf course of 8 holes has been laid out with very good greens, and there are both grass and hard tennis courts Summer dances are held on the hard courts and have been attended by as many as 1200 patients at one time Among other sports and pastimes provided are archery (with regulation targets, and standard strength of bows equipped with steel tipped arrows), "housey housey" gatherings, variety parties, concerts, bands, inter ward cribbage, checker and chess tournaments, crossword and cryptogram contests, quiz shows, picnics, horseshoe pitching, music appreciation, and club swinging, and field and sports days Patients are encouraged to organise their own sports activities

The buildings are scattered over a large estate, and the grounds have been beautifully laid out as a park by an expert from Kew Gardens This park is freely open to the public, who are encouraged to picnic there at week ends, and who often drive out there to spend a few hours in the open air This is a way—and a good way—of teaching people that mental hospitals are not places to be dreaded On public holidays, I was told, hundreds of people come and wander round the grounds

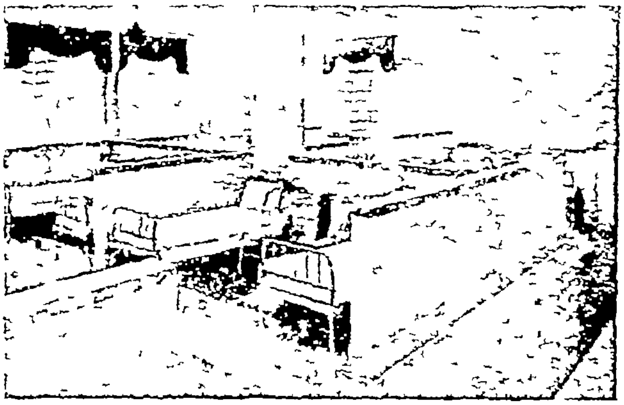
Admission to the mental hospital is broadly on the same basis as in England Some patients are certified but there is a steady increase of those who seek admission as voluntary patients. As in this country difficulty has been caused in mental hospitals in Canada through the admission of elderly senile patients who are accepted because there is no other suitable accommodation for them. No person over the age of 70 can be received at Essondale without the special approval of the medical superintendent, but he has to accept a large number because no other care may be available for them. One major difference between the administration of this mental hospital and similar hospitals in Great Britain is that there is no local committee. The medical superintendent is responsible to the Provincial Department of Welfare, for all matters connected with administration, but there is also a business manager who is responsible to the medical superintendent for the general running of the establishment, I was told that in practice he has a free hand since it is considered that the general administration is better undertaken by a lay specialist.

STAGES OF TREATMENT

Treatment in the hospital may be divided into early and active treatment of the acutely mentally ill with a view to early recovery and rehabilitation, and continued treatment for those patients who require treatment for a long time. The social service department of the hospital works closely with both classes of patients and the staff of the psychiatric department visit the homes of all patients admitted from local areas. There are ten psychiatric social workers on the staff, and they supply detailed accounts of the patient's life and circumstances to the psychiatrist, so that he is fully informed of the factors contributing to the mental illness. Visits in other areas of the Province are made by the Field Welfare Service, which undertakes general welfare work. The officers of this service are social welfare workers without a psychiatric qualification. While the patient is in hospital one of the psychiatric social workers keeps in touch with him and with his home. Rehabilitation plans are worked out between the psychiatrist and the psychiatric social worker and supervision is continued for six months after a patient's discharge. To carry the rehabilitation of women patients further, a small communal home has been established in Vancouver where a recovered patient may, if necessary, live a normal unrestricted life until she is able to find employment and be self supporting.

THE CLINIC

In the hospital grounds, at some distance from the main building, a fine new building for 325 patients has been erected as a clinic of psychological medicine, and as a teaching unit in the new faculty of medicine in the University of British Columbia, at Vancouver. The building is most luxurious, both the construction and furnishing being as good as would be found in any high-class hotel. There has apparently been no public criticism of the expenditure. This is a new development in Canada, and I was told that even the United States have no counterpart on the same scale. The clinic is a teaching centre, and provides active treatment for those patients suffering from early mental illness whose recovery and rehabilitation may be anticipated within four months. This is felt to be a distinct advance beyond the usual mental hospital type of treatment, being a step closer to community and general hospital types of care. The clinic houses a group of specialties representing all branches of medicine surgery, and psychiatry. The X ray department is fully equipped for radiology, and also has an operating theatre and special apparatus for cranial and brain studies. The clinical laboratories can undertake all types of investigation, and the staff are also engaged in teaching and research. The department of cardiology has the means for full study of the heart and cardiovascular system, and for the determination of the basal metabolic rate, the neurological department undertakes electro encephalography, and there are also a well equipped department of physiotherapy and an ear, nose, and throat department. The department of occupational therapy and the recreational department have already been mentioned. A special Act of the Provincial legislature provides for the admission of voluntary patients to the clinic, but patients may also be admitted on the certificate of two medical practitioners (no legal certification is required). The maximum period during which any patient may be retained at the clinic is four months, after which he must be transferred to the main building if he requires further care. Those responsible for the scheme believe that this intensive approach to the treatment of mental illness will bring psychiatry close to other branches of medicine and will do much to gain the confidence of the population in seeking early advice in such matters. It is hoped also that it will do much to place mental illness on the same plane as physical illness and help to remove any stigma which uninformed people may have regarding sickness of the mind.



The old people's dormitory

HOMES FOR THE AGED

In the same grounds as the mental hospital, but again at some distance and not visible from the main building are two storey buildings which have been erected to meet the needs of elderly patients. A special feature of these buildings is the provision of ramps instead of staircases from the ground floor to the first floor. The grade of the ramp is such that it permits comfortable walking as well as the use of wheel chairs and stretchers. The front entrance is also ramped, and leads to spacious lawns for outdoor activities. All floor space, including the ramps, is indirectly lighted at floor level, so that the old people can easily see their way, and all the ramps and corridors are provided with handrails.

In Canada, as in this country, a major problem is caused by the ageing population and this is due, it is considered, very largely to advances in medical and surgical care which are increasing the average life span. Provision of new institutions or old people's homes to replace the out of date poor law buildings, still to be found in many parts of Canada as in this country, is proceeding slowly, but the arrangements at Essondale are of rather a different type and seem well worth studying by those trying to relieve mental hospitals of some of their senile patients.

Many applications for direct admission are received, but since the main purpose is to relieve the pressure on the mental hospital all admissions must be made through the hospital itself. Like other patients, old people may be voluntary or certified. If certified on admission to the main hospital, they remain certified on transfer to the home. When the clinic is in full operation, elderly persons, like younger people, will be admitted to the clinic instead of the main building After treatment many of them, it is hoped, will be able to return to their own homes but those who need care for more than four months will be transferred to the residential home when they come to the end of their period of treatment in the clinic

The home is perhaps too large to give quite the same easy domestic atmosphere as the small type of residential home in which we have begun to specialise over here But it must be remembered that Essondale provides for elderly patients who would otherwise be in a mental hospital They could perhaps be classed as senile, although some of those I saw were in fact very little different from many of those to be found in institutions, and even old people's homes, in Great Britain The 'institutional atmosphere" as we know it, however, had been very largely avoided There were several comparatively small—and very comfortable—sitting-rooms where the old people could divide up into small groups, and in the grounds I saw them in small companionable parties, reading or chatting together In the central dining room of each block they eat at small tables capable of seating four The food is cooked centrally and taken in containers to the kitchens of each block

The dormitories are broken by low partitions, as shown in the photograph, which give some privacy for either one or two old people, but also allow of adequate supervision I think this plan might be copied in erecting similar buildings in this country Bed-ridden patients are not normally taken in these blocks

The cost of maintenance is higher in the old people's home than in the mental hospital, where much of the domestic work is done by the patients themselves Most of the older patients in the home are incapable of doing any work There was a very friendly atmosphere about the place, and the relationship of the patients and the staff was excellent

NATIONAL HEALTH SERVICE TRIBUNAL

REMOVAL OF PRACTITIONER'S NAME FROM LIST

THE Minister of Health has issued a report of an inquiry held by the tribunal at Maidstone last August when the Complainant was the Kent and Canterbury Executive Council and the Respondent Dr Archibald Blair, of Strood, Rochester The tribunal consisted of Sir Reginald Sharpe, K C (chairman), Mr H Lesser (standing member), and Dr S A Winstanley (practitioner member) The Complainant alleged

(*a*) That, in breach of his terms of service, the Respondent had (i) neglected on Sept 28 and 29, 1949, to visit and treat one Betty Irene Smith, deceased, who was then his patient, when her condition required that he should so visit and treat her (ii) neglected on the said dates to render all proper and necessary treatment to the said deceased woman and (iii) on various dates between Aug 21, 1948, and May 12, 1949, failed to forward to the Complainant 775 records which he was required to forward

(*b*) That the neglect and failure aforesaid was the culmination of a series of earlier complaints of a similar nature against the Respondent, which complaints had been respectively substantiated in September, 1929, July, 1943, March, 1946, and July, 1946

The Respondent admitted the failure to forward the records But this part of the complaint was not pressed, and the tribunal did not pay any attention to it

THE FATAL ILLNESS

Dr Blair who is 55 has practised in Strood for 23 years—since 1940 without a partner On July 5, 1948, he had 3041 patients on his National Health Service list

On April 13, 1949, a daughter was born to the deceased woman (aged 26) and her husband Gunner Smith (aged 19) Dr Blair was not asked to attend either before, at or after the birth On Friday, Sept 23, 1949, when Gunner Smith arrived at his home on five days' leave he found his wife in good health and spirits, and she remained normal until about 4 45 P M on the following Wednesday, Sept 28, when she complained to her husband of pains in her right side About 6 P M the pains became more severe and (according to her husband) she "went rigid" Gunner Smith thereupon went and saw Dr Blair at his surgery and told him about his wife's pains, that she had that day eaten two ripe pears and an apple, and that her menstrual period was due Dr Blair gave Gunner Smith a prescription for mist kaolin, which the latter on his way home caused to be made up by a chemist. Gunner Smith reached home about 7 P M and gave his wife some of the medicine and also some hot water, which Dr Blair had also advised him to do According to Gunner Smith, Mrs Smith got progressively worse and kept fainting

At 2 30 A M on Thursday, Sept 29, Gunner Smith went out and telephoned to Dr Blair from a public call box (The main conflict of evidence arises over what he said.) Dr Blair did not visit Mrs Smith following upon this telephone conversation Gunner Smith returned home and continued to administer to his wife the medicine and hot water, as again directed Mrs Smith fell asleep and apparently died about 3 30 A M , she was lying on her right side with her knees drawn up Gunner Smith had already fallen asleep and it was not until he woke up at 8 20 A M that he was aware that she had died He at once went and saw Dr Blair at his surgery (just after 8 30 A M) and told him of the death

Dr Blair's morning surgery begins at 9 A M and lasts about an hour, so it was not till about 10 45 A M (on Sept 29) that he saw the body (Rigor mortis had by then set in.) He examined the body, such examination only occupied a few seconds consisting, as it did, in touching the eyeballs and a glance at the body to see if there were any signs of violence (which there were not) Dr Blair certified the cause of death as (*a*) cardiac failure and (*b*) myocardial degeneration

QUESTIONS OF FACT

In his evidence Dr Blair told the tribunal that he had had no doubt in his mind as to the cause of death and had had no hesitation in issuing the certificate which he did Though he was not expecting it, her sudden death did not surprise him, he saw no need for a post mortem examination, and it never occurred to him that it might be advisable to have an inquest He further stated that on a Saturday morning in September, 1949, the deceased had consulted him at his surgery, that he had then examined her and found that her heart was not sound He did not then (so he told the tribunal) form the opinion that she was likely to die at any moment, he gave her on that occasion a prescription for mist digitalis and advised her to have reasonable rest and not to overwork herself for some little time

"The Tribunal has had to decide whether or not the deceased did in fact consult the Respondent on a Saturday morning in September, 1949 It is highly improbable that the deceased would have consulted the Respondent on the first morning of her husband's leave without telling him about it, and the Tribunal can see no reason why Gunner Smith should have withheld from it such an important fact, if to his knowledge it actually happened The Tribunal sees no reason to consider Gunner Smith an untruthful witness, and it is satisfied by his evidence (which, incidentally, was not challenged on behalf of the Respondent on this point) that on the morning of Saturday, the 24th September, the first morning of his said five days' leave of absence, the deceased and her husband were turning out and scrubbing the floors of two of their bedrooms. It also seems very unlikely that the deceased would have joined her husband in the task of scrubbing if she had been advised by the Respondent a few days earlier (or at most a week or two earlier) to rest and not to overwork Nor is there any record to be found of any such visit by the deceased to the Respondent on any other Saturday morning in September 1949 Nor, indeed, is there any record of the Respondent having prescribed anything for the deceased on any occasion in 1949 except the mist kaolin on the 28th September, which was prescribed on the information given by her husband Secondly, another female patient of the name of Smith who was also on the Respondent's list, namely, Mrs Florence May Smith, had been under the care of the Respondent for heart trouble for a great number of years the Form E C 6 relating to her case shows that the Respondent did prescribe mist digitalis for her when she called at his surgery on the 26th September 1949 the Tribunal thinks it more than likely that recollecting that a Mrs. Smith had been to see him about her heart trouble on the 26th September, the Respondent when he discovered that a Mrs Smith had died, apparently from cardiac failure, on the 29th September, confused the two patients in his own mind and was under the mistaken belief that the deceased had been to his surgery a few days before her death. Either this confusion was never resolved in the Respondent s mind, or, if the Respondent did subsequently realise the mistake he had made, he decided that it would be better to keep to the story that the deceased had visited him about her heart shortly before her death ' Further evidence supported the idea that Dr Blair confused the two Mrs Smiths

Gunner Smith and his mother believe that Mrs Smith died of appendicitis Such an opinion cannot be reconciled with medical science Even the Doctor who was called as a witness on behalf of the Complainant did not think that appendicitis would kill in such a short time (that is to say from 4 45 P.M. one day to 3 30 A.M. the next day) Furthermore, there is no evidence that the cause of death was not cardiac failure indeed the Tribunal is upon the material available *of the opinion that some form of cardiac failure* was the cause of death. There does not however appear to the Tribunal to be any sufficient ground for saying, as the Respondent did, that the secondary cause of the death of this young woman of 26½ years of age was myocardial degeneration. Such a cause of death in a woman of that age would have been a matter of considerable clinical interest to her doctor Neither the deceased s mother in law nor her husband had any knowledge that the deceased suffered from any form of heart disease and, as the Tribunal has found the Respondent had not given the deceased advice concerning an ordered life

The Tribunal is clearly of the opinion that not only upon the facts as found by it but even upon the Respondent s own version of the facts the Respondent ought to have reported the death of the deceased to the Coroner

The Tribunal has some satisfaction in being able to place on record its unanimous opinion that the deceased did not die as a result of any negligence or lack of professional skill on the part of the Respondent The evidence adduced before the Tribunal has not indicated any failure on the part of the Respondent to give such treatment as might have saved the life of the deceased. The evidence indicates that the deceased died at 3 30 A.M. while the Respondent could not in any event have reached her until 3 A.M (or perhaps a few minutes before) since Gunner Smith did not telephone to the Respondent until 2 30 A.M. The Tribunal is unable to visualise any treatment which the Respondent could have given the deceased only half an hour (or at most thirty five or forty minutes) before her death which would have saved her life "

A BREACH OF THE TERMS OF SERVICE

But a failure to visit a patient when called upon to do so may well be a breach, and possibly a serious breach, of the terms of service of a Medical Practitioner under the National Health Service notwithstanding that such failure to visit the patient has in no wise been detrimental to that patient s health and/or physical condition. In the opinion of the Tribunal a medical practitioner is by virtue of his terms of service, under an obligation to answer a night call by visiting the person to whom he is called if in all the circumstances of the case it would be reasonable to require him to do so notwithstanding the fact that he has formed the view that possibly no benefit can accrue to the patient as a result of his visit It may sometimes be difficult to say whether it would or would not be reasonable to require a practitioner to answer a night call by visiting the patient concerned The Tribunal is of the opinion that generally speaking when proceedings are taken before this Tribunal the burden is upon the Complainant of showing that it would have been reasonable for the practitioner to have visited the patient and, if a prima facie case of such reasonableness is made out by the Complainant then the burden shifts to the Respondent of showing that it would not have been reasonable to have required him to visit the patient

'Each case must of course depend upon its own facts and naturally a great deal will always turn upon what the practitioner knows already and or is told at the time when he is summoned, about the particular case in question. Hence the importance in the present case of the Tribunal s finding as already appearing that the deceased had not consulted the Respondent within the four weeks preceding her death. But of even greater importance is the view which the Tribunal has formed as to the terms in which he was asked to pay a visit to the deceased in the early hours of the morning of the day on which she died

'Put shortly Gunner Smith s version of his telephone conversation with the Respondent at about 2 30 A.M. on the 29th September, 1949 was this that he told the Respondent that the deceased was considerably worse (meaning, worse than when he had seen the Respondent at about 6 P.M the previous evening) and that she was writhing on the bed in pain and was fainting and he asked the Respondent to come and see the deceased there and then. To this request (according to Gunner Smith) the Respondent said that he could not go and see the deceased because he was not expected to work all night Gunner Smith then said he would not have rung up the Respondent if he had not thought it necessary to do so The Respondent refused to go and visit the deceased despite the repeated requests of Gunner Smith that he should do so

' The Respondent s version of this telephone conversation is, briefly this that Gunner Smith *told him that the deceased* was still in pain but did not say either that she was writhing in agony or that she was fainting , that he (the Respondent) asked if Gunner Smith wanted him to go and see her, to which the reply was No, Sir The Respondent thereupon asked why he had telephoned, to which Gunner Smith replied that he wanted a medical certificate to cover himself against his over staying his military leave of absence on account of his wife s condition. The Respondent told the Tribunal that this was not the first time that Gunner Smith had asked him for a medical certificate to cover himself against his over staying his military leave of absence (Gunner Smith admitted in cross-examination that he had made such a request on a previous occasion, and that on the present occasion he did also ask for a medical certificate for such purpose) The Respondent further said in evidence that he certainly expressed himself forcibly upon the telephone on this occasion , that he said he would go and see the deceased in the morning, and that Gunner Smith ought to come for his medical certificate in surgery hours According to the Respondent the only purpose of Gunner Smith in telephoning to him was (so far as could be judged by what he—Gunner Smith—said) to ask for the said medical certificate

The Tribunal s finding of fact, as between these two stories must be prefaced by this statement that it has seen no reason to think that Gunner Smith is not a truthful witness at any rate in regard to his evidence as to what he and the deceased did on the morning of the 24th September, 1949 while on the other hand it has found that the Respondent was an unreliable and untruthful witness when he said that the deceased consulted him one Saturday morning in September 1949 shortly before she died The Tribunal considers it highly improbable that the sole purpose of Gunner Smith in going out at 2 30 A.M to a public telephone call box was to ask for a medical certificate It may be thought a little surprising that he troubled to mention the medical certificate at all but the Tribunal is of opinion that it is not improbable that he might have added a request for such a certificate after he had made clear the real purpose of his telephone conversation (namely to ask the Respondent to visit the deceased at once) and had had his request refused. The Tribunal has unanimously come to the conclusion that Gunner Smith did tell the Respondent over the telephone some details about the deceased s worsened condition and did ask him to come and see her It finds it impossible to believe that if the Respondent had asked over the telephone (as he says he did) whether Gunner Smith wished him to visit the deceased. the latter would in the circumstances have replied in the negative '

In coming to this conclusion the Tribunal has not overlooked the evidence of the Respondent s wife who stated on oath that she heard the Respondent ask Gunner Smith over the telephone (and heard him repeat the question) whether he would like him to go out and visit the deceased. Nor has the Tribunal overlooked the evidence either of Marian Helen Offord (the Matron of a Nursing Home at Strood) or of Kathleen Rose Shorthouse (a State registered nurse employed as a District Nurse in Strood) that the Respondent does a considerable amount of night work (although the Respondent himself put the number of his night calls at only three a month, a figure which the Tribunal regards as very low indeed) and has always answered a night call made by them and visited the patient concerned

THE TRIBUNAL'S DECISION

"The question now remains was it reasonable to have required the Respondent to visit the deceased on the night in question when asked so to do ? The Tribunal is unanimously of the opinion that the Respondent ought to have visited the deceased and that he had no reasonable excuse for not so doing The Tribunal takes a very serious view of the Respondent's conduct in the present case, but might not, possibly, consider that, if this were an isolated instance of such a breach of his terms of service, it would be justified in coming to the conclusion that his continued inclusion in a Medical List would be so prejudicial But there are other allegations of a similar nature against the Respondent The Tribunal is unanimously of the opinion that when the Respondent's failure to visit the deceased in the present case is considered in the light of his three said previous failures to visit a patient it is impossible to say otherwise than that his continued inclusion in the Medical List of the Kent and Canterbury Executive Council would be prejudicial to the efficiency of the General Medical Services The Tribunal has necessarily come to this conclusion with very real regret, realising as it does that such a decision must, to all intents and purposes, mean the end of the Respondent's professional career, or at least its suspension for a considerable period, after which he would necessarily have great difficulty in achieving any worth while position in his profession But the Tribunal has felt that its duty compels it to arrive at the conclusion which it has done"

An appeal was made by Dr Blair against the tribunal's decision, but, after careful consideration of all the circumstances of the case, was dismissed by the Minister Dr Blair's name must accordingly not be included in future in any medical list until the tribunal or the Minister directs to the contrary

THE DENTAL BOARD

OPENING the last session of the sixth board on May 9, Dr E W Fish said that although the hazards of the Parliamentary time table had not yet permitted the introduction of a new Dentists Bill, it was at least unlikely that the seventh board would run its full course

This sixth board, Dr Fish recalled, had taken office four years ago at the beginning of a period of great expansion in the accepted functions of central government and shortly after the publication of the final report of the Teviot Committee This committee had recommended that an independent "Dental Council" should succeed the board, and Ministerial assurance had been given that a Bill would be introduced into Parliament to bring this change about He and his colleagues had therefore, during their term of office, been concerned, with the transfer of responsibility for existing commitments, and had been limited in the scope of their activity by having to avoid new commitments which might hamper their successors

During the last five years they had enjoyed cordial relations with the General Medical Council The council had undertaken a visitation of dental examinations and were even now revising their recommendations concerning the dental curriculum In both these enterprises they had shown sympathetic understanding of dental problems and had offered the board every opportunity of taking part in making plans and in carrying them out Dr Fish felt, however, that despite these helpful and friendly relations, it was clear that the Act of 1921 was out of date For instance, in carrying out the work of the committees the board had to call upon the advice of more practitioners than the Act permitted the profession to elect to the board Similarly, in revising the curriculum the council had thought fit to invite representatives of the academic body from the dental teaching schools to join them in their deliberations The National Health Service Acts had placed upon the dental profession responsibilities which more than ever required that it should be a self governing profession, responsible for its own standard of education, its own registration, and its own discipline To discharge these additional responsibilities provision must be made, Dr Fish affirmed, for a "General Dental Council" on which the profession was more widely represented, and whose membership would include those with special experience of the matters with which the new council would be called to deal

---

Medicine and the Law

Insanity and Intention

THE House of Lords in Crowther *v* Crowther (reported in the *Times* of May 10) met with an intriguing legal question and answered, in effect, "It depends" A wife sought divorce on the statutory ground of three years' desertion On the husband's side it was contended that, after two years' absence from her, he had been received into a mental hospital by virtue of an order under the Lunacy and Mental Treatment Acts Thereafter, it was argued, the period of desertion could not continue to run, a person who is *non compos mentis* cannot have the *animus deserendi*

Mr Justice Ormerod was obliged to decide against the wife in the trial court, he was bound by previous rulings of the Court of Appeal in the cases of Williams and Rushbrook, decided some eleven years ago The Court of Appeal could not vary its previous opinion, the House of Lords, however, was free to review the position The question was whether a spouse could be held guilty of desertion without cause, while suffering from such a degree of unsoundness of mind as justified detention under a reception order Some previous authority could be cited for the view that desertion, originating in a deliberate intention to desert, continued until brought to an end, and in Drew *v* Drew (1888), where the husband was sentenced to prison, it was held that the physical inability to terminate the desertion did not prevent its continuance On the other hand it has been decided that insanity may operate as the withdrawal of a client's authority to solicitors to proceed with litigation

Lord Porter solved the problem by saying that persons who are abnormal in some respects may be normal in others, evidence alone could answer the question in which category the individual should be placed If no evidence was called on the point, or if a petitioner failed to prove that the mental patient was capable of forming an intention, the court was not entitled to draw an inference of continued desertion from the intention revealed in periods either before or after certification The House of Lords has therefore sent the case back to the court of first instance in order that evidence, if available, may be received and a conclusion reached in the light of the principle enunciated

The problem thus seems not unlike that which arises where parties seek to upset a will on the ground of the testator's insanity One side will produce testimony of insane delusions, the other side will maintain that, in spite of the delusions (if any), he had at the moment of making his will a sound disposing mind The issue may not be wholly settled by medical evidence An older generation of lawyers will recall a famous case where a testator's will was witnessed by four medical practitioners, all of whom were called to give their opinion that he knew perfectly well what he was doing The will was nevertheless upset

In England Now

A Running Commentary by Peripatetic Correspondents

FACILIS descensus Averno! Idle musings in the bath lead rapidly to Dangerous Thoughts, the Circumcellion Heresy, and even Tito deviationism. I saw the pit that was yawning at my feet when I caught myself wondering whether 60 registrars and residents pullulating where previously only 6 pranced must inevitably make the service ten times as efficient.

It began with our maid's thumb going septic. She produced a fluctuant swelling in the ball of the thumb which, in my days of practice thirty years ago, would have meant a half-inch cut, complete relief, and cure in three days. What happens now? Reluctantly laying aside a razor-blade, I send her to her family doctor. He prescribes a kaolin poultice and invites her to see him again in three days' time unless it gets worse, when she can come back earlier. After a painful night, she goes back with a humble note from me suggesting that perhaps he might think fit to open it or arrange for it to be opened. He sends her to the big local general hospital, where she is given penicillin injections and attends twice daily for the next two days, after which, during an attempt to "remove some dead skin," there is a gush of pus and she comes back a different girl. But since the hole was made by accident it is too small, so she is still attending five days later for penicillin and having the thumb soaked and squeezed and kept warm with infra-red rays.

One must make every allowance for "What the patient says isn't evidence," but if this sort of thing is going on all over England it must be costing the country a pretty penny. Are students no longer taught to recognise fluctuant purulent swellings? Or are they taught never to open them? Or am I just an old fogey who is hopelessly out of date?

* * *

The waiting-room door was ajar and I heard one patient tell another: "I always come here. The magazines are so good."

And talking of magazines, I suppose that, the cry of "Bring out your Dead!" has not been heard in England since the days of the plague, but in 1951, O Fellow Peripatetics, we have "Bring out your Junk!" instead. What a chance for us to make some real money. Yesterday, when my char told us she got 8s. from a rag-and-bone merchant for a pile of national dailies our thoughts turned with a bang to my husband's old medical journals, piled ceiling high in the cellar. Since then it's been a race. Who'll get to the merchant first,—he or I? Somehow we're not quite so ruthless with our *Lancets* as with the others—there are back numbers in every room in the house and on both sides of the bed. When I thought of a Spring hat and started to gather them together I found myself stopping to read the old peripatetic columns and I'm still surrounded by a sea of *Lancets* dating back to 1945. My eye has just been caught by a comment on the remuneration of G.P.s under the "proposed scheme." Sorry, fellow writers, your words of wit and wisdom are doomed. I'll be able to afford a hat with flowers on it.

* * *

What is the cause, other than incipient sleep, of head-nodding in one's audience? It would be an interesting field for study. Is it an effort on the part of the nodder to impress the speaker with his knowledge or attentiveness or with his open mind—his ability to be converted by such powerful logic as that of the speaker? Is it merely an attempt to show that he at least has listened while all the others are asleep, or that he at least is intelligent enough to follow the speaker's confused utterances? Or is it a sort of reflex, set in motion each time the speaker strikes a chord by saying something which the listener has heard before?

Nodders are rarely equipped with sufficient experience or knowledge to justify their hearty manifestations of approval. I suspect that investigation would show that the I.Q. of nodders is lower than in non-nodding controls.

* * *

I keep meaning to have something done about my recurrent sinusitis, but somehow I can never find time; the same goes for my plantar callosity. A colleague of mine has been carrying about a grumbling appendix for over a year, and another has worn elastic stockings for years because he cannot get round to having a Trendelenburg done on his varicose veins. If we were laymen, we would promptly demand proper medical attention—and probably a holiday at the taxpayers' expense to boot. Why don't we do the same? Are we just a bunch of suckers, or hard-working idealists who are too conscientious to take time off from the service of humanity, or masochists? If we had to decide we would probably say cynically that our experience has taught us not to expect much substantial improvement from the therapeutic efforts of our professional brethren.

* * *

Tired of waiting for a health centre and of trying to do 20th century practice in 19th-century premises, our firm has mortgaged its children's future and built itself a new surgery. It has cost the earth, but at last each of us has a separate room with running water (h. and c.), a trolley for drugs and dressings, an examination couch, and a telephone. No more of this sharing ("After you with the auriscope, old boy"). No more making shift. The youngest doctor, who modestly disclaims any ability to hear anything through a stethoscope anyway, has the front room nearest the traffic. Next comes her immediate senior, the ham in the sandwich, and finally senex ipse, the outer crust, right at the back, remote and inaccessible. No longer can the patients gate-crash. All must put their heads through the dispensary hatch and tell the receptionist what they want or whom they wish to see. In a comfortable waiting-room they must wait their turn. Already (we hope) our standards have improved 50%. Perhaps the nicest thing of all is that we shall hear no more of that infernal squeak from the old front door as patients come in or go out.

* * *

In the days when a pound was worth twenty shillings I went to the extravagance of buying two pairs of tortoise-shell spectacles, in case one met with an accident. The other day, feeling that I needed my eyes tested again, I thought I would have this done under the National Health Service. The examination was carefully and patiently carried out, and I felt confident that my sight would soon be greatly improved by the new lenses. It was at this point that the optician raised the question of frames. "I've already got two pairs of real tortoise-shell," I told him, "and I want the lenses fitted to them. They're old pals." "I'm afraid that can't be done," the optician replied, 'and I would advise you to get this model at 12s. 6d. extra. Very similar, don't you think?' Seeing my embarrassment, he continued, "Tortoise-shell rims now cost about £6—only people with more money than sense can afford such things." I began to repeat, "I've already got two pairs . . .," but I suddenly thought, 'Be hanged to all this, I'll get these State affairs as a standby and go and get tested privately by someone who can use my good old blinkers." Whether I'll get satisfaction I do not know. What I do know is that I'm the proud possessor of £12 worth of spectacle frames that a generous State doesn't wish me to use, and that unless I dip into an already depleted pocket I shall soon, willy-nilly, join the growing ranks of the plastically standardised.

* * *

"M.R.C.V.S." writes: My fellow peripatetic of May 12 (p. 1068) has grossly misrepresented the destination of the *Observer's* 'nose to tail procession of vesicles." Owing to traffic conditions in Trafalgar Square the procession was so late in arriving that the clinical meeting which was to have been held at the Institute of Veterinary Psychiatry had to be abandoned. A short impromptu discussion was arranged instead, the subject being "Therapeutic Anosmia."

* * *

From a consultant's letter: "Her childhood was happy. Her father died at the age of 4."

Cause and effect?

Letters to the Editor

COLONIC REPLACEMENT OF THE STOMACH

SIR,—Mr Moroney is to be congratulated on doing something to the stomach which has not been done before By excising a large part of that organ together with the ulcer and replacing the deficiency with transverse colon on 22 occasions, he has shown considerable operative skill Suture lines in colon leak more readily than in other parts of the gut, though less so in patients with benign lesions By including in his article (May 5) postoperative thoughts on pH, "dog's stomachs," and "mucus," he has also shown a capacity to rationalise

Though the operation may be featured in the Dome of Discovery in the next Festival of Britain, it may have to wait as long to see if it is worthy of the honour It has taken half a century to remove the rose coloured spectacles which Moynihan, with others, succeeded in placing over the eyes of British surgeons when he encouraged anastomosis of stomach to jejunum Now that the stomach remnant is once more creeping back to its natural exit, the duodenum, it seems a pity that it should have to be via the colon

I hope Mr Moroney, together with Mr Aylett,[1] whose recently announced operation appears from subsequent letters to have given violent indigestion alike to men and dogs long years ago, will both tell us more later, and that others will not rush to these new fields merely from the delight of their spring greenness

For those who would like to try something new to many but even older than Billroth II (Polya to most), I can recommend that they do just as Mr Moroney does, only leaving out the part about the colon The operation is best known as Billroth I This will require excision of the ulcer, and even in large adherent duodenal ulcers this is usually manageable with experience, patience, and mobilisation of the right side of the duodenum With adequate mobilisation of the greater curvature the customary amount of stomach can be taken and junction made without tension Only one suture line is required instead of three as in this new procedure Excision can be just as complete as with the Billroth II types The operation has eminent supporters, with their own variations of detail, including Grey Turner, Morley, McEvedy, Schumaker, and Walton in later years, and younger adherents include Hickey,[2] Franklin at Hammersmith, and Bohn at Reading (personal communications) My own practice is to use the Billroth I operation, at times for carcinoma, almost exclusively for gastric ulcers, and latterly predominantly for duodenal ulcers My cases have shown no fresh ulcers, but occasionally a small stomach syndrome for a few months which seems to right itself There have been no "efferent loop dumping," no "afferent loop stasis" with bilious regurgitation, and no stomal blockage This is no place for details, which I propose to announce later

Mr Moroney, by his pioneering, has added to our knowledge and opened up new fields, and I hope he is right about the transverse colon As it tolerates fæces, lower ileal contents directly as in right hemicolectomy, and urine, it should not be offended by mere pabulum The effect of long standing acidic corrosion is yet to be established To replace a total loss of stomach, the colon may serve as it can in total loss of bladder For gastric carcinoma the operation is likely to fill a "long standing gap" But we do not look forward to an aftermath of articles on both early and late complications in cases with benign lesions

Billroth used his gastroduodenostomy for carcinoma initially I hope Mr Moroney will try, now and then, a Billroth I for benign ulcers I wish him and his adherents (may they be few when early) good fortune, a long silence, and an ultimate loud report

Radcliffe Infirmary
Oxford

G E MOLONEY

---

[1] Aylett S O *Brit med J* March 3 1951 p 451
[2] Hickey, B B *Ibid* April 14 1951, p 818

C S F CHANGES WITH PNEUMO-ENCEPHALOGRAPHY

SIR,—We read with great interest Dr Bickerstaff's paper[1] on changes in the cerebrospinal fluid (C S F) produced by intrathecal insufflation of air

The changes described by him, which we can confirm, are usually accompanied by very interesting vegetative reactions, and notably by blood changes, which we have studied Lumbar insufflation provokes, after a short period of leucopenia, well marked neutrophil leucocytosis lasting some hours F Hoff and others concluded from this that there exists a cerebral vegetative centre regulating the blood picture, and Beer believes that this is in the diencephalon, near the nucleus paraventricularis By this hypothesis the leucocytosis following pneumoencephalography would be an expression of direct irritation of the centre

We found that lumbar air insufflation causes, besides leucocytosis, leukergy[2] Leukergy[3] consists in the clumping of white cells in citrated blood, immediately or after incubation at 37°C for 1–3 hours This reaction is a very sensitive test in febrile diseases and inflammatory processes, its degree can be expressed as percentage of clumped cells The cells tend mainly to form cytologically homogeneous groups—i e, one often sees separate groups of neutrophils, lymphocytes, and monocytes, with 3 to 20 or more cells in a single group Leukergy is a cellular, and not a humoral, phenomenon, for leukergic leucocytes transferred to normal plasma clump as in their own plasma, whereas normal leucocytes do not clump in an inflammatory plasma Heating to 46°C or transfer to a 2–4% solution of saline disintegrates the clumps The clumping is due to increased adhesiveness of the cells and to their random collisions. Experimentally leukergy can be induced by intravenous injection of killed gram negative bacteria or by intrapleural injection of turpentine The condition is associated with bone marrow irritation, evident in a shift to the left in the Arneth count, and the quantitative parallelism between the percentage of leukergic cells and the leucocytosis and shift in the Arneth count suggests that leukergic cells are newly released from the bone marrow

It may be assumed that these adhesive white cells, liberated in the presence of inflammation, have a special function, and there is some evidence that they have enhanced powers of migration, bacteria adhere to the clumps and platelets, thus favouring phagocytosis The development of leukergy after lumbar air insufflation can be rationally connected with the pleocytosis of the C S F Leucocytosis and leukergy after encephalography may be attributed to either (*a*) an inflammatory reaction to irritation of the arachnoid by the air, or (*b*) direct irritation of the supposed diencephalic blood regulating centre The first of these two explanations seems the more likely, for the cellular content of the C S F in the lumbar region rises actually during insufflation of air, and the cells are mainly monocytes As to the second possibility, we repeated the classical experiment of Freund and Grafe in rabbits

We transected the spinal cord between the 7th cervical and the 1st dorsal segment—i e, below the spinal centre for innervation of the diaphragm and above the rami communicantes albi Hoff and Linhardt found no peripheral leucocytosis in such rabbits after injection of bacteria, and they concluded that a blood regulating centre existed. We, too, found that peripheral leucocytosis did not develop, but five hours after transection there was well marked leukergy, reflecting stimulation of the bone marrow which was also evident in marrow counts and increased leucopoiesis.

---

[1] Bickerstaff E R *Lancet* 1950 ii 683
[2] Stein W *Ann U M C S* 1949 4 553
[3] Fleck L *Sang* 1949 20 1

If there is a centre regulating the blood picture, either it is concerned only with the number of peripheral white cells (possibly by vasomotor innervation) or it acts at least partly by humoral mechanisms. After injection of bacteria, both in normal rabbits and in those submitted to transection of the cord, the number of circulating neutrophils rises and there is a shift to the left in the Arneth count, but in the animals with a transected cord the total number of leucocytes does not exceed the initial count. Rabbits deeply narcotised with Sodium amytal reacted in the same way as those with transection of the cord.

On the whole the existence of a distinct cerebral centre regulating the blood picture remains questionable. Undoubtedly the central nervous system influences blood morphology, but this influence is exerted rather through the many different vegetative functions, and after pneumo encephalography the C.S.F. pleocytosis is probably due to meningeal irritation.

Medical Academy
Lublin, Poland

LUDWIG FLECK
WIKTOR STEIN

OBTURATOR HERNIA

SIR,—In the following instance of the rare obturator hernia the patient was an African woman of middle age, a member of the Efik people of Southern Nigeria.

On admission to hospital on April 1, 1951 she had already been suffering for one week from complete constipation and frequent vomiting. Two days before admission a painful lump had appeared on the inner and upper part of her right thigh. She was a para 5 and gave no history of previous similar attacks of pain.

The patient was thin and in very poor condition when first seen. There was well marked visible peristalsis of the ladder pattern, but no abdominal tenderness or rigidity. The right thigh was partially flexed and externally rotated; all hip movements were painful. A soft, diffuse, and fluctuant swelling could be seen, extending 15 cm. down the thigh; it was of vague outline and had no cough impulse. Rectal examination revealed a ballooned rectum very tender on the right side.

Preoperatively strangulated obturator hernia with a ruptured sac was diagnosed, and operation was performed under spinal anæsthesia. Incision was first made over the swelling, which was found to consist of soft fæces lying free in the tissues deep to the pectineus muscle. A necrotic sac 1 cm. long, was seen in the region of the obturator foramen, but there was no recognisable intestine. A thin trickle of fæcal matter continued to come through the remnants of the sac. A lower abdominal approach was next made in order to examine the upper aspect of the hernia. The loops of intestine entering and leaving the hernial orifice were readily identified and there was no peritoneal infection. Both loops were firmly adherent to the orifice and a side to side anastomosis between loops above and below the obstruction was done. The thigh wound was left widely open and drained. The patient died on the third postoperative day in profound toxæmia.

This case conforms well to the usual features of obturator hernia, which is generally seen in multiparous women of poor physique and is often strangulated when first encountered. Preoperative diagnosis was made easier in this case by the presence of the large swelling in the thigh, although the Howship Romberg sign was absent. The double approach to the hernia from thigh and abdomen was an obvious necessity in this case.

It may interest young surgeons who are considering service abroad to know that recently in the course of ten days I operated on 8 cases of acute intestinal obstruction in this small country hospital. They included volvulus of small intestine due to peritoneal bands, intussusception due to a tumour of the ileum, fibrous stricture of the ileocæcal region, massive mesenteric hæmorrhage, agenesis of the rectum in a newborn child, obstruction and peritonitis following reduction en masse of a strangulated inguinal hernia, colic intussusception in a child, and the strangulated obturator hernia already described. This list should surely whet the appetite of anyone looking for experience in abdominal surgery. But he who would come to this type of work must be ready to rely solely on his clinical acumen for diagnosis, and to adapt his operative technique to the conditions of a plainly equipped theatre. Not for us are the ever more elaborate technical aids to medicine. In the volcanic age in which we live, however, such training may prove providential. And there is no doubt of the immediate good that will be done by any surgeon who decides to practise his art in this part of the world.

I wish to thank Dr H. Souster, acting medical superintendent, for permission to publish this case.

Methodist Hospital Ituk Mbang
East Nigeria

J R ROSE

ASPIRATION OF EMPYEMA THORACIS

SIR,—Your annotation on the article by Dr Asher and Dr Davies (April 28) particularly concerns assessment of the value of penicillin administered intrapleurally.

I am encouraged to refer to my experience of the mechanical aspect of aspiration in pre antibiotic days. In my series of 558 cases of lobar pneumonia during the 1914–18 war,[1] I recorded 116 as complicated by empyema. Of these, only 30 underwent rib resection, the remaining 86 were treated by aspiration alone with satisfactory resolution. Whilst such a procedure might well be expected to clear up effusions in the early stage containing few pus cells, I was surprised by the efficacy of this simple treatment when, as in 60 instances, really thick pus was present. In 24 of these pneumococci or streptococci were identified.

Modern chemotherapy and the systemic and local employment of penicillin must surely be an encouragement to practise aspiration as a measure that may in itself be adequate, as well as a valuable preliminary when it becomes clear that to ensure complete drainage surgery is essential.

London W 1

ADOLPHE ABRAHAMS

POLIOMYELITIS

SIR,—I should like to add the following experience to that recorded by Dr Harrington in your issue of May 5.

In each of the four cases of poliomyelitis encountered by me in 1947 the site of paralysis appeared to be related to trauma, as follows:

CASE 1.—Tonsillectomy followed a fortnight later by bulbar palsy.

CASE 2.—Injury to the left thumb, followed about a fortnight later by paralysis of the left forearm and shoulder. This man's wife had a two months' abortion at the same time as the acute disease that preceded his paralysis.

CASE 3.—Injury to left hand followed about a fortnight later by paralysis of the left arm.

CASE 4.—Impetigo of the left thigh, much scratched, followed by mild poliomyelitis with left quadriceps paresis. The time interval could not be assessed in this case because of the chronicity of the skin lesion.

At about the same time we encountered an old case of poliomyelitis which we regarded as belonging to the same series.

CASE 5.—A little later a girl aged 9 years attending for some other trouble, was found to have paralysis of the left arm and inquiry elicited the fact that paralysis had occurred about a fortnight after an injection of A.P.T. on Nov. 2, 1942.

This was our first encounter with post inoculation poliomyelitis, and we included it in the traumatic series. It was possible to trace most of the other children inoculated at the same time, and none of these had suffered ill effects from their inoculation.

Public Health Laboratory Service
Epidemiological Research Unit,
Cirencester

R E HOPE SIMPSON

---

[1] *Lancet* 1920 ii 545

AN UNUSUAL ASSOCIATION WITH TOBACCO

SIR,—In the following case smoking seems to have been the cause of an unusual syndrome

In 1926 a woman, aged 40, fainted while playing tennis On questioning she complained of severe pain between the eyes, her pulse was irregular, and she appeared to be so shocked that she was put to bed Within 24 hours the second and third toes of the right foot became painful, swollen, tender, and red, this condition gradually spread until it involved the whole foot and the leg to just below the knee, and the temperature reached 102°F The focal pain in the head gradually passed off after 24 hours, the leg lesion subsided, and after about 10 days the skin of the whole area desquamated the heart resumed its normal rhythm, and after about a fortnight the patient appeared to have recovered

A similar attack occurred 6 months later, and gradually attacks became more frequent until by 1941 they were taking place at intervals of little more than a month The patient was examined by a number of my colleagues, various diagnoses were made, including angioneurotic œdema, erysipelas, and an unusual manifestation of rheumatism After one attack she was put on salicylates, but these appeared to gravely increase the intensity of the attack X ray examination of the sinuses showed them to be clear, the frontal sinuses were small in development An aural specialist advised washing out the antrums to ascertain if there was any infection, but this was refused

I had noticed through the years that the attacks were related to exacerbations of a chronic bronchitis which the patient had had for some years, and these exacerbations seemed to be definitely related to smoking In 1941 I suggested that the smoking was responsible for the exacerbations of bronchitis and advised that the smoking should be stopped Accordingly it was reduced to two or three cigarettes per day, but this did not diminish the exacerbations, and further attacks affecting the foot and leg occurred with steadily increasing severity In 1943, when it was suggested that a surgical attack should be made on the sinuses, I advised that complete abstinence from smoking should first be tried

This was secured, and since that time no further attack affecting the foot and leg has been experienced, though the patient still has attacks of bronchitis whose severity increases at intervals

Birmingham **J F BRAILSFORD**

β-NAPHTHYL-DI-2-CHLORETHYLAMINE

SIR,—Reports on this substance in your columns[1,2] prompt me to relate briefly our experience with it in Italy, where the results obtained by Spigliati,[3,4] Introzzi and Ninni,[5] and De Ritis and Negroni[6] differ somewhat from those in Britain

Whereas British workers have sometimes administered up to 600 mg daily,[1] Italians have not usually given more than 300 mg (in one case Introzzi[5] gave up to 400 mg) Differences in the method of preparation may have something to do with the lower tolerance noted in Italy here the drug is given as a powder in cachets, whereas in Britain it is given in tablets

No depression of hæmopoietic function has been noted, even with protracted treatment[4] With leucopenia due to Hodgkin's disease, the white cell count has gradually returned to normal levels[4,5], while in hyperleukæmic leukæmia, sometimes quite severe, the number of circulating white cells, and more especially of their precursors, has fallen Prolonged treatment has not given rise to severe leucopenia Both in lymphogranuloma and in leukæmia therapy has produced an increase in the circulating red cells, during treatment marrow function seems to revert towards normal

Of 13 cases of Hodgkin's disease, 11 have responded satisfactorily, and in 4 the improvement has been maintained for over eighteen months In chronic myeloid leukæmia the response has been less constant and sustained, though still satisfactory, in each of 8 cases that have been treated pyrexia has decreased and the state of blood and bone marrow has improved 1 case of acute myeloid leukæmia, after some initial improvement, relapsed 2 cases of chronic lymphatic leukæmia responded very satisfactorily both by improvement in the general condition and by lessening of the glandular enlargement

Institute of Pathology,
University of Florence **PAOLO SPIGLIATI**

COMPLICATIONS OF INTRAVENOUS FLUID THERAPY IN CHILDREN

SIR,—A conclusion which I wish that Dr Todd had drawn from his work described in your issue of May 5 is that "cut downs" should only be performed on infants and children when no other means of giving parenteral fluid is possible There has been a tendency in the past to regard "cut downs" and parenteral fluid therapy as synonymous, and this is regrettable since the operation is often unnecessary, and sometimes even disfiguring (are the fashionable ankle bracelets worn to hide the scars of "cut downs" in infancy ?), and, as Dr Todd has shown, it carries a high morbidity

In my opinion the method of choice for giving parenteral fluid (at least in infancy, with which Dr Todd's article mainly deals) is by the subcutaneous route using hyaluronidase Few infants, in my experience, are so severely shocked that they cannot absorb fluid rapidly enough by this route, but, if they are, shock can first be combated by direct intravenous injection using a Kaufmann's syringe, and the restoration of blood-volume can then be completed by subcutaneous fluids

For blood transfusion similarly the method of choice is the use of a Kaufmann's syringe I cannot agree with Dr Todd that this technique is more difficult to learn than that of "cutting down" It is merely a refinement of the technique of venepuncture in adults with which every doctor is familiar, whereas "cutting down" is frequently learnt for the first time in a children's hospital

In practice it is certainly possible to make a "cut down" exceptional without resorting to special units for intravenous therapy Of 290 medical cases admitted under my care in the past year to the Leicester Royal Infirmary, 34 required parenteral fluid therapy, in 23 cases this was given subcutaneously and in 13 intravenously (2 patients were given fluid by both routes) In the intravenous group 19 infusions were given to the 13 cases (these figures do not include patients given blood transfusions as outpatients), in the subcutaneous group repeated or continuous infusions were given In only 3 cases was a "cut down" performed, in 2 this could probably have been avoided by a more expert, operator Thus of the 34 cases in hospital who required parenteral fluids, 9% had to have a "cut down" I feel sure that others could show a lower figure

Leicester **W J MATHESON**

VITAMIN-B DEFICIENCIES AFTER GASTRIC OPERATIONS

SIR,—The interesting article by Mr Welbourn and his colleagues in your issue of April 28 emphasises the liability of patients who have had a subtotal gastrectomy to develop symptoms and signs of vitamin B deficiencies, particularly hyporiboflavinosis and mild peripheral neuritis

Similar conditions may occasionally be seen at present in people whose diet is inadequate or whose gastric juice contains no free acid I have met two possible examples in recent weeks

The first, a woman of 28, had complained of numbness and tingling of her hands and legs with slight unsteadiness in walking during the previous nine months She had lost a stone in weight, suffered from flatulence fatigue and depression, and had received psychiatric treatment She said that she had recently had a very sore tongue and sore lips There had been no disturbance of vision or of micturition The only clinical abnormalities were very feeble knee jerks, absent ankle jerks, and absent vibration sense in both legs Test meal showed a histamine fast achlorhydria There was slight anæmia, but no abnormality of sternal bone marrow She had been eating poorly for a considerable time, and it was thought that her condition was the result of a vitamin B deficiency She was given intramuscular vitamin B therapy as an outpatient, and after two weeks she shows marked subjective improvement She says that she can now walk easily again in high heeled shoes and her paræsthesiæ are less The physical signs remain unchanged

---

[1] Matthews W B *Lancet* 1950 i 896
[2] Gardikas C Wilkinson J F *Ibid* Jan 20 1951 p 137
[3] Spigliati P *Min med* 1949 ii, 305
[4] Spigliati P Congresso di Ematologia Salsomaggiore May 10 1950 *Min Med* 1950 ii 490
[5] Introzzi P Ninni M *Hæmatologica* 1950 34, 925
[6] De Ritis F Negroni G *Min med* 1951 i 75

The second patient, a woman of 58, complained of severe pins and needles and tenderness in the limbs with burning sensations in the feet She could not easily fasten her buttons was unsteady on her feet, and had had several falls She felt very tired her tongue and lips had sometimes been sore, and she had had difficulty in holding her water These symptoms had been noticeable for several months She lived alone on a very poor diet On examination there was slight glossitis, and slight weakness of her hands and lower limbs Incoördination was slight in the hands but marked in the legs Superficial sensibility was impaired in a glove and stocking distribution, and vibration sense was much impaired at the knees and ankles The tendon reflexes were very brisk and were equal, there was bilateral ankle clonus, and both plantar responses were extensor There was some œdema of the ankles Blood count and sternal puncture showed no abnormality, and gastric analysis showed free hydrochloric acid It was thought that this might be a form of nutritional neuropathy with spinal cord involvement She was treated by rest in bed, some walking exercises, and an adequate diet with extra vitamin B (including 'Benerva, Marmite, and 'Multivite by mouth, and 'Cytamen 50' intramuscularly) The power and coördination of her limbs improved so that in a few weeks she became able to walk normally without support and her paræsthesiæ disappeared The objective sensory changes and reflexes remained unaltered

These examples afford no proof of the nature of the complaints, and it is well known that under normal circumstances vitamin B deficiency rarely occurs Possibly, however, a persistently inadequate diet, particularly in the presence of achlorhydria, may lead to a nutritional neuropathy where it would not ordinarily be expected

London W 1 **ERIC C O JEWESBURY**

Parliament

Miners' X-ray Scheme

On the motion for the adjournment in the House of Commons on May 7, Mr E H C **LEATHER** urged that full advantage should be taken of the work of Dr Charles Fletcher of the Pneumoconiosis Board by instituting a compulsory annual X-ray examination for miners This would reveal the disease in its initial stages when the miner could be given a surface job and a chance of recovery Mr Leather claimed the scheme would cost £135 000

Mr **HAROLD NEAL**, parliamentary secretary to the Ministry of Fuel and Power, said the question had been remitted to a committee presided over by the deputy chief medical officer of the Ministry of Health, and arrangements for an experimental scheme must await the conclusions of this expert committee, the first meeting of which was to be called shortly

The National Joint Pneumoconiosis Committee had advised that the experimental scheme was more likely to succeed if it was not linked directly with the X ray and dust-environmental surveys at coalmines which were being carried out by, or under the auspices of, the Pneumoconiosis Research Unit of the Medical Research Council Instead, it was aimed to confine the experimental scheme to the routine detection of pneumoconiosis by X rays and to build up a technique of safeguarding men found with the disease by confirming that they worked in, or were given every opportunity to work in approved dust conditions underground Extensive facilities for X-ray examinations were already available Every miner who felt that he might be suffering from the disease could make a claim for benefit, and if he did so he was automatically X-rayed

In the two years ended Dec 31, 1950, about 31,000 X ray films had been used, and 10,000 miners were diagnosed as having pneumoconiosis All of these, whether or not they had decided to remain in the coal-mining industry, were required to report periodically for re examination by a pneumoconiosis medical board The increased confidence of the men in the advice of these boards and in the arranging of test prevention diagnosis was shown by the fact that up to the end of 1950 about 5500 of the 10,000 cases diagnosed had remained at work in the industry

Compensation for Pneumoconiosis

In the House of Commons on May 8 Mr **LEATHER** asked leave to introduce a Bill to allow compensation to be paid in respect of persons who acquired pneumoconiosis as a result of their employment before July 5, 1918, and who were excluded from the then Workmen s Compensation Acts or regulations made under those Acts because of time limits contained in them Developments in X-ray technique and wider knowledge made it clear that a five-year time limit was unfair The disease was so long in its progression that 15 or 20 years might elapse before symptoms could be diagnosed Leave was given to bring the Bill, which was formally read a first time

National Health Service Bill

On May 9, Lord **HADEN-GUEST**, Lord-in-Waiting, moved the second reading of the National Health Service Bill The Bill passed through its remaining stages and was read a third time at the same sitting

QUESTION TIME

Membership of Hospital Committees

Lieut Colonel W H **BROMLEY DAVENPORT** asked the Minister of Labour whether his attention had been called to the withdrawal of the manager of the Sandbach employment exchange from the Arclid Hospital House Committee, and why it was now the general practice of his department not to allow his department s officials to serve on such committees —Mr **FRED LEE** replied I understand this took place over a year ago No general rule has been laid down about officers of the department serving on a hospital house committee, but it is the general practice of the department not to allow members of the staff to accept office on bodies whose functions include the engagement of labour Lieut Colonel **BROMLEY DAVENPORT** Is this not gross interference with the liberty of a subject who wants to serve others in his spare time? Why cannot he do it? No further reply was given

Hospitals Expenditure

Lieut Colonel D L **LIPTON** asked the Minister of Health what action he proposed to take arising from the Auditor-General's report on hospital expenditure —Mr H A **MARQUAND** replied I think that these matters should best be left to the normal machinery The report will shortly come before the Committee of Public Accounts and in due course be embodied in their report and published evidence, with subsequent action by Treasury minute

Amendment of Dentists Act

In answer to a question, Mr **MARQUAND**, Minister of Health said that proposals were under consideration for the amendment of the Dentists Act It was not possible to introduce a Bill in the present session but the Government intended to do so at an early opportunity

Red Cross in Korea

In answer to a question Mr **JOHN STRACHEY**, the Secretary of State for War, stated that the International Red Cross Committee had made repeated attempts to enter North Korea but permission to do so had been refused The Soviet and Chinese governments had previously informed the International Red Cross Committee that they did not feel able to interfere with the sovereign decision of the North Korean government in this respect However the president of the International Red Cross Committee had announced that he was recently permitted to visit Peking, where he saw the prime

AN UNUSUAL ASSOCIATION WITH TOBACCO

SIR,—In the following case smoking seems to have been the cause of an unusual syndrome.

In 1926 a woman, aged 40, fainted while playing tennis. On questioning she complained of severe pain between the eyes, her pulse was irregular, and she appeared to be so shocked that she was put to bed. Within 24 hours the second and third toes of the right foot became painful, swollen, tender, and red; this condition gradually spread until it involved the whole foot and the leg to just below the knee, and the temperature reached 102°F. The focal pain in the head gradually passed off after 24 hours; the leg lesion subsided, and after about 10 days the skin of the whole area desquamated; the heart resumed its normal rhythm; and after about a fortnight the patient appeared to have recovered.

A similar attack occurred 6 months later, and gradually attacks became more frequent until by 1941 they were taking place at intervals of little more than a month. The patient was examined by a number of my colleagues; various diagnoses were made, including angioneurotic œdema, erysipelas, and an unusual manifestation of rheumatism. After one attack she was put on salicylates, but these appeared to gravely increase the intensity of the attack. X-ray examination of the sinuses showed them to be clear; the frontal sinuses were small in development. An aural specialist advised washing out the antrums to ascertain if there was any infection; but this was refused.

I had noticed through the years that the attacks were related to exacerbations of a chronic bronchitis which the patient had had for some years, and these exacerbations seemed to be definitely related to smoking. In 1941 I suggested that the smoking was responsible for the exacerbations of bronchitis and advised that the smoking should be stopped. Accordingly it was reduced to two or three cigarettes per day; but this did not diminish the exacerbations, and further attacks affecting the foot and leg occurred with steadily increasing severity. In 1943, when it was suggested that a surgical attack should be made on the sinuses, I advised that complete abstinence from smoking should first be tried.

This was secured, and since that time no further attack affecting the foot and leg has been experienced, though the patient still has attacks of bronchitis whose severity increases at intervals.

Birmingham. J. F. BRAILSFORD.

β-NAPHTHYL-DI-2-CHLORETHYLAMINE

SIR,—Reports on this substance in your columns[1,2] prompt me to relate briefly our experience with it in Italy, where the results obtained by Spigliati,[3,4] Introzzi and Ninni,[5] and De Ritis and Negroni[6] differ somewhat from those in Britain.

Whereas British workers have sometimes administered up to 600 mg. daily,[1] Italians have not usually given more than 300 mg. (in one case Introzzi[5] gave up to 400 mg.). Differences in the method of preparation may have something to do with the lower tolerance noted in Italy: here the drug is given as a powder in cachets, whereas in Britain it is given in tablets.

No depression of hæmopoietic function has been noted, even with protracted treatment.[4] With leucopenia due to Hodgkin's disease, the white-cell count has gradually returned to normal levels[4,5]; while in hyperleukæmic leukæmia, sometimes quite severe, the number of circulating white cells, and more especially of their precursors, has fallen. Prolonged treatment has not given rise to severe leucopenia. Both in lymphogranuloma and in leukæmia therapy has produced an increase in the circulating red cells; during treatment marrow function seems to revert towards normal.

Of 13 cases of Hodgkin's disease, 11 have responded satisfactorily; and in 4 the improvement has been maintained for over eighteen months. In chronic myeloid leukæmia the response has been less constant and sustained, though still satisfactory; in each of 8 cases that have been treated pyrexia has decreased and the state of blood and bone-marrow has improved. 1 case of acute myeloid leukæmia, after some initial improvement, relapsed. 2 cases of chronic lymphatic leukæmia responded very satisfactorily both by improvement in the general condition and by lessening of the glandular enlargement.

Institute of Pathology,
University of Florence. PAOLO SPIGLIATI.

COMPLICATIONS OF INTRAVENOUS FLUID THERAPY IN CHILDREN

SIR,—A conclusion which I wish that Dr. Todd had drawn from his work described in your issue of May 5 is that "cut-downs" should only be performed on infants and children when no other means of giving parenteral fluid is possible. There has been a tendency in the past to regard "cut-downs" and parenteral fluid therapy as synonymous; and this is regrettable since the operation is often unnecessary, and sometimes even disfiguring (are the fashionable ankle bracelets worn to hide the scars of "cut-downs" in infancy?), and, as Dr. Todd has shown, it carries a high morbidity.

In my opinion the method of choice for giving parenteral fluid (at least in infancy, with which Dr. Todd's article mainly deals) is by the subcutaneous route using hyaluronidase. Few infants, in my experience, are so severely shocked that they cannot absorb fluid rapidly enough by this route; but, if they are, shock can first be combated by direct intravenous injection using a Kaufmann's syringe, and the restoration of blood-volume can then be completed by subcutaneous fluids.

For blood-transfusion similarly the method of choice is the use of a Kaufmann's syringe. I cannot agree with Dr. Todd that this technique is more difficult to learn than that of "cutting down." It is merely a refinement of the technique of venepuncture in adults with which every doctor is familiar, whereas "cutting down" is frequently learnt for the first time in a children's hospital.

In practice it is certainly possible to make a "cut-down" exceptional without resorting to special units for intravenous therapy. Of 290 medical cases admitted under my care in the past year to the Leicester Royal Infirmary, 34 required parenteral fluid therapy; in 23 cases this was given subcutaneously and in 13 intravenously (2 patients were given fluid by both routes). In the intravenous group 19 infusions were given to the 13 cases (these figures do not include patients given blood-transfusions as outpatients); in the subcutaneous group repeated or continuous infusions were given. In only 3 cases was a "cut-down" performed; in 2 this could probably have been avoided by a more expert operator. Thus of the 34 cases in hospital who required parenteral fluids, 9% had to have a "cut-down." I feel sure that others could show a lower figure.

Leicester. W. J. MATHESON.

VITAMIN-B DEFICIENCIES AFTER GASTRIC OPERATIONS

SIR,—The interesting article by Mr. Welbourn and his colleagues in your issue of April 28 emphasises the liability of patients who have had a subtotal gastrectomy to develop symptoms and signs of vitamin-B deficiencies, particularly hyporiboflavinosis and mild peripheral neuritis.

Similar conditions may occasionally be seen at present in people whose diet is inadequate or whose gastric juice contains no free acid. I have met two possible examples in recent weeks.

The first, a woman of 28, had complained of numbness and tingling of her hands and legs with slight unsteadiness in walking during the previous nine months. She had lost

---

1. Matthews, W. B. *Lancet*, 1950, i, 896.
2. Gardikas, C., Wilkinson, J. F. *Ibid*, Jan. 20, 1951, p. 137.
3. Spigliati, P. *Min. med.* 1949, ii, 305.
4. Spigliati, P. Congresso di Ematologia, Salsomaggiore, May 10, 1950; *Min. Med.* 1950, ii, 490.
5. Introzzi, P., Ninni, M. *Hæmatologica*, 1950, 34, 925.
6. De Ritis, F., Negroni, G. *Min. med.* 1951, i, 75.

Notes and News

WORLD HEALTH ORGANISATION

THE Fourth World Health Assembly was opened at Geneva on May 7 by Mme Amrit Kaur, India s minister of health and president of last year s assembly At the first session Dr L A Scheele, surgeon general of the United States Public Health Service and leader of the U S delegation, was elected president of the assembly, and Dr D A. Dowling (Australia), Dr A. H. Taba (Iran), and Dr Karl Evang (Norway) were elected vice presidents Colonel M. Jafar (Pakistan) was appointed chairman of the committee on programme Dr G A. Canaperia (Italy) chairman of the committee on administration, finance and legal matters, and Dr M T Morgan (United Kingdom) chairman of the committee on international sanitary regulations Tributes were paid to the late Dr Khalil Bey Egyptian under secretary of State for health, and the late Dr Geraldo de Paula Souza, director of the school of hygiene and public health at the University of São Paulo, Brazil Both were eminent in the field of public health, and Dr de Paula Souza was described as one of the ' founder fathers of W.H O At a ceremony *held in the afternoon, Mme Amrit Kaur presented the Léon* Bernard Foundation prize, for practical achievements in *social medicine to Prof* Réne Sand.

In his report for 1950 which was presented to the assembly Dr Brock Chisholm director general of W.H O, said that 100 countries and territories had received help directly from W H.O, while world wide technical services were made available to all nations to fight epidemics, and in other fields An important factor in the progress made by W.H.O in 1950 has been the decentralisation which has taken place, and, with the establishment of regional offices for the Western Pacific and for Africa, the regional network is almost complete A great problem is the shortage of health workers of all kinds said Dr Chisholm, but the organisation has tried to solve it by awarding more study fellowships and by arranging more conferences and seminars A serious development during 1950 was the announcement by 6 more governments of their intention to withdraw from W.H.O and the director general said that if it continued, the negative attitude of the U S S R, Byelorussia China, the Ukraine, Albania, Rumania, Hungary Czechoslovakia Bulgaria and Poland towards W.H.O would have an adverse effect on the organisation

MEDICINE AND THE FESTIVAL

THE Royal Society of Medicine and the British Medical Association have joined forces to play the medical host to Festival visitors at a series of symposia which they are holding at 1, Wimpole Street, London, W 1, *from June 4 to July 9* The beam of the debates will range widely, yet focus sharply The first meeting on Monday June 4, over which Sir Henry Dale O.M F.R S will preside, is to be devoted to the Peripheral Nervous System and belongs to the group of systematic discussions, of which other representatives are the Central Nervous System (June 14) under the chairmanship of Dr Russell Brain, F.R.C.P, and the Vascular System (June 8) under Sir John Parkinson. The different specialties claim their due, and Dr A. W S Sichel president elect of the B.M.A., will preside over Ophthalmology (June 11), Sir Gordon Gordon Taylor over Plastic Surgery (June 12) Sir Philip Manson Bahr over Tropical Medicine (June 26) and Sir William Kelsey Fry over Odontology (July 9) Turning from the general to the particular and from the knowledge of the past to the possibilities of the future, the organisers have chosen as further subjects Antibiotics, over which Sir Alexander Fleming F.R.S presides (June 7) and Cortisone' and A.C.T.H. with Prof G R Cameron, F.R.S (June 25) as chairman. The problems of the present are suggested by the meetings on Cardiovascular Disease in an Ageing Population, with Dr J H Sheldon in the chair (June 22) and the fears of the future by Burns, under Dr Leonard Colebrook, F R.S (June 19) The changing fashions of disease are illustrated by the meeting on the Decline of Infant Mortality, which Sir Allen Daley convenes (June 19) and the meeting on the rise in Peptic Ulcer (June 20) at which Sir Henry Cohen, president of the B.M.A. will be in the chair

There are *many other interesting and* important topics to choose from, and all doctors are welcome to attend the meetings A full *programme* and application forms for tickets may be had from the joint secretary of symposia, B.M.A House, Tavistock Square W C 1

BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION

ADDRESSING the British Empire Leprosy Relief Association in London last week, the Earl of Halifax, the president spoke of the newer methods of treating leprosy with the sulphone drugs and with thiacetazone The outcome of these advances, he said, had been remarkable, and, while the more *conservative still reserved final judgment, all agreed that the* change of outlook among the patients was almost miraculous The increasing use of the parent sulphone, diaminodiphenyl sulphone, had so reduced the cost of treatment that in many British territories local funds could at last be found to meet the needs of all cases at present within reach of treatment The association, Lord Halifax said was pleased that its work had earned the unqualified praise of the United Nations Trusteeship Mission which visited West Africa last year, it had been described as an example of human as well as medical achievement worthy of the highest commendation. *Another cause for satisfaction* was that in 1950 leper children discharged as cured numbered 349—nearly twice as many as in the year before Nevertheless the campaign against leprosy was young and in some areas the need was still very great a recent survey in East Africa showed that the proportion of cases within reach of effective treatment is only 1 in 80 The association s work must be expanded, and fortunately its income was sufficient to enable it to embark on new schemes, though to maintain any new effort the *need for funds would be as great or perhaps even greater* than ever before The association was ready and anxious to expand, but the difficulty had been the shortage of doctors. The president paid tribute to the work of Dr G A. Ryrie during his four years as medical secretary, and sympathised with him on the decline in health which had compelled him to resign his appointment At the same time he welcomed Dr R G Cochrane who had returned to take up the post of medical secretary after many years in Madras

Dr Cochrane said that progress had been made, not only in the drug treatment of leprosy, *but also in understanding* of the pathology and in orthopædic methods for preventing and correcting deformities Leprosy was not the hopeless disease it had been, and when doctors realised this then perhaps it would be easier to recruit helpers for the work

---

University of Oxford

Sir John Conybeare has been re elected a member of the board of the faculty of medicine He was the only candidate nominated by the general medical electorate

University of London

At a recent examination for the postgraduate diploma in psychological medicine the following were successful

Derek Anton-Stephens Karel Bobath, R B Carr Mani Bomanji Contractor W A Cramond H W D Davies John Denham L H Field G F J Goddard E S Goller Herta Graz B A J C Gregory L G W J Hannah Mercy I Heatley David Irwin M. A. Jackson, W G Joffe J C Kerridge Hazel W Liddell, J S B Lindsay J S Pippard Ebben Roderic Evans, P D W Shepherd Stanley Smith G F Spaul, S J G Spencer H P Tarnesby E L Udwin A A Valentine, K. R H Wardrop Letitia Woodvine

Mr G G Simpson, curator of fossil mammals and birds at the American Museum of Natural History New York, will deliver a lecture at University College, Gower Street, W C 1 at 5 30 P.M. on Wednesday, June 13 He will speak on Origin and Early Evolution of the Primates

Royal College of Physicians of London

Dr W E Lloyd will deliver the Mitchell lecture at the college, Pall Mall East, S W 1 on Thursday June 14, at 5 P.M. He is to speak on Pulmonary Tuberculosis in Young Adults—Observations on Minimal Lesions revealed by Routine Radiography

Royal College of Physicians of Edinburgh

At a meeting of the college held recently, with 'Sir David Henderson in the chair, the following were elected to the fellowship

A. P Agnew M B Glasg Thomas Semple M.D Glasg R W B Ellis M.D Camb

The following were elected to the membership

Alexander Kahan Kahan Chand Kandhari Kurt Aaron Ali Mohammad D R Barry Odhavji Tribhovandas Samani J D Robertson P W Wishart K G Lowe Abul Kalam Siddiqui Muriel M. McLean C M. B Field C D T MacLean B C Sinclair Smith, W J Bell A S Douglas James Hingston J F C Waterston K. B F Witcombe Durgadas Banerjee N P Bector George Selby H J Stott H W Macintyre A S Thambiah Madan Mohan Pradhan M F Oliver

minister and minister for foreign affairs, and had lengthy discussions with the president of the Chinese Red Cross Society In these discussions the Chinese Red Cross Society were asked whether, as an interim measure, while the International Red Cross Committee were unable to carry out their traditional duties in North Korea, they would act on the committee's behalf They were particularly requested to distribute medical supplies to United Nations prisoners of war and others, to provide assistance in the transmission of correspondence, and to assist in the transport of food parcels to United Nations prisoners of war The president of the International Red Cross Committee had emphasised that his talks with the Chinese Red Cross were most satisfactory

Diary of the Week

MAY 20 TO 26

Monday, 21st

Institute of Ophthalmology Judd Street, W C 1
5 30 P M Mr A B Nutt Congenital Ocular Palsies
West London Medico Chirurgical Society
8 30 P M (1 Wimpole Street, W 1) Bishop of Birmingham Over-population. (Cavendish lecture)
Institute of Laryngology and Otology 330 Gray's Inn Road W C 1
5 P M. Miss D T Collier Treatment of Facial Paralysis
University of Birmingham
4 P M. (Medical School) Sir Edward Mellanby F R.S. Nutritional Effects on Bone and the Nervous System (First William Withering lecture)

Tuesday, 22nd

Royal College of Surgeons, Lincoln s Inn Fields, W C 2
3 45 P M Dr James Craigie, F R.S Phase-contrast Microscopy of Mouse Sarcomas (Imperial Cancer Research Fund lecture)
University of London
5 30 P M (Westminster Medical School, Horseferry Road, S W 1) Prof Warren H Cole (Chicago) Surgery of the Biliary System (First of two lectures)
Wright Fleming Institute of Microbiology, St Mary's Hospital Medical School, W 2
5 P.M Dr C H Andrewes, F R.S Aspects of Immunity to Influenza (Almroth Wright lecture)
Royal Eye Hospital St. George s Circus, Southwark, S E 1
5 P M Dr T H Whittington Diplopia
West End Hospital for Nervous Diseases, 40, Marylebone Lane W 1
2 30 P M Dr Colin Edwards Sciatic Pain.
Institute of Dermatology St John's Hospital Lisle Street W C 2
5 P M Dr R M. B MacKenna History of Dermatology
Institute of Ophthalmology
5 30 P M. Dr Dorothy Campbell Vision in Conditions of Low Illumination
University of Birmingham
4 P M Sir Edward Mellanby Nutritional Effects on Bone and the Nervous System (Second William Withering lecture)

Wednesday, 23rd

Royal Eye Hospital
5 30 P M Mr R P Crick Theory and Management of Squint.
Institute of Dermatology
5 P M Dr H Haber Precancerous Conditions of the Skin
University of Birmingham
4 P M. Sir Edward Mellanby Nutritional Effects on Bone and the Nervous System (Last William Withering lecture.)

Thursday, 24th

University College, Gower Street, W C 1
4 45 P.M Mr D J Bell Biological Syntheses Concerning Carbohydrate Radicles (First of four lectures)
Royal Eye Hospital
5 P.M Dr S Nevin Myopathies in Ocular Practice
St George s Hospital Medical School Hyde Park Corner, S W 1
4 30 P.M Dr Denis Williams Neurology lecture-demonstration
Institute of Ophthalmology
5 30 P.M Dr F A Elliott Visual Attention.
Medico Legal Society 26, Portland Place W 1
8 15 P M Dr Leslie Narman Medicine in Industry
Honyman Gillespie Lecture
5 P M. (University New Buildings Teviot Place, Edinburgh) Dr N W Horne Tuberculous Meningitis
University of St Andrews
5 P M. (Medical School, Small's Wynd, Dundee) Prof J D Boyd Pigment Cells of the Body

Friday, 25th

Royal College of Obstetricians and Gynæcologists, 58, Queen Anne Street, W 1
5 P M. Prof H L Sheehan Anuria in Obstetrics (Blair Bell lecture)
Royal Eye Hospital
5 P M. Miss M. Savory Uses of Thrombin and Fibrinogen in Ophthalmology
Institute of Dermatology
5 30 P M Dr Brian Russell Clinical demonstration

Obituary

PERCIVAL MACLEOD YEARSLEY

F R.C.S

Mr Macleod Yearsley, formerly consulting aural surgeon to St James' Hospital, Balham, and to the London County Council, died at Gerrard's Cross on May 4, at the age of 83

A collateral descendant of Dr James Yearsley, the pioneer ear, nose, and throat surgeon in this country, he was educated at Merchant Taylors' School and the Westminster and London Hospitals In 1890 he qualified, and he took his F R C.S three years later

He was appointed to the staff of the old Royal Ear Hospital, then in Soho, of which in due course he became senior surgeon, and he was the first aural surgeon to the London County Council, for whom he carried out important investigations among school children. He also interested himself in the welfare of deaf-mutes

A man of many interests, Macleod Yearsley wrote some delightful fairy tales, studied the story of the Bible, discussed the sanity of Hamlet and doctors in Elizabethan drama, took a scientific interest in the Zoological Society, translated Forel's *Sensations des insectes*, and was an archæologist of repute In his own specialty he wrote a *Textbook on Diseases of the Ear* (1908) and another on *Nursing in Diseases of the Throat, Nose and Ear* Later he became greatly interested in the Zünd-Burguet electrophonoïd treatment of deafness, on which he wrote a monograph in 1933 Energetic, open-minded, and many-faceted, he was looked upon as rather a stormy petrel by his contemporaries, but he mellowed with time, to be regarded with respect and admiration by otologists of today

In his later years Yearsley retired to Gerrard's Cross, where he became ear, nose, and throat surgeon to the local hospital He married Florence Louise, daughter of the late Dr C M Cooper, and she survives him with a son.

GERALDO HORACIO DE PAULA SOUZA

M D

International health has suffered a loss in the death after a short illness of Prof G H de Paula Souza, director and professor of public health at the University of São Paulo, Brazil Beginning his career in international health as a medical officer of the Health Organisation of the League of Nations, he served for a time with UNRRA during the war and represented Brazil at the Technical Preparatory Commission in Paris and the World Health Conference in New York in 1946, and on the Executive Board and at the World Health Assemblies of W H O He will chiefly be remembered for his successful insistence, with the representative of China, that the San Francisco conference should include health in the functions and structure of the United Nations, as well as for his concern for the wider issues of public health, his stand against parochialism, and his never-failing personal courtesy and kindness

Appointments

Butler, N G P M.B Lond. anæsthetic officer, Stoke Mandeville Hospital, Bucks
Cheffins, E M. M B. Lond asst. chest physician Cambridge Chest Clinic
Cleminson K. L M.B Lond orthopædic registrar, Peterborough and District Memorial Hospital
Drennan V K M B M.CH. (ORTH.) Lpool F R.C.S E consultant orthopædic and traumatic surgeon Clwyd and Deeside Hospital Management Committee
Edmunds P K. D M.R C.S , D.M.R.D radiologist (S.H.M.O grade) Merthyr and Aberdare Hospital Management Committee
Fletcher P F M B Glasg , D P.M psychiatrist, Stanley Royd Hospital, Wakefield.
Hopkin D A B , M.D Lond , D T M & H., D.A consultant anæsthetist Lambeth group of hospitals
Lidgate M. M. M.B. Birm psychiatrist Menston Mental Hospital, near Leeds
McCauley, Peter, M.B. N U.I. D.P M asst. psychiatrist, St. Andry s Mental Hospital Suffolk.
Simons E L M.B. Camb asst clinical pathologist, Kingston General Hospital and Western General Hospital Hull.
Watson, Kathleen, M.B Lond D.A consultant anæsthetist, Huddersfield and Storthes Hall Hospital Management Committee groups
Wilson Peter, F.R.C.S.E D O.M.S consultant in ophthalmology, hospitals in Leeds A group
Wishart James M.B Glasg F R.F.P S , F R C.S.E consultant in orthopædic surgery hospitals in Bradford Wakefield, and Ilkley and Otley Hospitals Management Committee groups.

PHYSICAL EXERCISE *

ITS CLINICAL ASSOCIATIONS

SIR ADOLPHE ABRAHAMS
O B E , M.A., M D Camb , F.R C P
CONSULTING PHYSICIAN TO WESTMINSTER HOSPITAL

PHYSICAL exercise may be defined as exertion of muscles, limbs, and bodily processes regarded with reference to its effect on the subject But it is customary to limit such exertion to that which is undertaken with a view to the maintenance or improvement of health Indeed so established and intimate is this special association, that we are accustomed to append qualifying adjectives such as open air, carriage , horse , walking-, and others, according to particular requirements of exercise as a therapeutic prescription

In what respects does the subject interest or concern the clinician ?

In the first place he will naturally be credited with knowledge of the anatomical and physiological principles of exercise in general, and expected to explain and advise the type, the limitation of its extent, and the individual requirements according to age, sex, social position, and opportunities These are details which regard exercise as commensurate with other hygienic principles upon which advice is habitually asked , such as food, clothing, alcohol, tobacco

What is popularly termed violent exercise—that is, exertion to the limit of capacity or endurance—occupies an important place and fulfils an important function in civilised countries The clinician will be expected to pronounce upon the possible danger to the admittedly healthy, especially to the cardiovascular system when exposed to extreme stress or so called strain He will be asked to decide the significance of certain lesions and conditions—whether they may be completely disregarded of should be accepted as interdictory of unlimited effort He will, rightly or wrongly, be assumed to be an authority on " training "—that is, the preparation for athletics—and in consequence consulted on such matters as the selection of appropriate foods or so called stimulants The familiar associations of stitch, cramp, stiffness, and staleness will also be regarded as within his province

There are special gynæcological considerations that call for his attention, such as the place of exercise during pregnancy and after delivery, more especially on account of the increasing proclivity of girls and young women to participate in activities hitherto regarded as the male prerogative

The injuries that occur in sports and competitions—such as sprains, bruises, fractures, dislocations, concussion, indeed traumata of all kinds—require the applications of fundamental surgical principles with certain technical requirements, as when an athlete requests exceptionally rapid or immediate results These need not be comprised within my present thesis, a conclusion that applies to remedial exercises in general. Yet I may diverge in parenthesis to recall the application of graduated exercises in the treatment of some forms of *cardiac disease* and of *pulmonary tuberculosis* In *diabetes*, exercise is accorded a prominent therapeutic place along with diet and insulin Prolonged inactivity lowers sugar tolerance in the non diabetic confined to bed (Blotner 1945), for with lessened demand for the rapid storage and utilisation of sugar the pancreas is rested, and diabetic reactions may occur even with a normal fasting blood sugar At least one diabetic subject has despite his disability reached top ranking in lawn tennis, although reduction of his insulin dosage demanded by severe competitive exercise calls for some circumspection in the avoidance of hypoglycæmia Even sufferers from *myasthenia gravis* have under the influence of neostigmine been capable of strenuous exercise, although the wisdom of such indulgence may well be questioned

INSTINCT AND INSTRUCTION

In a state of Nature the demand for physical exercise is satisfied as instinctively as the demands imposed by hunger, thirst, and cold the mere circumstances of existence ensure a sufficiency But in civilised life the relative increase in sedentary work and the shift to mental and intellectual forms of human endeavour are so predominant that, with the exception of certain natural occupations such as farming, hunting, and lumbering, physical exertion is reduced to negligible proportions And even in these, the introduction of machinery encroaches continuously upon the physical application Fifty years ago, the urban population of the United States was estimated at 2% it is now 60% Comparable changes have occurred in this country The necessity or craze for speed together with the convenience of improved and increasingly rapid means of locomotion make the city dweller less and less inclined to utilise his own natural means of progression

There are other elements in urban life that contribute to the necessity of regarding exercise as essential to health The ever increasing protective influence of clothing, of wind sheltered dwellings, and of artificial heating withdraws people more and more from a struggle with the rigours of Nature City dwellers become concentrated in an atmosphere charged with gases of imperfect combustion, and through a canopy of soot and dust deprived of direct sunlight Amusements and recreations inevitably mean congestion in crowded public places, with exaggeration of these disadvantages and the addition of infection Open air exercise must then be designed for its antidotal effect In many instances an instinctive urge ensures a sufficiency, in others it will be more or less deliberately undertaken as a measure of hygiene If exercise is instinctive and to a considerable extent a vital necessity, why should advice be needed ? Because it differs from such essentials as food and clothing, and similar familiar requirements, in which, when error in their application is committed, it is either from some inevitable cause of hindrance or from wilful infringement of laws ignorance of which cannot be pleaded In the case of exercise, although the evils which arise from abuse or misapplication are really as direct as those that follow the non observance or misapplication of any other agent of health, they follow less suddenly on committal of the fault Reminders of neglect speak not with the imperative voice of hunger or thirst or cold or oppressive heat or fatigue

Were the physical component the only one to be considered it would suffice to proceed on simple dynamometric lines But, fortunately, the psychical side, the factor of recreation, the satisfaction of the play instinct, perpetually operate to secure Nature's requirement indirectly but more advantageously When, for example, walking alone is avoided as too insipid, and the claim to its traditional constitutional value is disregarded, all kinds of accompaniments may be introduced to increase attractiveness As is well known, a man who would not willingly walk a dozen yards when a hospitable vehicle presents itself, can easily be persuaded to follow a little white ball over several miles of varying country Shooting, fishing, croquet, bowls, butterfly hunting, collecting fossils, and similar outdoor pursuits, undertaken according to taste and fancy, ensure a sufficiency of fresh air and exercise for the less vigorous

In fact, when called upon to discuss the necessity or at least the advantage of exercise with a patient who regards the advice in the light of a conventional prescription, the practitioner will pay particular attention

---

* The first Lumleian lecture for 1951 delivered before the Royal College of Physicians on April 10

Royal College of Obstetricians and Gynæcologists

At a recent examination for the diploma in obstetrics, the following were successful

E A Agius A S Arneil, Janet M Bell D G B Bennett E I Boxer H S Brown, J A C Brown C B Burdett Smith R K Burt J D Chalmers, R A Chesterfield Joanne M Clements, J F Connolly J S Cox T I Crichton J M A Critchley Margaret E Davies J A Dow A J Dinn H G Dixon D C Dymond, Emrys Evans Harriet Earls Margaret M Farrell Ethel A Fisher, Hanora H Forde J M Frew, D C H Garrod, H S Gavourin Nagendra Nath Ghosh H J Giwelb, N G O Gourlay Michael Grant, Kenneth Greig Peter Griffiths Harry Haigh J S Happell W T Harrott J W S Harris Kathleen J Harrison Patricia E Hartley M M Herbert G J S Herdman Ruth N E Hinckley J G Inglis, W G Irwin Bernard Isaacs W C Jamieson Dorothy M Jennings A T Johnson A W Johnson Krystyna Maria Kawa H M Kent Gordon Kettlewell H M Kirkpatrick, Po Chuen Lai Catherine M Lamplugh, D C Langwell Joyce H Lazarus J J Lee William Lees, T P Linehan C D Linton H A R Loxdale H S M Callum Austin McCawley D P McDermott James McDowall Susanne M Macgregor W J M Mackenzie F J McKenna, L P Mackie Cynthia J McPherson, L J Mann J G Mathie Brian Measday, Margaret L Meikle A L Mintz Rhona E Morgan F J Mouser Jessie M B Muirhead Anne M M Oriel Eliasz Perelman Evelyn Peters Violet M J Procter Margaret D F Quinet A J H Reford A M Reid D H Richards J H Ridgwick Freda M Roberts D J Rodger I P Ross Mark Sackwood I N Samuel Joycelyn H W Sandison Muriel J Scudamore Henryk Seid Parmeshwar Narain Sinha June M Smith P M Smith Isobel M W Stark, R G O Taylor O H Taylor Eirian Thomas Somasundram Thurairetnam W L Timmins F L Trott A C Turnbull Ethel M Wallis Alexandra C Watson Pamela L C Watson Margaret L Watt, Grace A M Webster H M White H W Wilson M B Wingate P A T Wood Frances M E Wylde

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting held on Monday, May 7, with Mr Walter W Galbraith, the president, in the chair, the following were admitted fellows of faculty

A C McDougall Mallaraj Basavaraj Urs *qua* physician, B McK Dick *qua* surgeon

Faculty of Ophthalmologists

The following have been elected officers for 1951–52 president, Mr O M Duthie, vice presidents, Mr R C Davenport and Mr A B Nutt, treasurer, Mr E G Mackie, secretary, Mr J H Doggart

West Midlands Physicians Association

The second meeting of this association will be held at the North Staffordshire Royal Infirmary, Stoke on Trent, on Saturday May 26, at 11 A M

Conference on Maternity and Child Welfare

The National Association for Maternity and Child Welfare are holding their annual conference at Church House, Westminster, London, S W 1, on June 27, 28, and 29 The conference will be opened by Princess Elizabeth at 10 15 A M on June 27, and the speakers will include Dr E Ashworth Underwood, Dr R C Lightwood, Dr Mildred Creak, Dr J L Burn, and Dr Alex Russell Further particulars may be had from the secretary of the association, 5, Tavistock Place, W C 1

Harveian Society of London

At this society's Buckston Browne dinner on May 10, the toast of The Society was proposed by Mr L S Amery, who spoke with humour of the difference between politics and medicine Politicians, he declared submitted to none of the exacting tests undergone by those who attended the temple of Aesculapius Our only qualification is our own good opinion of ourselves as members of the body politic We politicians shamelessly advertise our nostrums Of Harvey he spoke with admiration as the first person to make our blood circulate' Mr Amery remarked that in a life time the pulse beat 2500 million times To what purpose ? he asked, and went on to provide some thought provoking answers In his reply Mr W L Tucker the president, suggested that in the National Health Service professional harmony was tending to become disrupted, partly owing to the wages policy This disruptive trend should be arrested, and the Harveian Society could make its own contribution by bringing together all manner of doctors Sir Alexander Maxwell and Mr Basil Cameron replied for The Guests to a toast proposed by Dr Brian Warren Sir Alexander Maxwell urged the need for close understanding between Britain and the U S A, for without this the outcome for the world might be catastrophic He implied that one factor dividing the two nations was their common language which obscured the need for effort "We must get to know our American friends'

Lebanon Hospital for Mental and Nervous Disorders

The 52nd annual meeting of this hospital will be held at the Cora Hotel Upper Woburn Place, London, W C 1, on Monday, May 21, at 3 P M, when the Earl of Feversham, the president, will take the chair The speakers will include Dr J C Sawle Thomas and Dame Katherine Watt, R R C, both of whom have visited the hospital during the past year

National Council for the Unmarried Mother and Her Child

A meeting of this council will be held at the County Hall, Westminster Bridge, S E 1, on Wednesday, May 23, at 2 30 P M Miss Robina Addis, Miss Eve Kennedy, and Prof R M Titmuss will open a discussion on Unmarried Parents—the Background for the Social Worker

Students' Clinical "At Home"

On April 20 the Junior Common Room Society of the Middlesex Hospital was at home to 6 students from each of the other London teaching hospitals, and the programme consisted of both clinical and social functions The visitors were directed, as far as possible in accordance with their own choice, to one of ten teaching rounds or to some urological operations One round was given by Sir Gordon Gordon Taylor, and the others by present members of the hospital staff Altogether over 200 students attended these various rounds After tea Dr C E Lakin gave a lecture entitled Nec Silet Mors A sherry party for the visitors and members of the staff was held in the evening, and was followed by a dinner

Chelsea Clinical Society

Proposing the toast of the Chelsea Clinical Society at the annual dinner on May 8, General Sir Ronald Adam, chairman of the British Council, spoke appreciatively of the work of those members of the profession with whom he had been associated in the Army He went on to speak of the council's work in bringing the successes of British medicine to the notice of other countries The retiring president, Mr Geoffrey Parker, replied to the toast The toast of The Guests was proposed by Dr N L M Macmanus, and Lord Horder and Prof E C Dodds, F R S, replied The president then made a presentation to the retiring secretary, Mr H Paxton Baylis, and Dr K E Eckenstein, the treasurer, spoke of Mr Baylis's long and loyal service to the society After the presentation, Dr J H Dunn was inducted as president for the coming year

---

Births, Marriages, and Deaths

BIRTHS

BESWICK —On May 4 at Brantingham, Yorks the wife of Dr T S L Beswick—a son

CARDEW —On May 7 the wife of Dr P N Cardew—a son

COOLING —On May 3 at Ipswich the wife of Dr C I Cooling —twin sons

DAVIES —On May 6 at High Wycombe, Bucks the wife of Dr L W Davies—a son

DIGGLES —On May 7, at Davyhulme Lancs the wife of Dr Harry Diggles—a daughter

FOWLER —On May 6 at Bromley Kent the wife of Dr Bruce Fowler—a son

HALL.—On May 3 the wife of Dr R G Hall—a daughter

MACDONALD —On May 6, at Chesterfield the wife of Dr J A MacDonald—a son

ROBERTSON —On May 4, in Liverpool, the wife of Dr A J Robertson—a son

ROSTRON —On May 6 at Lelant, Cornwall to Dr Rosemary Rostron (née Arkwright) wife of Dr Kenneth Rostron—a son

WARIN —On May 11 at Bristol the wife of Dr Robert Warin —a son

MARRIAGES

BALL—ILLING —On May 5 at Ashtead Surrey Michael Joseph Ball, M R C S, to Elizabeth Katherine Illing

PARK—KENNARD —On May 2 at Hobart Tasmania Charles Leslie Park M D to Joyce Kennard M B

SOOTHILL—THORNTON —On May 7 at Wyther Leeds John Farrar Soothill, M B to Brenda Thornton

SPALDING—FALLE —On May 5 in London John Michael Kenneth Spalding M R C P to Elizabeth de Carteret Falle, M R C P

DEATHS

ARNOTT —On May 6 in London William Arnott, M B Lond aged 69

LAMBALLE —On May 5 at York Frederic William Lamballe M.B Durh lieut.-colonel, R.A.M C retd

WALLACE —On April 26 George Smith Wallace O B E M B Glasg D P H colonel R A M C retd aged 72

YEARSLEY —On May 4 at Gerrard's Cross Bucks Percival Macleod Yearsley F R C S aged 83 means to that end, including the obvious one of muscular exertion Physiologists have shown what preposterous misconceptions were generally held about this alleged aid to reduction

Since in the performance of any exercise the oxygen consumption can be accurately measured, and since a litre of oxygen is the equivalent of 5 calories, the exertion corresponding to the oxidation of a standard pound of body-weight in the form of fat (i e, 4230 calories) is merely an affair of simple calculation To those who have hitherto thought only vaguely of the potentially reducing power of exercise the revelations are startling Thus, at the ordinary reasonable walking pace of $3^{1}/_{2}$ miles an hour, which requires an oxygen consumption of 0 75 litre per minute, one mile is the equivalent of 65 calories, so combustion of the pound of fat would necessitate a constitutional of some $65^{1}/_{3}$ miles spread over about 19 hours

Terpsichore is from this angle a not very efficient adjuvant, for 16 hours of the foxtrot would be necessary for the same reduction

Of course the oxygen consumption is much greater with strenuous exertion A sprinter at full speed is expending energy that demands approximately 6 litres of oxygen in 10 seconds Even so, were it humanly possible to continue at this extreme speed, $7^{1}/_{3}$ miles would have to be covered to draw on the pound of fat And turning to a practicable physical achievement, running at the rate of 10 miles an hour, which is the pace of a good marathon runner, no less than 43 miles would be necessary

Almost certainly there is some other factor that is more elusive Is it not likely that regular exercise sets the basal metabolic rate at a higher level operating throughout the twenty four hours? Superficially it would seem that appropriate estimation ought to prove or disprove such an explanation, but in actual practice it has not been found easy to obtain convincing evidence

It is generally agreed that getting fat is not due to anything so simple as want of energy expenditure It is a habit of the body, and exercise, especially if undertaken regularly, in some way helps to acclimatise the body to it, as in the case of almost everything to which the human body may be subjected Yet even the greatest enthusiast is compelled to admit the comparatively limited application of exercise, more especially as the subjects most desirous of reduction are obviously incapable of exertion of great severity or prolonged duration

Loss of weight must of course be distinguished from genuine loss of fat In strenuous exercise there may be considerable loss of water from the body from perspiration and to a lesser degree, through respiration I found in myself a loss of three pounds in weight in half an hour's climbing in Switzerland A loss of from four to ten pounds has been noted in a marathon runner This loss is restored within the ensuing three days, sometimes within twenty four hours

DIET AND FITNESS

The clinician will be expected to advise upon the nature and quantity of food likely to contribute to physical fitness and athletic prowess His task will be neither easy nor agreeable in attempting to reconcile fetishism with sober physiology He will strip the mystery from much that has no greater foundation than tradition, and the iconoclast is never popular

Diet in athletic training has always received more than its proper share of attention It has been credited with attributes and possibilities always exaggerated and largely imaginary Although most of the outrageously unphysiological precepts of old time training have largely disappeared, a few survive as if something must be retained amid the shifting quicksands To this day belief persists that energy, stamina, strength, and endurance are directly obtainable from what one eats rather than from what one does, and advice will be sought upon articles of food that can increase respiratory power or cardiac efficiency Although his opinion will be greeted with some degree of incredulity, the practitioner will be of service in pointing out that the energy expended is comparatively so little that there is no justification deliberately to increase the usual food intake, especially of animal protein, a practice which will often lead to indigestion and other disturbances Alternatively, the reputation of articles of diet said to be bad for training has in the majority of cases no foundation of any kind There are psychological reasons for the admission of some alimentary generosity in order to avoid the bugbear of staleness, but these are outside laboratory calculations

The practitioner will have more difficulty in discrediting the alleged value of concentrated comestibles or complex vitamin preparations

During World War II, some anxiety being felt that stereotyped rationing might lead to undernutrition and malnutrition, a number of investigations were undertaken to estimate the effect of administering vitamins One series of experiments showed considerable improvement in performance of various physical tests Another series, however, showed convincingly that there was no evidence whatever of any such benefit, and the most reliable conclusion to be drawn is that given an adequate diet, supplementation with vitamins serves no useful purpose (Keys and Henschel 1942) Nor did parenteral injections lead to any increase in muscular efficiency (Foltz et al 1942)

These laboratory investigations confirm the observations of those who have been in intimate contact with great athletes. Machines differ in their fuel requirements and the human machine is no exception Dietetic peculiarities are simply those of individual taste, the dictates of natural inclination

THE HEART IN EXERCISE

Since, rightly or wrongly, solicitude is applied to the work undertaken by the heart in extreme exertion and the possibility of strain and permanent injury, a few details relating to the circulation will not be out of place

In an average healthy subject at rest, each ventricular contraction at the rate of 72 per minute, expels 100 ml. ($3^{1}/_{2}$ ounces) or about 7 litres ($1^{1}/_{2}$ gallons) of blood per minute During extreme exertion the ventricular output may be more than doubled and the cardiac frequency rise to 160 and on occasion higher The minute volume thus increases to 37 litres (8 gallons) Expressed in more homely statistics, this is the equivalent of a bath room tap turned full on Such spectacular figures encourage the presumption of danger and damage, apart from the symptoms of discomfort that may arise and the appearance of distress so alarming to an onlooker The traditional expectation of injury is that of a dilated heart, but it would appear that some confusion of thought is related to the terminology

When such discrepant statements are made as that the heart enlarges in exercise and that the heart after exercise is smaller, it is clear that technique in estimation and measurement must in one of these circumstances be incorrect or that there is some fundamental misconception

It is universally accepted that at the beginning of exercise, when the coronary blood supply has not reached its maximum, the heart dilates in order to increase the efficient contraction of its individual fibres Dilatation then is an essential part of the mechanism by which it can increase or maintain its output in response to a greater venous inflow or a higher arterial pressure. It is a perfectly normal process, and the extent to which it can take place is limited by the pericardium Even so, a considerable addition to its content of blood at the to the psychological side, remembering that even if accepted as medicine it is not necessary that medicine should be unpalatable. There cannot be one best form of exercise for all persons. One man's pleasure is another man's madness. The ascent of high mountains, for example, is a penal discipline: one of the fiercest torments of the Greek Hell is regarded as one of the sublimest pleasures of an English holiday, a commentary on the saying that some of us take our pleasures very sadly. The exercise that gives unqualified enjoyment to one may inspire boredom in another and be interpreted as a form of torture by a third. Formally to advise or order exercise without regard to the individual's tastes, quite apart, of course, from his physical capacity, is equivalent to the employment of a universal prescription or a dietetic régime on Procrustean lines.

OUTLETS FOR AGGRESSION

The more strenuous forms of exercise which include the element of competition to a greater or less degree, represent the primitive instinct of strife, which, however stifled and suppressed by civilisation, nevertheless survives, and survives to some purpose. It seems that human beings were not born to be the gentle kind creatures that religion would desire. Judging by the past, and unhappily, too, the present, the lion who may some day achieve the prediction of the prophet and lie down with the lamb will be a very senile lion on the point of death.

Modern games and athletics are basically conventionalised outlets which help the civilised citizen to express his emotions vicariously and to control his radical aggression, the aggression for which the organism was constructed and which all animals to survive must practise. Aggression is thus expended in a regulated fashion without resorting to primitive ways. As William James says: even if the day ever dawns in which muscular vigour will not be needed for fighting the old heavy battles against Nature, it will still always be needed to furnish a background of sanity, serenity, and cheerfulness, to give moral elasticity to our disposition, to round off the wiry edge of our fretfulness, and make us good humoured and easy of approach.

BENEFITS OF ACTIVITY

The picture of the unnatural conditions of urban life represents the ill effects of taking no exercise. Considered from the positive aspect, activity will be directly or reflexly related to all the functions of the body, chiefly as a result of an increased provision of oxygen.

First, one naturally considers the circulation, the tide on which is brought up all fresh material for incorporation in the tissues and on which is borne away all that is effete. The call for increased cardiac frequency on effort results in decreased frequency during rest, with improved output and lower blood pressure. A reserve is created which may be utilised in the maintenance of life under adverse conditions. In general, the body is educated to deal with emergencies.

Ventilation of the lungs is increased, especially at the apices. The mechanism of temperature control is tuned up; the nervous system is trained in coordination. A higher level of motor integration automatically ensues. Muscular movements are conducted with greater economy, whilst latent fibres are employed and more oxidising and metabolic enzymes are developed. The integrative effect is not confined to the voluntary muscular sphere: it extends deeply into the autonomic field. A sense of strength and well being engenders, colours, and reacts upon the outlook and actions as a whole.

The bone marrow is stimulated by the oxygen want which is a temporary consequence of vigorous activity. There is a reflex enlargement of the suprarenals. Bodily movements lead to massage and increased motility of the alimentary canal with improved coordinated control of the mechanical factors of digestion.

The relationship of exercise to the gastro intestinal functions demands a more critical examination than traditional everyday experience can supply. The so called constitutional walk to create an appetite is not simply the exponent of physical exertion as is popularly supposed—a misconception which, as I shall show later, is particularly related to obesity. Appetite has a far greater psychological background in the stimulating effect of moving air upon the exposed parts of the body and the enjoyment which depends upon a number of influences according to tastes and temperament.

Campbell and his colleagues (1928) found by the employment of test meals, that walking at the easy pace of $3^1/_2$ miles an hour increased the rate of emptying of the stomach, and that simultaneous agreeable conversation was more effective than exercise alone. In exercise of greater severity, both the gastric secretion and the rate of emptying were decreased. Presumably cutaneous vasodilatation with relative anæmia of the stomach is the main responsible mechanism.

They found considerable individual differences, corresponding no doubt to natural ability for exertion and the customary degree of participation. They found that on the whole the rate of digestion was increased in any exercise that did not produce discomfort—an observation supporting the common experience that a child often takes vigorous exercise after a meal, a practice of which an adult is quite incapable, an example of the value of instinct as a guide to what is physiologically sound.

By enthusiasts too much may easily be claimed. Contrary to popular belief, there is no evidence to support the view that a high standard of physical fitness is associated with, or conducive to, the attainment of special resistance to infectious diseases. Muscular efficiency and athleticism are special features. They are not incompatible with health and resistance to illness but they are not necessary accompaniments. Physical training as such improves the ability of the body to deal with situations with which exercise confronts it, an adaptation, an automatic utility irrespective of whether the organism is healthy or not. Properly conducted recreational activities impart a psychological release and so enhance equanimity but are incapable of generally improving a man's health or resistance to illness. A great number of sedentary workers take little or no deliberate exercise but seem to be quite as normal in respect to infection as their physically more strenuous fellows.

The remarkable improvement in the physique of the subnormal recruit to the Fighting Services may be unduly attributed to the physical training. This, of course, plays its part, but one has to remember the many concomitant advantages—abundant wholesome food, the discipline of regular habits and other hygienic circumstances, freedom from the pecuniary and social anxieties of a precarious life with intermittent unemployment, and so on and so on.

EXERCISE AND OBESITY

Although the association of physical activity with obesity must always have been recognised, until comparatively recently little attention was paid to this or for that matter any other method of reduction. The tendency to put on weight, the middle aged spread as it was called, or the rather euphemistic and chivalrous expression, the well covered woman, was accepted as inevitable; and so far as exercise was related, most people were not at all clear in the differentiation of cause and effect.

At the end of World War I, when for some reason or other the natural feminine conformation became unfashionable, the craze for slimming (still persisting) encouraged and demanded investigation of all possible women of a particular physique and temperament are likely to be interested in sport, in which they see an opportunity to compensate for what is felt to be the inferiority of being feminine

Even in men, the anxiety and tension, the disturbing influence of the limelight of adulation and hero-worship, may adversely affect the nervous system It might be contended that such influences would be still more deleterious to young women—a presumption which is, however, stoutly denied by those who claim for women a capacity for adjustment and stability superior to that of men

In the year preceding World War II, a committee was appointed to investigate the details upon which obstetricians and gynæcologists have expressed widely differing opinions We interviewed many women prominent in the world of sport as active participants or as officials or entrusted with the charge of girl athletes. In addition, a questionary was circulated among a considerable number who in their youth had indulged in athletics and other competitive exercise and had subsequently borne children, with inquiries as to their pregnancies, deliveries, and general health. Many stated that dysmenorrhœa, so far from being aggravated since engaging in such exercise, was markedly improved. No indication was forthcoming of relative sterility, of disturbances during pregnancy, or of difficulty in delivery The criticism is obvious that we were dealing with enthusiasts but what other material was available ?

The outbreak of war terminated the inquiry, which would have been extended particularly in the direction of psychology It must be admitted that the unæsthetic accompaniments that on occasion cannot be overlooked may inject a degree of prejudice that handicaps judgment on the physical side This is an unavoidable weakness in human nature most people see what they wish or expect to see

SEQUELÆ OF RADICAL GASTRIC RESECTIONS

CLINICAL AND METABOLIC FINDINGS IN 35 CASES

R H F Brain
M.B Birm. F.R.C.S

CONSULTANT THORACIC SURGEON MID WORCESTERSHIRE GROUP OF HOSPITALS LATELY SENIOR SURGICAL REGISTRAR THORACIC UNIT QUEEN ELIZABETH HOSPITAL, BIRMINGHAM

With an Introduction by

F A R Stammers
C B.E , Ch.M. Birm., F.R C S

PROFESSOR OF SURGERY, UNIVERSITY OF BIRMINGHAM

Surgical technique, aided by its modern adjuncts and ancillary services, has become so safe that hardly any operation is inherently impossible Hence the fashion is for more and more radical procedures , but the time has now come for surgeons to ask themselves whether, from the patient's point of view, such and such an eradication is psychologically and physiologically justifiable. Furthermore, every effort should be made to explain, with the aim of preventing or at least mitigating, the secondary discomforts of radical surgery that sometimes lead patients to question the value of their operations I therefore suggested that Mr Brain should investigate the sequelæ of total and near total gastrectomies, particularly the failure of these patients to gain weight and strength, and their liability to diarrhœa, anæmia and deficiencies of vitamin B complex

---

In the past 3½ years some 40 total or near-total gastrectomies were performed at the Queen Elizabeth Hospital Birmingham, and 35 of the patients had some form of special investigation We paid particular attention to the postoperative period, and made detailed metabolic studies of some of the cases

TABLE I—CLINICAL FINDINGS IN FOLLOW UP OF 33 GASTRECTOMY PATIENTS

Clinical feature		Total gastrectomy		Near total gastrectomy	
		For cancer (13 cases)	For other conditions (4 cases)	For cancer (10 cases)	For other conditions (6 cases)
Appetite		Good	Good	Good	Good
Capacity for food					
Limited		12	4	8	4
Increased		1		2	2
Dumping syndrome					
Mild		11	2	5	2
Severe		1	1	3	1
Dysphagia due to					
Stomatitis	Regurgitation of alkaline juices	3	2	3	3
Œsophagitis					
Spasm	Vitamin B deficiencies	6	1	3	
Organic obstruction		1			
Diarrhœa		12	4	9	4
Constipation		1		1	
Weight					
No gain		12	4	8	4
Rise to normal		1		2	2

Most of the patients were operated on for cancer of the stomach, often of the cardiac end , and it must be emphasised that our inquiry was concerned only with the most radical resections Nevertheless, the cases still varied both in the nature of the lesions present and in the severity of their operations , the patients were therefore divided into four parallel series, as follow

Series 1 —Total gastrectomy for cancer
Series 2 —Total gastrectomy for non malignant conditions
Series 3 —Near total * gastrectomy for cancer
Series 4 —Near total gastrectomy for non malignant conditions

On the whole, the postoperative findings were much the same in each series

CLINICAL PICTURE

Both surgeons and physicians have lately become increasingly aware that patients who have a gastric resection, particularly a radical one, are by no means normal afterwards (see leading article in *The Lancet*, 1950, ii, 373) Even after a " routine " partial gastrectomy for simple ulcer, loss of weight and excessive excretion of fat in the stools are often noted (e.g , by Wollaeger et al. 1946) The follow-up findings in a large series of cases of duodenal ulcer treated at the Queen Elizabeth Hospital by vagotomy alone,† when compared with a similar series treated by partial gastrectomy, revealed striking differences in the general nutrition of the two groups In the vagotomy series, the patients who became symptom free often gained up to 2 stone in weight after the operation , whereas the gastrectomy patients, though they seemed otherwise well, gained only a few pounds at best Where total gastrectomy was done, even for non malignant conditions—e g , a case of gastric polyposis—the patients looked almost like the wasted inmates of Belsen Camp

It seems that a radical gastric resection initiates a state of " katabolism " leading ultimately to stabilisation of the patient's metabolism at a body-weight much below end of diastole will produce a comparatively slight increase in the diameter of the heart. At the termination of exercise clinical estimation of the heart size is prone to error: widespread vigorous pulsation precludes accurate localisation of the apex beat. Radiography, however, points to a reduction in size, as would on mechanical grounds be expected.

---

* The terms near total and "subtotal are both used in this paper to describe gastrectomies closely approaching total

† The treatment of duodenal ulcer by vagotomy alone was subsequently abandoned at this hospital.

But, protest the alarmists, it is an ultimate permanent enlargement that is to be feared. And since cardiac hypertrophy is so intimately identified with a pathological condition of the vascular system, or of some other system with cardiovascular repercussions, an indictment of violent exercise is comprehensible. The pertinent features to be examined would appear to be the following:

1. Is there evidence of cardiac hypertrophy in those accustomed to violent exercise?
2. If such hypertrophy occurs, is it pathological or is it a hypertrophy homologous with that of the voluntary muscles?
3. When cardiac hypertrophy is apparently related to athleticism, is it necessarily the result of exercise? May it not be evidence of a naturally large heart in a human being constitutionally fitted for protracted exertion?

When with hypertrophy the muscular fibres enlarge without increase in the number of capillaries, each capillary has to supply an increased mass of muscle. Efficiency is in consequence impaired because the exchange of oxygen and metabolites is impeded. That is the condition of a heart enlarged through some pathological state. On the other hand, hypertrophy in the sense of increased capillarisation is not necessarily enlargement in the clinical sense.

Tung (1934) found that 45% of rickshaw pullers had enlarged hearts. But pathological influences can by no means be excluded. The life of the rickshaw pullers is extremely precarious. Owing to their small earnings, they cannot feed, clothe, and house themselves properly, and they are exposed for long hours to all the inclement weather the climate imposes. Moreover the physical output is comparatively small.

Radiological investigation of athletes who have exerted themselves over long periods provides no evidence of recognisable enlargement. Lee (1915) satisfied himself that there was no difference between the size of the heart in men who had been rowing for two years and in those who had been rowing for ten years, and very little if any difference from those in a younger group who had not rowed at all.

Turning to the constitutional factor. May not man share the privilege of selection, as in the Animal Kingdom generally? The wild hare has, weight for weight, three times the heart muscle of the wild rabbit. The greyhound by virtue of generations of strenuous exercise, or as a result of selection, is endowed with a proportionately large heart at birth—a heart which responds, to schooling and training, by hypertrophy. Thoroughbred colts have comparatively larger hearts than the ordinary run of horses (Herrman 1925–26). How far this is evidence of the inheritance of acquired characteristics or the result of selection through generations of racing stock is a matter for speculation. In the case of man, any such investigation is in the vast majority of cases limited to X-ray estimation of the volume of the heart, calculating its weight and relating this to body weight. Using this method, Bramwell and Ellis (1931), working with competitors at the Olympic Games at Amsterdam in 1928, found that the marathon runners had relatively large hearts, with a ratio to body weight of 1/46·4 as compared with 1/63·8 in shorter-distance runners. Opportunities for the more accurate direct estimation of the heart weight are naturally very rare. The isolated example I am able to advance is of exceptional interest (Abrahams 1946).

A man of 78 died suddenly during a course of deep X-ray therapy for malignant disease of the thyroid. As a necropsy was permitted, I requested particular attention to the heart and blood-vessels, for his career as an athlete in his youth had been of almost legendary order.

He was, in the opinion of authorities, the greatest long-distance cyclist of all time. At the age of 18 he broke records for the bicycle and tricycle rides from Land's End to John O'Groats, for which achievement he had an insatiable partiality. Contemporary members of our profession warned him that every such performance reduced his life expectation by 10 years; but he accomplished it on 24 occasions. After terminating his career as a long-distance cyclist he continued as an outstanding performer at cricket, hockey, swimming, and lawn tennis for the remainder of his life, during which his health remained excellent.

At the necropsy the cause of death was found to be an embolus in the left pulmonary artery. The heart was conspicuously large, weighing 18 ounces (509·4 g.). The muscle was firm and without fatty changes or infarctions. The coronary vessels were entirely free from atheroma. The aorta was in a remarkable state of health. The valves were normal. All other viscera were healthy.

It is probable that similar examples of natural hypertrophy would be discovered if necropsies on famous athletes were performed, and if, in the case of those who died at an advanced age, care was taken to assess the usual degenerative changes.

In this connection a reference is desirable to the condition known as "idiopathic" hypertrophy of the heart—a term that suggests, superficially at any rate, the possibility of confusion with the constitutional hypertrophy of the super-athlete, but in fact a grave pathological state. Termed "idiopathic" because of an unknown ætiology, it is usually fatal in early childhood, but three examples have been described in which the patients survived to the ages of 18, 29, and 31 (Levy and Rousselot 1933). There was in these young adults no history of violent exercise or of excessive fluid intake; the hearts post mortem weighed 740 g. (26 oz.), 750 g. (26½ oz.), and 640 g. (22½ oz.) respectively. Areas of degeneration and necrosis were visible in the myocardium. Microscopically, the heart muscle cells showed hydropic degeneration with vacuolisation of the sarcoplasm similar to the condition of the myocardium in fatal cases of diphtheria.

Whittle (1929) described the case of a student aged 20 who fell off his bicycle and died within a few minutes. Post mortem his heart was found to weigh 800 g. (28 oz.). Although the only exercise indulged in had been that of ordinary cycling, Whittle considered the muscular exertion to have produced this remarkable cardiac hypertrophy, a conclusion surely quite unacceptable. This patient must have belonged to the group alluded to by Levy and Rousselot when describing the three cases under their care.

EXERCISE FOR WOMEN

The physiological and recreative advantages of exercise apply to women equally with men; but when the more strenuous forms and especially those involving competition are in question, some circumspection is desirable. The modern tendency towards participation in track athletics calls for inquiry whether woman's special function in Nature may not be seriously prejudiced. For guidance, we look to our gynæcologist colleagues and we find conflicting opinions. Some regard athletics as harmful by increasing the incidence of disturbances of genital functions, especially menstrual disorders and sterility. Others not merely deny these ill effects but believe the very opposite. Some obstetricians are convinced that in women who have indulged in a great deal of exercise difficulties occur at parturition through muscular rigidity. Others of equal experience have failed to identify any such influence.

There is the psychological factor. Sport, especially of a highly competitive character, is held to bring about changes of a masculinising nature, with production of the virago type. An alternative explanation is that only

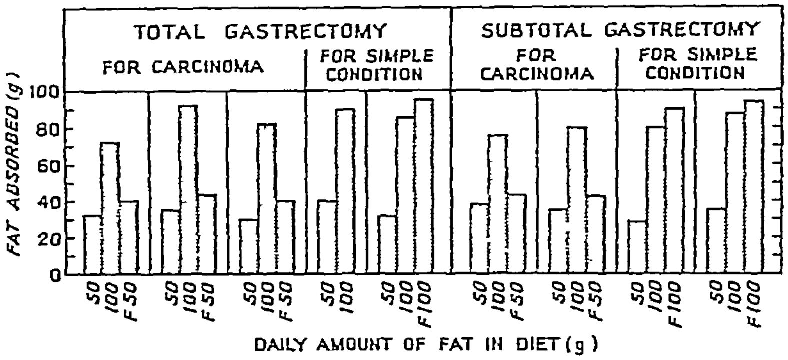


Fig 4—Amount of fat absorbed from different diets after gastrectomy F = fractional

still further, in some cases raising the proportion absorbed to 90%, which closely approaches normality

These findings seem to be of considerable clinical importance, and they have lately been applied in the treatment of 2 patients, to find out whether the patients' general nutrition could be improved in this way and whether there were any adverse effects This presented some difficulties in practice, for it was necessary to keep the patients in hospital for a further month in addition to their stay of at least a month for routine investigations Only 2 patients agreed to this, but one of them gained 12 lb and the other 6 lb in the month There do not appear to be any adverse effects, and the daily number of stools is not increased In our experience these patients like a high-fat diet, but some other writers on this subject, for example Muir (1949), find that after partial gastrectomy many patients " go off fats " Naturally we have recommended this régime to patients discharged from hospital, and with some satisfactory results, but many complain that the present ration scales make it very difficult and often impossible to follow unless sympathetic members of their family are willing to give up their fats

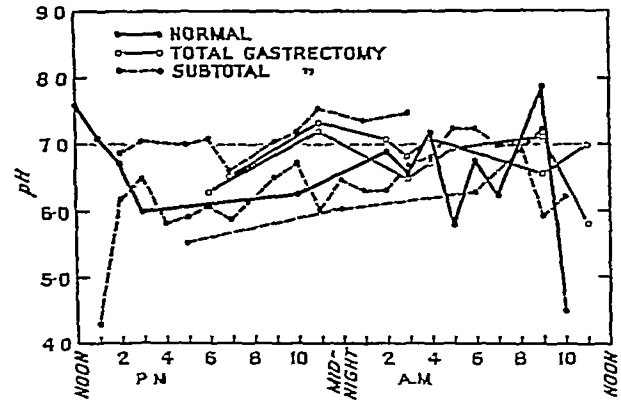


Fig 5—Values of pH in upper jejunum in 2 cases of total and 3 cases of near total gastrectomy for carcinoma and in 1 normal person

Our present view is that the " dumping syndrome " mechanism is responsible for the defective fat absorption When a meal is dumped mechanically en masse into the jejunum, the pancreas does not receive either " neurogenic " or " hormonal " warning until too late, whereas when the fat is given in multiple small meals (" fractionation "), even if the first meal misses the pancreatic enzymes, almost certainly the remainder will be more fortunate because they will utilise the enzymes secreted as a result of the stimulus of the preceding meal. This might be called " pancreaticocibal asynchrony "

Experiments have been undertaken with duodenal and upper jejunal intubation in order to assess pancreatic function and intestinal pH (fig 5) Unfortunately, no satisfactory quantitative test could be devised, but qualitatively it can be said that normal enzymes are present The pH findings have proved of great interest because many writers in the past referred to a " stabilisation of pH " following radical gastrectomy and suggested that it might be responsible for the poor absorption of " ferric " iron, resulting in anæmia From fig 5 it will be seen that the upper jejunum seems to be mainly " acid ", one case even had a pH of 4·2 at one stage in the day

In order to dispose of the possibility of an obstruction to the absorption of neutral fat through the lymphatics or even the cisterna chyli, blocked as a result of the operation, chylomicrograms were done on a series of cases with results shown in fig 6, these can, I think, be considered normal, though slightly delayed

Bowel motility, judged by giving barium with normal meals, appeared to be normal in the few cases tested, and so also were the cholecystograms and liver function tests.

BLOOD PICTURE

Anæmia

Iron deficiency was apparently not present in our cases except in the immediate postoperative period, when it seems to be directly due to loss of blood before and at operation and the consequent depletion of iron stores When the depletion is corrected the patient remains stable On the other hand, other workers—e g, Ransom (1948)—have often pointed out that " hypochromic microcytic anæmia " is a common sequel to gastrectomy

Macrocytosis

Macrocytosis in the peripheral blood was present in 11 of our cases—about a quarter of the total. This is intriguing but of academic interest only, since none of our patients has had an associated anæmia requiring treatment This subject was investigated by estimating the mean corpuscular volumes (M C V) and noting the general appearance of cells in stained films Price Jones curves were not done, but we are assured by our hæmatologist that the M C V results given in fig 7 almost certainly represent an " understatement," since these cells are " thinner " than normal. Bone marrow biopsies were made in most of the cases and showed uniformly that the source of the macrocytosis is the macronormoblast in a hypercellular marrow

Even more interesting are the cases that show a waxing and waning macrocytosis, including those with a preoperative macrocytosis that returns to normal

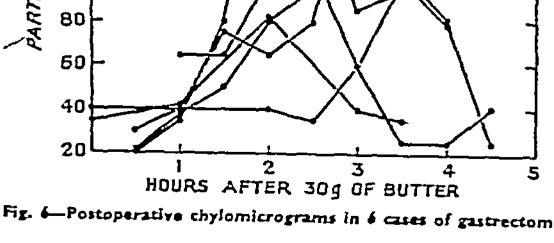


Fig. 6—Postoperative chylomicrograms in 6 cases of gastrectomy.

his normal level Among the possible causes of these changes we have considered the following

(1) Difficulties of ingestion—e g , dyspepsia and dysphagia
(2) Defects of absorption
(3) Disturbance of fluid balance
(4) Increased utilisation of food

Up to now only the first two have been seriously investigated , the third is strongly suspected to play a part, though without direct evidence The follow up findings in the 33 cases are summarised in table I

DIFFICULTIES OF INGESTION

Capacity for Food —The total amount of food taken in 24 hours was almost invariably less than before operation , it tended to increase with time but rarely reached normal The intake was usually rather larger after subtotal than after total gastrectomy An important finding was that 5 patients ate "more food than they had ever eaten in their lives," by the simple expedient of taking frequent small meals, as a result, these 5 patients had returned to about their normal weights

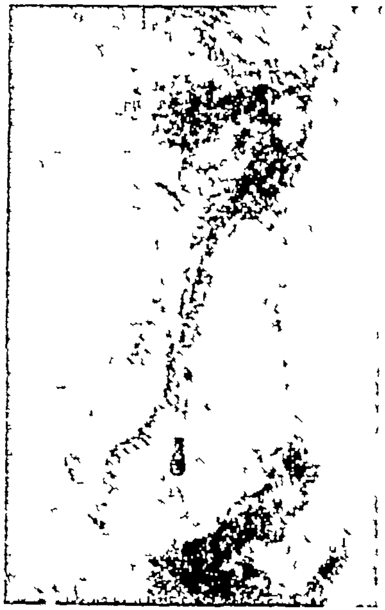


Fig 1—Balloon introduced into efferent jejunal loop ; before infection

Dumping Syndrome —In the 20 "mild" cases there was postcibal fullness, not severe but definitely limiting the patient's capacity for food The 6 "severe" cases also showed evidence of autonomic stimulation, such as sweating, palpitation, or faintness, and in 1 case actual loss of consciousness The mechanism of these symptoms was established in 2 severe cases by the introduction of a balloon into the efferent jejunal loop (fig 1) , when the balloon was inflated the dumping symptoms were exactly reproduced twice in one patient and once in the second This had previously been reported by Alvarez (1940)

Dysphagia —Except in the cases of frank vitamin B deficiencies (see below), dysphagia was rarely a distressing symptom and patients seldom complained of it except on direct questioning Where the dysphagia appears to be related to the regurgitation of intestinal juices, the type of œsophago intestinal anastomosis done probably plays a part in its causation On the whole, we now believe that the Roux Y anastomosis is more satisfactory The simple loop technique, even when combined with an entero anastomosis, seems liable to produce manifestations of regurgitation One patient in this series had an œsophagoduodenal anastomosis, and this has been followed by a persistent and highly disabling œsophagitis

TABLE II—INCIDENCE OF METABOLIC DEFECTS IN 40 GASTRECTOMY PATIENTS

Type of gastrectomy	No of cases	Deficient fat absorption	Vitamin B deficiencies	Macrocytosis	Iron deficiency
Total					
For carcinoma	15	8	5	6	0
For other conditions	4	3	1	3	0
Near total					
For carcinoma	13	7	3	1	0
For other conditions	6	3	0	1	0
Whole series	40	21/21*	9/32†	11/32†	0/25‡

* Only 21 cases were submitted to fat absorption tests
† Excluding 5 patients who died within five days of operation and 3 who did not attend for follow up
‡ Excluding 12 patients who died within three months of operation and 3 who did not attend for follow up

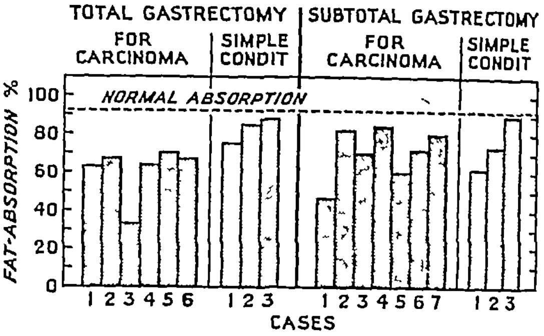


Fig 2—Fat absorption of patients on diet containing 50 g fat daily, three months after gastrectomy

Diarrhœa was invariably present in the early stages after operation, but it was not a distressing symptom and within three months it usually settled to 1 or 2 stools a day

Constipation was unusual, but it was very troublesome in 2 patients during their fat balance tests

DEFECTS OF ABSORPTION

Steatorrhœa

It will be seen from table II that steatorrhœa was demonstrated in all the cases that were thoroughly investigated by giving diets of known fat content (usually 50 g daily) over six days and collecting the stools during the last 72 hours This régime was repeated roughly at three month intervals to note the effect of time

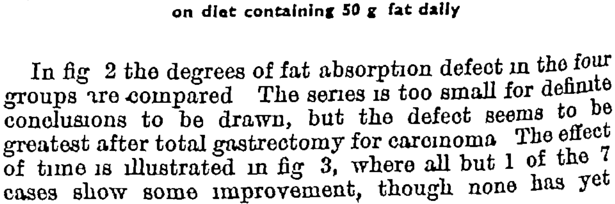


Fig 3—Effect of time on fat-absorption of gastrectomy patients on diet containing 50 g fat daily

In fig 2 the degrees of fat absorption defect in the four groups are compared The series is too small for definite conclusions to be drawn, but the defect seems to be greatest after total gastrectomy for carcinoma The effect of time is illustrated in fig 3, where all but 1 of the 7 cases show some improvement, though none has yet reached a normal level of absorption

The most significant experiments were those comparing the effects of doubling the amount of fat in the diet (giving 100 g instead of 50 g a day), "fractional" feeding of fat (i e , giving small amounts in hourly feeds throughout the day) , or a combination of (1) and (2) Fig 4 shows the results in 9 typical cases

It seems clear from these results that doubling the fat content of the diet at least doubles the amount of fat absorbed Dividing the daily ration into small hourly feeds also raises the percentage of fat absorbed And a combination of the two methods improves absorption

PREVENTION AND TREATMENT OF TRAVEL SICKNESS WITH PROMETHAZINE CHLOROTHEOPHYLLINATE

JOHN HARPER
M.B. Belf., D.T.M. & H.
OF THE MEDICAL TRIALS UNIT, MAY & BAKER LTD

TRAVEL sickness is not a disease but a normal physiological reaction to various types of oscillatory motion, at least 90% of normal people are susceptible to it in some degree (Morton et al 1947), and its severity and duration are conditioned by many psychic, somatic, and environmental factors. The difficulties in assessing the value of any remedy for travel sickness have been emphasised by all who have written on the subject. Objective criteria are few, there is extreme personal variation among the victims, and there is the added complication of spontaneous recovery in a matter of days.

REMEDIES USED PREVIOUSLY

The many remedies recommended and used for sea sickness include compounds acting on the central nervous system, such as barbiturates, caffeine, and amphetamine, those acting on the autonomic nervous system, such as atropine and other alkaloids, and local anæsthetics such as chlorbutol and cocaine. During the late war premeditated trials, in which many of the peace time variables were eliminated or overcome, were designed and made on a large scale (Noble et al. 1947). The results showed that hyoscine hydrobromide in doses of 0·6 mg (gr $^1/_{100}$) was effective (Holling et al. 1944) and safe, even under tropical conditions (Hill and Guest 1945).

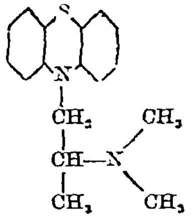
Many of these war time trials of solanaceous alkaloids and barbiturates were conducted with the particular object of preventing seasickness in fit trained men exposed for short periods in landing-craft and other small vessels. The conditions were not therefore comparable with those experienced by civilian passengers on longer voyages.

Chance and the independent observations of McEvedy (1949) and Gay and Carliner (1949) have led to trials of other compounds under conditions more like those of civilian travel. McEvedy, while in charge of the sick bay of a British troopship, observed that patients treated with anti histamine compounds were less affected by seasickness than other patients. He showed, by a planned comparison of 'Anthisan' and hyoscine, that anthisan was at least as acceptable a remedy as hyoscine and was free from some of the disadvantages of that drug. Gay and Carliner, working in an allergy clinic in North America, were investigating the possible value of 'Dramamine' in hay fever and urticaria, when one of their patients noticed that, though she had suffered from car sickness all her life, she could control it completely if she took 50 mg of the drug a few minutes before boarding a street car. These workers then investigated the effects of dramamine in cases of motion sickness and later in cases of seasickness. Trials were conducted in a North Atlantic troopship, groups of subjects living under the same conditions were studied, and controls were given lactose. Further trials of anti histamine drugs include those of Rust and Fosberry (1949) on dramamine, Beaumont (1949) on anthisan and 'Phenergan,' Ambrus and Ambrus (1950) on phenergan in seasickness, and of Strickland and Hahn (1949) on dramamine in airsickness. A summary of dramamine trials under various conditions has been published by Shaw (1950), and Wright (1950) has recently compared older remedies of the barbiturate hyoscine group with some anti histamine drugs and their derivatives both prophylactically and therapeutically under troopship conditions. Scandinavian workers have also reported similar work. Santesson (1949), using 'Amosyt' which is similar to dramamine, has recorded his findings in a variety of conditions including sea, train, car, and air sickness, and Engquist (1950) has described the use of 'Lertigon,' the hydrochloride of a phenthiazine base very similar in composition and action to promethazine chlorotheophyllinate known as 'Avomine'.

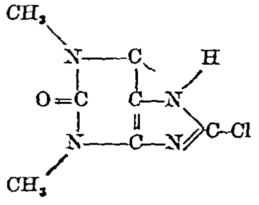
The prevention and treatment of seasickness with avomine during four crossings in a large North Atlantic civilian passenger liner in the winter of last year is described here.

PHARMACOLOGY

Avomine, which is chemically N (2 dimethylamino-n propyl) phenthiazine 8 chlorotheophyllinate (i.e., the 8 chlorotheophyllinate of promethazine), has the following structural formula:



Promethazine



8 chlorotheophylline

It is a white powder sparingly soluble in water and was prepared for use in small uncoated tablets of 10 mg and 25 mg (equivalent to 56·2% promethazine) for oral administration.

The clinical pharmacology and practical applications of promethazine hydrochloride (phenergan) have been described by Bain et al.(1948) and by Bain (1949). It has a powerful protracted anti histamine action as well as other effects, which include local anæsthesia and reduction of capillary permeability. Like many of the other anti histamine drugs it has a sedative effect which varies from person to person, but this seldom lasts as long as its anti histamine action.

Cusic (1949), in an attempt to counteract the drowsiness which may limit the applications of anti histamine drugs in some cases, tried the effect of combining a xanthine derivative with an anti histamine grouping. Many of these salts were unstable, but the 8 chlorotheophyllinate was an exception and formed a stable salt. Recently Mitchell (1950) has described some preliminary research which suggests that the introduction of 8 chlorotheophylline, apart from altering the incidence of side effects, may actually alter the anti emetic action of the anti histamine grouping.

CLASSIFICATION OF CASES

It is difficult to draw an objective dividing line between prevention and treatment in a condition in which the victim passes, by imperceptible stages, varying in sequence, duration, and severity, from a state of well-being to one of abject misery. And it is revealing to note how few people, even among those who know of their high susceptibility to motion sickness, seek medical advice on embarkation or soon after. The small number of people asking for preventive treatment is extremely regrettable in view of the findings of Quigley et al. (1943) and Wolf (1943) which indicate that if prevention of nausea by oral drug administration is to be attempted, it should be commenced early—preferably before even

---

MR BRAIN REFERENCES

Alvarez, W C (1940) An Introduction to Gastro Enterology New York p 409
Machella T E (1949) *Ann Surg* 130 145
Muir A (1949) *Brit J Surg* 37 165
Ransom H K (1948) *Sth Surg* 14, 15
Wollaeger E E Comfort M W Weir J F Osterberg, A E (1946) *Gastroenterology* 6.

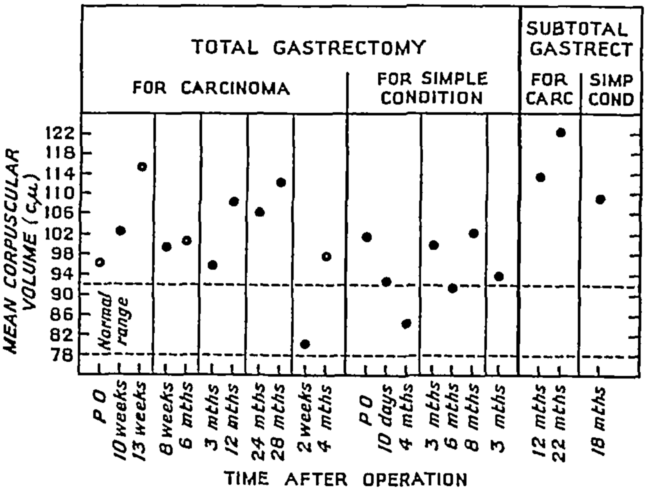


Fig 7—Mean corpuscular volume in 10 cases at various times after gastrectomy P O = postoperative

after operation More detailed preoperative investigation, I feel, would reveal many more instances of incipient macrocytosis, particularly in the carcinoma group In one recent case where an œsophagojejunostomy was performed for a simple stricture, leaving an intact normal stomach in situ, a macrocytosis developed postoperatively

There seems no doubt that this blood picture commonly accompanies other types of steatorrhœa—e g , idiopathic steatorrhœa and sprue—and also vitamin B deficiencies In the present series 6 patients with vitamin B deficiency were found to have macrocytosis and the other 5 are strongly suspect but no absolute blood counts were done because they occurred very early in the series

The question arises whether our present cases of macrocytosis will become megaloblastic some years after operation, a sequel reported by several surgeons and well illustrated by Moynihan's famous case

DEFICIENCY OF VITAMIN B COMPLEX

The present series includes 9 cases of vitamin B deficiencies The diagnosis was made on the clinical observation of glossitis (fig 8) (often ulcerative), pharyngitis, œsophagitis, cheilosis, corneal hypervascularity, and (in 1 case) generalised rash, together with the response to nicotinic acid, riboflavine, and occasionally pantothenic acid The onset has been on the 6–10th postoperative days, except in 2 cases which started three months and one month after operation, the last case coinciding with a large empyema

All the cases that were recognised were cured, but 2 patients early in the series died with gross pharyngitis and œsophagitis so severe that nutrition became impossible

Our present routine is to give large doses of nicotinic acid and riboflavine before and after operation This has reduced the incidence of vitamin B deficiency, though 3 further cases have been encountered which illustrate the important effect of sepsis (fig 9) This seems to be bound up with what we now regard as the ætiology of the condition—rapid multiplication and migration of the organisms in the upper alimentary tract, and a consequent increased demand for the vitamin B complex If infection occurs elsewhere—e g , subphrenic space or pleural cavity—the demand will be even greater, and hence the common association of vitamin B deficiency in these cases with septic complications Thus we now give vitamin-B complex as a routine after gastrectomy, and if signs of vitamin B deficiencies still arise we search for and deal with any focus of sepsis and reinforce the dosage of vitamin B complex

We intend to extend our researches on the intestinal flora after gastrectomy both high up in the jejunum and in the colon, for in the colon steatorrhœa must play a part by permitting a gross proliferation of *Bact coli* where normally these organisms may be destroyed when their vitamin B complex is possibly reabsorbed

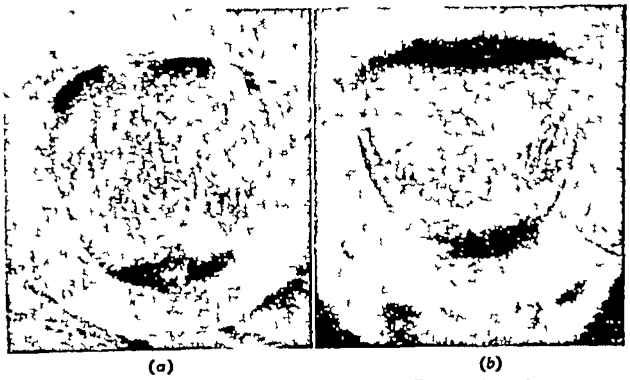

(a) (b)

Fig 8—Glossitis due to deficiency of vitamin-B complex after gastrectomy (a) before and (b) a fortnight after, treatment with nicotinic acid and riboflavine.

CONCLUSIONS AND SUMMARY

A great deal of work remains to be done particularly on the possible defect in the absorption of proteins and carbohydrates On the present evidence, which we have drawn almost entirely from studies of fat metabolism, it seems likely that the main causes of wasting after radical gastrectomy are poor capacity for food associated with the dumping syndrome , and malabsorption of fat

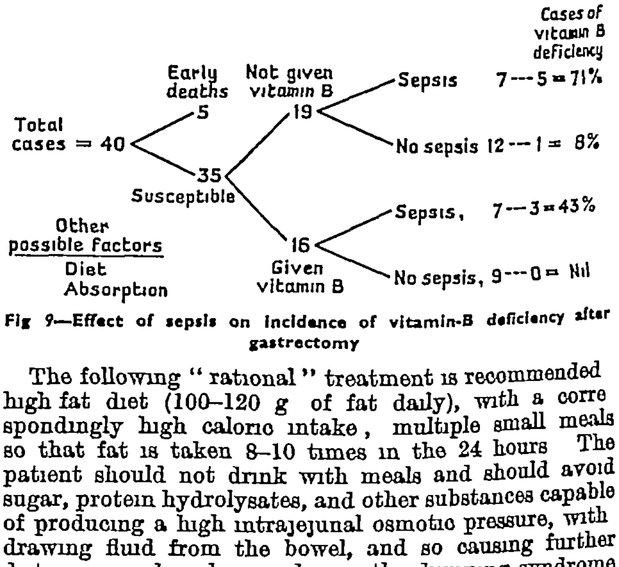


Fig 9—Effect of sepsis on incidence of vitamin-B deficiency after gastrectomy

The following " rational " treatment is recommended high fat diet (100–120 g of fat daily), with a correspondingly high caloric intake , multiple small meals so that fat is taken 8–10 times in the 24 hours The patient should not drink with meals and should avoid sugar, protein hydrolysates, and other substances capable of producing a high intrajejunal osmotic pressure, with further drawing fluid from the bowel, and so causing further distension and perhaps inducing the dumping syndrome (Machella 1949) On this régime some patients in the present series have managed to eat more than their normal preoperative intake and have therefore gained weight

The blood picture after radical gastrectomy is characterised by a high incidence of macrocytosis No evidence of iron deficiency was found

Vitamin B deficiencies can be prevented by the routine administration of vitamin B complex and by the eradication of sepsis

The biochemical estimations were made in the biochemical department of the Queen Elizabeth Hospital and in the pharmacological department of the University of Birmingham I wish to thank Dr Garfield Thomas and Prof A. C Frazer for the advice and assistance rendered by them and their departments, and Dr A L P Peeney for help in hæmatology , Mr A. L d'Abreu, Mr A. Gourevitch, Mr B N Brooke, Mr D M Morrissey and Mr J L Collis, under whose care the patients were admitted, for their coöperation , and Sister Simpson and her nurses at the Queen Elizabeth Hospital for their care of these patients

References at foot of next column

seasickness (a prevention rate of 92%) leaving 4 cases (8%) in which prophylaxis was unsuccessful. These 4 failures included 2 patients who asked for treatment to be continued because they were bad travellers, 1 who admitted having had a "surreptitious" tablet of unknown strength from a friend, and 1 for whom the dose was obviously inadequate but in whom prophylaxis was eventually successful with 25 mg twice daily.

Therapeutic Group

In this group of 274 cases all were treated with 25 mg tablets, given two on the first day of treatment (one immediately and one at night) and one the next evening.

TABLE III—THERAPEUTIC GROUP

Direction of voyage	No of cases	More than 1 visit only	More than 3 tablets only	More than 1 visit and 3 tablets	Treatment successful	Treatment unsuccessful
Out	216	2	7	18	27	189 (*87·5%*)
Home	58	0	5	3	8	50 (*86·2%*)
Total	274	2	12	21	35	239 (*87%*)

In 239 (87%) treatment was successful with one visit and three tablets, and the remaining 35 (13%) required further treatment: 2 required an additional visit only, 12 required additional tablets only, and the remaining 21 required both additional tablets and an additional visit. Among these 35 are included 2 patients visited to investigate reports of possible side effects; 9 requesting, or considered likely to benefit from, prophylactic treatment for the remainder of the voyage; 4 who vomited the first dose; and 20 who had relapsed after a period of freedom from symptoms and asked for further treatment.

SIDE EFFECTS

In only 3 cases were there any side effects which might possibly be related to the treatment.

Case 1.—A frail elderly woman had one 25 mg. tablet at night. The next morning vomiting had stopped, nausea had gone, and she ate a light breakfast in bed. When dressing about two hours later she felt dizzy and could not stand; but after lying down for a few hours she became completely normal.

Case 2.—A well-built young man was confined to bed for three days before calling for help. He had spent the whole of three previous transatlantic voyages in bed. Two 25 mg. tablets were given at 6 P.M., because he was reported to have slight streaks of blood in his last vomitus, and two were left for the next day. He slept until 1 A.M. and then took his remaining two tablets. Nausea and vomiting had gone the next morning and he got up despite severe giddiness lasting some hours.

Case 3.—An elderly woman whose vomiting had been controlled by self-administered dramamine was unable to be up and about, because of drowsiness and dizziness; she was given 10 mg. at night and the next morning while on the sun-deck—five decks above her cabin—she fainted. She recovered spontaneously after lying down for a few minutes.

COMPLICATED CASES

Two types of cases are grouped under this heading: those in which motion sickness was superimposed on some other condition, and those in which other remedies had already been used. The first group included 7 pregnancies, 4 cases of diabetes, 1 systemic vaccinia reaction, 1 patient taking phenobarbitone after operative removal of a brain tumour, 1 person who took anthisan to relieve migraine, 1 case of myxœdema, 1 severe hypertensive with orthopnœa, and 1 woman who had recently undergone a complete perineal repair. In all these cases seasickness was successfully prevented with routine doses.

The second group consisted of 44 patients who were treated because other remedies, either self-administered or prescribed by their doctors ashore or afloat, had failed, or who had asked for treatment because of residual symptoms of seasickness or obtrusive and unpleasant side effects of previous medication. It included 25 persons who had taken other anti-histamine compounds or their derivatives and 17 who had taken one or other of the solanaceous alkaloids; in many of these cases the original drug had been taken irregularly, and often in inadequate doses, after the onset of the premonitory symptoms and even later. Among those who had taken the anti-histamine compounds, nausea and vomiting were controlled to a large extent, but those requesting treatment were confined to their cabins because of drowsiness, dizziness, or headache; one woman was extremely agitated, and another so drowsy and disorientated that she said with some feeling that she would rather have been sick. Among those who had taken alkaloids, nausea and vomiting were often still present, and one woman, a nurse, presented the typical picture of belladonna poisoning—hot flushed skin, dry mouth, and widely dilated pupils. All these cases at the first visit were given avomine in routine prophylactic or curative doses, and none required any further treatment either for seasickness or for side effects.

DISCUSSION

How or why the anti-histamine compounds and their derivatives act, not only in motion sickness but also in a wide range of conditions in which nausea and vomiting are prominent presenting symptoms, can be little more than armchair speculation until the fundamental physiology of nausea and vomiting has been elucidated, and the various pharmacological actions and antagonisms of these new synthetic agents have been more surely assessed.

Their successful use in abolishing these symptoms suggests that the site and mode of action are more likely to be found in the blocking mechanism on the effector side of the reflex arc. Of interest in this connection is the clinical finding that dizziness, whether it be a residual symptom of seasickness or a side effect of the drugs themselves, may remain after the nausea and vomiting have been abolished. Hill (1937) has noted that, in some cases of seasickness treated with amphetamine, partial cures were obtained in which headache and dizziness were abolished while nausea remained. Whether the agent "blocked" be histamine, acetylcholine, or some other substance of importance to the physiological economy of the central or autonomic nervous system, time and experiment must be left to say. In the meantime, the drugs we have are very valuable in controlling nausea and vomiting and so preventing biochemical imbalances and dehydration which result from uncontrolled vomiting.

SUMMARY

'Avomine' (promethazine 8-chlorotheophyllinate) is a safe and effective remedy for seasickness.

In the dosage recommended its side effects are insignificant.

In 92% of cases treated prophylactically and at least 87% of cases treated therapeutically success was achieved with three tablets of 25 mg. given (but not all taken) at one visit.

Prevention or treatment does not seem to interfere in any way with the normal mechanism of adaptation to the disturbing motion.

I wish to thank the directors and the medical superintendent of the Cunard Steam Ship Company Ltd., whose kind coöperation made this trial possible; the ship's doctors, nurses, and dispensers for advice and help; and the stewardesses and stewards for their willing assistance.

References overleaf

premonitory symptoms have appeared In this present trial an attempt was made to divide those passengers who called for aid into prophylactic and therapeutic groups The prophylactic group includes (1) those persons who came for advice before or soon after sailing, (2) those who came at the threatened approach of rough weather, and (3) those who came in the initial stages of their reaction to the ship's motion, when their symptoms were confined to malaise

Most of the therapeutic group were in the later stages of seasickness, and many of them could not leave their cabins, having failed to respond to the ministrations of friends and cabin staff, various forms of self medication, or the remedies prescribed by their own doctors

ROUTINE OF TREATMENT

Dose—Tentative variations of dose from case to case in the early stages of the first outward voyage showed that avomine 10 mg once, or even twice daily, was adequate in some cases but not in others It was also found that avomine 25 mg even when given twice daily was unexpectedly free from the usual anti histamine side effects From these encouraging preliminary observations the routine dosage was adopted of one 25 mg tablet each evening at bedtime for prevention, and, in established cases, two 25 mg tablets on the first day (one when the case was first seen and one the same evening), and a third 25 mg tablet on the evening of the second day

Administration—The tablet was to be placed on the tip of the tongue and rapidly washed down with a small drink In established cases, the patient was advised to stay in bed for one to two hours after the first dose to minimise the chances of the tablet not being retained Otherwise no restrictions were imposed, the patients were encouraged to get up and about as soon as they felt able, and to eat what and when they fancied Many patients were able to retain not only fluids within an hour but also solid food soon afterwards If, as occasionally happened, the first dose was not retained it was repeated immediately The small size of the tablet used, and the ease with which it was swallowed, was appreciated by those in whom nausea was a prominent symptom, and by those who had had experience of larger tablets, or of several tablets at once, on other occasions Children aged 5 years or more were able to take the 10 mg tablets without difficulty and without any unpleasant side effects, some of the heavier children aged 9–12 years were given the same dose as adults from the start Though suppositories had been prepared in readiness, the administration of avomine otherwise than by mouth was not found necessary, and parenteral fluids were not required in any case All patients—the majority of them tourist class—were successfully treated in their cabins, none requiring transfer to the ship's sick bay

Supervision—Since the cases were not evenly spread out over the duration of each voyage but concentrated into the second and third days (out of 372 cases on four voyages, 221 were first seen on the second day out of port and 106 on the third day out), administration of each dose, either personally or by the ship's medical staff, was impracticable To ensure that patients, if not rapidly relieved, would be seen again, and to reduce as far as possible surreptitious transfer of tablets from person to person, only three tablets were left at the first visit

ASSESSMENT OF RESULTS

Rigid assessment of a remedy for seasickness under peace time North Atlantic travel conditions is unsatisfactory for many reasons It is difficult to control the almost endless variables Patients may not cooperate, or if they do and are quickly cured, they may never be seen again Personal follow up of a large number of cases is impracticable when the voyage takes only 5–6 days and most of the patients are seen in the first two days The use of an inert substance as a control is unjustifiable in the case of fare paying passengers who are either on long planned voyages or important business trips Despite these difficulties it was hoped that regular reporting by cabin staff, limitation of tablets to three at a time, and check up of those still in their cabins on the later days would enable some estimate to be made of probable failures Though there are many obvious loopholes the criteria of cure—or perhaps, more accurately, of failure to control—have been taken as the need for more than one visit, or more than three tablets, or both These criteria are far from ideal but provide some measure of the success of any treatment if only from the somewhat selfish point of view of the sick-bay A single visit, at which three tablets are prescribed is not an "unsuccessful" course of treatment for established motion sickness Further visits or additional tablets do not necessarily mean that the original treatment failed, they may indicate a relapse or a request for preventive treatment for the remainder of the voyage The fact that one tablet prophylactically on each of three successive nights, or three tablets therapeutically over 24–36 hours, proved adequate, without continued medication, in such a high proportion of cases suggests that this treatment does not interfere with the normal mechanism of adaptation to the disturbing motion but "blocks" the annoying symptoms so often experienced during the process

ANALYSIS OF RESULTS

The data collected on 372 cases were considered complete enough for tabulation, but in the final tables 48 of these are not included Of this group of 48, 26 were children of various ages Those aged over 5 years had avomine 10 mg, and those aged under 5 years, phenergan 5 mg, 15 were adults treated with 10 mg tablets in the early dosage estimations, and the remainder were given 10 mg doses only, on account of complicating factors or doubt about their symptoms being due to seasickness This leaves 50 cases in which avomine was used for prevention, and 274 in which it was used for treatment

TABLE I—ANALYSIS OF TOTAL CASES

Direction of voyage	No of cases	Day of voyage							Prophylactic cases (table II)	Curative cases (table III)	Other cases
		1	2	3	4	5	6	7			
Out	287	2	201	59	19	5	1	0	35	216	36
Home	85	1	20	47	12	1	3	1	15	58	12
Total	372	3	221	106	31	6	4	1	50	274	48

'Out' and 'Home' = from and to United Kingdom

Prophylactic Group

Of this group of 50 cases, 6 were treated with 10 mg tablets and 44 with 25 mg tablets given one each evening for three successive evenings Of the 6 given 10 mg tablets 5, and of the 44 given 25 mg tablets 41, had no

TABLE II—PROPHYLACTIC GROUP

Direction of voyage	No of cases	More than 1 visit only	More than 3 tablets only	More than 1 visit and 3 tablets	Prophylaxis unsuccessful	Prophylaxis successful
Out	35	0	2	2	4	31 (*88 5%*)
Home	15	0	0	0	0	15 (*100%*)
Total	50	0	2	2	4	46 (*92%*)

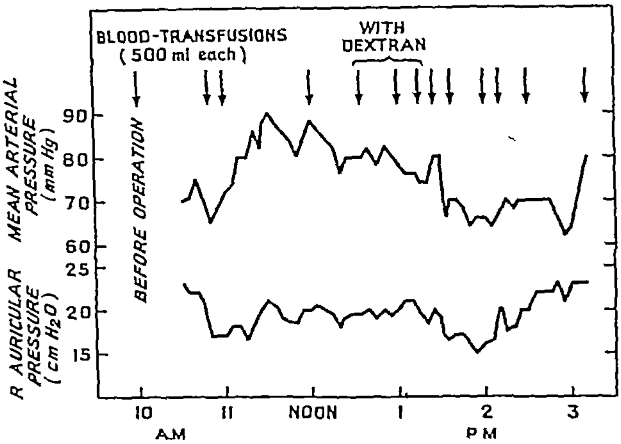


Fig 9—Blood pressure and right auricular pressure during hindquarter amputation in a man aged 59

arterial blood pressure at the end of a total gastrectomy lasting five hours was virtually the same as it was during the pre anæsthetic period On four separate occasions during the operation the mean blood pressure fell to 75, 90, 85, and 78 mm Hg, but on each occasion it was rapidly restored by blood transfusions of 175, 325, 300, and 300 ml at rates varying from 90 to 325 ml a minute The greatest rise in right auricular pressure was 11 cm of saline solution and was only temporary

Fig 9 shows the blood pressure responses and the right auricular pressures in a patient transfused intra arterially The mean blood pressure at the beginning of the operation was only 70 mm Hg At the end of a lengthy major operation the mean blood pressure was 80 4 litres of blood and 1 5 litres of dextran were given intermittently during the operation The right auricular pressure was never raised above its pre anæsthetic level

CONCLUSIONS

The replacement of rapid and severe blood loss at rates similar or equal to the rate of loss may, on occasion, be a life saving procedure Our experience leads us to state that transfusion at rates up to 350 ml. per minute can be effectively achieved with a rotary pump and is safe, provided that care is taken to ensure that not more than 70% of the estimated blood loss is replaced rapidly A raised venous pressure is a warning to stop the transfusion

SUMMARY

The rationale is given for the use of rapid transfusion Circulatory collapse from severe hæmorrhage—e g , during operations on the heart, large blood vessels of the body, and vascular tumours—must be rapidly treated if irreversible shock is to be avoided

The fluid mechanics and dynamics of transfusion are presented

Limitations of rapid replacement by standard gravity techniques are explained only 70 ml. of stored blood can be transfused intravenously in one minute through a single large Hamilton Bailey cannula if gravity alone is used and the height of the reservoir is 4 ft (the usual height of a transfusion bottle above a patient)

Blood replacement at a rate greater than 70 ml. per minute requires either multiple transfusions or some form of pressure delivery

The use of a rotary pump and a large Hamilton Bailey cannula allows delivery of 350 ml. of blood per minute at a pressure of 440 mm Hg

A simple straight silver cannula of special design allows delivery of 350 ml of blood per minute at a pressure of 120 mm Hg

The dangers of rapid pressure transfusion are discussed Replacement at a rate of 350 ml per minute increases the normal stroke volume of the heart by only about 9% and has proved safe A raised jugular venous pressure is evidence of overloading of the circulation and is an indication to stop the transfusion The risk of air embolism is minimal if a rotary pump is used, and hæmolysis is not a direct complication of the method Local venous thrombosis is a common sequel of pressure transfusion but is not serious

Not more than 70% of the estimated blood loss should be rapidly replaced in the presence of vasoconstriction The remainder should be given slowly

Pressure transfusions were given to twelve patients undergoing major surgery, intravenous and intra arterial routes were used Restoration of blood pressure followed rapid replacement of blood and was achieved without untoward sustained increases of pressure in the right auricle of the heart

The rotary pump has been made available to us by the kindness of Mr Schranz, of the Genito Urinary Company, London, W 1.

REFERENCES

Aird I (1949) A Companion in Surgical Studies Edinburgh
Barcroft, H Edholm, O G (1945) *J Physiol* 104, 161
Churchill E D (1948) *Ann Surg* 128 799
Dodge R A Thompson M J (1937) Fluid Mechanics New York and London
Glaser O Page I H (1948) *Amer J Physiol* 154 297
Gregersen M. I (1941) in McCleod s Physiology and Biochemistry in Modern Medicine 9th ed St Louis , p 1078
Holden W D Cole J W , Portmann A F (1950) *Surg Gynec Obstet* 89 455
McMichael J (1944) *J Amer med Ass* 124 275
Pierce V K Robbins, G E Brunschwig A (1949) *Surg Gynec Obstet* 89 442
Riddell V H (1939) Blood Transfusion London
Robbins M A Olson W H Rolnick H C (1950) *Surgery* 27 254
Walton, J N (1947) *Lancet* 1 662
Zweifach B W (1950) *Circulation* 1 433

SICKLE-CELL ANÆMIA IN GREECE

C Choremis
M D Athens
PROFESSOR OF PÆDIATRICS

N Zervos
M D Pisa
ASSOCIATE PROFESSOR OF PÆDIATRICS

UNIVERSITY OF ATHENS

V Constantinides
M D Athens
REGISTRAR

L Zannos
M D Athens
RESIDENT MEDICAL OFFICER

ST SOPHIA S HOSPITAL FOR CHILDREN

Sickle cell anæmia is usually regarded as essentially peculiar to the Negro race Sporadic cases have been described in white people, but in many of them it has been impossible to rule out admixture with Negro blood Such cases have been mostly in Americans of Greek or Italian origin (Wintrobe 1946), but a few cases have also been described in Italy (Powell et al. 1950) and Greece (Makrycostas 1940, Zaberdinos 1950, Comninos et al. 1950)

We now report the discovery of foci of sickle cell anæmia in villages situated around Lake Copais * It was so common that the villagers gave it a special name —*kokkali*, from *kokkalo* meaning " bone " *in colloquial* Greek, probably because of the characteristic pains in the joints

We visited one of these villages, Petromagoula,† and examined 11 children and 10 of their parents, indicated to us by the local physicians Besides a careful clinical examination we made blood counts and examined their blood in dry smears and wet preparations sealed with soft paraffin Sickle cells were found in the wet preparations from 12 persons, of whom 9 were children The case records are summarised below and easy flow Acute bends or kinks in the tubing are to be avoided, and the drip nozzle in the drip chamber should be of the same internal diameter as the rubber tubing of the system Ideally, the cannula or needle should slope gently, as in the French's type of needle, while the connecting tubing should fit over the outside of the needle shank

---

* *Copais* was a swamp which was dried out by an English company a few years ago The neighbouring villages comprised one of the most malaria stricken areas of Greece

† The ancient town of Orchomenos

Such recommendations are equally applicable both to rapid and to slow transfusion techniques, and their adoption would tend to minimise the risk of spontaneous stoppage in slow drip transfusions (Walton 1947)

Provided that these refinements of technique are adopted, then with the usual pressure of 100 mm Hg (or a head of water 4 ft —the average height of a transfusion bottle above a patient), 125 ml of saline solution, or 70 ml of stored blood, can be delivered in a minute through a large Hamilton Bailey cannula To increase this rate of transfusion it is necessary either to increase the pressure or to use more than one cannula If the pressure is raised to 280 mm Hg, 350 ml of saline solution can be delivered in one minute, to deliver blood at this rate the pressure must be raised to 440 mm Hg If the pressure is not increased above 100 mm Hg, four large Hamilton Bailey cannulæ are needed to deliver blood at a rate of 280 ml a minute

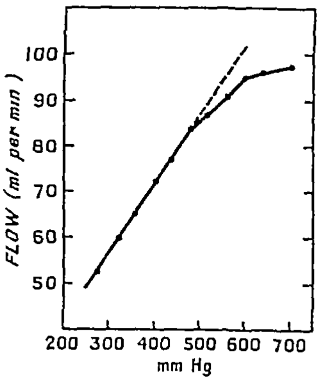


Fig 6—Flow through Luer needle 20 g × 1½ in, showing critical pressure beyond which rate slows

The flows referred to occur only if there is free outflow beyond the cannula Vascular spasm will cause a considerable diminution in rate of the transfusion if gravity alone is used For this reason we prefer to use a rotary pump, modified from Riddell (1939), and connected by rubber pressure tubing to a cannula of silver tubing 0 063 in in internal diameter With this equipment (fig 7) a flow of 350 ml of blood per minute can be obtained at an operating pressure of 120 mm Hg, and the rate of flow is not affected by variation in resistance to the outflow Such a system may be used equally well for intravenous or intra arterial transfusion

DANGERS OF RAPID TRANSFUSION

The risk of overloading the heart by a high speed transfusion is not so great as might first appear, for, even if the rate of transfusion is 350 ml a minute, the normal stroke volume of the heart is increased by only some 9%, and, when the stroke volume has become less than normal as a result of hæmorrhage, the extra amount of blood provided by the transfusion will hardly do more than make up for the acute deficiency

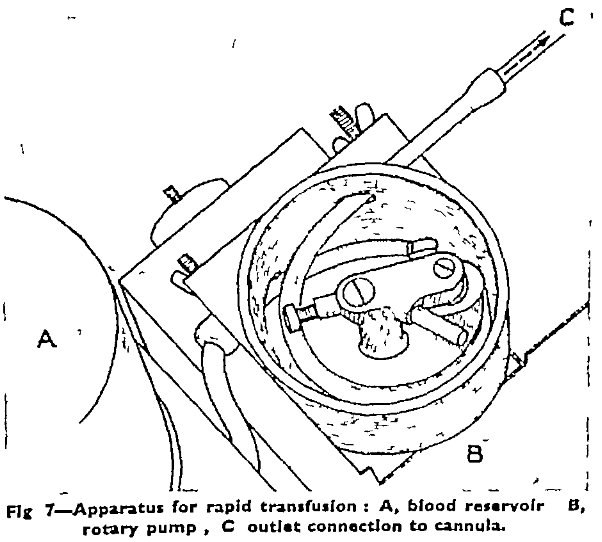


Fig 7—Apparatus for rapid transfusion : A, blood reservoir B, rotary pump, C outlet connection to cannula.

The danger of overloading the circulation by excessive transfusion has been re emphasised by Holden et al (1950) A rapid increase above normal in the total circulating blood volume is reflected by a rise in venous pressure and may be followed by serious cardiac embarrassment, especially if the myocardium is unhealthy or ischæmic To avoid such risk it is important to ensure that the amount transfused does not exceed the blood loss A raised jugular venous pressure must be taken as a warning to stop the transfusion

Glaser and Page (1948) have shown, in animals made hypotensive by hæmorrhage, that intra arterial transfusion of blood in amounts not greater than 70% of the blood loss is sufficient to restore the blood pressure fully, if greater amounts are given in the presence of compensatory vasoconstriction, irregular cardiac action and cardiac failure may develop This principle should be accepted for man, and only 70% of the estimated blood loss should be rapidly replaced, the remainder should be given slowly as vasoconstriction decreases and the patient's pallor disappears

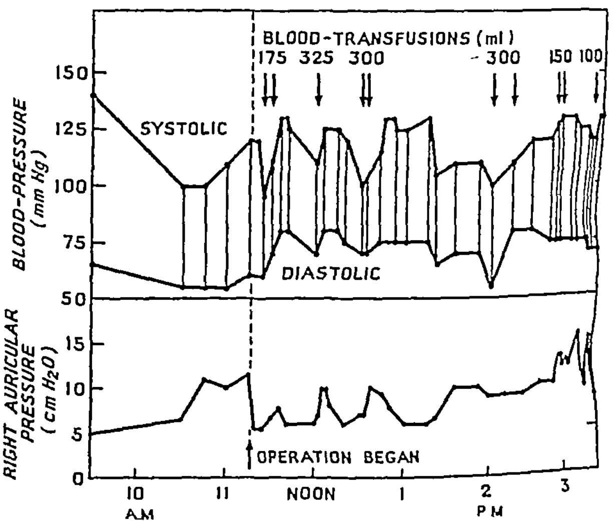


Fig 8—Blood pressure and right auricular pressure during total gastrectomy in a woman aged 68

Hæmolysis resulting from the action of a rotary pump driving the blood is negligible, but we have, on one occasion, seen a severe degree of hæmolysis following transfusion of a large volume of stored blood, a sequel not necessarily due to the method An excess of serum bilirubin may prove dangerous if pre existing liver damage is present, but the risk of renal tubular blockage by blood pigments can be discounted if protracted hypotension is avoided and adequate fluid replacement is maintained (Robbins et al. 1950) Air embolism should never occur if the rubber tubing is sound and the reservoir is never completely emptied Local venous thrombosis is a common sequel of pressure transfusion (Aird 1949), but in our experience it is not a serious complication

PERSONAL EXPERIENCE

Twelve patients have been transfused with the cannula and rotary pump described Nine transfusions have been given into veins at the elbow and three into radial arteries

Fig 8 shows the blood pressure responses and the right auricular pressures in a woman, aged 68, who was transfused intravenously It can be seen that the mean cases (leaving out the 5 from the neighbouring villages) to the previous 9, we have 15 children, or 0 25% of the population, suffering from sickle cell anæmia, compared with about 0 2% in the Negro race in America We are undertaking a study of the incidence of the sickle cell trait in Petromagoula Our findings up to the present moment seem to confirm the high incidence of the disease in this village

REFERENCES

Comninos D Bacalos, D Katsirumbas P (1950) *Bull Athens med Soc* April *Ibid* November
Makrycostas K (1940) *Wien Arch inn Med* 33 339
Powell W N, Rodarte J G, Neel, J V (1950) *Blood* 5 887
Wintrobe M M. (1946) Clinical Hematology Philadelphia
Zaberdinos, A (1950) *Scient. Union Evangelismos Hosp* Feb 24

STENOSING TENDOVAGINITIS AT THE RADIAL STYLOID PROCESS

REVIEW OF THIRTY CASES

D A C Reid
M B Lond, F.R C S

SENIOR REGISTRAR IN PLASTIC SURGERY, ROOKSDOWN HOUSE BASINGSTOKE, LATE SURGICAL REGISTRAR, HASLEMERE AND DISTRICT HOSPITAL

STENOSING tendovaginitis at the radial styloid process, though characterised by well defined signs and symptoms, is often wrongly diagnosed as "sprained wrist" (the patient often gives a history of injury), fracture of the scaphoid, neuritis, or rheumatism

De Quervain (1895) was the first to recognise and describe this condition, reporting 5 cases, 2 of which showed, at operation, the typical fibrous thickening of the tendon sheath He later reported 8 more cases, all of which responded to surgical treatment Hoffman (1898) also described the condition

Winterstein (1927) reviewed 154 cases, and Finkelstein (1930) recorded 24, all of which were operated on after failure of conservative treatment

Brown (1935) was the first to report a case in this country Clinically it appeared to be typical, but operation was refused The pain was relieved by immobilising the wrist in plaster, but recurred subsequently necessitating further periods of immobilisation

Burns and Ellis (1936) reported 28 cases

ÆTIOLOGY

Most of the patients are women and of the present series of 30 only 4 were males The ages ranged from 14 to 78, average 42 Of Finkelstein's (1930) 24 patients, 20 were women, and the majority were houseworkers The underlying cause appears to be chronic or repeated trauma, rarely is there a history of acute onset following injury The main incidence in women doing routine housework seems to be significant It is easy to understand that repeated trauma could cause inflammation of the tendons lying directly on the bone at the wrist and bound down by the extensor retinaculum Eichhoff (1927) explains that the cause in many cases seems to be a constantly repeated movement of the wrist, especially in adduction with the thumb fixed in grasping some object, when the affected tendons are stretched over the radial styloid process and maximally constricted This happens typically in wringing—an action very often used by the housewife

Of the 26 females in the present series 13 were housewives and 6 others were employed in housework, 2 were schoolgirls, and the remaining 5 included 1 nurse, 1 typist, 2 clerks, and 1 mill worker The 4 males were a sanatorium nurse (incidentally an amateur lawn tennis champion), a painter, a gardener, and a post office engineer Although no examples occur in this series, stenosing tendovaginitis is often seen in physiotherapists

Some of the patients attributed their symptoms to particular types of work—e g excessive gardening, machinery, and routine housework—and 10 attributed their symptoms to an injury

ANATOMY

The tendons affected are those of the abductor pollicis longus and extensor pollicis brevis muscles These two tendons have a common synovial sheath lying in very close contact at the wrist, the extensor being to the inner side of the abductor Where the sheath is thickened they lie in a groove on the lateral aspect of the lower end of the radius and are held close to the bone by the attachments of the extensor retinaculum

PATHOLOGY

As already described, the condition is thought to result from repeated trauma Initially this gives rise to œdema of the tendon sheath, which later becomes permanently thickened from dense fibrosis In the most advanced cases the thickened sheath has an almost cartilaginous consistence This thickening of the sheath compresses the tendons, which tend to become constricted and flattened Apart from this purely mechanical phenomenon, the tendons are not involved in the pathological process

The mesotendon is often thickened, and, together with the sheath enveloping the tendons, is often dull grey and less transparent than the normal synovial lining, this gives the tendons a dull lustreless appearance very different from the glistening transparent appearance of healthy tendons

On exposure at operation the affected part of the sheath appears as a pearly white thickening Microscopy of the hypertrophied sheath reveals fibrosis Sometimes there is slight cellular infiltration suggesting non specific inflammation Sometimes the thickened sheath is lined with granulation tissue, and the amount of fluid in the tendon sheath is often increased

CLINICAL FEATURES

The onset of symptoms is usually gradual The patient may attribute the disability to a sprain or some other trivial injury A continuous dull nagging pain, aggravated by movements of the thumb and wrist, is felt over the radial aspect of the wrist and extends to the dorsum of the thumb and into the forearm The site of maximal pain is localised by the patient accurately to the radial styloid process

Examination reveals a definite hard swelling felt on palpation over the radial styloid process, and not infrequently visible Passive movements of the thumb, particularly extension and abduction, and adduction (ulnar deviation) of the wrist, cause severe pain Excruciating pain on adduction of the wrist with the thumb flexed is pathognomonic, according to Finkelstein (1930)

DIFFERENTIAL DIAGNOSIS

Crepitus is not elicited on movement, this fact distinguishes the condition from traumatic tenosynovitis

True bony injuries—e g, fracture of the scaphoid—are excluded by radiography, which in stenosing tendovaginitis is usually negative, but Schneider (1928) reported finding calcium salts deposited near the lesion in some of his cases, and Brown (1935) found radiological evidence of periostitis—newly formed bone—just above the styloid process

Neuritis of the terminal branch of the radial nerve may give rise to a similar distribution of pain, but it will probably be associated with a corresponding area of hyperæsthesia Moreover the nerve can be palpated as it crosses to the dorsal aspect of the wrist $1^1/_2$ in above the radial styloid process This aggravates the pain, which is unaffected by movements of the thumb

CASE RECORDS

Case 1—A boy, aged 18 months, was subject to periodic painful œdema of the forearms and lower legs His conjunctivæ were slightly icteric, and his mucosæ very pale The spleen was palpable three finger breadths below the left costal margin

Red blood cells numbered 3,700,000 per c mm, and white cells 6700 A dry blood smear (fig 1) showed conspicuous anisocytosis, with many target and oval cells A wet preparation examined after twenty four hours showed many sickle cells

Case 2—A boy, aged 9 years, was subject to periodic œdema and pain in the joints and long bones His skin was pale The spleen was not palpable, but the liver could be felt two finger breadths below the right costal margin

Red cells 2,500,000 per c mm, and white cells 10,400 Dry blood smears showed moderate hypochromia and anisocytosis, with more than 40% target cells, 5–6% oat cells, and rare sickle cells Wet preparations showed sickle cells ten minutes after the blood had been taken

Case 3—The mother of case 2 had no relevant past history, and physical examination was negative A wet preparation showed sickle cells after twenty four hours

The father's blood was also examined in a wet preparation, but no sickle cells were found, even after three days

Case 4—A boy, aged 14, had had pains in the joints and long bones until four years ago Since then he had felt well His spleen was not palpable, but the liver extended three finger breadths below the right costal margin

Red cells 4,800,000 per c mm, and white cells 8000 A dry smear showed more than 50% ovalocytes, and rare target and sickle cells A wet preparation showed sickle cells

Case 5—A boy, aged 1, had no relevant past history His spleen was palpable, one finger breadth, and liver two finger breadths, below the costal margin The liver was hard

A dry blood smear showed normal red cells A wet preparation, examined after twenty four hours, showed sickle cells

Case 6—The mother of case 5 provided a wet preparation showing sickle cells Her husband was not examined

Fig 1

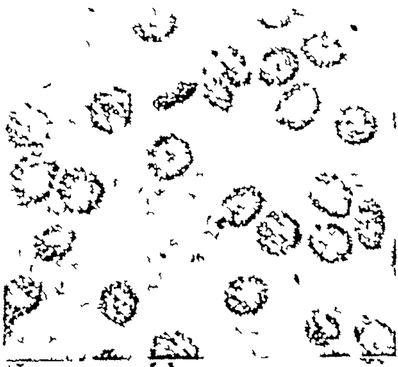
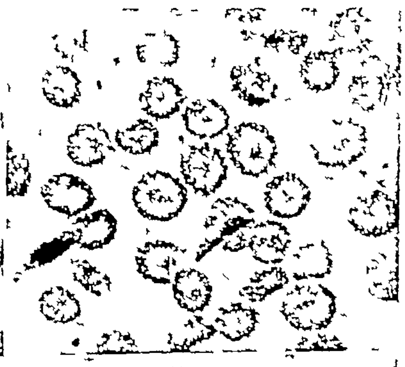


Fig 2



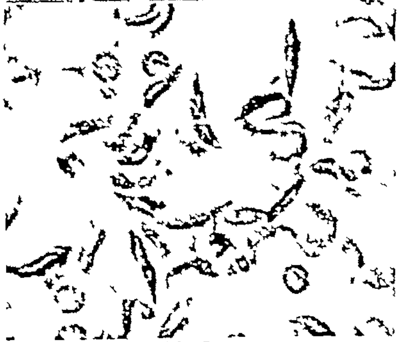


Fig 3

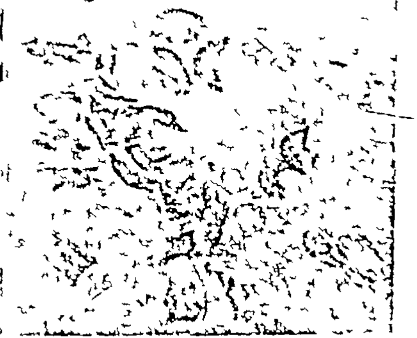


Fig 4

Fig 1—Dry blood smear from case 1 showing anisocytosis, with target and oval cells

Fig 2—Dry blood smear from case 7, showing anisocytosis target cells and oat cells.

Fig 3—Wet blood preparation from case 7, showing sickle cells.

Fig 4—Wet blood preparation from case 9 showing sickle cells

Case 7—A girl, aged 5, was very pale and had had pains and œdema of the joints for a year Her liver was hard and palpable three finger breadths below the right costal margin

Red cells 2,200,000 per c mm, white cells 7600 A dry smear (fig 2) showed obvious anisocytosis, macrocytosis, and hypochromia, more than 20% target cells, and about 10% elongated red cells A wet preparation (fig 3) showed sickle cells

Case 8—The twin sister of case 7 was subject to periodic fever and pains in the joints Her mucosæ were very pale and the conjunctivæ slightly icteric Cheek-bones prominent nose flat Her spleen was not palpable, but the liver extended three finger breadths below the costal margin and was very hard

Red cells 1,800 000 per c mm, and white cells 11,000 A dry smear showed obvious anisocytosis and 20–30% target cells A wet preparation showed sickle cells

Case 9—A girl, aged 18, had had, since the age of 2 months pains in the joints, long bones, and abdomen Menstruation had started at the age of 15 One of her brothers had died with anæmia and pains in the joints Her liver and spleen were palpable two finger breadths below the costal margin

Red cells 4,000,000 per c mm and white cells 10,000 A dry smear was unsatisfactory A wet preparation (fig 4) showed sickle cells

Case 10—The mother of case 9 provided a wet preparation which showed sickle cells, but the father of case 9 had no sickle cells

Case 11—A boy, aged 12, had had pains in the joints for some years His liver was palpable two finger breadths below the costal margin, but his spleen was not felt

Red cells 3,300,000 per c mm and white cells 5800 A dry smear showed slight anisocytosis, rare target cells, and about 10% ovalocytes A wet preparation showed sickle cells.

Case 12—A boy, aged 13, had had periodic pains in the joints and long bones The mucosæ were pale, and conjunctivæ slightly icteric Cheek bones prominent, nose flat. The spleen was palpable three finger breadths, and the liver one finger breadth, below the costal margin

Red cells 4,500,000 per c mm, and white cells 9600 A dry smear showed 4–5% target cells A wet preparation showed sickle cells

CONCLUSION

So great a number of cases of sickle cell anæmia among whites in a small area has never been described before, and raises several questions (1) Are malaria and chronic undernourishment ætiological factors in this disease? (2) What is the anthropological significance of the occurrence of sickle cell anæmia among Greeks? (3) In order to have sickle cell anæmia, is it indispensable to be homozygous for the sickle cell trait? (4) Can the sickle cell trait and the Cooley anæmia trait, which is so common among Greeks, interact and produce sickle cell anæmia in the carrier of both traits?

ADDENDUM

Since this article was completed we have found in Petromagoula 11 more children with sickle cell anæmia Of these 11, 5 were from neighbouring villages Only one parent was found to be positive for the sickle cell trait. The histories, physical findings, and dry smear preparations of blood were similar to those already described in the previous cases We also estimated total serum bilirubin, and found values above normal (0 6 mg per 100 ml) in 9 of these children, 5 of whom had values above 1 2 mg per 100 ml

Petromagoula has about 6000 inhabitants Thus if we add these 6 new

The results of surgical treatment are excellent

A case is also described in which a similar condition affected the flexor carpi radialis tendon at the wrist

I am extremely grateful to Mr Gerald N Golden, F.R.C S, for permission to publish his cases and for his help in preparing this paper

REFERENCES

Brain W R, Wright A D Wilkinson M (1947) *Lancet*, i 277
Brown W M. (1935) *Brit Med J* ii 538
Burns B H Ellis V H (1936) *Lancet* i 717
De Quervain, F (1895) *KorrespBl schweiz Ärz.* 25 389
Eichhoff E (1927) *Beitr klin. Chir* 139 746
Finkelstein H (1930) *J Bone Jt Surg* 12 509
Hoffmann P (1898) *Trans Amer orthop Ass* 11 252
Schneider C C (1928) *Surg Gynec. Obstet* 46 846
Winterstein O (1927) *Münch med Wschr* 74 12

"TENNIS THUMB"

TENDINITIS WITH CALCIFICATION IN FLEXOR POLLICIS LONGUS

MICHAEL C OLDFIELD
M.B.E D.M. M.Ch Oxfd F R C S
SURGEON, GENERAL INFIRMARY AT LEEDS

ACUTE tendinitis with calcification in the supraspinatus and other tendons near the shoulder-joint is fairly common, and has been recognised since Painter's original account of the condition in 1907 and Wrede's confirmation of it in 1912 But calcification near the insertion of other tendons has been less often reported

CASE REPORT

History—My patient was a schoolgirl aged 15, who was right handed During the summer of 1949 she was in her school tennis team and played strenuously and often. Before the end of the term she noticed ' a lump under the ball of the right thumb At first it did not cause any pain, nor did it interfere with tennis or writing It gradually increased in size, and she noticed that it looked white ' Later it became tender and caused discomfort when she was gripping her racquet At the end of the term she went on holiday to France for three weeks Though she only played tennis three times while she was there the lump remained tender

On returning home, she had acute tonsillitis and was in bed for ten days After recovering from this she returned to school One day quite suddenly while she was doing lessons, she noticed that her thumb was generally swollen In the evening it became more swollen and painful Pain was so severe during the night that she could not sleep and her mother poulticed her thumb but the pain became worse Next day treatment with intramuscular procaine penicillin was started

Examination (Sept 26 at Dewsbury Infirmary)—The patient was in excellent general condition Temperature 98°F, pulse rate 86 respirations 24. Her right thumb was held in semiflexion and was generally swollen and inflamed The redness, induration swelling, and tenderness were greatest on the volar aspect Flexion and extension at the interphalangeal and metacarpophalangeal joints were limited and painful The movements of the other fingers and wrist were unaffected There was no swelling or tenderness in the palm or above the wrist The supratrochlear and axillary glands were not tender nor enlarged

X ray examination of the right thumb showed irregular calcification in the course of the flexor pollicis longus tendon over the proximal phalanx and the base of the distal phalanx (fig 1) X ray examination of the left thumb and chest revealed no abnormality The erythrocyte sedimentation rate (Wintrobe corrected) was 1 mm. in 1 hour The Wassermann and Kahn reactions were negative

Treatment—The right thumb and wrist were immobilised by a plaster of paris slab in the position of rest ' with the wrist somewhat dorsiflexed and the thumb semiflexed The right hand was supported in a sling Intramuscular procaine penicillin 300 000 units was given twice a day for ten days The pain disappeared within twenty four hours and the redness and swelling gradually subsided during the next two weeks On Oct 5 a new plaster slab was applied and the patient was allowed to go home but was asked to attend regularly as an outpatient On Nov 1 she returned to school with her right thumb immobilised by the plaster slab

The plaster was removed on Jan 3, 1950, when radiography showed that the calcification had almost disappeared (fig 2) The range of flexion and extension at the interphalangeal joint of the right thumb was only 10° less than that of the left

On Feb 14 1950, movements of the right thumb were natural and radiography showed that all abnormal calcification had disappeared (fig 3)

On Feb 14, 1951, the right thumb was as mobile and as strong as the left and there had been no pain or disability during the past year X ray examination showed no calcification in the region of the flexor pollicis longus tendon, and the patient was told that she could start playing tennis again next season

DISCUSSION

Tendinitis with calcification, though commonest near the insertion of the supraspinatus above the shoulder, can probably occur in almost any tendon and has been reported in the tendons round the elbow, wrist, hip, knee, and foot (Lapidus 1943) I have not found any record of calcification in the flexor pollicis longus, but Winchester and Mekie (1947) described calcification of the flexor carpi ulnaris near its insertion into the pisiform bone

Their patient was a male clerk, aged 42, and they suggested that repeated trauma, by pressure on the tendon when writing might have been the cause of the trouble On incision " yellow pultaceous gritty material ' was removed from within the tendon.

The most likely cause of the calcification is repeated friction or small strains Single sudden sprains and septic infections, such as tonsillitis, have also been suggested as occasional ætiological factors (Codman 1906)

Treatment in the acute stages is by rest and immobility Massage and movement are harmful, but short-wave therapy may relieve pain Open operation with incision of the tendon and evacuation of the gritty pultaceous material (containing calcium carbonate and calcium phosphate) has been practised with success (Codman 1906, Painter 1907, Emslie 1932, Winchester and Mekie 1947) but seems unnecessary Injection of 2% procaine

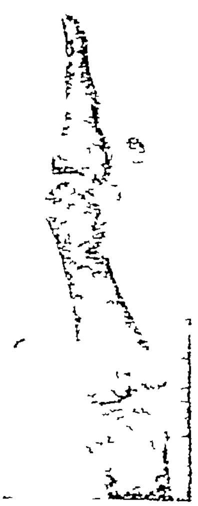


Fig 1

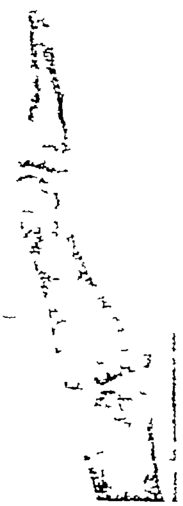


Fig 2

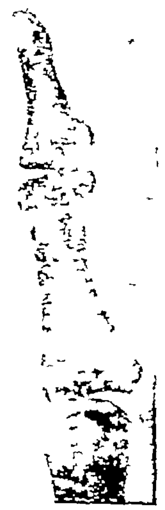


Fig 3

Fig 1—Radiograph Sept. 26 1949 Calcification in terminal portion of right flexor pollicis longus tendon.

Fig 2—Radiograph Dec. 12 1949 Showing that the calcification in the tendon has almost disappeared but there is a small nodule of exuberant bone present at the insertion of the tendon into the base of the distal phalanx.

Fig 3—Radiograph Dec. 19 1950 Calcification in the tendon has disappeared but the excrescence of bone is still present at the insertion of the tendon into the terminal phalanx.

TREATMENT

A case which presents the well defined syndrome as outlined above should, in my opinion, be treated surgically Only the acute case should be treated conservatively either by immobilisation in plaster or by physiotherapy—e g , short wave diathermy and wax baths

In chronic cases the condition is progressive and conservative measures usually fail to relieve the symptoms Even if temporary relief is achieved, cure cannot be effected by these means One of the cases in this series was referred after an unsuccessful period of plaster immobilisation , in 4 other cases conservative measures brought no improvement and operation had to be advised It seems unjustifiable to withhold surgical treatment for a condition which responds to it so readily In 28 of my 30 cases operation was advised, and in 28 it was performed

Operation

The skin over the site of operation is prepared two days before operation and again on the morning of operation After premedication with atropine sulphate gr $^{1}/_{100}$, a short general anæsthesia is obtained with thiopentone, nitrous oxide, and trichlorethylene This allows the application of an Esmarch bandage, which ensures a bloodless field for the operation As an alternative, regional anæsthesia produced by blocking the brachial plexus with 'Anethaine' is very satisfactory This method has been found useful in one or two elderly patients whose general condition precluded general anæsthesia

A small longitudinal incision, 2 in long, is made over the radial styloid process Care should be taken to avoid the terminal branch of the radial nerve as it crosses the tendons on to the dorsal aspect of the forearm about $1^{1}/_{2}$ in above the wrist joint, and the digital branch it gives off to supply the skin over the radial side of the thumb These nerves should be defined and suitably retracted The thickened tendon sheath is exposed and incised in the same line This incision should extend into normal sheath both above and below the thickened area, and a strip of the hypertrophied part should be completely excised This ensures that the tendons are no longer constricted, a fact which can readily be demonstrated by passively extending and flexing the thumb The wound is then sutured and a pressure bandage applied

RESULTS

The results of this small operation are uniformly excellent The patient can use his thumb fully without pain, and often notices complete relief immediately after operation

Two of Finkelstein's (1930) patients still complained of pain on pressure over the styloid process ten and eleven months after operation In both of them the tendon sheath was cartilaginous in consistence They were treated in the usual way by the removal of a strip of thickened sheath Finkelstein recommended that in such cases, which are most advanced an even better result could be ensured by the removal of the entire circumference of the sheath This was unnecessary in the present series

In all the 28 cases treated by operation (in 3 the condition was bilateral) the immediate result was excellent, the symptoms being completely relieved Reviewed after periods ranging from a few months to three and a half years only 2 cases show results not altogether satisfactory

A girl, aged 14, still complains of weakness and pain in both wrists, although she only had slight thickening of the tendon sheaths at operation

A woman, aged 53, still complains of numbness and vague pains in both wrists She is neurasthenic, and her symptoms are consequently difficult to assess

The 2 patients not treated by operation had mild symptoms These were temporarily relieved by physiotherapy but the pain comes back from time to time

DISCUSSION

Stenosing tendovaginitis at the radial styloid process is somewhat allied to trigger finger, in which a thickening develops, in the sheaths of the flexor tendons to the fingers, over the metacarpal heads in the palm of the hand The thickened sheath constricts the enclosed tendons and impedes their action Immediate relief is afforded by division of this thickened sheath

I have known a similar thickening to develop in the sheath of the flexor carpi radialis muscle at the wrist

A housewife, aged 52, had had for six months a painful swelling, over the anterior surface of the wrist, which was getting worse There was no history of injury She had had an exactly similar swelling in the left wrist eleven years previously This had been explored, but it was said that nothing abnormal was found

On examination a very tender swelling was found about the size of a finger tip, over the tubercle of the scaphoid Radiography was negative Immobilisation of the wrist in plaster having procured no relief, operation was undertaken The sheath of the flexor carpi radialis tendon was found to be much thickened and the tendon to be constricted The sheath was incised and part of the thickened area excised The flexor retinaculum was not thickened, and the median nerve was not compressed The patient made a good recovery

Histological examination of the thickened sheath revealed the presence of plasma cells and an appearance such as would result from a long standing inflammation

These three conditions—stenosing tendovaginitis at the radial styloid process, trigger finger, and thickening of the flexor carpi radialis tendon sheath—are manifestations of the same pathological process—namely, thickening and stenosis of the tendon sheaths, due to fibrosis, possibly the result of a low grade inflammation Though the precise ætiology is debatable, the consensus of opinion is that the condition is largely due to repeated trauma I do not think that stenosing tendovaginitis of the flexor carpi radialis (as described above) has previously been recorded, but Finkelstein (1930) observed similar changes in the sheaths of the extensor carpi ulnaris, flexor pollicis longus, and the extensor pollicis longus tendons

The syndrome of median nerve compression at the wrist described by Brain et al (1947) is a separate condition in which the median nerve is compressed by the flexor retinaculum (annular ligament) at the wrist as it lies in the carpal tunnel Various degrees of median nerve palsy arise, and the condition is relieved by surgical division of the flexor retinaculum

In the case described above in which tendovaginitis affected the flexor carpi radialis tendon, the flexor retinaculum was not thickened and the median nerve showed no evidence of compression, being normal in appearance Median nerve compression at the wrist would, because of similar subjective symptoms, enter into the differential diagnosis

SUMMARY

Stenosing tendovaginitis at the radial styloid process is usually a chronic condition, found mostly in women employed in housework

The patient very often gives a history of injury

The tendon sheaths are locally thickened and compress the tendons of the abductor pollicis longus and extensor pollicis brevis muscles

Conservative treatment should be applied only to the rare acute case following trauma

The established case should be treated by incision of the tendon sheath and excision of that part of it which is thickened

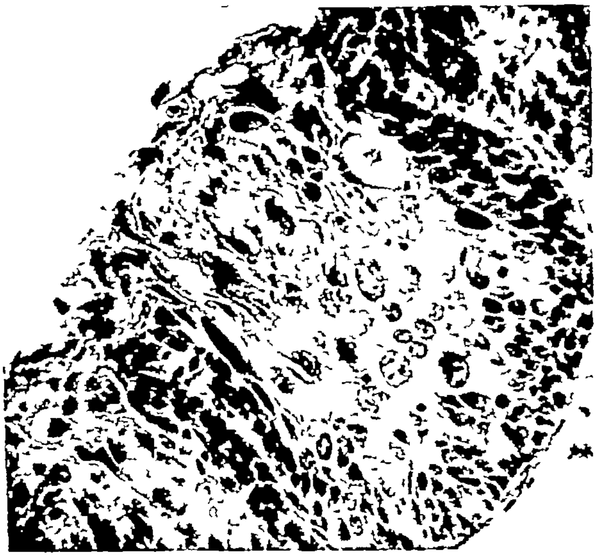


Fig 4—Malignant squamous epithelium (× 270)

Traut (1941), or in surface biopsies from the cervix, as suggested by Ayre (1947), is leading to the discovery of a new crop of early cancers, even by those with no special intensive training, though naturally a lower incidence of errors follows from training and long experience The smear or surface biopsy could be arranged for every woman at a gynæcological clinic, whatever her complaint, and should probably be done in every parous woman over 30 who is admitted to a gynæcological ward for any reason Many hospitals in the U S.A do not now undertake cauterisation of the cervix until malignancy has been excluded so far as possible by smear or biopsy But the interpretation of these smears can be both difficult and time consuming, and is so far only being undertaken in a few of our larger teaching centres

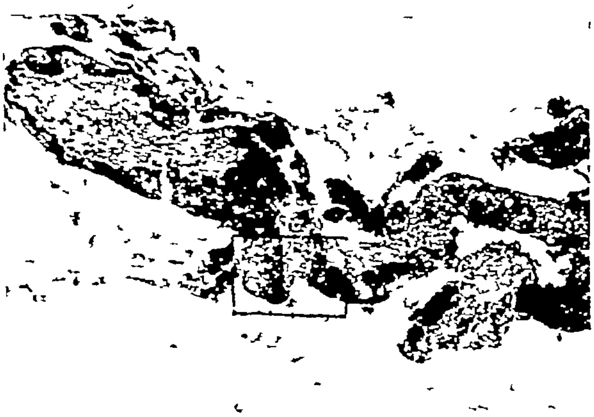


Fig 5—Cervical curetting showing malignant epithelium (low power)

When a "positive" (malignant) smear is found yet to the clinician the cervix presents no special site demanding biopsy, Schiller's iodine test is the only simple intermediate method between a surface smear and a "ring" biopsy of the entire junctional epithelium, as advocated by Ayre (1948), for finding the possible malignant area Wespi (1950) combines Schiller's test and inspection of the cervix with Hinselmann's colposcope, and believes he can discover the majority of early growths, but again this is not easy, nor have such few colposcopes as there may be in this country led to results making the learning and practice of their use obligatory A "ring" biopsy is not always easy to obtain properly, and Novak (1949) prefers a sharp spoon with which he lifts off the surface junctional epithelium This is still most efficiently obtained under anæsthesia with a volsellum on the cervix, though it can be done without, and the epithelial strips resulting are essentially more accurately and more easily interpreted than are single cells in a smear It is really a simple method of searching for the early cancer in all cases admitted for gynæcological operation, and is intermediate in thoroughness between the smear and the ring biopsy, obviating the difficult interpretation of the one and the trauma of the other, to which none of us would subject all our patients routinely The curved spoon curette (fig 1) is merely a modification of the straight spoon curette (still best used for the endocervix) A special sharp cutting edge is applied, and the curette is angled so that it may be used against the junctional epithelium by rotating the handle in the axis of the vagina Figs 2 and 3 show a strip of squamous epithelium so obtained, the specimen being fixed and mounted in paraffin as usual. A strip of malignant epithelium is shown in fig 4 Figs 5 and 6 show malignant epithelium found by curetting the cervix The discovery of this epithelium led to a "ring" biopsy, which in turn led to the discovery of a superficial early but probably invasive, epidermoid cancer (figs 7 and 8)

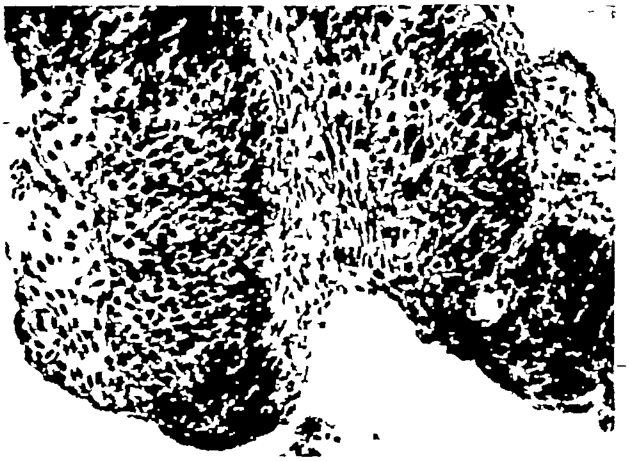


Fig 6—High-power view of area marked in fig 5

It is more difficult to draw off strips of epithelium from some cervices than from others, but it is always possible Should suspicion have been raised by examination of a smear previously, the endocervix also should always be inspected after dilatation and the straight spoon curette used to obtain endocervical scrapings—a step too easily omitted With such fragile strips as the curved scoop obtains it is essential that they should all

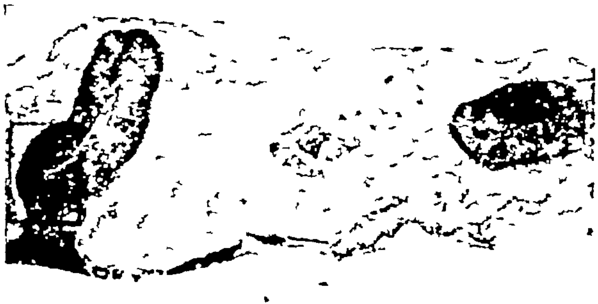


Fig 7— Ring biopsy specimen taken from cervix after the findings shown in figs. 5 and 6. A superficial early but probably invasive epidermoid cancer

into the tendon may relieve pain if this is severe Injection of local anæsthetic solution and saline solution followed by aspiration has been used with success, and Sandstrom (1938) advised local rest combined with X ray therapy

I consider that complete rest, which entails plaster immobilisation in the acute stages, is all that is usually necessary

I am indebted to Dr G R Sunley for referring the patient to me and for his help in her treatment, and to Prof A S Johnstone for his kind advice

REFERENCES

Codman, E A (1906) *Boston med surg J* 154 613
Emslie R C (1932) *Brit J Surg* 20 190
Lapidus P W (1943) *Surg Gynec Obstet* 76 715
Painter, C F (1907) *Boston med. surg J* 156 315
Sandström, C (1938) *Amer J Roentgenol* 40 1, 7
Winchester, J W Mekle E C (1947) *Brit J Radiol* 20, 482
Wrede L (1912) *Arch klin Chir* 99 259

CURETTAGE IN THE DIAGNOSIS OF CERVICAL CANCER

A MODIFIED SPOON CURETTE

A F ANDERSON
M B Edin, F R C S E, M R C O G
LECTURER IN OBSTETRICS AND GYNÆCOLOGY, UNIVERSITY OF EDINBURGH

THE need for reviewing the steps usually taken to diagnose cancer of the cervix comes from the realisation that this lesion commonly arises at the average age of 37, very much earlier than we have been accustomed to suppose The average stage I cancer ("established," invasive) is already an old cancer, presenting with well known symptoms and signs By this time there is usually some point on the cervix suggesting the site from which a biopsy should be taken, or else it is to be found in the endocervical canal These cases have already a 20% probability of lymph node involvement, and their average age incidence is 45–50 They are cases which are clinically suspected

But what of those cases not clinically suspected? These are of two types (1) those showing very early invasion of the connective tissue, and (2) those showing no invasion, in which the growth is confined to the superficial epithelial layer or its extension into the lumen of a cervical gland These two stages have an average age incidence of 42 in the first type (Auerbach and Pund 1945), and 37 in the second, and still younger, type (Auerbach and Pund 1945, TeLinde and Galvin 1944)

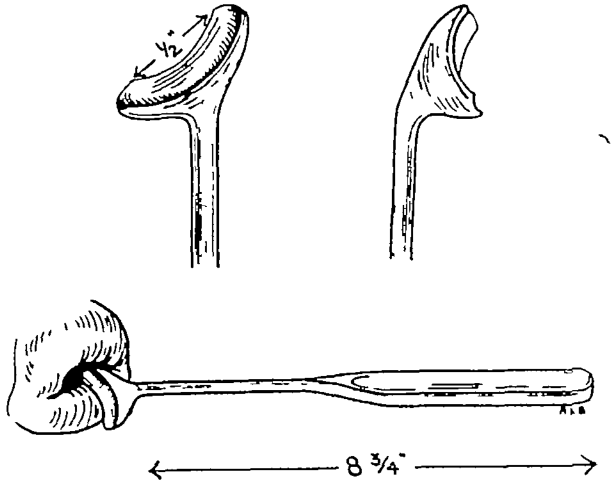


Fig 1—Spoon curette modified for routine use on junctional epithelium of cervix

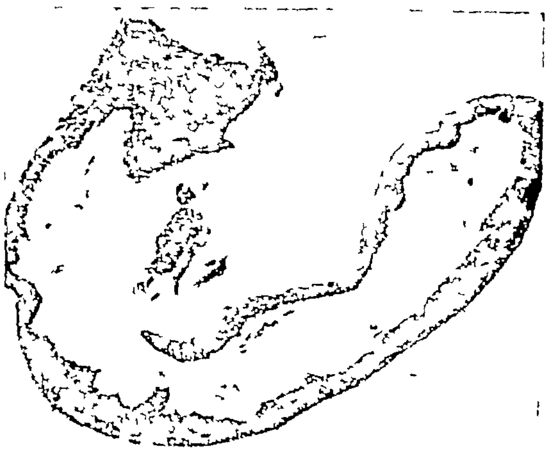


Fig 2—Strip of non-cancerous epithelium obtained with spoon curette (× 20)

Women with these really early cancers may have symptoms, but they are not symptoms suggesting cancer, and the appearance of the cervix with an intact epithelium does not suggest cancer A cervix with a "suspicious area" on it visible to the naked eye most commonly turns out to be benign ("erosion," ulceration) or quite malignant, with invasion already established, and very seldom a young superficial or pre invasive type of cancer

Foote and Stewart's (1948) excellent "mapping" of the extent of 27 such pre invasive cancers shows how the usual single biopsy fragment may only discover half these cases, and how biopsy from both anterior and posterior cervical lips may only discover three quarters, and it confirms Schiller's finding that these early cancers most commonly begin at the junction of the squamous and the columnar epithelium at the external os That this early cancerous change in the epithelium necessarily becomes an invasive cancer is as nearly proved as is possible by the number of such cases not radically treated owing to misinterpretation of the original picture and eventually developing an invasive cancer TeLinde (1949) mentions 18–20 such cases, I have since added 3 more in this country (Anderson 1950), and Younge et al (1949) report a case deliberately left untreated in which monthly biopsies showed invasive cancer eleven months later

The increasing practice of searching for malignant cells in vaginal smears, as suggested by Papanicolaou and

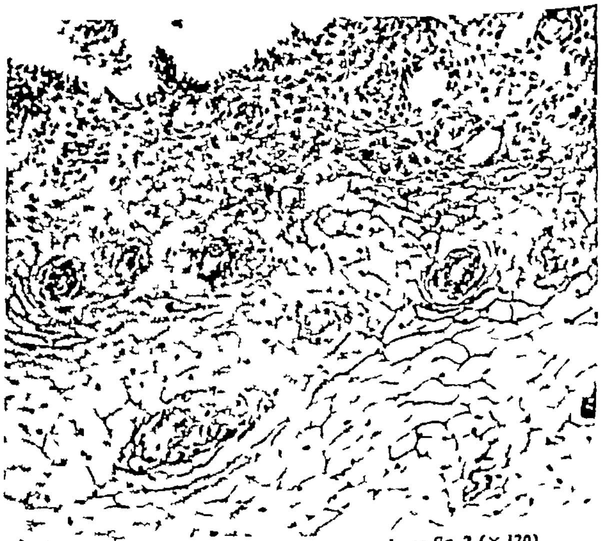


Fig 3—Higher-power view of same strip as fig 2 (× 120)

lesion of the upper lobe of the right lung, resembling a patchy pneumonic consolidation, with no cavity formation. This lesion had partially resolved by May 18

A week before admission he began to feel throbbing intermittent pain in his right leg with much tenderness. The pain caused him to limp and was not worse at night There were no symptoms referable to any other limb In 1938 he had similar pain and had been in hospital for a week.

On admission his appetite was good and his bowels regular Examination showed a cataract in the left eye diminished air-entry at right lung base a maximal cardiac impulse in the fourth space in the midclavicular line, and a small umbilical hernia. No abnormality was found in the central nervous system.

Two inches above the ankle joint the right leg was slightly swollen, hot and tender Slight pitting could be elicited. Shotty glands were present in both groins The left leg was apparently normal The urine contained urobilin (+ + +) and bilirubin (+ +) but was otherwise normal. A white-cell count showed 17 000 cells per c.mm. Hb was 10 g per 100 ml.

Initial Treatment—The patient was given penicillin 100 000 units three-hourly

Radiography of the chest on June 9 showed almost clear lungs with minimal shadowing in the right infraclavicular region, apparently the residuum of the patchy area of pneumonitis originally demonstrated on May 9 1949 Radiography of the right leg showed extensive erosion of the shaft of the tibia (fig 1a) involving the cortex on the anterior aspect and severest in the middle third In the upper third there was some erosion on the posterior aspect, with periosteal reaction. The swelling on the anterior aspect of the tibia was distal to the affected cortex. There was no change in the tibia near the joint surfaces There were no symptoms or signs referable to the left leg (fig 1b), which showed very similar erosion, chiefly of the middle third of the tibia on the anterior aspect. There was however some involvement of the medulla.

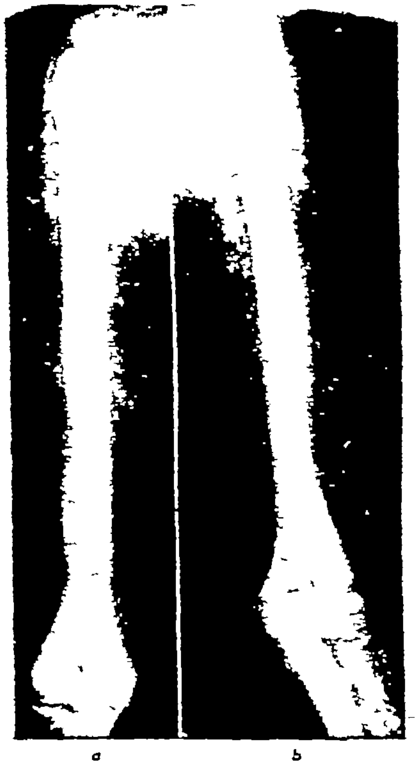

a b

Fig 2—Osteoperiosteal reaction limited to mid-shaft of humerus a right arm b left arm.

Because the appearance and distribution of the erosion was similar to that seen recently in a case from a neighbouring hospital it was suggested by one of us (M. F) that the infective organism in this case of osteomyelitis might be the Friedländer bacillus

Laboratory Investigations—An Ide test was negative The serum albumin 3·3 g and serum globulin 3·7 g per 100 ml. Thymol turbidity, 3·5 units thymol flocculation negative (—), Takata Ara test positive (+ + +) Alkaline phosphatase (King Armstrong) 15·5 units Icteric index 8, and bilirubin test direct positive 0·5 mg per 100 ml. Blood-culture negative for *S typhi* A specimen of cerebrospinal fluid 3 lymphocytes per c.mm., total protein 60 mg., chloride 0·660 mg and sugar 80 mg, per 100 ml Wassermann reaction negative Agglutinations for typhoid paratyphoid *Brucella melitensis* and *Br abortus* negative

Aspiration—On June 11 1949 the abscess of the right leg (lower third anteriorly) was aspirated and 5 ml. of brownish bloodstained pus was withdrawn. Microscopy of the pus showed pus cells and gram negative capsulated bacilli. Culture yielded a pure growth of an organism culturally and biochemically resembling Friedländer's bacillus. The bacterium was sensitive to streptomycin in a concentration of 100 μg per ml. but insensitive to penicillin 100 units per ml and to sulphadiazine, sulphapyridine, and sulphathiazole in a concentration of 1 5000 Aspiration was repeated on June 14, 1949 The pus contained pus cells and gram-negative bacilli Cultivation yielded an abundant growth of Friedländer's bacillus On June 17 a further specimen gave a similar result, and next day examination of pus from the thigh showed numerous pus cells and gram negative bacilli.

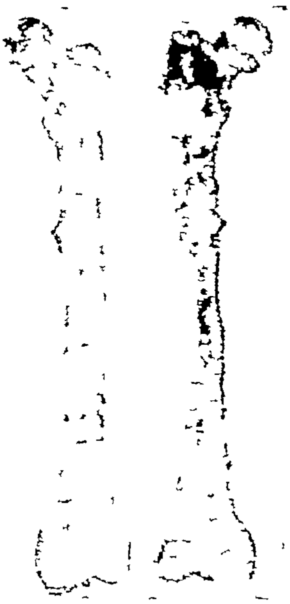

a b

Fig 4—Extensive pitting and periosteal reaction of entire shaft of left femur a anterior view b posterior view

Blood examination on June 14 showed Hb 10 g per 100 ml., colour index 0·96, red cells 3 370 000 per c.mm., leucocytes 16 300 per c.mm. (neutrophils 87·0%, mononuclears 5·5% lymphocytes 7·5%, eosinophils 0) On June 23, 1949 the serum agglutinated Friedländer's bacillus to a titre of 1 25 only Culture yielded an abundant growth of Friedländer's bacillus and scanty coliform bacilli insensitive to Aureomycin.

Other Bones—More detailed examination of the arms revealed deep-lying induration over the lower third of the humerus on both sides, and radiography showed osteomyelitis in both humeri (fig 2) more extensive on the right than on the left, involving the cortex more than the medulla, and with marked periosteal proliferation. As in the tibiæ the distal and proximal ends of the bones were not involved. The left ulna showed some erosion in the cortex on the posterior aspect of the middle third. The bones of the forearms were otherwise uninvolved. In the left femur (fig 3) there was extensive erosion of the cortex and medulla, most marked on the posterior aspect, and with profuse periosteal proliferation. There was a similar lesion in the middle third of the right femur affecting chiefly the cortex on the lateral aspect The whole of the rest of the skeleton was radiographed with negative results All these bone lesions, except that in the right tibia were neither painful nor tender

Fig 3—Profuse periosteal proliferation in shaft area of left femur

Progress—On June 20 1949, the left leg and thigh became swollen The left calf was tender and Homans's sign was positive. There was an effusion in the left knee joint The whole leg became extremely painful Acute thrombophlebitis was diagnosed. Two days later the thigh was somewhat indurated, and underlying infection was suspected.

Aspiration and Operation—Subsequently 60 ml. of thick brown pus was aspirated Open drainage was advised but the patient refused operation. Aspiration followed by instillation of penicillin was persevered with until July 19 1949 when the patient consented to operation. By this time the thigh was grossly swollen and the knee joint infected.

be sent for examination, and *immediately* floated off the curette by immersion in fixative solution, because the drying, and possible loss, which may take place if they are laid on a gauze swab may be so considerable as to confuse the picture and entirely nullify the trouble taken by clinician, technician, and pathologist The endocervical fragments, if any, should always be dropped into a separate container of fixative

No doubt, even if this procedure were a regular practice, some early cancers might still escape discovery, but it is probably a much more fruitful "routine" step in the examination of a gynæcological patient than are many curettages now being done for no very obvious reason other than that the patient is anæsthetised, as pointed out by Bowes (1949), and certainly it should make us more "cervix conscious" The reward of the discovery of these very young and early cancers should be a survival rate approaching 100%

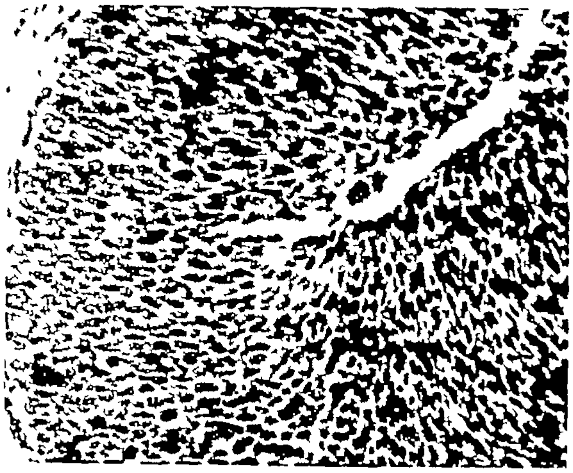


Fig 8—High power view of epidermoid cancer

Some workers still incline towards the view that the finding of more stage I cancers holds out the greatest promise of reducing the mortality of this most common and distressing tumour, but the onus cannot be entirely placed on the patient, and the very accessibility of the cervix, coupled with the absence of symptoms in the earliest type of case, cannot but shift more of the onus on to the gynæcologists

The modified spoon curette was made by the Medical Supply Association Ltd

REFERENCES

Anderson A F (1950) *J Obstet Gynæc* 57 1
Auerbach S H Pund E R (1945) *Amer J Obstet Gynec* 49 207
Ayre J E (1947) *Ibid* 53 609
— (1948) *J Amer med. Ass* 138 11
Bowes K (1949) *Practitioner*, 163, 118
Foote F W, Stewart, F W (1948) *Cancer* 1 431
Novak E (1949) *Amer J Obstet Gynec* 58, 581
Papanicolaou G N Traut H F (1941) *Ibid* 42 193
TeLinde, R W (1949) *Surg Gynec Obstet* 88, 792
— Galvin G (1944) *Amer J Obstet Gynec* 48 774
Wespi H (1950) Early Cancer of Uterine Cervix New York
Youngo P A Hertig A T Armstrong D (1949) *Amer J Obstet Gynec.* 58 867

' There are about 200 medical officers of health employed by Local Health Authorities, and though figures are not available probably about 2000 doctors are employed altogether in the preventive services Is it right that there should be one doctor in the hospital and specialist services for every 13 or 14 patients and one general practitioner for 2200 panel patients? Is one doctor per 20,000 of the population the correct proportion of the country's medical man power to be allocated to the prevention of disease? The time has obviously come when some authoritative body should investigate the relative claims on the available pool of man power for the medical services, indeed, for the utilisation of all the professional services, and its primary task should be to find out what proportions are desirable for each branch of service —Dr Hugh Paul *Med Offr*, May 19, 1951, p 201

OSTEOMYELITIS DUE TO FRIEDLANDER'S BACILLUS

D A Muskat
Ch M Rand
ASSISTANT SURGEON

M Findlay
M R C S, D.R Edin.
SENIOR RADIOLOGIST

CORONATION HOSPITAL, JOHANNESBURG

Multiple metastatic osteomyelitis, excluding that due to *Treponema pallidum*, is uncommon The organisms usually responsible are staphylococci, streptococci, pneumococci, *Salmonella typhi*, or *Mycobacterium tuberculosis* Until recently Friedlander's bacillus has not been reported as causing osteomyelitis, though it had been found in almost all the organs of the body (Wilson and Miles 1946, Browning and Mackie 1949) Two cases, however, have occurred in Bantu patients in another hospital in Johannesburg (Comins et al 1950), and a third is reported here The clinical findings were peculiar and the radiological features so characteristic that, while awaiting the report on the culture of pus aspirated from the abscess, one of us (M F) was able to suggest the diagnosis

CASE RECORD

A Bantu male, aged 41, a printer's assistant, was admitted on June 8, 1949, with pyrexia He complained of tightness in the chest and hiccup, and for a week his right ankle had been painful

History—The "tightness in the chest" started about March 21, he had no pain in the chest and did not cough. On April 23 he was admitted to another hospital, whose notes stated that he looked very ill, and had herpes labialis acute pharyngitis, and generalised abdominal tenderness. He was found to have severe normochromic anæmia and was given a transfusion of 500 ml of blood He improved, but two weeks later his condition necessitated a further transfusion of 500 ml His temperature ranged between 99° and 103°F Large doses of penicillin (for a month) and streptomycin (for two weeks) caused no improvement Thirteen specimens of urine and nine of fæces were negative for *S typhi* Blood culture and Widal and Vi tests were negative, and no *M tuberculosis* were found in the sputum There was a "pronounced leucocytosis" Radiography on May 9 showed a

a b

Fig 1—Periosteal reaction limited to shaft of tibia: a right leg b left leg

use Depression of the cough reflex is, in itself, much less important

If morphine has already been given, and the onset of ill effects noticed in the form of shallow and infrequent breathing, increased cyanosis, and coma, nikethamide 5–10 ml. should be given slowly intravenously, and oxygen administered

The essence of the danger seems to lie in the failure to differentiate between the useless dyspnœa of other forms of heart failure and the compensatory hyperpnœa of cor pulmonale In the former morphine is life saving, in the latter lethal.

SUMMARY

Morphine is deadly in heart failure secondary to chronic lung disease

Six patients are described who illustrated this

Nikethamide, given intravenously, is valuable in rescuing the patient if the ill effects are noticed in time

I am indebted to Dr A H Holmes and Dr N Kletts for their kind permission to report these cases

REFERENCES

Daley R (1945) *Brit Heart J* 7 101
Donald, K W Christie R V (1949) *Clin Sci* 8 33
East T , Bain, C (1948) Recent Advances in Cardiology 4th ed London p 361
Friedberg C K (1950) Diseases of the Heart Philadelphia and London p 899
Levine S A (1945) Clinical Heart Disease 3rd ed Philadelphia and London p 271
McMichael J (1947) *Advances in Internal Medicine* 2 64
Price F W (1941) A Textbook of the Practice of Medicine. 6th ed , London p 873
White P (1945) Heart Disease. New York
Wood P (1950) Diseases of the Heart and Circulation. London p 473

STREPTOMYCES FERMENTATION DERIVATIVES IN ACUTE LEUKÆMIA

ROBERT D BARNARD
M D
OF LAURELTON, LONG ISLAND, NEW YORK STATE

EARLY in 1949 I began giving acute leukæmic patients a crude *Streptomyces griseus* fermentation by product, sold as a hog and poultry feed supplement It had been noticed that in cases of amyotrophic lateral sclerosis this product created a ravenous appetite and a strongly positive nitrogen balance—effects beyond those obtained with relatively pure B_{12} preparations (Barnard 1950) Unexpectedly, within 24–72 hours most of the acute leukæmia patients who were given the streptomyces residue went into what was apparently a remissive phase of the disease with sudden abatement of fever, cessation of bleeding, and a remarkable clinical improvement Unfortunately, however, in these cases there was seldom any comparable improvement in the blood picture, though in a few cases the remission was hæmatological as well as clinical (Barnard and Fox 1950, Barnard and Appel 1950) Later in 1949, when a new batch of the product was used, the results became entirely negative, though its vitamin B_{12} content was similar, and a chance observation led to the discovery that a residual antibiotic, not the B_{12}, was responsible for the remission in acute leukæmia, and also for improvement in other atopic diseases and in animal growth (Barnard 1951a) The conclusion was finally reached that any of the streptomyces derived antibiotics ('Terramycin ' 'Aureomycin,' chloramphenicol, streptomycin), given in such a way as to suppress the usual coli aerogenes intestinal flora, may induce remission of acute leukæmia and that this remission will be maintained until (usually in a few days or weeks) antibiotic-resistant strains repopulate the intestinal tract, after which relapse is rapid Nevertheless an occasional patient did not show this relapse, and it was found that those who happened to be taking large quantities of milk had developed and maintained a lactobacillus type of intestinal flora which probably suppressed the coliforms

To produce convincing statistics is difficult because so many other factors seem inseparable from the life and death of the acute leukæmic once he has been so diagnosed Of the 50 patients who have now purposely * been treated with antibiotic containing streptomyces derived materials, many were transfused occasionally or repeatedly; and though sometimes these transfusions were probably not harmful † they often appear at such a time in the case history as to prevent rigorous appraisal of the rôle of the antibiotic My statement that hæmatological improvement was seldom apparent, should be qualified by saying that almost always there was deceleration or cessation of the usually progressive anæmia the erythrocyte count seemed to stabilise itself at a level which was lower than normal but which apparently was physiologically adequate, for many patients were able to return to school or to work This small blessing did not satisfy some of the attending physicians, or some member of the patient's family—after all, the blood picture was " bad "—and the bulk of the series made exitus via the " antifol " route, after discontinuance of maintenance antibiotic therapy or after what must be regarded as a purely elective blood transfusion Some died from acute congestive heart failure imposed by the (then) unappreciated salt and water retentive effects of adrenocorticotherapy , though I must add that, strangely enough, administration of the streptomyces derived antibiotics, or the change in intestinal flora this may entail, has likewise produced profound adrenocorticomimetic effects which were not always in the interests of the patient Diuretic doses of ammonium chloride are now given to most patients receiving sustained oral antibiotic therapy, but the corticomimetic effects are still so conspicuous that we cannot expect to evolve a satisfactory supportive régime in acute leukæmia until we have considerably more clinical experience Accordingly—and because there have only been 6 one year survivals among 50 patients—I shall confine myself here to describing 3 cases which illustrate (1) the rôle of the streptomyces fermentation product in the induction of remission, (2) the probable identity of the active factor, and (3) its possible mode of action

ILLUSTRATIVE CASES

Case 1 —A girl, aged 17, developed a viral " pneumonia in November 1949, and was treated at home throughout her illness When she did not respond to penicillin (fig 1), and when gum bleeding became pronounced and the spleen was found to be palpable, the blood was examined on Dec, 13 The peripheral smear itself was diagnostic of an acute myeloblastic leukæmia, there being a complete granulocytic hiatus between " blast " and mature forms , but marrow aspiration was also performed (Dec 22) and revealed over 80% of nucleated forms to be undifferentiated and while megakaryocytes were absent On Dec 25 40 g of *Streptomyces griseus* residue (now known to have a B_{12} equivalence, per gramme of 6 µg on the basis of L *leichmanni* assay and 220 " units ' of streptomycin equivalence in terms of *Bacterium coli* suppression) was begun in four divided daily doses, the material being emulsified in milk with linseed oil and Tween 80 At the end of 24 hours the patient, though still febrile, was so much better that consent was obtained to discontinue the parenteral penicillin. Temperature was normal within 72 hours of commencing the residue ingestion and the patient left her bed A strong revulsion developed against the residue mixture at about the end of the second week of its exhibition, and attempts to force it were met with retching and vomiting Relapse was manifest

---

* Many acute leukæmic patients are now of course receiving aureomycin terramycin or chloramphenicol as a supportive measure for the control of the infective component supposedly connoted by fever The possibility that chloramphenicol may be the cause of some purported antifol remissions has been noted (see McNeil 1950) The patients in my series ordinarily received an antibiotic dosage which was considerably less than that used for the treatment of infections and was actually of the same order of magnitude as that found to induce optimal growth in hogs

† In many instances I believe they actually killed the patient as when blocking type antibodies were present (Barnard 1951b)

Under thiopentone anæsthesia 4 pints of pus was removed Three days later the leg had subsided greatly, but the patient's condition generally did not seem to improve commensurately Two transfusions of 500 ml of blood were given On July 25 the right thigh became swollen. On July 28, 400 ml of pus was evacuated through a deep incision. The patient's condition deteriorated, and he died on July 30, 1949, apparently from profound toxæmia

Treatment had been mainly supportive A high vitamin, high protein, and high carbohydrate diet was given A course of penicillin and sulphadiazine was given despite the insensibility of the causal organism Streptomycin was given continuously in doses of 2 g a day For a fortnight before death the dose was increased to 3 g a day (there being no signs of toxicity) Aureomycin was given in the last week without benefit

Necropsy Findings —There was evidence of general toxæmia, particularly affecting the heart and spleen The liver was soft and showed fatty degeneration In the right lobe of the liver was a small necrotic abscess filled with yellowish green pus The left femur was bathed in pus, and the surrounding muscles were necrotic The left femur was irregular, with some periosteal new bone formation posteriorly (fig 4) The findings on the right side were similar but not so pronounced Nothing abnormal was found in the lungs

COMMENTS

This case presents interesting and unusual features Although throughout the clinical course there was no cough, expectoration, or clinical evidence of a lung lesion, the initial radiological finding did show a lesion

The condition was characterised by high remittent pyrexia, becoming intermittent, severe toxæmia, moderately high persistent leucocytosis, and osteomyelitis of almost all the long bones, either simultaneously or in rapid succession

Even with definite radiological changes the clinical findings of pain, tenderness, and swelling (before the onset of gross suppuration) were slight

Friedlander's bacillus produces abundant brown blood stained pus, with a musty, but not foul, odour, and can be isolated in pure culture It is apparently, in vitro, sensitive to streptomycin, but in the present case intensive streptomycin therapy had no effect

Pathologically the main changes were an extensive periosteomyelitis, with a definite tendency to form new bone No sequestra, cloacæ, or sinuses developed

REFERENCES

Browning C H, Mackie T J (1949) Textbook of Bacteriology 11th ed, London p 322

Comins C, Kay, S Skapinker S (1950) *Brit J Radiol* **23** 168

Wilson G S Miles A A (1946) Topley and Wilson s Principles of Bacteriology and Immunity 3rd ed London, vol I, p 668

LETHAL EFFECT OF MORPHINE IN CHRONIC COR PULMONALE

N J Roussak

M B, B Sc Manc, M R C P

MEDICAL REGISTRAR, MANCHESTER ROYAL INFIRMARY

No physician would disagree with Sydenham's oft quoted eulogy of opium, and yet this drug, no less than newer potent therapeutic aids, may be a double edged weapon It is the purpose of this communication to re emphasise the extreme danger attending the use of opium in heart disease of pulmonary origin

Five patients whose deaths were precipitated by the drug are described, and one in whom the fatal result was averted

CASE RECORDS

Case 1 —A man, aged 58, was admitted to hospital with bronchitis and emphysema and recent superadded infection. He showed cyanosis, dependent œdema, and venous congestion, and the liver was enlarged Given oxygen, penicillin, and morphine gr $^{1}/_{4}$, he sank into coma with shallow respirations and died in a few hours

Case 2 —An emphysematous man, aged 62, had a chest expansion of only $^{1}/_{2}$ in Moderate cyanosis, œdema of the legs, and an enlarged liver were present He was comfortable, though slightly dyspnœic, in bed 'Nepenthe' 30 minims resulted in diminished amplitude of respiration, coma and death followed

Case 3 —After operation for perforated ulcer a man, aged 64, with bronchiectasis found his exercise tolerance much reduced, and signs of right sided heart failure developed This responded to treatment, and the sputum diminished and became less offensive One night the patient was given morphine gr $^{1}/_{6}$ for ulcer pain, sleep merged into coma, and he died.

Case 4 —A man, aged 28, was admitted with bronchiectasis and congestive heart-failure Rapid and unexpected deterioration followed the administration of morphine gr $^{1}/_{4}$, cyanosis deepened, and the patient died shortly afterwards in coma.

Case 5 —A man, aged 30, with bronchiectasis and right sided heart-failure was treated in hospital on several occasions. Ultimately he was given nepenthe 30 minims, respiratory movements weakened, cyanosis increased, and he lapsed into coma Oxygen was of no avail, and he died

Case 6 —A grossly obese man, aged 42, had unexplained right-sided heart-failure which responded well to digitalis and diuretics Emphysema and bronchitis, not at first considered very severe, were shown to be the cause of the failure when, instead of his nightly barbiturate, he was unfortunately given nepenthe 30 minims Seven hours later he was found in deep coma, almost apnœic, and heavily cyanosed Oxygen was given, and nikethamide 10 ml. administered slowly intravenously Respiration increased in depth and his colour improved while the needle was still in the vein, and within five minutes he was conscious, although rather dyspnœic This patient is still alive two years later

These patients had congestive heart failure secondary to chronic lung disease, and some were already showing gratifying signs of improvement The condition of each deteriorated dramatically after morphine or nepenthe had been given

DISCUSSION

Apart from the statement that morphine *should not* be given in bronchial asthma or in the presence *of copious* bronchial secretions, "because of depression *of the cough* reflex," little mention is made in textbooks or the literature of the danger of morphine in cor pulmonale

Discussing the treatment of congestive heart failure, East and Bain (1948) write "Ventilation may well be diminished without harm if the reflexes provoking it are quieted A less than normal oxygen tension can quite well be tolerated" "Morphia is dangerous in heart failure secondary to kyphoscoliosis, also when the failure is complicated by sepsis Old people are sometimes very sensitive to morphia Otherwise its use is free from all risk" The danger in kyphoscoliosis (Daley 1945) is due to the associated reduced vital capacity Price (1941) advises that small doses of morphine should first be given in heart failure, and the effects noted, but no special mention is made of cor pulmonale White (1945) does not mention the matter, but Levine (1945) and Wood (1950) warn against the use of morphine in cor pulmonale Friedberg (1950) writes "Morphia causes serious respiratory depression and occasional fatalities in patients with pulmonary failure, and is therefore contra indicated"

In the presence of greatly diminished vital capacity sufficient oxygenation of the blood may only be achieved by maximal respiratory effort (hyperpnœa) Such hyperpnœa is produced by stimulation of the respiratory centre by the decreased oxygen tension of the blood, the arterial oxygen saturation being often 70–35% in emphysema (McMichael 1947) Afferent vagal impulses from the lungs, and impulses from the carotid bodies, also play a part, but it is thought that the centre becomes insensitive to the continuously raised carbon dioxide tension (Donald and Christie 1949)

It is essential that the respiratory centre remain responsive to such stimuli, and it is the depressing effect of morphine on it that causes the deaths following its frequently, aureomycin does so occasionally, and oral penicillin appears to have done so in 4 instances The efficacy of these antibiotics in this connection is strikingly parallel with their efficacy in promoting growth in poultry and hogs, and the underlying mechanisms may be the same My present working hypothesis is that the proteosæmia ("peptonæmia") repeatedly demonstrated in acute leukæmia (Erben 1900) arises from a predominantly proteolytic flora in an intestinal tract of increased permeability, and that this proteosæmia is responsible for the depression of blood cholinesterase, whose level is lower in acute leukæmia than in any other condition (Barnard et al. 1946) The rôle of the blood-cholinesterase in the general regulation of cellular permeability has only recently become an open topic (Holland and Greig 1950), its function in regulating hæmopoiesis has been subject of surmise (Barnard 1948) On this hypothesis, the proper antibiotic for suppression of proteolytic species may vary in different subjects

Case 3—A school teacher, aged 69, was admitted to hospital on May 12, 1950, with developed stranguary, abdominal pain, and hæmaturia. A diagnosis of acute prostatism led to plans for transurethral resection, but a severe anæmia was found, and operation was postponed until the patient could be "built-up with transfusions What was overlooked in the routine blood count was a leucocyte figure of 8000, which the technician stated were all lymphocytes,' and a note that platelets were sparse Aureomycin administration was begun on admission. Transfusions before operation had little effect Examination of the original blood film and of a routine blood-count record made in November, 1949, when the patient enrolled in a local health insurance plan, led to the tentative diagnosis of acute lymphoblastic leukæmia During the first four weeks in the hospital the leucocyte count fluctuated from 8000 to 80 000 (fig 2) but the percentage of 'blast' forms among these also varied with the total leucocyte-count, the absolute numbers of blasts like the small numbers of granulocytes, remaining remarkably constant

Transurethral resection was performed during the second week in hospital, and bleeding from this site continued. A double transfusion five days after operation almost killed the patient The course completely altered on the substitution of terramycin and chloramphenicol for the aureomycin, all bleeding and fever abating The patient himself noticed that the change over had produced an almost odourless stool, and this state of affairs has continued with a predominantly gram positive intestinal flora. When last heard from, about eight months after the apparent remission began, the patient was in the best of health and at work.

In this case terramycin apparently eliminated an aureomycin resistant strain of *Bacterium aerogenes* Relapse may have been prevented by a liberal intake of milk which maintained a predominance of lactobacilli antagonistic to the coli-aerogenes group This case also illustrates how cessation of bleeding may indicate the beginning of a remission The effect seems not entirely due to the anti heparin effect of terramycin (Barnard 1951b), since aureomycin likewise neutralises heparin (Barnard 1951b)

The long term 'hæmatinic effect' of continued small doses of antibiotic is well shown by this patient, whose erythrocyte count continued to climb without the necessity of transfusion This effect, identical with that observed when streptomyces fermentation derivative was given for the usually refractive anæmias of glomerulonephritis, hypersplenism, and protracted radiotherapy, is perhaps the most promising feature of the use of this product in acute leukæmia Another is its tendency to abrogate "allergic" manifestations, a history of which is so common among leukæmic patients and members of their families

SUMMARY

Food supplements obtained by fermentation with *Streptomyces griseus* have been given by mouth to patients with acute leukæmia In some cases the clinical condition has greatly improved, but the blood picture has not shown corresponding changes.

Though the products used are rich in vitamin B_{12} their effect in leukæmia is more probably related to their content of antibiotic Streptomyces derived antibiotics alter the intestinal flora, suppressing the coli-aerogenes organisms, and the clinical remissions seem to last until antibiotic resistant strains emerge to repopulate the gut This event was apparently postponed in patients whose large intake of milk promoted the growth of lactobacilli

Untoward effects on salt and water balance have been observed in some cases treated with streptomyces fermentation products, and more experience will be needed before any satisfactory régime for their use can be evolved

ADDENDUM

Since this report was prepared examples of remission in the leucoblastoses, including Hodgkin's reticulioma and disseminated myeloma, apparently due to small doses of streptomyces-derived antibiotics, have continued to accumulate, and the concomitance of an odourless stool and remission remains striking That these effects have not always emerged with regular large doses of antibiotic may be explained by Kersey's (1951) finding that the streptomyces derived antibiotics, thought not ordinarily suppressing lactobacilli, develop this action at a critical level which depends partly on the amount of B_{12} present Kersey's data indicate that the lactobacillus would probably survive in the intestine at a terramycin concentration which would result from administration of small doses, but that it would not survive with ordinary doses This probability is being borne out by studies on fæcal flora

I wish to acknowledge my indebtedness to Chas Pfizer and Company, Brooklyn, for providing generous quantities of *Streptomyces griseus* residues as well as to Dr Elliott R Weyer and other members of the scientific staff of that company for their encouragement, kindly constructive criticisms, and suggestions.

REFERENCES

Barnard R. D (1948) *J Amer med Ass.* 136 573
— (1950) *N Y St. J Med* 50 1852
— (1951a) *Urol. cutan Rev* (in the press)
— (1951b) *N Y St J Med* (in the press.)
— Appel A (1950) *Urol. cutan Rev* 54, 345
— Fox H L (1950) *Ohio St med J* 46 784
— Sprinz H. Fitch H M. Lehman R. A Walker R. A (1946) *Science*, 104, 449
Chow B F Lang C. A Davis R Conley C L Ellicott C E (1950) *Bull. Johns Hopk. Hosp* 87 156
Erben D (1900) *Z klin. Med* 40, 282
Holland W C Greig M. E (1950) *Arch Biochem* 26 151
Kersey R C (1951) Proceedings of the Society of American Bacteriologists March 20
McNeil D L (1950) *Canad med Ass J* 63 248 614

FIBROSARCOMA OF THE TONGUE AFTER INTERSTITIAL IRRADIATION

REPORT OF A CASE

PETER DELLER
M B Camb
LATE CANCER REGISTRAR, UNIVERSITY COLLEGE HOSPITAL, LONDON

In the following case a fibrosarcoma of the tongue developed nineteen years after interstitial irradiation at the same site

CASE RECORD

A man, aged 48 was first seen in October 1929 He then had a lump under his tongue noticed for a month, and an ulcer measuring 2 by 1 5 cm., with hard raised everted edges on the left side of the undersurface of his tongue and extending into the floor of the mouth. The base of the ulcer was indurated but induration did not extend appreciably beyond its edges No glands were palpable in the neck Carcinoma was diagnosed, and the growth was treated with interstitial radium in a total dosage of 1210 mg hr or about 10,000 r A biopsy was not done A fortnight later a gland dissection of both submaxillary triangles was done followed a year

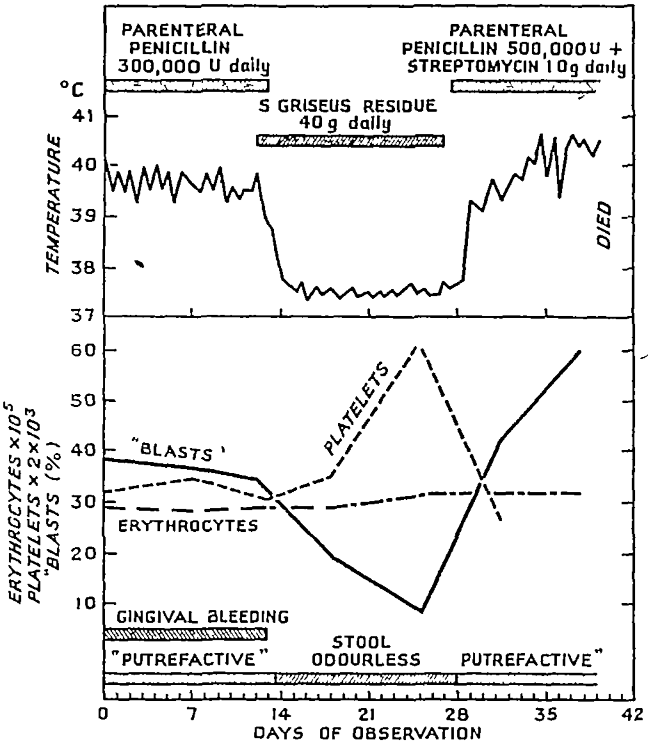


Fig 1—(Case 1)

within 48 hours of its discontinuance The patient died on Feb 2 from what was apparently a cerebral hæmorrhage, necropsy was refused

Remissions of the kind seen in this case are common even in untreated children (I regard them as the rule rather than the exception and have seen them occur merely on sending an unhappy sick child home from the hospital), but they are seldom spontaneous in adults What the graph cannot depict is the rapid reversal in course, under the same environmental conditions at home, amazing alike to the family and the attendants, during which the colour changed from corpse like to ruddy and the appetite became ravenous, within 48 hours after beginning to take the crude fermentation residue The latter, incidentally, turned out to be among those in which the presence of a coliform suppressor antibiotic, assayed as "streptomycin," was found accountable for the accelerated growth of chicks and hogs On the basis of subsequent calculations it appeared that the patient had been daily ingesting about 0 3 milligrammes of B_{12} and 8 0 milligrammes of antibiotic (in terms of streptomycin, aureomycin, terramycin, or chloramphenicol coliform suppressor equivalence) This amount could hardly have resulted in any significant distribution of the antibiotic through the blood stream, and it was also significant that parenteral penicillin and/or streptomycin did not alter the course of the disease Unfortunately, the stools were not examined bacteriologically, but it is probable that the emergence of resistant coli aerogenes strains in the intestinal flora coincided with the relapse, which had undoubtedly begun before the rejection and discontinuance of the fermentation residue

The fermentation residue contains vitamin B_{12} Though massive doses of the latter have been given parenterally in acute leukæmia without advantage, there may be differences in the pharmacodynamics of oral and parenteral B_{12}, at least in animals (Chow et al 1950) The next case permitted comparison of the two known components of the product used

Case 2 —A boy, aged 12, was treated at home from the middle of March, 1950, with a refractory "viral" pneumonia, and had daily injections of penicillin During the first week in April, splenomegaly and hepatomegaly were noticed On April 23, the peripheral smear showed a macrocytic anæmia with 13% of myeloblasts, marked thrombopenia, and a moderate erythroblastosis the sternal marrow showed marked "blast" infiltration, 70% of all nucleated forms being undifferentiated On the same day the child was transferred to the hospital, and was given, by mouth, 10 g daily of a streptomyces derived residue containing 55 µg of B_{12} per g but devoid of coliform suppressor substance During the next 12 days deterioration was rapid The spleen continued to enlarge, as did the cervical glands, and the patient was prostrated The temperature spiked higher each evening, reaching 41 7°C on May 5 Only by special pleading was a transfusion withheld, and on the morning of May 6 1 5 g of terramycin hydrochloride daily was substituted for the antibiotic free streptomyces concentrate The temperature was normal by the morning of May 8, and the child was out of bed The appetite had become voracious by May 10, and on the 14th, as it was evident that all glands, the spleen, and the liver were receding in size, he was allowed to go home in definite clinical remission

I must gratefully acknowledge the kindness of Dr Harry Bloch and Dr Margaret Rice, of the King's County Hospital, for permitting my supervision of the care while the child was there Later developments, which were reported to me, were less happy Though the hæmoglobin was definitely higher than during the hectic stage of illness, pressure for the orthodox transfusion ritual was resumed after the child had been home for some weeks Whether his death was the result of transfusion, I do not know, though in other cases I am more certain (Barnard 1951b)

As this patient daily ingested over 0 5 mg of B_{12} before he received any antibiotic, the question arises whether storage and continued activity of this vitamin was not responsible for the remission There is no way in which B_{12} can be completely eliminated from the human, since it is synthesised in the gut and stored in the liver, but it is significant that in our experience oral terramycin alone will usually induce some degree of clinical and hæmatological remission, oral chloromycetin does do so

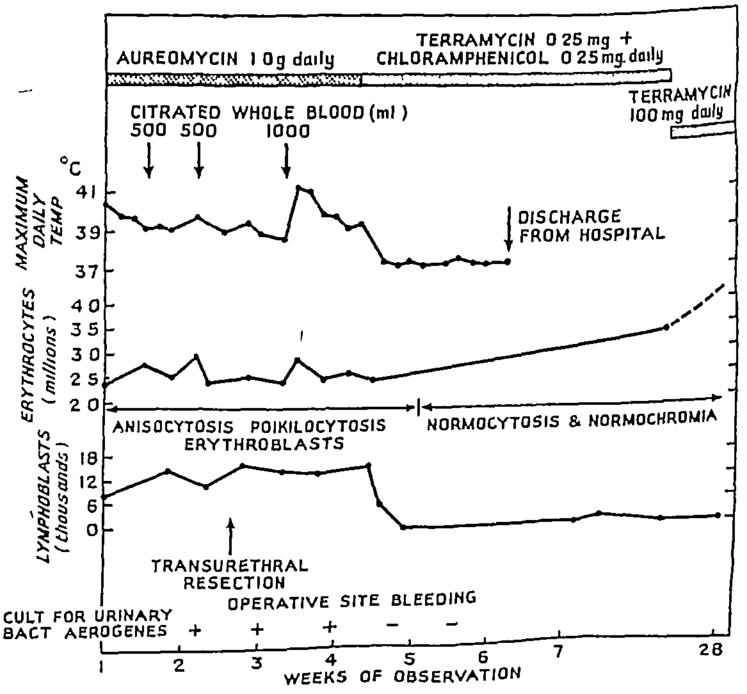


Fig 2—(Case 3)

eight expressed as a percentage of the normal standard woman of normal weight for height contains about °/o of fat, a man 16%

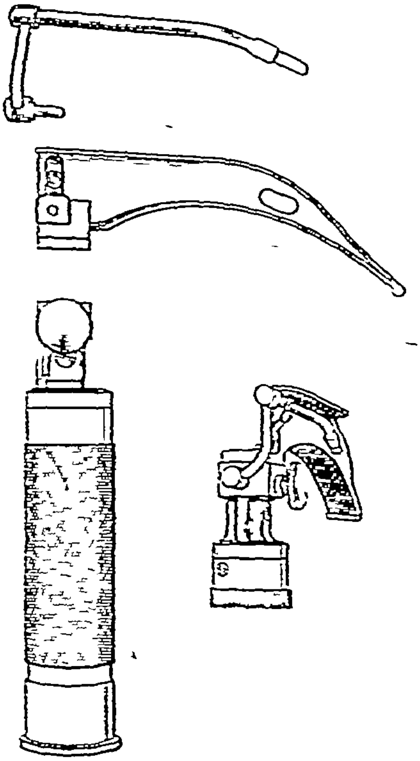
The highest figure obtained for fat was just over 60% or a woman weighing 25 stone This woman was carrying bout 15 stone of fat and she had no more muscular tissue han an under-weight person with which to do it

Dr D A W EDWARDS described two disorders of ubcutaneous fat—lipodystrophy and diffuse symmetrical pomatosis. The excessive tissue in lipomatosis is fat, nd Dr Edwards showed slides of parafin sections of atty tissue taken from normal and obese persons and rom persons suffering from lipomatosis. He demonstrated learly that in an obese person the number of fat cells is ormal, but there is an excessive amount of fat in each ell. In lipomatosis the number of fat cells is increased, nd not the amount of fat in each cell. The fat cells espond normally to undernutrition, and the normal nd abnormal parts of the body lose equivalent amounts f fat. In lipodystrophy there is a local disappearance r loss of function of the fat-storing cells. It is quite ommon to get both disorders in the same patient

New Inventions

MODIFIED LARYNGOSCOPE

THE laryngoscope illustrated here is a modification of R. R. Macintosh's excellent design In this instrument he blade has been lengthened and its side-wall increased n depth This gives an improved view of the larynx and, by opening the mouth more widely, an increased area for manipulation.



The entire electrical system can be removed from the blade, so that the latter can be put into the steriliser without fear of ultimately damaging the electrical insulation. It also makes for easy replacement of the lens fronted lamp, when required This instrument was made for me by Messrs A. L. Hawkins, of 15, New Cavendish Street, London, W 1

FRANCIS T EVANS
M.B. Lond,
F.F.A R.C.S, D.A

St Bartholomew's Hospital
London.

Reviews of Books

Current Therapy, 1951

Editor HOWARD F CONN M.D Philadelphia and London W B Saunders. 1951 Pp 699 50s

Conn's *Current Therapy* should make a special appeal to the general practitioner, who will be grateful for a book on treatment which is both comprehensive and up to date. This volume, with its round dozen consultant editors and nearly 300 contributors, seems to have both these merits. It aims at providing a brief but complete resume, by one or more authors, of the treatment of all the commoner conditions met with in practice. No details of surgical operations are included, but the descriptions of methods available to the general practitioner are full and for the most part clear The indexing is excellent and quick reference either to symptoms or to diseases proved possible for all the conditions looked for—with the exception of Halitosis (which seems to be omitted from almost every book on treatment), Proctalgia fugax, and (unless hidden out of sight) Periarteritis nodosa. A number of useful diagrams are given, and a roster of drugs ' at the end includes most of the best-known proprietary preparations The therapeutic methods differ in places from those current here, but the book certainly offers authoritative views on present-day American treatment

Neurosis and Human Growth

KAREN HORNEY M.D London Routledge & Kegan Paul 1951 Pp 391 21s

Dr Horney's latest work is a welcome addition to her psychoanalytical theory The fact that this theory is still developing—through the amplification here of the ideas embodied in *Our Inner Conflicts* in particular—is an indication of its clinical and intellectual vitality

It is too early to assess the extent to which her system is likely to constitute a non-Freudian school. Her contribution to the understanding of neurosis seems to lie mostly in the social biology of neurotic disorder Her concept of psychodynamics—far less a psychology of the unconscious than that of Freud—is, in its own field, equally illuminating Like most therapists, nowadays, she is well aware of factors outside the rigid Freudian canon of trauma, especially social factors, but she has a rather uncritical readiness to transfer conscious constructs to the patient. Modern anthropological work increasingly forces us to recognise the effect of social factors, and these are something which Freudian psychodynamics in their original form have not proved flexible enough to interpret satisfactorily It is in bridging this gap that Dr Horney's work has particular value She points the way to a full ultimate synthesis, not only between the sociological and Freudian approaches to mental ill health, but between the classical traumata and the conception of behaviour disorder (delinquency in particular) as a situation neurosis conditioned by faulty relationships. Her terminology is clear and will be welcome to teachers of social psychology

The therapeutic implications of Dr Horney's work extend throughout education politics, and social institutions This is a valuable book.

Contraceptive Technique

HELENA WRIGHT M.B London J & A. Churchill 1951 Pp 68 6s

THIS is a good short book which could well be in the hands of every general practitioner and medical student it is concise accurate free of fads and full of useful information especially in dealing with gynæcological difficulties which may modify the technique of choice. Dr Wright's ten-page survey of the scope, objects and requirements of contraception under modern conditions is a model of good sense, with which the rest of the book is in key Clinic and private-practice routine methods are well outlined the psychological background is at least as much in the author's mind as the hygienic. A brief account of contraceptive methods suitable for use in the tropics, or in countries which prohibit the sale of proper appliances, and an account of the British Family Planning movement, up to the report of the Royal later (i e , December, 1930) by a formal left block dissection None of the glands was reported as containing carcinoma, and the growth regressed satisfactorily The patient was seen regularly for nearly 19 years after this, and no evidence of recurrence was found

In September, 1948, he noticed another lump in his tongue, and reported immediately to hospital Deep to the irradiation scar was a firm irregular ill defined mass 1 5 cm in diameter No masses were palpable in the neck In October, Mr A J Gardham performed a left hemiglossectomy The excised portion included the left side of the floor of the mouth and the sublingual gland, and showed a grey fibrous tumour 1 cm. in diameter surrounded on every side by about 0 75 cm of apparently normal muscle On section a fibrosarcoma of low grade malignancy was reported by Prof G R Cameron There was no sign of recurrence up to 27 months later (December 1950)

DISCUSSION

Without histological proof one cannot say whether the original growth was a sarcoma or a carcinoma

If it was a sarcoma its clinical features were atypical (Ross 1935) and its local recurrence after 19 years was most unusual When a sarcoma recurs it usually does so within a few months, according to Koerth et al (1943), who summarised the published accounts of 61 primary sarcomas of the tongue

If the original growth was a carcinoma, the appearance of a sarcoma at the same site following interstitial irradiation is worth noting Nearly all the reported cases of irradiation sarcoma have followed protracted irradiation , Wilson and Brunschwig (1937) reported and reviewed 26 such cases However, one sarcoma occurred in a rabbit 18 months after a 1 mg, radium needle had been implanted at the same site for 20 days (Schürch and Uehlinger 1931) , and Gricouroff (1937 1943) described 4 human cases, of which 3 had a proved carcinoma of the tongue treated by interstitial irradiation, and fibrosarcomata developed at the same site after 12, 4, and 4 years , and the 4th case was one of carcinoma of the buccal aspect of the cheek in which a fibrosarcoma appeared at the same site 12 years later There is thus no doubt that sarcoma of the tongue sometimes develops after interstitial irradiation , but these cases are so rare that it is impossible to be certain whether there is any causal connection between the irradiation and the tumour

I am most grateful to Mr Gardham for his encouragement and his permission to publish this case , and to Professor Cameron for the pathological report

REFERENCES

Gricouroff G (1937) *Bull Ass franç Cancer* 26 378
— (1943) *Mém Acad Chir Paris*, 69 520
Koerth C J McCorkle R G Donaldson, J M jun (1943) *Dis Chest* 9 151
Ross, J C (1935) *Brit med J* 1, 54
Schürch O Uehlinger E (1931) *Z Krebsforsch* 33 476
Wilson, H , Brunschwig A (1937) *Surgery* 2, 607

Medical Societies

ROYAL SOCIETY OF MEDICINE

Experimental Approaches to Obesity

The section of experimental medicine of the Royal Society of Medicine met on May 8, with Prof R A McCance, F R S , president of the section, in the chair

Dr G C **Kennedy** described his work on experimental hypothalamic obesity in rats If the tuberal part of the hypothalamus of rats is damaged by electrolytic lesions the animals become very fat The cause of this obesity is overeating From the first day after operation the animal eats 2–3 times as much as normal , this hyper phagia goes on for 4–6 weeks, by which time the rat weighs about 50% more than an unoperated animal of the same age The increase in weight is entirely due to the deposition of fat, and the amount of water in a fat animal is exactly what one would expect in a normal animal of the same length. Even when the operation is performed on an animal which is still growing the body length is unaffected, the obese operated animal being exactly the same length as its unoperated control.

Rats with hypothalamic obesity seldom survive for more than a year after the operation The first signs of ill health are that the skin undergoes trophic changes and pressure sores appear on the feet After 8–10 months gross kidney damage ensues, with severe albuminuria and enlargement of the kidneys The adrenals are the only other organs which are hypertrophied The lesions in the kidney all lie in the tubules There is no vascular damage, and the glomeruli are unaffected The histological appearance is of pyelonephritis, and is similar to that produced by non specific stresses of various kinds

Dr Kennedy described experiments in which operated and control rats were fed unlimited amounts of the stock diet mixed with an equal bulk of kaolin The control animals responded by eating twice their usual amount so that their calorie intakes were unaltered The operated rats seemed unable to increase sufficiently their already high consumption of food, so that their calorie intakes were reduced Dr Kennedy concluded from this that calorimetric control is paralysed by operation on the hypothalamus The nature of the stimulus to which the hypothalamus responds is still a matter of controversy

Captain A R **Behnke**, speaking on measurement of the fat and water content of the body in relation to obesity, emphasised the distinction between the terms " overweight " and " obesity " Football players are very often overweight, and are turned down on this account by the insurance companies regardless of the fact that their excess weight consists largely of muscular tissue Obesity implies that the excess weight consists of fat

As a rough guide to leanness and fatness Captain Behnke recommended the comparative girths of the chest and the abdomen In lean men the chest measures about 8 in more than the abdomen, but in fat persons the abdomen measures more than the chest Captain Behnke went on to describe results which he has obtained on 100 naval personnel by measuring their specific gravities A body with a specific gravity of 1 100 has no excess fat at all Every addition of 1% fat to the body weight will cause the specific gravity to decrease by 2 units (i e., 0 002) Most people have a specific gravity between 1 090 and 1 050, which corresponds to fat contents of 5–25% Comparative measurements on a few obese subjects have shown that a reduction in body weight is solely at the expense of fat

It is not practicable to make specific gravity measurements on patients , but if advantage is taken of the fundamental concept that the fat free body tissue is of uniform structure, all that is necessary for the assessment of the amount of fat in the body is determination of the total body water

Miss E M **Widdowson**, D SC , described a method which she and Professor McCance have used for breaking down the body weights of living persons into terms of extracellular fluid, cell mass, minerals, and fat The extracellular fluid and total body water are estimated directly, and the difference between them is taken to be the intracellular water This, multiplied by $\frac{100}{70}$, gives the cell mass The minerals have been shown by direct chemical analysis of human bodies to comprise 7% of the fat free body weight, so that all the information is now available to enable one to determine " by difference " the total amount of fat in the body

Results obtained by this method for the amount of water and fat in 30 normal individuals, fat and thin, and in 10 undernourished German men before and after rehabilitation, were described and a slide was shown relating the percentage of fat in the body to the body-weight expressed as a percentage of the normal standard. A woman of normal weight for height contains about 17% of fat, a man 16%.

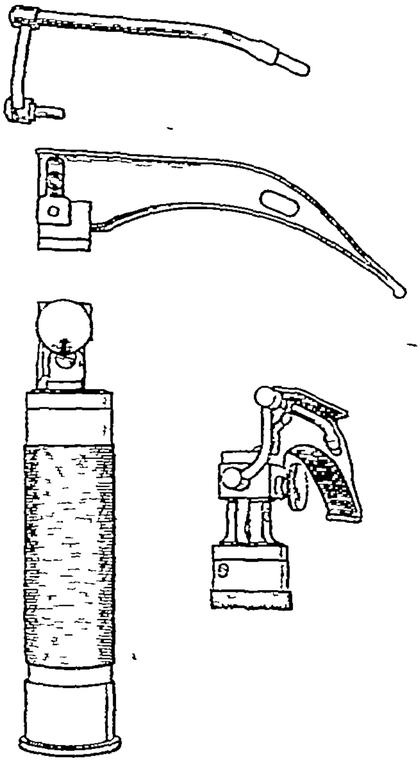
The highest figure obtained for fat was just over 60% for a woman weighing 25 stone. This woman was carrying about 15 stone of fat, and she had no more muscular tissue than an under-weight person with which to do it.

Dr D. A. W. EDWARDS described two disorders of subcutaneous fat—lipodystrophy and diffuse symmetrical lipomatosis. The excessive tissue in lipomatosis is fat, and Dr Edwards showed slides of paraffin sections of fatty tissue taken from normal and obese persons and from persons suffering from lipomatosis. He demonstrated clearly that in an obese person the number of fat cells is normal, but there is an excessive amount of fat in each cell. In lipomatosis the number of fat cells is increased, and not the amount of fat in each cell. The fat cells respond normally to undernutrition, and the normal and abnormal parts of the body lose equivalent amounts of fat. In lipodystrophy there is a local disappearance or loss of function of the fat storing cells. It is quite common to get both disorders in the same patient.

New Inventions

MODIFIED LARYNGOSCOPE

THE laryngoscope illustrated here is a modification of R. R. Macintosh's excellent design. In this instrument the blade has been lengthened and its side-wall increased in depth. This gives an improved view of the larynx and, by opening the mouth more widely, an increased area for manipulation.



The entire electrical system can be removed from the blade, so that the latter can be put into the steriliser without fear of ultimately damaging the electrical insulation. It also makes for easy replacement of the lens fronted lamp, when required. This instrument was made for me by Messrs A. L. Hawkins, of 15, New Cavendish Street, London, W.1.

St Bartholomew's Hospital.

FRANCIS T. EVANS,
M.B. Lond., F.F.A. R.C.S., D.A.

Reviews of Books

Current Therapy, 1951

Editor: HOWARD F. CONN, M.D. Philadelphia and London: W. B. Saunders. 1951. Pp. 699. 50s.

Conn's *Current Therapy* should make a special appeal to the general practitioner, who will be grateful for a book on treatment which is both comprehensive and up to date. This volume, with its round dozen consultant editors and nearly 300 contributors, seems to have both these merits. It aims at providing a brief but complete resume, by one or more authors, of the treatment of all the commoner conditions met with in practice. No details of surgical operations are included, but the descriptions of methods available to the general practitioner are full and for the most part clear. The indexing is excellent and quick reference either to symptoms or to diseases proved possible for all the conditions looked for—with the exception of Halitosis (which seems to be omitted from almost every book on treatment), Proctalgia fugax, and (unless hidden out of sight) Periarteritis nodosa. A number of useful diagrams are given, and a “roster of drugs” at the end includes most of the best-known proprietary preparations. The therapeutic methods differ in places from those current here, but the book certainly offers authoritative views on present-day American treatment.

Neurosis and Human Growth

KAREN HORNEY, M.D. London: Routledge & Kegan Paul. 1951. Pp. 391. 21s.

Dr Horney's latest work is a welcome addition to her psychoanalytical theory. The fact that this theory is still developing—through the amplification here of the ideas embodied in *Our Inner Conflicts* in particular—is an indication of its clinical and intellectual vitality.

It is too early to assess the extent to which her system is likely to constitute a non-Freudian school. Her contribution to the understanding of neurosis seems to be mostly in the social biology of neurotic disorder. Her concept of psychodynamics—far less a psychology of the unconscious than that of Freud—is, in its own field, equally illuminating. Like most therapists, nowadays, she is well aware of factors outside the rigid Freudian canon of trauma, especially social factors, but she has a rather uncritical readiness to transfer conscious constructs to the patient. Modern anthropological work increasingly forces us to recognise the effect of social factors, and these are something which Freudian psychodynamics in their original form have not proved flexible enough to interpret satisfactorily. It is in bridging this gap that Dr Horney's work has particular value. She points the way to a full ultimate synthesis, not only between the sociological and Freudian approaches to mental ill health, but between the classical traumata and the conception of behaviour disorder (delinquency in particular) as a situation neurosis conditioned by faulty relationships. Her terminology is clear and will be welcome to teachers of social psychology.

The therapeutic implications of Dr Horney's work extend throughout education, politics, and social institutions. This is a valuable book.

Contraceptive Technique

HELENA WRIGHT, M.B. London: J. & A. Churchill. 1951. Pp. 68. 6s.

THIS is a good short book which could well be in the hands of every general practitioner and medical student; it is concise, accurate, free of fads and full of useful information, especially in dealing with gynæcological difficulties which may modify the technique of choice. Dr Wright's ten-page survey of the scope, objects, and requirements of contraception under modern conditions is a model of good sense with which the rest of the book is in key. Clinic and private-practice routine methods are well outlined; the psychological background is at least as much in the author's mind as the hygienic. A brief account of contraceptive methods suitable for use in the tropics or in countries which prohibit the sale of proper appliances and an account of the British Family Planning movement, up to the report of the Royal

Commission on Population, round it off Moreover a book of this kind should have a wide circulation in countries where the development of contraception and the training of advisers are becoming economic necessities Those wishing for a more detailed account of the scientific background of the subject will need to consult larger works, such as *Problems of Fertility in General Practice*, published in 1948 and sponsored by the Family Planning Association.

Die Entzündungsbestrahlung

(2nd ed) Dr HABIL R GLAUNER, Dozent für Röntgenologie und Strahlenheilkunde, Chefarzt der Röntgenabteilung am Marienhospital, Stuttgart Stuttgart Thieme 1951 Pp 189 D M 18 60

THE first edition of this book on the radiation of inflammatory conditions was published in 1910, this second edition leaves the first part, which explains the action of radiation, little changed, but brings the second part, which deals with treatment, more up to date

Dr Glauner discusses biological reactions on conventional lines, and concludes that the localised effect of X radiation is mainly due to its effects on leucocytes and lymphocytes, and to increased enzymatic processes at the site of an inflammatory lesion These effects are produced by very small doses, ranging from 10 r in acute, to 20 r in chronic, inflammations Very small doses are given daily, higher doses at longer intervals The results of treatment on these lines, for a large variety of inflammatory lesions, are discussed at length Lesions which respond particularly well are furuncles of the face, carbuncles, infections of sweat glands, and puerperal mastitis Other conditions which benefit when treated by the techniques described are tuberculous lymph nodes, and infections of the tonsil and other regions in nose and throat, postoperative parotitis, some forms of pneumonia, and certain chronic gonococcal infections The pain and disability of some forms of chronic arthritis can be relieved Radiotherapy can therefore be useful in the treatment of many diseases when combined with other forms of treatment, chemotherapy in particular There is an extensive bibliography, and the book can be recommended to radiotherapists studying the treatment of these inflammatory lesions

Nobel The Man and His Prizes

Editors The Nobel Foundation Stockholm Sohlmans Förlag 1950 Pp 620 Sw Kr 30

THIS important book contains not only surveys of the sciences as exemplified in the awards, together with an account of the awards in Literature and Peace, but also what to the general reader may be of even greater interest, a penetrating analysis of the character of one who was little known to the public

Alfred Nobel, as an inventor of genius, of many things besides dynamite, could hardly escape becoming a man of great wealth Yet at no time did he obtain happiness Born in Sweden and never losing his affection for his country, he was so cosmopolitan that he wrote with greater facility in English and perhaps in German, than in his native tongue The poetry which poured from him as a young man, under the influence of his passion for Shelley, was English poetry, by no means without merit When not travelling on the business of the many undertakings which he controlled, he lived for long in Paris and at the end of his life in Italy a retiring, sensitive soul, considerate of others, detesting all publicity, always an idealist and always alone Once, ill and lonely, he wrote ' I can see in my valet's eye how much he pities me, but I cannot of course let him notice that "

In his life Nobel was always a generous giver but one who discriminated "My natural inclination is less to honour the dead who have no feelings and who must be insensible to our marble tributes than to help the living who suffer want " In a short will of doubtful validity he left his great fortune to found the prizes that we know, and it is interesting to read how dubious were many of the leading personages and institutions of Sweden as to the wisdom of accepting the trust By many it was thought "a magnificent intention and a magnificent blunder ' Only after protracted discussion and a bitter struggle for four years was the final realisation of Nobel's wishes achieved Today the task of distributing the prizes is regarded by all Sweden as a privilege

In the account of recent awards an interesting light is thrown upon the mentality of Hitler When Professor Domagk was invited to receive the prize, Hitler, who had never heard of the 'Prontosil' which was exciting all Europe and who advisers were unable to enlighten him, had Domagk's hou surrounded by armed guards and hurried him to prison. T Hitler it was clear that a professor who received an awar from a foreign nation could only have earned it by betrayin his own

The Meaning and Practice of Psychotherapy

V E FISHER, PH D, formerly director of the Menta Hygiene Clinic, New York University New York an London Macmillan 1950 Pp 411 37*s* 6*d*

ALTHOUGH written in a pleasanter, less involved style than most American books on this subject, the present volume fails to shed much light on the first part of its title Dr Fisher's theories about the psychopathology of the mental disorders he treats are not discussed at much length From his first section, on the approach to the patient and procedure, and from his bibliography, it may be inferred that he has a very open mind and does not feel bound by any of the orthodoxies, but this eclecticism results in some oversimplification of theory The three following sections, which comprise the bulk of the book, are more rewarding, for they contain over 20 case histories, showing Dr Fisher's methods of handling various conditions—psychotic, psychoneurotic, and socially maladjusted Perhaps the most interesting case is that of an early schizophrenic treated by what Dr Fisher calls "psychic shock," though the cases of phobia and of suicidal tendencies are also most unusual In this as in many other books on psychotherapy the contrast between obscure, even debatable, theories and the intuitive sureness of their proponent when it comes to dealing with a patient is curious Possibly psychotherapy has always been more a matter of deep calling unto deep than we like to think nowadays

Pediatric Allergy

ROBERT CHOBOT, M D, assistant clinical professor of pediatrics, New York University—Bellevue Medical Center New York and London McGraw Hill 1951 Pp 284 38*s* 6*d*

Dr Chobot's teaching on allergic problems in children is well known in America He has set out in this book the basic facts of pædiatric allergy that he has gleaned from his experiences The book could be said to be a synopsis of the clinical aspects of diagnosis and treatment of allergic complaints in children and, though it was not the author's intention to make the book a general synopsis on allergy, it could well serve this purpose It is easily and quickly read, though at times, in compressing his subject matter, Dr Chobot makes dogmatic statements which might be misleading to a student Thus he says that the term migraine should be reserved for the condition in which patients have unilateral headaches associated with nausea and vomiting, later, nausea and vomiting rather than headaches are said to be the prominent symptoms in young children But on controversial questions he usually presents both sides He knows that some will take issue with him over the importance he gives to focal infection, particularly over the frequency with which he advocates the removal of tonsils and adenoids Though he is hopeful of progress in the development of more effective anti-histamine drugs, he rightly observes that they are of no great use in asthma, where they can only be used for sedation The last part of this very reasonable book is taken up with illustrative case histories to bring out points in diagnosis and treatment

---

Blood Clotting and Allied Problems (New York 1950 Pp 224 $3)—The Josiah Macy, Jr, Foundation's Third Conference on this subject, held in January, 1950, gave most of its time to discussing anticoagulants and their control, with special emphasis on the newly introduced substances 'Tromexan,' phenylindandione, and paritol Six papers in this volume, edited by J E Flynn, deal with problems connected with prothrombin, one deals with the effect of surfaces on blood coagulation, and one with the application of zeta potential measurements for studying blood clotting All the papers are very technical but the volume remains of interest to specialists in the field, mainly because of the verbatim reports of the discussions, which seem reasonably uninhibited

THE LANCET

LONDON SATURDAY, MAY 26, 1951

International Sanitary Regulations

Last month a special committee, consisting of government delegations, met in Geneva to consider the final text of the new International Sanitary Regulations which it is proposed shall replace the existing International Aerial and Maritime Sanitary Conventions. The text had been worked on for three years by the World Health Organisation's expert committee on epidemiology and quarantine and by the secretariat of W.H.O., and had been sent to governments for comments, so it was already in a form likely to find general support. International quarantine discussions necessarily end in a measure of compromise between those countries which are highly receptive to the diseases in question, and therefore require the maximum protection, and those whose interests are mainly in international trade and which insist on the minimum interference with shipping and aircraft on international trade routes. On this occasion, however, there was a third group which held that the best protection for all countries against importation of disease is the immunisation of all travellers as a condition of international travel. With Dr. M. T. Morgan in the chair, the committee was in session for four weeks, during which the argument centred round these conflicting interests, but the final text did not differ greatly from the original. It is hoped that the W.H.O. Assembly, now meeting in Geneva, will accept this text, so that the new regulations will then be open to governments for acceptance.

The procedure on this occasion differs from that used for previous conventions. Governments will not now have to sign and ratify these new regulations individually, for they will come into force for all members of W.H.O. after a stated period. During this period governments may only contract out of the regulations as a whole and cannot make reservations substantially changing the intention of the regulations. For this reason any reservation made by a government must first be submitted to the Assembly, and, if it is rejected, the government concerned must either withdraw the reservation or reject the regulations as a whole. In the latter case the existing conventions will remain in force if the country concerned has ratified them. The new regulations provide for a continuous review of their working which will enable any amendments or additions to be made without the need for an entirely fresh set of regulations on each occasion. If a dispute arises between governments on a quarantine matter, W.H.O.'s existing machinery for dealing with it will be used, but if necessary a suitable committee may be convened to consider the case. There is also the final remedy of an appeal to the International Court of Justice. The measures prescribed in the regulations are to be regarded as maxima, and no country is likely to apply them in full.

The recent advances made in methods of destroying insects have been recognised by the abolition of some of the older measures in force for dealing with typhus, relapsing fever, and plague. Measures against yellow fever remain largely unchanged, but there is now a clause that allows local areas which keep the aedes index below 1% to be excluded from the yellow fever endemic zone. The smallpox and cholera measures have been simplified, though the measures themselves have been somewhat intensified: for instance, travellers on an international journey may be required to possess a certificate of vaccination against smallpox, but if they come from a local area infected with smallpox they *will* be required to possess such a certificate, or to submit to vaccination, or failing this to be isolated for the unexpired portion of the incubation period. The certificate of vaccination against smallpox has been revised: it will no longer contain a record of the result of vaccination but will become available immediately for three years from the date of vaccination. As regards cholera, stricter measures are now to be permissible; persons arriving from an infected local area within the incubation period of the disease may be isolated for the remainder of that period, unless they have a valid certificate of inoculation against cholera. Rectal swabbing and stool examinations of healthy persons are not permissible measures under the new regulations. The six diseases to which the regulations apply—cholera, plague, yellow fever, smallpox, typhus, and relapsing fever—are now to be termed the "quarantinable diseases," while the other infectious diseases for which no provisions are yet made in the regulations will be termed "epidemic diseases." Proposals were discussed in the committee for removing typhus and relapsing fever from the scope of the regulations as well as for establishing the maximum measures which may be applied for "epidemic diseases." Both proposals were dropped for the time being, though they will no doubt be raised again in the course of the work of review of the regulations.

Generally speaking it can be said that these regulations, if accepted, will be an important advance and will place the international system of quarantine on a more rational basis. A point of great importance is that there is now a convenient procedure for altering and revising the quarantine regulations at suitable intervals, to conform with advances in science and with changing epidemiological conditions.

Drugs in Amœbiasis

The pandemic of virulent amœbiasis that was widely predicted to mark the homecoming of expeditionary forces at the end of the late war has not materialised. In the U.S.A. the post-war rise in incidence seems to have been no greater than might be expected from improved diagnostic techniques and amœba mindedness among both doctors and the public. The American outlook has in places amounted to a phobia, and there has been a tendency for some clinicians to ascribe nearly every case of chronic looseness of the bowels to amœbic infection, and for some pathologists to report nonpathogenic strains as *E histolytica* Bargen[1] and other American authorities look now on the "amœba-carrier" as a person suffering from amœbiasis which is not causing manifestations severe enough to send the patient to his doctor , in fact most of these people have symptoms of the infection, though they are not necessarily those of colitis

The ideal amœbicide should be active by mouth , it should kill the organism in the trophozoite or cystic stages in the lumen of the gut, and should reach the liver and other infected tissues in a concentration high enough to deal effectively with trophozoites , and its toxicity must be low No known drug satisfies all these criteria The amœbicides now in use are of three classes First, there are those like emetine, carbarsone, and 'Vioform' which when given systemically will kill amœbæ in either bowel or tissues , they presumably act directly on the amœba, since they have little if any effect on associated bacteria or protozoa The second class act indirectly by rendering the bacterial flora of the intestine unfavourable for amœbæ , these include penicillin and some other antibiotics (probably 'Aureomycin' acts directly), sulphonamides, and hydroxyquinolines like chiniofon and 'Diodoquin' These may clear the lumen of the bowel of *E histolytica* but are not effective if the tissues have been invaded Unfortunately they only clear the bowel of the parasites for a few weeks or possibly months, and when the normal bacterial flora returns the pathogenic amœbæ flourish once more The third class of drug, exemplified by chloroquine, are concentrated in the liver and act well in amœbic hepatitis, but much less on the amœbæ inside the colon For this reason a combination of amœbicides is often more effective than any one alone Improved methods of in vitro testing have made it possible to see whether an amœbicide acts directly on the amœba or on commensal organisms in the gut

Several workers have been studying the effect of antibiotics in amœbic dysentery Penicillin is used only as an adjunct to other treatment,[2] since its therapeutic effect must be on the secondary bacterial invaders rather than on the amœba itself, which is resistant in vitro to concentrations of penicillin as high as 10,000 units per ml[3] Faust[4] noted that 'Bacitracin' is amœbicidal and Most[5] found that this antibiotic not only ends acute amœbic dysentery but also eliminates the amœbæ from the stools of two thirds of the patients treated It apparently acts selectively on clostridia and enterococci, as well as on other gram-positive organisms, but it does not prevent the subsequent reappearance of amœbæ in the stools , 80,000 units by mouth daily for 10 days is recommended Aureomycin seems to be even more promising McVay and colleagues[6] treated 37 cases with 2 g daily for a week with good results in 36 , symptoms were quickly relieved and the carrier state eliminated Most et al[7] treated 100 cases with satisfactory results, though 10% relapsed after 10 days' treatment Armstrong and others,[8] working in the Amœbiasis Research Unit at Durban, obtained an immediate cure rate of 94% —higher than with any other single agent—but the relapse rate was high In their view aureomycin is the drug of choice in acute ulcerative amœbiasis, but it should be given with other drugs, such as diodoquin, to prevent the relapses commonly seen in the first month after a course of aureomycin alone Hall,[9] who has been treating acute and chronic cases in veterans at Minneapolis, reports good results in chronic amœbic dysentery and in cyst-passers (i e , "carriers," now usually looked on as chronic cases of amœbiasis) , but he emphasises that "aureomycin should not be used alone in hepatic amœbiasis, but should be supplemented by emetine hydrochloride or chloroquine, or both" In his hands, chloramphenicol has been less effective than aureomycin against amœbæ in vitro Thompson et al[10] found that chloramphenicol would suppress amœbic colitis in dogs, but only temporarily , it worked better against cæcal infections in rats but had not yet been tried in human infections The amœbicidal activity of some of the new antibiotics have been compared by Watt and Vandegift[11] They head the list with polymyxin B and aureomycin, followed by polymyxin E Bargen[1] cites some excellent clinical results with 'Terramycin', and lately McCowen et al[12] have shown that 'Fumagillin' or H3, an antibiotic obtained from a species of aspergillus, will inhibit the growth of *E histolytica* at a dilution of 1 in 120 million in the presence of the intestinal bacterial flora, and will eradicate amœbic infection in rats in a dosage of 9 mg per kg If this newest recruit is well tolerated by man it may well be the best amœbicide among the antibiotics

Among other new drugs introduced for amœbiasis are 'Milibis' and chloroquine Milibis, or 'Win,' the bismuth derivative of *p*-N glycolylarsanilic acid, originally studied in infected kittens in Germany in 1943,[13] has been submitted to clinical trial in the United States by Dennis, Berberian, and Hansen[14] It is not absorbed and so can only act locally in the bowel Sixty-two out of sixty eight cases were cleared of amœbæ after taking 0 5 g three times a day for a week, but further investigation is needed Chloroquine [7-chloro-4-(4-diethylamino 1 methyl butyl amino) quinoline] has given encouraging results as an amœbicide[15] It is concentrated in the liver, the concentration in that organ being 400 to 600 times that in the plasma[16] A dose of 0 3 g twice daily for two days and then 0 3 g daily for an additional twelve to nineteen days is a valuable adjunct in the treatment of amœbiasis with liver involvement Chloroquine, despite its somewhat lower effectiveness in intestinal amœbiasis, is a satisfactory substitute for emetine in hepatic amœbiasis, and is considerably less toxic than emetine apart from mild gastric disturbances chloroquine appears to be relatively free from side effects Emetine is still favoured for the treatment of amœbic hepatitis, but care is required in its administration since in dosage slightly in excess of that used therapeutically it is a protoplasmic poison If the claims for chloroquine stand the test of time this drug may eventually replace emetine in the treatment of amœbic hepatitis

---

[1] Bargen J A *J Amer med Ass* 1951 **145**, 785
[2] Wright, A W Coombes A E R *Lancet* 1948 i 943
[3] Knoll, E W Howell, T H *Arch Path* 1946 **42** 594
[4] Faust, E C cited by Bargen (ref 1)
[5] Most H *Bull N Y Acad Med* 1949 **25**, 717
[6] McVay L V Laird R L, Sprunt D H *Sth med J* 1950 **43** 308
[7] Most H Miller J W Grossman E J *Amer J trop Med.* 1950 **30** 491
[8] Armstrong T G, Wilmot, A J Elsdon Dew R *Lancet*, 1950 ii 10
[9] Hall W H *New Engl J Med* 1951 **244** 495
[10] Thompson, P E Dunn, M C, Bayles A Reinertson, J W *Amer J trop Med.* 1950 **30** 203
[11] Watt J Y C Vandegift, W B *J Lab clin Med* 1950 **36**, 741
[12] McCowen M C, Callender M E Lawlis J F *Science* 1951 **113**, 202
[13] Hauer A *Dtsch tropenmed Z* 1943, **47** 153
[14] Dennis E W Berberian D A Hansen S S *Amer J trop Med* 1949 **29** 683
[15] Berberian D A *J clin Invest* 1948 **27** 525
[16] Conan N J *Amer J trop Med* 1948 **28** 107

Carbarsone, a trivalent arsenical compound, is often used in conjunction with emetine If the oxygen attached to the arsenic atom of carbarsone oxide is replaced by a sulphydryl group (SH) the toxicity is reduced Substitution of the hydrogen atom of the SH group by methyl or phenyl groups, and carboxylation of these to render the compounds soluble, results in amœbicides with an activity greater than that of the parent substance[16] After their administration arsenic can be detected in the bile, liver, kidneys, and intestinal tract Preliminary tests in man have shown that two of these compounds are about 90% effective against trophozoites in tissues and cysts and in the lumen of the colon[17 18] All arsenicals are, however, potentially toxic, and such compounds cannot compare in safety with antibiotics such as aureomycin and terramycin

The problem of relapse may be solved by using a combination of drugs ARMSTRONG, WILMOT, and ELSDON-DEW[8] found a combination of penicillin and sulphasuxidine, followed by emetine and diodoquin, 95% effective They believe that the dose of emetine could be drastically reduced if it were used with aureomycin, and that the combination of diodoquin with aureomycin would reduce the relapse rate still further

Mental Health and the Mother

"EVERY kind of parent makes a hash of it" is a despondent aphorism born of modern psychiatric teaching, but there is some comfort for parents in the more recent view that deprivation of parental love—and even deprivation of the love of bad or incompetent parents—makes a super-hash, a kind of witches' brew Dr JOHN BOWLBY, whose work on this theme is well known, has lately made, on behalf of the World Health Organisation, a report on *Maternal Care and Mental Health*,[19] as a contribution to the United Nations programme for the welfare of homeless children His review of the evidence of the effects on the child deprived of the care of his mother during his early years is extremely impressive Studies fall into three classes (1) direct studies made on the mental health and development of children in institutions, hospitals, and foster homes, (2) retrospective studies of the early histories of adolescents or adults who have developed psychological illnesses, and (3) follow up studies of groups of children deprived of maternal care in their early years It is noteworthy that all these studies, undertaken ' by people of many nations, varied training, and, as often as not, ignorant of each other's conclusions," very largely confirm and support each other Indeed, only three, all follow-up studies, throw any doubt on these conclusions Numerous careful direct studies indicate that, when young children are deprived of maternal care, their physical, intellectual, and social development is retarded, and retrospective and follow up studies make it clear that in some children the damage is serious and permanent All children under the age of about seven years seem to be vulnerable, and the effects have in some cases been noticeable in the first few weeks of life Among the direct studies quoted is that of H DURFEE and K WOLF who (using the Hetzer-Wolf tests) compared the developmental quotients (D Q) of 118 infants in various institutions, and correlated the results with the amount of maternal care the infants received They found no difference between normal and deprived children in the first three months, but differences steadily increased from that time onwards, and children who had been in institutions for more than eight months during the first year showed such severe psychiatric disturbances that they could not be tested The picture of the institution baby has been drawn by H BAKWIN from his own observations, as follows

> "Infants under 6 months of age who have been in an institution for some time present a well-defined picture The outstanding features are listlessness, emaciation and pallor, relative immobility, quietness, unresponsiveness to stimuli like a smile or a coo, indifferent appetite, failure to gain weight properly, despite the ingestion of diets which, in the home, are entirely adequate, frequent stools, poor sleep, an appearance of unhappiness, proneness to febrile episodes, absence of sucking habits"

Those who have seen R A SPITZ's film, *Grief, a Peril of Childhood*, will be aware how accurate is this description of the baby deprived of his complementary partner

SPITZ and K M WOLF have made systematic studies of four groups of children—three in which the babies were with their mothers, and one in which they were not Absolute levels of development differed according to social group, but babies living with their mothers showed no change in D Q during the year On the other hand, the 61 infants brought up in a hygienic institution, and kept in relative isolation in cubicles, showed a catastrophic drop in D Q between the ages of four and twelve months, from 124 to 72, by the end of the second year the D Q had sunk to 45, and the infants were gravely retarded Other studies, notably those by W GOLDFARB, show similar retardation in older institutional children In a thorough study of 30 children aged between thirty and thirty-five months, half of them in an institution and the other half in foster-homes, GOLDFARB found a difference of 28 points in the intelligence quotient (Stanford Binet test) between the two groups The institution children had an average I Q of 68—on the borderline for mental defect—while the children in foster-homes averaged 96 BOWLBY notes that such findings are often questioned on the ground that many children in institutions come of poor stock, physically and mentally, heredity, it is suggested, might account for the differences But, as he points out, the investigators in most of the studies he cites have taken care to ensure that their control groups are of a similar social class and spring from a similar stock

---

[17] Anderson H H Hansen E L Sah P T Cafiso J R *J Pharmacol* 1947 91 112

[18] Anderson H H Johnstone H G Bostick W Chevarria A P Packer A *J Amer med Ass* 1949 140 1251

[19] Geneva World Health Organisation Monograph Series no 2 1951 Pp 179 Obtainable from H M Stationery Office at 10*s*

The picture of apathy and retardation described by BAKWIN is produced most commonly in children who have had a happy relationship with their mothers up to six or nine months, and have then been suddenly separated from them. Of 95 children studied by SPITZ and WOLF, 20% reacted to separation by a severe depression, and 27% by a mild depression; this was considered to be the normal response. Most of those who escaped such depression had not had a close and happy relationship with their mothers, which suggests that their development was already damaged and their later capacity for love likely to be impaired. If the mother returns, recovery may be rapid and striking; but the longer she is away the more serious and lasting the damage, and the less the likelihood of complete recovery.

Retrospective studies suggest how serious the damage may be. In the '30s several independent workers noticed that those young delinquents who seem to have no capacity for affection or feeling for others had often had seriously disturbed relationships with their mothers in early years. Such children were often persistent thieves, violent, and egotistical, and sometimes guilty of sexual misdemeanours. If the disturbed relationship was a cause of the delinquency, as seems probable, society has a direct interest in preventing the separation of young children from their mothers. In a group of 44 young thieves whom BOWLBY himself studied, 14 were of the "affectionless" type, and 12 of the 14 had experienced separation from their mothers in early childhood. Among a control group of 44 emotionally disturbed children who did not steal none were affectionless, and only two had been separated from their mothers. GOLDFARB's comparisons of 15 children who had spent their first three years in an institution and 15 who had not, show a remarkable difference in such functions as intelligence, ability to conceptualise, reading, arithmetic, social maturity, capacity for friendship, and speech. In every instance the control group excelled the institutional children, often considerably. Three studies run counter to the general findings. S. Z. ORGEL has given a not very detailed or systematic account of 16 institution children, among whom he found only 2 with adverse personality features; F. BROWN judged that 100 institution boys aged between nine and fourteen were no more neurotic than 100 of the same age living at home in bad surroundings; and F. BODMAN, having found that 51 institution children had a lower social maturity score (Vineland scale) than 52 children living at home, regrouped all the children according to heredity, and found exactly the same difference. He concluded that constitutional factors are at least as important as environment, but BOWLBY considers that the statistical methods applied were not above criticism.

In the main the evidence is remarkably consistent and impressive; and BOWLBY holds that the case is now proved. If so, what are the remedies? They are urgently needed, he believes; for these deprived children grow up into ill adjusted adults, and reproduce in their own families the conditions which led to their own disablement. This is confirmed by the experience of psychologists and sociologists: deprived unhappy children grow up to make unsuccessful marriages in which discord, desertion, separation, and divorce are commonplaces; and they are thus poor parents. In this context he mentions the growing value of marriage guidance; and he might have added guidance about venturing on marriage at all. The notion that marriage is an exacting adult experience is not very general nowadays; it might well be more widely taught.

BOWLBY proposes some important preventive measures. First we need more research into the effects of deprivation. It would be useful to know, for instance, the length of time during which separation of the child from the mother can be permitted with safety, to allow for making good the damage done. Again, personality growth depends on the interaction between the growing child and the people about him, especially his mother, and we need closer studies of this process. Experiment presents obvious difficulties, but some of LIDDELL's work with animals is proving enlightening. Systematic clinical and psychometric studies of institutional and delinquent children could give further information and so, he thinks, could physiological and electro-encephalographic investigations. Meanwhile some social preventive measures suggest themselves. BOWLBY warns against a vested interest in the institutional care of children, and the temptation to suppose that because a child looks clean it must be well and happy. A rather grubby child playing boisterously in the home of its loving but feckless parents may be growing into a more mentally healthy citizen than a docile and physically cherished child in a clean bare ward. He is no lover of day-nurseries; not only do they separate mother and child for many hours of the day, but their rates of infection are high. Moreover, they are costly to run (£3 per head per week), and for every 100 women they release to industry they employ 50 to look after the children. We should give up the idea that because a mother is running her home badly she should be deprived of her children: it is often not only easier, but much cheaper, to give her some material help with the rent and the housework. BOWLBY quotes the saying of Sir JAMES SPENCE that at present mothers are "relieved of their children when they should be relieved of their chores." He also puts the case for the child detained for long months or years in hospital for orthopædic or other treatment. Most of these can spend their time at home between operations; and their segregation from normal life is damaging and unnecessary. When a young child must be separated from his mother—when she dies, or abandons him, or is kept from him by sickness or imprisonment—then he should whenever possible be provided at once with a substitute, a foster mother with whom he can make the same strong personal link that he should have made with his own mother.

BOWLBY concludes a capable survey of many other aspects of this world wide social problem by comparing our present position to that faced by the pioneers of public health a century ago. We must take action now, even though our evidence is incomplete; for "it must be remembered that evidence is never complete, that knowledge of truth is always partial, and that to await certainty is to await eternity." In this case, to await certainty may well be to await a spreading of our present social sickness until it is beyond all cure.

Annotations

HOUSING FOR SPECIAL PURPOSES

BOTH humane and economic considerations have directed attention to the housing of old people. A new booklet[1] on this subject goes further afield to study the accommodation required for single workers, including students and apprentices, dwellings for disabled persons, and the special needs of district nurses and midwives. There are even a few kind words for the house hungry higher income groups.

The recommendations dealing with the aged emphasise the importance of cooperation between the housing and the welfare authorities, especially at the moment when responsibility passes from the one to the other. The old people should be conscious of this close-working arrangement "they should not be troubled by the possibility of passing from familiar surroundings (the home or the room they have known for many years) to a completely strange place administered by strangers." In examining the various types of dwelling the committee have given much thought to hostel accommodation, for which an Exchequer subsidy is now payable under the Housing Act, 1949. They take the view that each hostel should provide for about 30 old people. The building should not have more than two storeys, and it should be planned for communal rooms, dining-rooms, kitchen, and some bed sitting rooms on the ground floor, with the rest of the bed sitting rooms and the warden's flat above. The building should be centrally heated, with a radiator in every room and, in addition, open fires in the communal rooms. It is rightly urged that each single old person should have a separate bed sitting room: they all want to have *one* room of their own. The equipment suggested for the bed sitting rooms is admirable: each with a fitted washhand basin, a built in cupboard with hanging space and shelves, an electric fire, a good central light, and a point for a bedside lamp. An electric bell near the bed is also an essential fitment. There is a further useful suggestion to fit up a number of guest rooms in each hostel.

The proposals for self contained dwellings follow the traditional pattern, but the committee go further than the Housing Manual in suggesting an auxiliary means of water heating by gas or electricity. They lay just emphasis on protection against fire, but almost in the same breath they say that a coal fire should always be fitted in the bedroom. The two proposals are incompatible. A coal fire is *not* safe in a bedroom of 120 sq ft or thereabouts, even when a kindly authority provides a fireguard. Coals drop out, and bedclothes leap to meet them. Why not a properly guarded gas or electric fire, or a hot water radiator as recommended for the hostel bedrooms? Another curious anomaly, explicit under the heading of hostels and implied in the separate dwellings, is that the W C should not be combined with the bathroom. No reason is given for this out of date advice, but it is well known that elderly people have increasing difficulty in maintaining cleanliness after using the toilet, and that the narrow, cold cell which constitutes the W C in England is the sworn enemy of hygiene. The committee show a common sense attitude towards the siting of dwellings, recommending that some of them should be dispersed among ordinary houses. At the same time there is a need for cottages in groups for old folk who prefer to live among people of their own generation. These grouped dwellings should be provided in each residential district in a town, so that the old need not leave the surroundings they know well. For those who have to be relieved of the heavier household tasks hostels are suggested, in the same area. Under existing legislation the home making of the aged is a responsibility of no less than three authorities: the local councils for small dwellings and hostels, the welfare authorities for the infirm, and the regional hospital boards for those who are sick.

The provision of hostels for single workers is still a matter for investigation in this country, since neither the extent of the need nor the most suitable design has been determined. The committee favour the adoption of standards identical with those for the aged for more or less permanent single workers, but for the young apprentice and the student a reduction of the floor area of the bed sitting room from 140 to 108 sq feet as a minimum. This seems reasonable, so long as the communal services are not curtailed—and this is the recommendation of the committee. Perhaps the most emphatic, as well as the wisest, proposal for this group is that a full service of communal meals should be provided:

> "Apart from the fact that the casual meals service can seldom be run economically, it seems to us that the alternative to a complete meals service too often means a hasty snack eaten in the canteen or improvised hurriedly between the return from the day's work and the evening activities and an inadequate supplement to a light midday lunch. In the case of young people we think the arguments against an arrangement of this sort to be quite conclusive and even amongst older people we feel that the communal service will be preferred to the meal cooked with the restricted facilities that could be provided in a bed sitting room."

In considering the needs of disabled persons the committee show imagination and generosity. The special requirements include ramps in place of steps, wide spaces and doorways to allow a wheeled chair to turn, a larger bathroom than normal, and a second W C compartment fitted with holding bars on both sides and a suspended ceiling grip. Many details of equipment have been thought out, especially in relation to ease of movement and avoiding the risks of slipping.

The report as a whole is simple and useful. It is well printed, and is illustrated by good photographs and by plans easily read by the layman.

THE STUDENT'S OUTLOOK

THE medical student learns much and in the end knows little, said Prof Andrija Stampar of Zagreb, at a discussion held the other day by delegates to the fourth assembly of the World Health Organisation. The present system of education, Dr Stampar declared, is out of date and in urgent need of reform. It persists in its traditional aim of training physicians to cure individuals of actual disease. But the rapid development of medical science, of public health services, of social medicine, and of social insurance demands a different attitude, and by learning about preventive, social, and constructive medicine the student should be given a healthy outlook on the nation's life and the doctor's rôle in society. Some medical faculties still have no special chairs in these important subjects, and many of them isolate themselves from their public health services. Only when they have rid themselves of this policy of isolation can they become centres of learning that will train doctors more for collective than for individual needs—doctors with more understanding of general health questions that concern people's lives, and their social and economic conditions. Recalling the principle, expressed in the W H O constitution, that governments have a responsibility for the health of their peoples, and that this responsibility can be fulfilled only by the provision of adequate health and social services, Dr Stampar said that if medical students had become used to this principle during their training we should not have witnessed such desperate opposition by medical men in some countries where national health services have been introduced or have recently been discussed. Is every young doctor (he asked) really convinced that everyone, rich or poor, has an equal right to health? Is he convinced that his services are not like other services, just another commodity to be sold for money? The spirit of preventive medicine should permeate the whole of medical education, and not, as at present, be taught in the last year of the curriculum when the student already has settled opinions.

---

[1] Housing for Special Purposes: a supplement to the Housing Manual 1949 prepared by a Subcommittee of the Housing Advisory Committee. H M. Stationery Office. Pp 43. 2s.

THE MEDRESCO HEARING-AID

HEARING AIDS are now so inconspicuous and such a familiar sight—1 in about 200 of our adult population wears one—that they often pass unnoticed. The earlier forms of electric amplifier were generally known as "deaf aids," and many of them did indeed advertise the wearer's deafness more than they helped his hearing. But in the last fifteen years, thanks largely to the development of miniature wireless valves and small but powerful batteries, easily wearable valve amplified hearing aids have been evolved which give remarkably clear and undistorted reproduction of speech. For many deaf people the only remaining objection to the use of an aid has been the price, and it is hardly surprising that, since the National Health Service began to provide (on free loan) and maintain hearing aids for those in need of them, the demand has exceeded the supply. To date, more than 120,000 deaf persons in England, Scotland, and Wales have been supplied with a 'Medresco' aid through the Ministry of Health, and almost an equal number are waiting to try one. The probable demand was estimated by the Social Survey [1] as being at least 300,000 from among the 1,750,000 hard of hearing persons in this country; and as further improvements in size and performance are made, the proportion of such persons who are prepared to use an aid may well increase. So it may be some time before the peak of the demand is reached.

As this scheme was something quite new, it was decided that, after it had been working for two years, an attempt should be made to ascertain how far the medresco hearing aids were actually being used. The Social Survey undertook this, and their findings are described by Mr Gray and Miss Cartwright on p. 1170. These support the anticipations of the Electro Acoustic Committee of the Medical Research Council,[2] who were responsible for the design and development of the medresco aid and who believed that the provision of one type of aid, with even amplification over the whole of the speech frequency range, would meet the needs of all but a few deaf persons. They will also quieten the qualms of those who feared that many, if not most, of the aids issued would not be used properly but would be stuffed away in a drawer—a fate that not infrequently overtook the earlier electrical aids. Perhaps the most interesting feature of this sample survey is that, with the help of the medresco aid, some 80% of deafened persons over the age of 75 were able to understand all or most of what was said to them; for it has been the general experience that sufferers from senile deafness will tolerate only the purest amplification and that they do not take kindly to electrical aids. In fact it will be seen that most of the criticism of users is directed not at the aid itself but at the batteries, which weigh five times as much as the rest of the aid and are more than twice as bulky. It is to be hoped that the recent advances made in battery construction and in the amount of current consumed by the valves will enable smaller batteries to be employed without increasing the running costs.

The medresco aid has thus come out of this test very well. In six years a hearing aid has been designed, tested, produced, and distributed on a large scale, and studied in action. What has not yet been revealed is the fate of those still awaiting trial with an aid. At some of the hearing aid centres, where the waiting lists now run into many thousands, it is thought that, at the present rate of issue, five or more years will pass before some deaf people get their turn. And, of course, as more aids are issued, so will more of the new aids be needed for replacement of those worn out; already, indeed, of every 100 aids issued, about 40 go in replacements. Probably most of the 47 hearing aid distributing centres could manage to distribute more aids than they have at present, without reducing the amount of instruction given to each person in the use and maintenance of the aid. Such instruction is a very necessary part of the scheme and should not on any account be cut.

It is important that the waiting lists should be worked off as quickly as conditions will allow. To know that the medresco aid is a success gives no satisfaction to those at the end of the queue; in fact, it only serves to sharpen their impatience. Let us hope that enough aids will continue to be produced to enable the existing centres to work at full capacity.

---

1. Williams L. T. *Acta otolaryngol* 1949, suppl. 90, p. 97.
2. Hearing Aids and Audiometers. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1947, no. 261.

THROMBOSIS OF THE INTERNAL CAROTID ARTERY

TRAUMATIC thrombosis of the internal carotid artery was first described by Verneuil [1] in 1872, and its importance as an occasional cause of hemiplegia after head injuries associated with trauma to the neck has been emphasised by Cairns.[2] Lately spontaneous thrombosis of the artery has been more often recognised as a cause of the syndrome. The introduction by Moniz of carotid arteriography made the diagnosis possible during the patient's life; and it was Moniz who, in 1937, first reported a group of cases.[3]

Thrombosis of the internal carotid artery occurs predominantly in men, and the highest incidence seems to be between the ages of 35 and 55.[4] It affects the left side more commonly than the right; and often premonitory symptoms are present for weeks or even months before the fairly sudden onset of severe hemiplegia. These warning symptoms are mainly of two types: (1) attacks of frontal headache on the side corresponding to the diseased artery, lasting for some hours at a time and usually stopping after hemiplegia has developed; and (2) transient disturbances of function of the cerebral hemisphere supplied by the diseased artery. These temporary disturbances consist of hemiparesis or of unilateral sensory symptoms, lasting for anything from a few minutes up to an hour or two; the symptoms clear up completely but recur again and again. These transient neurological disturbances tend to come on separately from the attacks of unilateral headache. Some patients also have attacks of transient impairment of vision on the affected side, due to retinal ischæmia. When hemiplegia finally develops it may come on suddenly; but in some cases the development is "stuttering," with weakness of one leg followed, over the course of days or even weeks, by gradual involvement of the arm and face and of speech. Probably the transient premonitory episodes are due to cerebral ischæmia; they may be the result of vasospasm of cerebral arteries due to nerve impulses originating in the diseased wall of the internal carotid artery.[5] Clinically the diagnosis is difficult, and Fisher [4] thinks that middle cerebral thrombosis is often diagnosed in these cases. In a large series of necropsies on cases of cerebral vascular disease no instance of thrombosis of the middle cerebral artery was found, though this lesion had commonly been diagnosed during life; unfortunately in this particular series the carotid arteries were not thoroughly examined, and he emphasises how often such an examination is omitted in routine necropsies. At times the

---

1. Verneuil A. *Bull. Acad. Méd. Paris* 1872, 1, 46.
2. Cairns H. *Lisboa méd.* 1942, 19, 375.
3. Moniz E., Lima A., de Lacerda R. *Pr. méd.* 1937, 45, 977.
4. Fisher M. *Arch. Neurol. Psychiat.* 1951, 65, 346.
5. Amell N. O., Ashby D. W. *Lancet* 1949, ii, 1078.

diagnosis may be suggested clinically by unilateral absence of carotid pulsation high up in the neck, but a thrombosed carotid artery may become recanalised, and pulsation on both sides some time after an ictus does not rule out the diagnosis At present the diagnosis can be proved with certainty only by demonstrating the block by arteriography

The thrombosis takes place most commonly in the carotid sinus at the beginning of the artery, but it may occur in the part of the artery in the carotid canal In an exhaustive study Hultquist [6] found changes in the brain in only one third of the cases of occlusion of the internal carotid artery below the origin of the ophthalmic artery, and possibly the lesion may sometimes give rise to no symptoms, whether symptoms are produced or not presumably depends on the adequacy of the circulation through the circle of Willis The commonest pathological basis for thrombosis appears to be atheroma in the carotid sinus, and, as Chiari [7] pointed out in 1905, atheroma of the carotid sinus can also be a source of cerebral emboli More rarely the underlying arterial disease is thrombo angiitis obliterans [8] The pathology and clinical characteristics of thrombosis of the internal carotid artery will be further clarified by routine post mortem examination of the whole length of the vessel, by keeping the condition in mind in cases of unexplained hemiplegia, and by arteriographic examination

TAKING THE CURE

To provide an authoritative statement on the place of the spa in modern practice, the British Medical Association appointed a committee under the chairmanship of Lord Horder [9] Its report [10] forms a guide to all the spas in Great Britain, and describes the various forms of treatment obtainable at each. Among the conditions in which the committee believes that spa treatment can be of great value are chronic arthritis of the rheumatoid and degenerative types, muscular, fascial, and fibrositic rheumatism, infections of the urinary tract, pelvic disorders in women, and certain cardiovascular and nervous disorders It also thinks that far more use could be made of the spas for patients recovering from acute illness, whether medical or surgical Anticipating the argument that the physical treatment available at spas could be given equally well at any suitably equipped hospital, it points out that, apart from the concentration of specialised medical facilities, the spas are attractive places with equable climates, and have the amenities of holiday resorts, hence the benefits of physical treatment are supplemented by the important psychological effects of a "complete change" in attractive surroundings with ample opportunity for recreation The committee concludes that the profession in general tends to underestimate the value of spas, and in many ways fails to appreciate the progress made at these centres in recent years Increasing cooperation between the spa hospitals and the universities and teaching hospitals will promote research, permit greater continuity of treatment and standardisation of investigation and follow up, and help the spas to take their proper place in the National Health Service

THE JENNER MEDALLIST

CELEBRATING the centenary of Jenner in 1896 the Epidemiological Society of London founded a medal to be awarded from time to time for distinguished work in epidemiological research or for pre eminence in the prevention and control of epidemic disease The ten recipients have been William Power, A Laveran, Patrick Manson, Shirley Murphy, John McVail, Monckton Copeman, T H C Stevenson, George Buchanan, Arthur Newsholme, and Major Greenwood, and last week a new name was added to the list—that of James Alison Glover In recounting Dr Glover's achievements to a meeting of the section of epidemiology of the Royal Society of Medicine, Dr W H Bradley, the president, singled out three of them as sufficient evidence of "great merit" First was his work on the Prevention of Cerebrospinal Fever, published by the Medical Research Council in 1920, which led the Army's director of pathology to say that "he has been a good friend to the private soldier" Second was his report to the Ministry of Health in 1924 on the Incidence of Rheumatic Diseases, still cited as basic And third were his Milroy lectures of 1930, including some of his early observations on the streptococcal tonsillitis preceding acute rheumatism "In all this work his concern has been for the sick person," and his qualities have endeared him to an ever increasing circle From 1934 he was the senior medical officer of the Board of Education, and now, ten years after reaching the Civil Service retiring age, ' he still puts in a good day's work at the Ministry of Health, giving wise counsel at the highest level, although his rank is only that of ' temporary ' medical officer "

On receiving his medal from Lord Webb Johnson, president of the Royal Society of Medicine, Dr Glover spoke of his father's work as a port medical officer and attributed his own epidemiological contributions to the influence and help of his father and his friends He commended the instruction graven on his medal—veniente occurrite morbo—"run to oppose the coming disease"

WORLD HEALTH ORGANISATION

AT a meeting of the Fourth World Health Assembly on May 16, Germany, Japan, and Spain were admitted to the organisation, this brings the total membership of W H O up to 78 full members and 1 associate member The six countries elected to nominate members to serve on the executive board for the next 12 months were Belgium, Ceylon, Cuba, Greece, Lebanon, and Liberia These members will replace those whose term of office expired this year, other members come from Chile, El Salvador, France, Italy, Pakistan, Philippines, Sweden, Thailand, Turkey, United Kingdom, United States of America, and Venezuela

---

WE have to record the death on May 16 of Surgeon Vice Admiral Sir BASIL HALL, K C B, medical director-general of the Royal Navy from 1934 to 1937

Dr R ST A. HEATHCOTE, F R C.P, formerly professor of pharmacology in the Welsh National School of Medicine, died in London on May 19, aged 62

THE death is also announced of Dr J R C GREENLEES, D S O, headmaster of Loretto from 1926 to 1945 and latterly chairman of the South Eastern Regional Hospital Board for Scotland

The MEDICAL REGISTER for 1951 contains 80,222 names of doctors, an increase of 1082 on last year's total. The new registrations in 1950 numbered 3160, which is 51 more than in 1949, and 32 above the average for the last ten years, but 808 less than in 1948 (the peak year) The Commonwealth list has increased by 491 to 7064, and the foreign list by 86 to 1991 The Register is published for the General Medical Council, 44, Hallam Street, London, W 1, by Constable & Co, Ltd, 10, Orange Street, W C 1 It is in two volumes, and the price is 42s

---

[6] Hultquist, G T Über Thrombose und Embolie der Arteria carotis und hierbei vorkommende Gehirnstörungen Jena 1942

[7] Chiari H *Verh dtsch path Ges* 1905 9 326

[8] Antoni N *Acta med scand* 1941 108 502 Andrell P O *Ibid* 1943 114 336

[9] The members of the committee were Dr R G ANDERSON Dr C W BUCKLEY Sir HENRY COHEN, Dr J E DAWSON Dr C R GIBSON Prof S J HARTFALL, Dr G D KERSLEY Dr T G REAH Dr F A SMORFITT Dr R W STEWART Dr D F WHITAKER Dr D WILSON Dr H B WOODHOUSE, and Dr W YEOMAN the Ministry of Health was represented by Dr E T CONYBEARE and Dr F S COOKSEY The secretary of the committee was Dr E E CLAXTON

[10] The Spa in Medical Practice B M A House Tavistock Square W C 1 1951 Pp 96 3s 6d

Special Articles

HE MEDRESCO HEARING-AID

ITS USE AND ITS VALUE

Gray **Ann Cartwright**
B Sc B Sc

the Social Survey Division of the Central Office of Information

aring aid service is part of the National Health When the Act came into operation on July 5, was decided that 'Medresco' hearing aids e issued on permanent loan to people who iem The size of the problem was uncertain, igh the Social Survey had estimated (Wilkins t at least 300,000 people would apply for hearing- rate at which they would apply, the extent they would use their aids, and the number ies and repairs that would be needed, was own

hout England and Wales 47 distribution centres been set up at selected hospitals In July, e were only 4 Suitably equipped, the centres d by trained technicians who fit the aids and minor repairs Each serves, on the average, gnostic centres, one of which is generally at hospital as the centre

THE MEDRESCO AIDS

ids are the result of research undertaken by the e on Electro Acoustics (1947), one of three es formed in 1943 after the Ministry of Health d the Medical Research Council (hence the l res co) for advice in dealing with the problem s

o main types of aid produced are shown in npanying figure The insert type is more than the external, over four fifths of patients ie former type Each aid consists of three s, the receiver or earpiece, the amplifier and ie, and the batteries

e insert type the receiver is clipped on to an ear ch is made from an impression of the patient's ie early days of the service, patients received, as ry measure, one of four sizes of a standard ear his standard fitting is not as comfortable and is it such a good support for the receiver as the y fitted ear mould which is finally issued The e of receiver cannot be worn by patients with or easily irritated ears, a fact they do not always So these patients are given the external type n earphone is held over the ear by a headband rse heavier and more conspicuous

lead connects the earpiece to the amplifier, which, icrophone is contained in a black 'Bakelite' case of the case is a combined switch and volume l at the back there is a clip for fixing the case to the A sunken screw at the back of the case enables ian to set a tone control to give the more suitable equency characteristics A further plastic lead he amplifier to the high and low tension batteries housed in a leather case fitted with an adjustable

ht of a complete aid is 1 lb 11 oz for the insert lb 3 oz for the external type

GETTING AN AID

person's first approach to the service is usually us doctor, who will refer him to a diagnostic ere he is examined by an otologist When it decided that the patient would benefit from o hearing aid, his name is put on a waiting- listribution centre Priority is given to young nd people who need aids for their work

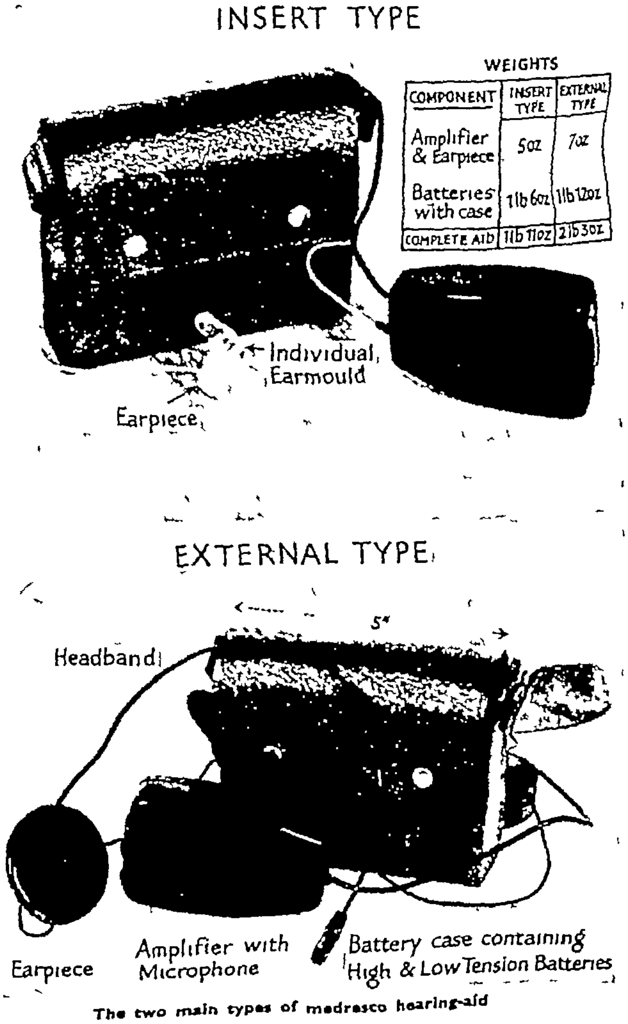
In due course the patient is called to the distribution centre After preliminary testing, he is fitted with the most suitable type of aid, and the tone control is adjusted to the one with which the *patient feels he can best under*stand speech He is then given instruction in the use of the aid, how to turn it on and off, how to adjust the volume, and how to connect up new batteries Often he is given advice about the best way to wear it, and he is usually warned that he may take some time to get used to it, and that he had better not wear it in the street until he is familiar with it

When the aid is issued, the patient is given a booklet containing printed instructions, and space for recording the number and date of battery issues and of any repairs He does not need to return to the distribution centre to obtained battery replacements, but chooses a convenient hospital where future issues are made But repairs are always made through the distribution centre

THE AID IN USE

At the end of the first two years the Ministry of Health asked the Social Survey to find out the extent to which patients were using their aids and whether they had any criticisms or suggestions to make about the aids or the service

A random sample of patients aged 16 and over who had been issued with aids before April 30, 1950, were interviewed A two stage sample design was used, the first stage units consisting of 10 distribution centres selected with probability proportionate to the number of


INSERT TYPE
WEIGHTS
Individual, Earmould
Earpiece
EXTERNAL TYPE
5"
Headband
Earpiece
Amplifier with Microphone
Battery case containing High & Low Tension Batteries

COMPONENT	INSERT TYPE	EXTERNAL TYPE
Amplifier & Earpiece	5oz	7oz
Batteries with case	1lb 6oz	1lb 12oz
COMPLETE AID	1lb 11oz	2lb 3oz

The two main types of medresco hearing-aid

TABLE I—PATIENTS ISSUED WITH MEDRESCO HEARING-AIDS

—	Estimated numbers	All patients issued with aids %	Patients still retaining aids %
Aids returned before this inquiry (August 1950)	4000	5·7*	—
(a) By patients	1800	2·6	
(b) By relatives of dead patients	2200	3·1	
Aids not in use and available for collection	2000	2·9	3·0
(a) From patients	1600	2·3	
(b) From relatives of dead patients	400	0·6	
Patients not using aids but wishing to retain them for further trial	1000	1·4	1·5
Patients claiming to use aids	63 000	90·0	95·5

* Corrected since for some centres these were not included in the sample.

patients issued with aids. This method of selection has been described by Gray and Corlett (1950). The names and addresses of the main sample of 1150 patients were selected from the records of these centres. A further supplementary sample of patients with the less common types of aid was also drawn so that comparisons could be made between patients with the different types of aid. Patients were visited[*] in their homes by trained interviewers who, using a standard questionnaire, recorded the answers to some 70 questions.

The interviewer first confirmed that the patient still had a medresco aid. Returns made by the distribution centres indicated that of the 70,000 adult patients[†] who had been issued with an aid before April 30, 1950, 66,000 or 94% still had an aid at the end of August, 1950, when this inquiry took place. More than half of the 4000 aids which had been returned belonged to patients who had died. It was next ascertained that the patient made some use of the aid and the interviewer collected any aids that were no longer wanted. It is estimated that 2000 aids, that is 3%, would be available for collection in this way, but some of these would be returned eventually in any case. A further 1·5% of the patients admitted that they did not use their aid, but wished to retain it for further trial (table I).

TABLE II—AVERAGE DAILY USE OF THE AID IN THE WEEK BEFORE INTERVIEW

	%	
Aid not used last week		13·7
Used during the interview	6·4	
Not used but in working condition	3·0	
In need of repair or batteries	4·3	
Aid used last week (hours per day)		86·3
less than 2	20·6	
2—less than 4	21·0	
4—less than 6	14·3	
6—less than 8	7·1	
8—less than 10	5·2	
10—less than 15	11·8	
15 or more	6·3	

Thus of the 66,000 adult patients still retaining their aids at the time of the inquiry, 63,000 or 95·5% claimed to use them. It is to these patients, who are later described as the medresco users, that the remainder of the questions were put.

HOW LONG?

They were asked a series of questions about the use they made of their aid. Some early questions dealt with the different occasions on which they might use the aid and these served to stimulate the memory. They were then asked how many hours they had used their aid on each day during the preceding week. The average daily use for all medresco users was 4·9 hours.

The validity of these estimates was tested by comparing them for consistency with the patients' answers to other questions and with observations made by the interviewer. The tests suggested that the estimates were sound. One such check may be illustrated:

Observed behaviour of patient	*Average daily use (hours)*
Patient was wearing aid when first seen	9·7
Patient immediately put on aid	3·7
Patient put on aid when asked to produce it	3·1
Patient put on aid at a later stage	1·9
Patient did not use aid for the interview	1·6

While the average daily use is 4·9 hours, table II shows there is a considerable variation between patients in their use of the aid.

Nearly 14% of the patients did not use their aid during the week before the interview, but half of these people used their aid for the interview. Answers to other questions suggest that a sixth of this group or about 2% of medresco users make little, if any, use of their aid. At the other end of the scale 18% used their aid for an average of 10 hours a day or more, and at least 6% must have used them throughout each day.

TABLE III—VARIATION IN DAILY USE WITH TYPE OF AID AND AGE OF PATIENT

—	Average daily use (hours)		Proportion of medresco users %
Type of aid			
Insert with individual ear mould	5·9	5·2	40·8
Insert with standard ear fitting	4·5		44·4
External (earphone type)	3·1		14·8
Patient's age in years			
16–34	5·3		5·8
35–44	6·1		11·3
45–54	5·4		25·6
55–64	5·1		23·8
65–74	4·0		32·3
75 and over	3·1		11·2
All medresco users	4·9*		100·0

* Standard error 0·2 hours

The amount of use patients make of their aid is affected both by the type of aid and the age of the patient. Insert type aids are used more than the external types, and the insert types fitted with an individual ear mould more than those with only a standard ear fitting. The average daily use made of the aid by different groups of patients, and the proportion of medresco users in these groups are shown in table III.

The average daily use is highest for patients aged 35–44 years and then it decreases with age, reaching its lowest at 3·1 hours for the group aged 75 and over. A third of the medresco users are aged 65 or over, and 11% are 75 or over.

WHAT FOR?

In addition to the questions about hours of use patients were also asked about the occasions on which they used their aid. Analysis of these answers shows that the external type aids are used less than the insert ones on all occasions.

Of the medresco users who were workers 44% used their aids when working (table IV). Nearly all the patients, 92%, said they used their aids when visited by friends; the next most frequent use, 88%, was when patients visited their friends. More patients listened to the wireless than went to the cinema, 89% compared with

---

[*] Not all the patients were found. For example, 11% of the main sample were not interviewed because they had moved or for other reasons. A comparison of the known characteristics of the whole sample with those of the sample interviewed suggests that the loss had little effect on the sample.

[†] A year later, by April 21, 1951, a further 55 000 adult patients had received an aid, making a total of 125 000 patients.

74%, but of the people who did so similar proportions used their aids Of the patients who went shopping 63% used their aid and of those who went out 62% used it in the street The proportion of medresco users who did not go to the cinema at all, 26%, is not higher than has been found in the general population when allowance is made for the age composition of medresco users A slightly lower proportion of medresco users however listened to the wireless than would be expected for a group with this age composition

ABILITY TO HEAR WITH THE AID

The reproduction of speech with maximum intelligibility was the aim of the Committee on Electro Acoustics, who considered that "the greatest inconvenience and loss suffered by deaf people arises from their inability to understand speech" How far this aim has been achieved is shown by patients' answers to the question "When you are wearing the aid and people are talking directly to you, can you understand all that is being said, most of what is being said, or only some of what is being said?" In reply to this question 65% of medresco users claimed to understand all that was being said, 26% could understand most of what was being said, while 9% could understand only some of what was said

Some idea of the relative values of these answers can be obtained by comparing them with tests carried out at one centre on some patients when they were first issued with an aid This test recorded the proportion of words correctly repeated by the patient listening with the aid to test word lists from a speech audiometer corresponding to the level of a moderately loud voice at 3 ft from the person 86 of the patients included in the sample had been tested in this way and the average percentages of words understood by patients giving the three answers were

TABLE IV—SHOWING (A) THE PROPORTION OF PATIENTS WHO ENGAGE IN VARIOUS ACTIVITIES, AND (B) THE PROPORTION OF THESE PATIENTS WHO USE THEIR AID FOR THAT ACTIVITY

Activity	Percentage engaging in activity	Percentage of those engaging in activity who use aid for it
Work	46	44
In the street	98	62
Shopping	83	63
At the cinema	74	85
Listening to radio	89	87
Visiting friends	98	88
Visited by friends	100	92

Understands	*Average of percentage*
All	91
Most	82
Some	73

A 91% average score on this test is not necessarily inconsistent with claims to understand all in the question Since connected speech is more easily understood than discrete word lists and many patients will normally lip read, it is not necessary to hear 100% of the words in conversation to understand it all

The proportion understanding all that was said was higher for patients with insert aids than for those with external aids—70% as compared with 48% It is not possible to say from the evidence of this survey to what extent this difference is due to the aid itself, since patients receiving the two types of aid themselves differ considerably However the difference cannot be accounted for simply by age of patient, although this also affects the patient's ability to understand speech as can be seen from table v

TABLE V—VARIATION IN ABILITY TO UNDERSTAND SPEECH WITH AGE OF PATIENT

Extent to which patient claims to understand speech when wearing aid	All medresco users	Patient's age in years					
		16–34	35–44	45–54	55–64	65–74	75 and over
	%	%	%	%	%	%	%
All	65	72	83	72	69	55	43
Most	26	24	14	25	24	31	35
Some	9	4	3	3	7	14	19
Sample (medresco users)	950	50	109	240	236	214	101

The proportion understanding "all" is highest (83%) for patients aged 35–44, but again, as with use of the aid, it reaches it lowest value of 43% for those aged 75 or over

Another factor affecting a patient's ability to understand speech is his type of deafness The type of deafness was obtained from the otologist's report, where available, and has been classified as conductive, perceptive, or mixed The proportion understanding "all," "most," and "some" is given for patients with the three types of deafness in table VI

Three quarters of the patients with conductive deafness claimed to understand all that was said, as compared with only half of those with perceptive deafness

All three factors, the type of aid, the patient's age, and the type of deafness, which have been shown to affect the patient's ability to hear with the aid are associated Thus while over half the patients with external aids are aged 65 or over, less than a third with insert aids are so old Again, elderly patients tend to suffer more from perceptive deafness than younger patients It can be shown, however, that, independently of age, the type of deafness affects a patient's ability to hear More over an appreciable difference still exists between patients with insert and external aids even when age and type of deafness have been standardised

SATISFACTION

With as many as 91% of the patients claiming to understand all or most of what is said when using the aid, it is scarcely surprising to find that the service has been enthusiastically received The main criticism of the aid concerned the weight of the batteries A third of the patients found this troublesome With the case, the batteries weigh about $1^1/_2$ lb and account for four fifths of the weight of the aid The aid works efficiently with smaller batteries, but the running costs are increased

TABLE VI—VARIATION IN ABILITY TO UNDERSTAND SPEECH WITH TYPE OF DEAFNESS

Extent to which patient claims to understand speech when wearing aid	All medresco users	Type of deafness				
		Conductive	Mixed	Perceptive	No diagnosis	No records available
	%	%	%	%	%	%
All	65	73	66	53	65	63
Most	26	23	21	34	29	27
Some	9	4	13	13	6	10
Sample (medresco users)	950	220	99	74	35	430

Towards the end of the interview the patients were ed for their comments on the service generally ly 17% of patients made no approving comment quarter of this 17% indicated that they could not hear properly with the aid and the remainder repeated criticisms made earlier in the interview—mostly about the weight of the batteries 30% of the patients were satisfied with the aid and service, a third of these making some qualification such as "It's a very good aid, but a little bulky—otherwise there is very good reception from it" Just over half the patients, the remaining 53%, made some really enthusiastic comment, a third of these adding some critical remark Typical of the last group is the patient who said "It's only the batteries are rather heavy, otherwise they're marvellous —a very, very good invention—otherwise everything is perfect" Purely enthusiastic comments came from over a third of the patients, such comments as "They are very helpful and beneficial in a hundred and one ways I've no fault to find with it at all."

Such comments and the knowledge that half the patients come from households where the weekly income of the head is £5 a week or less leave little doubt as to the success of and need for the hearing aid service

SUMMARY

Of the patients who had medresco hearing aids at the time of the inquiry, 95 5% claimed to be using them These patients used their aids for an average of 4 9 hours a day 65% of them say that with the aid they can understand all that is said when someone is talking directly to them Both the amount of use made of the aid and the patient's ability to hear are at their maximum for the 35–44 year age-group and then decrease with age of patient Patients with a conductive deafness are more likely to hear well with the aid than those with a perceptive deafness

We wish to acknowledge the help we have received from all concerned with the inquiry We particularly wish to thank Dr Littler and Mr Terence Cawthorne of the Medical Research Council and the technicians of the Bradford Hearing Aid Centre

REFERENCES

Committee on Electro Acoustics (1947) *Spec Rep Ser med Res Coun Lond* no 261 H M. Stationery Office

Gray P G Corlett T (1950) *J R statist Soc* 113 150

Wilkins L T (1949) Social Survey H.M Stationery Office

REGIONAL HOSPITAL BOARDS

THE Minister of Health has made the following appointments to fill vacancies caused by the retirement of a third of the members of the 14 Boards in England and Wales Out of 121 appointments, 90 are reappointments of retiring members, 8 appointments are still outstanding Those now appointed will hold office until March 31, 1954 The names of medical members are shown in bold type

NEWCASTLE REGION

Reappointed A J Best J.P Leslie Bird M.B.E Jack Cohen J.P P S Hancock, O B.E J.P T B Harston, **R. R Jowett,** M.R.C.P Prof **F J Nattrass,** F.R C.P

New Members S Hills A. C R Punnett one appointment outstanding

LEEDS REGION

Reappointed S Clayton Fryers Mrs N Fienburgh, J C Hunter Mrs I Barbara Shaw Alderman R E Smith, **Donald Watson,** F R C.S

New members **R. A. Murray Scott,** M D, **P J Moir,** M C F R.C.S (until March 31, 1952) one appointment outstanding

SHEFFIELD REGION

Reappointed Mrs. Gladys Buxton, J.P Prof **E. F Finch,** F.R C.S, **J L. A. Grout,** M.C, F.F.R, W B Jarvis, O B.E, J.P, Lieut Colonel N Gervis Pearson, D.S O, M.C, G H. Round, J.P W Scholey, J.P

New members **H. Temple Tate,** M.B.E F.R C O G, Mrs Clark, John Roberts (until March 31, 1952), one appointment outstanding

EAST ANGLIAN REGION

Reappointed Prof **A Leslie Banks,** F R C.P, **R W Butler,** F R C.S, Mrs N R Dow, C Dudson R B Keefe Miss C McCall, Sir Cecil Oakes, W H York.

New member Prof T G P Spear

NORTH-EAST METROPOLITAN REGION

Reappointed H. W Butler M.P, **George Graham,** F.R C.P **Robert Poots,** M.B, **R. W Reid,** F.R.C.S, Alderman C H Simmons, J.P W V Wakefield, Mrs A. Hollingsworth

NORTH WEST METROPOLITAN REGION

Reappointed F J Ballard, G B Jeffery D.SC, F.R.S, Miss **Katharine C Lloyd-Williams,** M.D Alderman H. R Neate, A. C de Rothschild.

New members **V Zachary Cope,** F.R.C.S, A. E Ward, Frederick Lawrence, Kenneth Robinson, M.P one appointment outstanding

SOUTH EAST METROPOLITAN REGION

Reappointed **C W Brook,** M.R.C.S The Hon Ruth Buckley, Sir **William Kelsey Fry,** C B.E., M.C, F.R C.S, F D.S R C S, S C Harris, J.P **J B Hunter,** C.B.E, M.C, F.R C.S, **W G Masefield,** M.R C S

New members The Hon. Mrs. Sylvia Fletcher Moulton O.B.E J.P Alderman J C Maclean, E J Mount (until March 31 1953).

SOUTH WEST METROPOLITAN REGION

Reappointed E F Crundwell A. G Linfield, C B.E **David Stark Murray,** M.B Richard Sargood J.P

New members **G S Todd,** C V O, O.B.E F.R.C.P, Alderman Mrs. V King Colonel C Chieveley Williams, O.B.E Alderman W A. J Case, M.B.E., J.P, **H. E Harding,** F.R C S

OXFORD REGION

Reappointed Miss **Janet Vaughan,** F.R C P (reappointed chairman) H A. Goddard, Sir David Lindsay Keir, LL.D, W R Robins Sir George Schuster K C.S.I K.C.M.G, C B E, M C

New member J E S Clapp one appointment outstanding

SOUTH WESTERN REGION

Reappointed Prof **R. J Brocklehurst,** D M, Victor Collins O B E, **C J Fuller,** F.R.C.P, Alderman Mrs. J Marshall G G Gilmour White, O B.E M.A., J.P Prof. **R. Milnes Walker,** F.R C.S

New members W N Scott Lady Katherine McNeille, Mrs D E. King Alderman F A. Parrish, C B.E J.P (until March 31 1953)

WELSH REGION

Reappointed Captain W J Canton, H T Edwards Alderman Thomas Evans William Evans, J.P, Mrs K. W Jones Roberts J.P Thomas McDonald J T Morrison, Prof **R. M. F Picken,** M.B **J H. O Roberts,** M.D J.P **Roy Thomas,** F.R.C.S Alderman the Rev W D Thomas

BIRMINGHAM REGION

Reappointed Alderman A. F Bradbeer Major L E Bury, O.B.E J.P Alderman W T Bowen Alderman W L Dingley, V W Grosvenor, J.P (appointed chairman) C O Langley, **J H. Sheldon,** F.R.C.P Prof **A. P Thomson,** M.C F R.C P **A. J Watson,** F.R.C.S

MANCHESTER REGION

Reappointed F Bussy, W A. Davies, C.B.E J.P, **R. L. Newell,** F.R C.S Prof **Harry Platt,** F.R C.S

New members C C Sumner, Sir James Lythgoe, Councillor A M Watson, S H Hampson, M B E, A C C Robertson, J.P (until March 31, 1952), two appointments outstanding

LIVERPOOL REGION

Reappointed Councillor E A Ashton, Alderman N Birch, J.P, Prof W M Frazer, O B.E, M D, J T Morrison, O B E, F R C S, J Taylor, J.P

New members Mrs Annie Cain, J.P, one appointment outstanding

GENERAL PRACTICE IN SCOTLAND

In its second report the Scottish Medical Practices Committee remarks that even in areas where the need for additional doctors seems to be clearly established there has been no influx of new practitioners This, says the committee, may be due to two causes (1) that even with a fixed annual payment a doctor setting up in practice will normally face a period of financial stringency unless he takes over the nucleus of a practice, and (2) that he may experience difficulty in finding either a living place or premises from which to conduct his practice (In one area the executive council's first, second, and third choice for an advertised vacancy all failed to find accommodation) "It follows, therefore, that some practical steps may require to be taken by Executive Councils and the medical profession if there is to be a more satisfactory distribution of general practitioners In the Committee's view the most satisfactory way of increasing medical strength is by the formation of medical partnerships"

The committee remarks that since the first report was published,[1] responsibility for selecting doctors to fill vacancies has been placed with executive councils, in consultation with local medical committees, and any appeal lies to the Medical Practices Committee Furthermore, the concurrence of the Medical Practices Committee is now necessary before a proposal by an executive council not to advertise a vacancy may be made effective, and the committee may, where it deems this desirable, require an executive council to advertise a vacancy

Discussing the remote areas, the committee observes that applications to practise are few, the response to advertisements of vacancies is poor, and applicants are mostly fairly young This may be due to two factors (*a*) reluctance to take a step which might seem to lead to isolation, and (*b*) the difficulty experienced by younger men in establishing themselves in general practice, and their desire—if not need—to seize any opportunity to do so The committee asks that executive councils and local medical committees, when filling vacancies in less remote areas, should give special consideration to applications from doctors in remote areas, so as to provide an avenue of outlet to those who have worked for some time in isolation and apart from normal contact with professional colleagues

The number of doctors providing general medical services was 2409 at July 1, 1950, compared with 2419 at Dec 1, 1949

Executive council areas, or part thereof, where the need for additional doctors appears to the committee to be established, are as follow

County of Dunbarton	Dumbarton, Alexandria/Renton
County of Fife	Buckhaven, Methil, and East Wemyss, Dunfermline, Rosyth, Inverkeithing, Charlestown, Cowdenbeath, Lochgelly, Lochore, Glencraig, Kelty, Cardenden, Crossgates
Galloway	Stranraer
County of Lanark	Airdrie, Bellshill
Lothians and Peebles	Musselburgh, Bathgate
County of Orkney	Kirkwall
County of Renfrew	Paisley, Johnstone, Port Glasgow
County of Ross and Cromarty	Barvas
Counties of Stirling and Clackmannan	Bannockburn, Falkirk, Grangemouth.

Addition to the number of doctors would be desirable in the following executive council areas, or part thereof

Counties of Aberdeen and Kincardine	Laurencekirk, Ellon
County of Angus	Forfar
County of Caithness	Wick
County of Dumfries	Annan, Dumfries
County of Dunbarton	Clydebank
Galloway	Whithorn
County of Inverness	Inverness
Lothians and Peebles	Armadale, Bo'ness, Haddington, Tranent
Counties of Perth and Kinross	Blairgowrie, Stanley and Bankfoot
County of Ross and Cromarty	Ullapool
Counties of Roxburgh, Berwick, and Selkirk	Galashiels
Counties of Stirling and Clackmannan	Alloa, Kilsyth, Stirling
County of Zetland	Lerwick and the Island of Bressay

GENERAL MEDICAL COUNCIL

Opening the 181st session of the council last Tuesday, Prof David Campbell, the president, spoke with regret of the death of Sir Leonard Parsons, F R S, a member of the council, and of Dr Thomas Fraser, a former member, also of Prof J A Nixon, who during the late war was inspector of qualifying examinations in medicine.

The President recalled that, under the Medical Act, 1950, the council's legal name [formerly the General Council of Medical Education and Registration of the United Kingdom] was now the General Medical Council During the present session members would be invited to make regulations under this Act which (subject to approval by the Privy Council and to Parliamentary scrutiny) would fix the period of service as house-officer before a doctor could be fully registered, and to make further regulations determining how the whole period was to be divided between medicine and surgery, how far time spent in the practice of midwifery might be counted as time spent in one of the other two main subjects, and the maximum time spent in a health centre which might similarly be reckoned towards the completion of the periods spent in medicine or surgery The new Medical Disciplinary Committee had already made the Medical Disciplinary Committee (Procedure) Rules, 1951, which came into operation on April 18 The first meeting of the Penal Cases Committee, now a statutory body, was held on April 24, and the first disciplinary cases referred to it by the Medical Disciplinary Committee would be heard on May 24 Except for the remnant of old disciplinary cases reserved to the council, the transfer of cases to the Medical Disciplinary Committee was complete, and on April 14 this committee also became responsible for dealing with applications for restoration to the Register after disciplinary erasure Also under the Act, the normal fee for registration had been increased from £5 to 11 guineas, and an addendum to the *British Pharmacopœia* had been published and would come into force on Sept 1

Finally, the President spoke appreciatively of the work of Mr Michael Heseltine, C B, the registrar, who was shortly to be succeeded by Mr W K Pyke Lees Mr Heseltine's eighteen years in this appointment had included the difficult war years in which "there continued to flow from his eager and able brain and pen important memoranda written in fine, clear, and cogent language, and a joy to read" Latterly Mr Heseltine had done great work on the Medical Bill, now the Medical Act, 1950 Mr Heseltine was to continue to work on the historical, educational, and legal aspects of the council's activities

---

[1] See *Lancet* 1950 i 176

The Wider World

A CITY OF THE MIDDLE WEST

FROM AN AMERICAN CORRESPONDENT

THE city lies within 200 miles of Chicago, complicated nexus for four north central States thriving richly on agriculture and industry. Its over 100,000 inhabitants are matched by an equal number in the neighbouring, small cities, towns, villages, and farms. Many machine tool shops turn out a variety of products, from electric motors to automotive pistons; the international giants of heavy industry are well represented elsewhere in the State.

In 1940, in a population somewhat smaller than it is now, more than 90% were native born whites, 4% foreign-born whites, and 2·5% Negroes, with a scattering of a dozen Asiatics. Few cities of comparable size boast so homogeneous a population, the large majority stemming from German stock whose descendants scarcely know German or even the derivation of their names. One fifth are Catholics, and an equal proportion highly conservative Lutherans, the remainder comprising the numerous Protestant sects whose churches help swell the city's total to more than 120.

Except for the "downtown" business and shopping areas and the factory foci at irregularly distributed points, architecture is mainly confined to single family frame houses, painted white and set back from the tree-lined streets like minor monuments on the expanse of green lawn. Two thirds are occupant owned, the majority costing less than $10,000 to reproduce at current prices. The owners themselves do much of the necessary painting, plumbing, electrical wiring, and upkeep. A motor car is taken for granted; only the lack of one causes comment. The adult male's wage now probably averages $65–70 weekly before deduction of the national withholding tax on income; although the State's per caput income is only median, the city's ranks among the nation's highest.

Marriage takes place 3–5 years earlier than in large cities; and children are so much the normal life pattern that the decision to have children, how many, or at what time, rarely comes up for discussion. Compared with the standards set by outstanding schools in the East, the educational level is low, but not lower than the national average. The percentage of young people entering college from local secondary schools is reportedly more than double the national figure. Conformity in most things is the rule; no one wants to be conspicuous for divergent opinions or activities. A recent analysis of a small population sample revealed a greater than average degree of submissiveness among adults. The cultural level approximates that of other non university cities of its size, raised somewhat above these by an excellent free public library supported by its own taxation independent of other governmental agencies, a semi-professional symphony orchestra and a competent amateur theatre. Veterans societies' club houses serve as social centres for their members. Sports competitions, chiefly football and basketball (the latter played both by high school teams and by professional athletes) provide the chief recreation.

Two hundred physicians and four hospitals with a total capacity of 800 beds represent medicine. One of the four hospitals plans the early erection of a substitute with double the old capacity. Another is under the Veterans Administration, but because of shortages in medical and nursing personnel only 50% of its 200 beds are filled. Of the two hundred physicians, fewer than a quarter profess to be specialists; the rest are general practitioners. Many are graduates of the State university medical school, which is yet to be included among the nation's best. Of these, a large proportion have had only a single year's internship in a local hospital, entailing the expected concomitant disadvantages of such limited experience.

General practice is what the term implies; in fact, the usual office sign assigns the doctor a broad field—physician and surgeon. No hospital attempts to restrict the doctor in his practice, nor are the results of his labours ever genuinely reviewed or criticised, despite the efforts of the American College of Surgeons. The little existing criticism derives from a small lay minority transferred by business firms or coming by choice from large Eastern cities. The indigenous population protests little. *Vis mediatrix naturæ* is often mistaken for professional skill, especially when aided and abetted by copious doses of antibiotics, one succeeding another until the gamut is run.

Office calls are $2–3, home visits $3–5, depending on the hour of the day. A few physicians see 150–200 persons a day, apart from hospital surgical patients; 60–70 patients a day is not uncommon, while doctors more recently embarked on practice see 25–30 daily. Appendicectomy brings not less than $150, children's tonsillectomy $65–75—fees ordinarily reserved for specialists in large cities. Anæsthesia administration at $25 by a general practitioner is extra, and the specialist anæsthetists usually receive no more. Ironically, appendicectomy (scarred appendices heavily outnumber the acutely inflamed) brings twice the price of an obstetrical delivery with its prepartum and postpartum care. *Medical Economics* has periodically surveyed medical incomes, and finds the highest averages in cities of 100,000–200,000; this city is no exception.

The Negro community dwells in a slum area where fewer than a score of houses have been built in forty years. Limited as well in employment opportunities by the forces inherent elsewhere in the country, it is served by several Negro physicians in the ratio of 1 to each 2500 persons. These physicians, in general practice and professionally comparable with their white colleagues, number some whites in their practices as white physicians number a few Negroes.

Employment among all groups is universal; collections are good. The general prosperity boosts the tax funds made available by local authorities for the care of the indigent and disabled, and, consequently, the physician's income as well. The local medical society yearly contracts with the authorities, for a stated sum, to care for the indigent and disabled as if they were private paying patients. Each month office and home calls and surgical procedures are prorated and charged against the fund, which for at least ten years has been large enough, with the indigent patients few enough, to return the doctor a private patient fee.

Such is the background against which layman and physician view "socialised medicine." A further description of the community may clarify the local attitude: a high percentage of conservative Catholics and Lutherans; a numerically greater orientation toward the Republican than the Democratic party, and virtually everyone in both parties on the right wing; a nearly universal reading of the local newspaper (a less skilful but even more conservative version of the *Chicago Tribune,* which itself outsells all other out of town dailies); a practically non-existent readership of liberal dailies or weeklies, and perhaps less reading of serious books or periodicals than the excellence of the local library warrants; little foreign travel except for the several thousand young men who saw service abroad in the late war and who hold no very flattering opinion of "foreigners."

The local medical body actively supports A.M.A. policies but with considerable reluctance to foot the high costs of implementing those policies. In part this reluctance may be attributed to a general unwillingness to spend money; physicians are said to be poor contributors to local philanthropies, one possible source of the resentment of the laity against the elevated medical income

(Incidentally, income tax officers in the United States review a higher proportion of physicians' returns than of any other group) Any contemplated change in the status quo is a threat to income and to established patterns , and the doctor and, in turn, the layman are suspicious of any innovation as a Socialist (read "Communist ") plot to overthrow the American Way of Life "Socialised medicine in Germany led to Hitler " , "the National Health Service has been established with American dollars " , "Do you want to have to stand in line to see your doctor ? "

Physicians in this part of the country have pioneered in the establishment of an Association of American Physicians and Surgeons, one of whose activities is a competitive essay contest among secondary school students, to whom both material and references are furnished by the association Essay subjects concern the superiority of the status quo to other systems of medical practice, with special emphasis on the former's unique American aspects At one time the association included in its constitution a clause to become effective should "government medicine" be instituted by law This provided that wherever 75% of physicians voted to stay out of the scheme, these would then boycott those doctors who decided to enter The realisation that the association would be liable to prosecution under a charge of "conspiracy in restraint of trade" prompted cooler heads to delete the clause

As it now functions there is no pressure to alter the established patterns of medical practice, and this for several reasons (1) the indigent receives the same standard of care as does his employed brother, who can in addition find relief in Blue Cross, Blue Shield, and other forms of reduced cost hospital and medical care insurance , (2) the doctor is paid for all services regardless of the patient's economic status , and (3) the present trend in the United States is deeply conservative, a trend consistent with basic local inclinations

Public Health

Public-health Salaries

In December, 1950, the Industrial Court gave its award on the salaries of assistant medical officers, of senior medical officers, and of medical officers of health [1] The salary scales for deputy medical officers, for divisional or area medical officers, and for officers holding mixed appointments were referred back by the court, to be determined by joint negotiation, and in the event of failure to reach agreement either party was at liberty to report such failure to the court Agreement was not reached, and on Jan 15, 1951, the secretary of the staff side of Medical Whitley Committee C made formal application to the court to determine the matters in dispute The court heard the parties on these matters at three sittings during April and issued its award on May 7 Copies may be had from H M Stationery Office

The management side, "reinforced in their view that doctors employed by local authorites have, as regards salaries and conditions of service, an affinity with other local authority employees rather than medical practitioners," proposed nine scales which they are discussing in other negotiating machinery, of which the top seven (with a minimum salary of £1050 in the third and a maximum of £2000 in the ninth scale) would be appropriate to the grades of medical officer in question Local authorities would place these officers into a scale they consider appropriate to the post and the person occupying it, with a refinement of the scale in the case of mixed appointments

For deputy medical officers of health the staff side claimed a commencing salary which is 75% of the minimum of the scale selected by the employing authority for the medical officer of health within the appropriate range as awarded for medical officers of health by the Industrial Court, plus annual increments which depended on population and aggregated to £200 minimum and £300 maximum The court have awarded a commencing salary of two thirds of the minimum adopted by the employing authority for its medical officer of health, and annual increments equivalent to those of the medical officer of health The following table, for a few selected populations, illustrates the claim and the award

Population not exceeding	*Staff side claim salary*	*Award*
100,000	£1162 10s –£1387 10s	£1033–£1233
250 000	£1462 10s –£1687 10s	£1300–£1500
600 000	£1725–£2025	£1533–£1800
600 000 +	At discretion	At discretion

Increments claimed and awarded aggregate £250–£300 for different populations

Divisional or area medical officers receive an award based on the salary previously awarded to senior medical officers (£1250–£50–£1650) , where the population of the division does not exceed 150,000, 250,000, and 400 000 there is added to these scales £50, £150, and £250 respectively Where the population of the division exceeds 400,000, the addition is at discretion For this class of officer, the award is £100 less than the claim (The position of divisional or area medical officers whose responsibilities do not cover the whole range of health services—including the school medical service—is still being considered by Committee C)

For mixed appointments the court award the appropriate proportion of the salary of the county post (as assistant medical officer, divisional, or area medical officer) and the appropriate proportion of the salary of the county district medical officer of health, plus the appropriate proportion of £100

This, like all other such awards, is a compromise It was as natural for the public health service to insist on its affinities with other branches of medicine as it was inevitable that the local authorities should emphasise that in matters of salary they could not ignore the effect of awards to one profession on other professions For the time being the issue is settled , but that does not imply that all discontents are removed or all anomalies rectified On the contrary, the whole time divisional medical officer, regarding the salary of his colleague the district medical officer, may well have cause to think that the anomalies are intensified

The newly qualified man, weighing his choice of a career, will naturally compare the financial rewards of the consultant service, of general practice, and of public health The next year or two will shed light on the numbers seeking a postgraduate public health qualification and competing for posts Among other things, that light will illuminate the profession's opinion of the attractiveness or otherwise of the new salary scales

The Registrar-General's Review

It may be that the period 1946–47, covered in the latest review from the Registrar General,[1] will prove more remarkable for the establishment of national systems of morbidity recording, for use both in hospital and home, than for the mortality experience of these years An international working party produced an agreed system of classification of disease , pilot record schemes were started in four teaching hospitals , and the Survey of Sickness by sampling and house to house visits was well established

Some at least of the preliminary results of the survey are now to hand to supplement the data already published [2] e long spell of exceptionally cold weather in the first ree months of 1947, for example, produced an increase the number of severe rather than minor illnesses

---

[1] *Lancet* 1950 ii 918 *Ibid* Jan 6 1951 p 58

[1] The Registrar General's Statistical Review of England and Wales for the two years 1946–47 Text vol I Medical London H M Stationery Office 1951 Pp 325 6s 6d

[2] Sickness in the Population of England and Wales in 1944–47 Studies in Medical and Population Subjects no - London 1949

The first fruits of morbidity recording should not, wever, obscure the vital facts of mortality, particularly this review is wisely insistent on the need for careful spection of the detail of statistical tabulation Thus ile for most purposes a simple measure of the risk to fant life is given by the ratio of the number of deaths ider 1 year of age in 1947 to the number of births gistered in that year, the use of such a value in 1946 d 1947 would have suggested that in 1947 there had en a check to the satisfactory decline in infant mortality recent years A more accurate rate, based on the timated number of births to which the infant deaths 1947 could be related, showed that in fact the 1947 fant mortality experience was better than in 1946 he acid test of inter regional comparisons, however, owed that there could be no grounds for complacency ot only were death rates in the North and in Wales % above the rate in South East England but the gap as widening quickly Similar caution is needed in terpreting such summary measures of mortality as age andardised death rates A detailed study of age x-specific death rates shows that though mortality general declined between 1946 and 1947, there were itical changes in the experience of certain groups of the opulation Among men, for example, despite the fact at the crude death rate was the same in 1947 as it was 1946, mortality increased in every age group over 45 ome of this was due to the continued increase in deaths om cancer of lung and coronary and myocardial disease omen, particularly if they have taken the elementary recaution of being married, fare much better , as always, cardiac mortality is an index of resilience, women were uch less affected by the cumulative effects of war than ere their weaker brothers In tuberculosis, too, milar factors operate The "generation" effects f childhood environment in determining tuberculosis ortality in later life do not appear among women over 0 , but their menfolk show in their relatively adverse xperience the cumulant effects of stress during the two ars and the selective thinning of their ranks by the eaths of the fittest of their generation in the first world ar

Diphtheria Immunisation

The Ministry of Health has expressed concern at the lling off in the numbers of babies and children immunised against diphtheria In England and Wales more han 140,000 fewer babies were protected in 1950 than n 1949 , the figures fell by 23,000 during the first half f the year, and by 117,000 in the second half

Since the immunisation campaign began in 1941 over million babies and children have been immunised Diphtheria deaths have fallen from a pre-war average of 800 per annum to 49 last year—a new low record. Cases have declined from 55,000 per annum to 980—also a new low record

Mortality in 1950

The Registrar General announces[1] that in England and Wales during 1950 the death rate (provisional) for respiratory tuberculosis was 321 per 1,000,000 population, and the rate for other forms of tuberculosis 43 per 1,000,000 The death-rate from cancer was 1991 per 1,000,000 The maternal mortality, based on deaths primarily classed to diseases of pregnancy, childbirth, and the puerperal state as arranged in the Manual of the International List (6th revision) was as follows

No	Cause	Mortality per 1000 live and still births
651	Abortion with sepsis	0.09
650 652	Other abortion	0.05
640 649 670 678	Complication of pregnancy and delivery	0.54
681	Sepsis of childbirth and puerperium	0.03
680 682-689	Other complications of the puerperium	0.15

In England Now

A Running Commentary by Peripatetic Correspondents

THE plea that the labourer is worthy of his hire is cynically regarded as the conventional assertion of the overpaid. There must be few recorded examples of anyone admitting that he was paid more than he deserved, whereas protestations to the contrary are almost universal. All the obvious anomalies can no doubt be explained on the principle of supply and demand The buffoon who receives an astronomical salary must be worth it to his employers , who, as they are accustomed to point out, are not in business for their health So many factors enter into the question of remuneration—the pleasantness or otherwise of the occupation , the possession of some monopoly, whether a natural gift or a laboriously acquired technique , the preference of some for kudos rather than financial gain, and so on.

I often think that literature is a serious claimant for the world's poorest recognition There are, it is true, the plums for the giants in this as in all professions. Conan Doyle claimed as much as seven and sixpence or ten shillings a word when in his heyday, and O Henry, I am sure, had he possessed any commercial sense could have asked (and would have received) double that rate And this in the days when money was really money Among medical works there are, I understand, a sprinkling of best-sellers that ensure a steady if modest trickle into the exchequer , but many writers would be content with the glow of authorship plus the cost of ink and paper

A few years ago, tempted by the glamour of association with the learned, the eminent, even the titled, I accepted an invitation to participate in a textbook symposium From time to time I received encouraging reports of the book's success, and last week a balance-sheet showing the profit to date which had been divided among the contributors in proportion to the length of their contributions and enclosing as my share, a cheque for 15*s* 10*d* Deducting income and super tax—I am still, but probably for the last year of my life, in the super class—I reckon this works out at a penny for 30 words or, say, three lines It would be difficult to represent this on a time-work basis, but, even excluding the elements of study, technical knowledge and experience, I think sixpence an hour would not be far from the mark So assuming an eight-hour working day, even with my modest requirements, it is barely a living wage

* * *

Whether you look on the rabbit as a useful supplement to the meat ration or as an unmitigated pest, you cannot deny that it is a remarkable animal Their young, for instance, instead of having the disproportionately large head, spindly legs, and general ugliness characteristic of most animals in their early stages, are perfect miniatures of the adult rabbit Then a doe is said to give the richest milk of all mammals, though so far my extensive search of the literature has not unearthed any supporting evidence The calorie value of milk seems to vary inversely with the size of the animal producing it

—	Composition of milk (%)							Calorie value per 100 ml.
	Water	*Protein*	*Fat*	*Lactose*	*Ash*	*Calcium*	*Phosphorus*	
Human	87.5	1.0	4.4	7.0	0.21	0.35	0.01	70
Cow	87.2	3.5	3.7	4.9	0.72	0.12	0.09	74
Ewe	82.7	5.5	6.4	4.7	0.92	0.20	0.17	109
Goat	86.5	3.6	4.0	5.1	0.81	0.13	0.10	79
Mare	89.0	2.7	1.6	6.1	0.51	—	—	54
Sow	82.0	6.2	6.8	—	0.96	0.25	0.15	113
Bitch	75.4	11.2	9.6	3.1	0.73	—	—	163

These figures may not be so remarkable when one remembers the different rates of growth of the youngsters If you want to rear baby rabbits by hand, you should fortify cow's milk and even proprietary baby foods with cream and sugar But bringing up rabbits is an art not easily acquired, though some children, including my daughter have a gift for it Her technique (personal communication) is to give them very frequent feeds with numerous remedies and which completely stopped as soon as hyoscine was given

---

[1] Registrar General's Return for the Week ended May 5 1951 H.M. Stationery Office Pp 20 9d

Statistical evidence for the value of any drug in this condition is impossible to obtain, but it seems clear that this drug is of the greatest value, and that it should always be the first to be tried as soon as breath holding or carbon dioxide have failed

Ruislip Middlesex J D LAYCOCK

PUBLICITY IN CANCER

SIR,—Professor Russ has added to his many public services by raising again (March 24) the urgent importance of publicity in cancer, and has quoted as examples two of the most important cancers of all—breast and cervix They are important not only because of the number of cases but because the cure rate is very high (of the order of 70%) if treatment is given in the early stages

Mr Malcolm Donaldson (April 28) has supplemented the plea by stressing the importance and value of educational campaigns among the laity, for which he has himself long been a devoted worker There is by now a considerable amount of experience of such propaganda efforts, especially in America and some Continental countries, no one, I think, will deny that they carry a definite risk of increasing cancerphobia in susceptible individuals, yet many of those who have the requisite experience are satisfied that the public benefit achieved outweighs the disadvantages The medical profession should be acutely aware by now of the dangers of the wrong type of "health" propaganda, and doctors know full well how dangerous a little knowledge can be The mother whose thoughts fly to poliomyelitis each time her child is off colour, the hypochondriacs who plague our consulting rooms and outpatient clinics—these are to some extent victims of the wrong kind of propaganda Yet what is the alternative ? A public that is beginning to be educated will insist on a certain minimum of knowledge, and if it cannot get it from wholesome sources will undoubtedly get it elsewhere However much we may be irritated at times by the undigested 'information" picked up by our patients we should realise that it is, on the whole, a healthy sign of the times, and that in the long run a higher level of general education and awareness is our best ally in the campaign against disease

Cancer is, I think, a special case It seems to be an inevitable accompaniment of civilisation, and the more effective our hygienic and anti infective measures, with consequent increased longevity, the greater will its relative incidence become Civilised communities must develop a cancer consciousness, which is not the same thing as cancerphobia, it means an awareness of the high curability rate of most cancers and of the importance of early diagnosis Mr Donaldson sets great store by popular lectures and can point to a large personal experience, one doctor has told me, however, that after a good deal of such lecturing he gave it up as relatively ineffective in comparison with the effort needed Two methods suggest themselves as particularly suitable owing to their high publicity value—the radio and screen There have been at least two recent programmes, one on television and the other on sound only, dealing with cancer, and the speakers, I am told, emphasised the importance of early diagnosis in forthright words I think there should be more programmes to the same end, to spread the net as widely as possible Broadcasts in the Woman's Hour series would also be invaluable, and they should be repeated, with suitable background variations, at not too long intervals Short documentary type films shown at cinemas alongside the usual programmes would also reach a large public

Another line of approach is the periodic medical examination The theoretical ideal of a thorough overhaul for most of the population at regular intervals is clearly impracticable for a long time to come, but a breast-and-pelvis examination of all women between 40 and 70 is much more practicable At a rough estimate, for every 1500 women examined annually we could expect to pick up 2 cancers of breast and 1 of cervix—1 of these two most important and curable of cancers for every 500 women In addition, about the same number of skin cancers would be noted, though these are less important for our purpose since the mortality from skin cancer (apart from melanocarcinoma) is now very low A very occasional case of cancer of rectum, tongue, vulva, or other easily accessible site would also be added Women of 40–70 form about 18% of the populace—say 1 in 6, a general practitioner's list of 3000 patients therefore might include some 500 for examination If 10 were examined each week they would all be seen within the year, and the time taken would be relatively short

I would like to see a pilot experiment on these lines. Moreover there is another advantage in such a personal examination—subtler than conventional propaganda but in the long run perhaps more important than anything else—I mean the genuinely educational value of the process It would tend to make the subjects "prophylaxis minded" and impress on them the value of early detection The presence of the doctor would lead many to declare their secret fears and hearten them to come regularly for routine examination—at least there is British and American evidence that this is what tends to happen These people would also be the best advocates among their own families and friends

Medical man power and harsh economics may make even this limited programme difficult to realise, though as between these two major lines of approach—mass propaganda and individual examination—I should much prefer the latter Is it really too much to ask ?

J WALTER

Deputy Medical Director
Sheffield National Centre for Radiotherapy
Graves Institute of Radiotherapy Sheffield

PSYCHOSOMATIC APPROACH TO PULMONARY TUBERCULOSIS

SIR,—May I be allowed a few observations in connexion with Dr George Day's article of May 12, which I have read with great interest

Dr Day wonders whether tuberculosis, cancer, and other destructive diseases should not sometimes be regarded as "psychotic conversions" This is a view which has developed over many years in my own mind, and I am wont to use the term "psychotic conversion" in a colloquial way It appears to me that the same character which enables a process to surmount the somatic barrier manifests itself in the mental sphere in a quasi psychotic way

About two years ago I visited the Mount Sinai Hospital in New York There a psychosomatic approach is cultivated on a large scale, in that to each specialty is attached at least one psychiatrist (in most cases a psychoanalyst) and they number more than fifty in all When I spoke to some of them, expounding this view, they were greatly interested and told me that they had of late seemed to be moving in exactly the same direction.

I am not familiar with Dr Day's statement that it is "notorious that, if one succeeds in depriving an asthmatic of his asthma, there is a chance of his becoming schizophrenic", but he may well have had in mind an experience of which I told him

In this case a young married woman lost severe and frequent asthmatic attacks which had been occurring since early youth as a result of a few months of psychotherapeutic treatment However, after a holiday interruption I found her in a paranoid state with delusions centred upon myself She was unable to continue, relapsed and went back to her ordinary physician for treatment by injections as before A year later I saw her again in a sanatorium where she had returned to the care of a physician to whom she had long formed a very strong attachment. She had been heavily sedated and was now in a psychotic state very reminiscent of schizophrenia, overlaid by gross toxic hallucinations. She had to be transferred to a private mental nursing home, since she was too restless and difficult to be kept in the physician's nursing home. She recognised me at once, and had good contact with me despite her deranged state of mind. She made a good recovery, could soon be allowed home, and had, on balance, probably benefited by this "reconversion" of her asthma.

This case illustrates very well the exchange of a psychosomatic syndrome for a psychotic state. It appears to me also interesting that this patient's condition did not correspond to any of the known "textbook" psychoses and was, in my opinion, not a schizophrenic episode.

These observations lend colour to Dr Day's view that extreme caution and judgment are required in the approach to somatic disorders from a psychological point of view.

London W 1 S H FOULKES

PROPRIETARY PREPARATIONS

SIR,—The Cohen Committee recommended that doctors should avoid prescribing proprietary medicines advertised direct to the public. The most recent reaction to this is the packing of two proprietary products of identical composition, by either the same manufacturer or associated companies, under different names, one being advertised to the public and the other to the medical profession.

The solution to the question of prescribing proprietary preparations is not easy. There are many objections to the list of equivalents included in the *National Formulary* before the war, mainly because some were not exact equivalents. The only practicable way, to my mind, is to produce a list, suitably cross referenced, giving the formulæ (adjusted by calculation to a common basis) of both proprietary products and similar preparations in the *B.P.C.*, &c. In producing this, regard should be given to the limited time at the disposal of doctors, and it should preferably be produced in similar size to the *N.F.*

Newcastle upon Tyne A FORSTER

ORGANIC HYPERINSULINISM TREATED WITH ALLOXAN

SIR,—In his letter of April 28 Dr Mårtensson has ably outlined a number of provocative points arising from the article of Feb. 24 by Dr Gilchrist and myself.

Though we cannot be sure that other blood constituents did not contribute to the enormous citric acid level, it would appear from other factors—namely, the high fatty acid and pyruvic acid levels—that there existed a stepped up Krebs's cycle with damming up at the citric acid stage, and probably occasioned by the altered metabolism on the part of the hepatoma—akin to enzymic fluoro acetate derangement at least in effect. Indeed, it is well known that citric acids have been found to be increased in hepatitis and cirrhosis.

Positive proof of hyperinsulinism cannot be adduced, and from this aspect the title of our article might have been better chosen. However, there were factors present which pointed to hyperinsulinism. Evidence for a normal though fast moving, anaerobic or phosphorylation cycle of glucose metabolism was found in (*a*) the sharp fall repeatedly seen in the blood glucose level following the peak elevation on oral administration of large doses of this sugar, (*b*) the normal creatinine excretion, and (*c*) the high blood pyruvic acid levels, though these probably also reflected some increased alpha ketoglutarate.

In the pancreas there was presumptive histological evidence for hyperinsulinism. Islet tissue was exceedingly abundant: frequently up to 15–20 islands were seen in one low power (× 75 field).

The maximum and minimum diameters of 71 islets, measured in succession and without selection by traversing completely on a projecting microscope one small section taken from the tail of the pancreas, gave a mean size of 215 × 130 μ. Of these 71 islets 38 had maximum diameters in excess of 200 μ, 28 had greatest diameters of 250 μ or more, 13 exceeded 300 μ in this measurement, while 7 were in excess of 350 μ and 4 passed 400 μ. The largest islet seen measured 660 × 360 μ. 50 islands from two normal organs of cases in the same age-decade, and measured similarly, gave average greatest and least diameters of 117 × 84 μ. Of these only 4 exceeded 200 μ in maximum diameter, and none had a dimension greater than 240 μ.

Further evidence for the large size of the islets was found in the total cell counts, in performing which very small islands having less than 15 cells were omitted in the controls as well as in the case in question. The cells were counted in the plane of one section. 24 islets from the case under discussion gave a mean cellular content of 336 cells per unit—a figure which does not include the giant islet mentioned. 25 islets from three control normal organs gave a mean content of 152 cells per island. These comparative figures are more impressive when it is realised that a large number of beta-cells had been completely destroyed by the alloxan.

The islet hyperplasia and probable hyperinsulinism may be interpreted as in some way secondary to deranged metabolism occasioned by the hepatic carcinoma—e.g., evoked by some accumulated member or members of the tricarboxylic acid cycle, or by the formation of abnormal metabolites on the part of the tumour. It is not assumed that the clinical hypoglycæmia was due only to this; indeed, it is very probable that the hepatic neoplasm was the greater culprit.

General Hospital
Sudbury Ontario Canada M J G LYNCH

PREVENTION OF TUBERCULOSIS IN YOUNG PEOPLE

SIR,—Last week's article by Dr Anderson and his colleagues is evidently based on a very careful survey, and we should do well to ponder the findings.

In one sentence, however, the authors conclude that our methods of detecting tubercle bacilli in the sputum of patients are poor, on the ground that there were an unexpectedly high number of conversions among apparently negative cases. I suspect that in many of these cases the conversions were due to contact with an unexamined, unknown positive case among the contacts, such as a friend or neighbour. If this is so the original negative patients and the converted contacts were the contacts of, and infected by, undetected sources common to both parties.

C O S BLYTH BROOKE

Public Health Department
Finsbury Health Centre London E C 1

URETHRAL CARUNCLES

SIR,—I appreciated the comments (April 28) of Mr Mills and of Dr Taylor and Professor McLaren on my short article of April 14. I have no objection to the name "caruncle" but deplore a symptom masquerading as an entity.

Mr Mills states "... the exquisite tenderness of pedunculated fragments of granulation tissue are lesions whose existence can hardly be doubted." On the contrary, they are the classical group and very much subject to doubt. I should certainly like to hear more about specific instances of exquisitely sensitive and painful masses with narrow pedicles situated on an otherwise normal urethral mucosa in the absence of present or past infection of the urinary tract. Most of the so called "caruncles" are not particularly tender, though I have seen one or two conditioned iatrically or by mirror contemplation, as a Yogi his navel. In these the agony was manifested before the probe had made contact. If, as Mr Mills asserts, the mother country still boasts of a few of the veteran type of caruncle, I must reduce my negative generalisation—always hard to prove—to a close approximation In any case I am sure he will agree that a long range battle of the "caruncles" would be unprofitable and inconclusive

My chief purpose in writing at all was to discredit the "caruncle" as a cause of dysuria, and put the blame firmly where it belongs on infection or the after effects of infection in the urinary or genital tract The impostor must not continue to divert attention from the real nigger in the woodpile Not all doctors can be expected to be au fait with all the nuances of innocent and guilty "caruncles," if any of the latter exist

A primrose by a river's brim
A yellow primrose was to him,
And it was nothing more

Johannesburg R CAMPBELL BEGG

SURGERY OF MITRAL DISEASE

SIR,—In your annotation of April 21, you point to the need for the right word for the new operation, which neither "valvulotomy" nor "commissurotomy" quite describes I would like to propose the following names

(1) cuspidotomy (derived from *cuspis*),

(2) (Tri)glochinotomy (see Quain's *Elements of Anatomy* 11 ed, vol 4, part 3, p 43),

(3) annulotomy ("the annulus fibrosus, a ring of fibrous tissue at the atrio ventricular junction, to which the bases of the cusps are attached," *Ibid*) I believe that the third name would be the most correct

Budapest Hungary LAJOS LÉVY

SPECIALISATION IN TEACHING

SIR,—From time to time correspondence centres around the matter of specialisation in teaching in the undergraduate sections of the medical schools In view of the more usual absence of comment by the teachers it may be as well that a few notes be recorded in reply to Dr Richards's remarks in your issue of May 12, especially in view of his obvious awareness of particular situations in and around teaching departments I would suggest, however, that Dr Richards is too sweeping when he says that the average undergraduate does not "come under the influence of a teacher who would describe himself simply as a doctor, able to help him fit his specialised learning into its proper perspective"

A not inconsiderable number of clinical teachers are well versed in the art and science of general practice, and in fact are giving increasing attention to those essentials in method and outlook which will engender, as early as possible, in the mind of the undergraduate, the notion that for "every practical reason the patient's body is indivisible", and, moreover, the essential linkings of the physical trends of the individual, whether a child or an adult, to the social, occupational, environmental, temperamental, and psychological aspects, is constantly brought forward in clinical discussion and demonstration It must not be assumed that the teachers are necessarily mentally isolated from the world of general practice On the contrary, many of them have had years of experience with general practitioners and domiciliary consulting practice, and in some cases a personal experience of general practice itself As a result of that a clinical teacher becomes a great asset in the department and has an approach to the undergraduate scheme hardly obtainable otherwise, and he does not fail to create a realistic and effective manner in his teaching methods He comes to realise that vacillation and vague diffuseness is to be avoided, that general practice is not a compendium of specialties but a carefully planned synthesis The suitable training of new general practitioners is something much more than "a more modest goal"—it must be calculated in terms of the best beginning to a life's study of human nature The general practitioner is the field worker and observer of morbidities

Departments which carry one or two men as "passengers" (using Dr Richards's definition) are never at a disadvantage The "passenger" may distinctly enlighten the scene when "knowledge comes, but wisdom lingers" No medical school should be without them The busy general physician or general surgeon, who hardly ever has time to put pen to paper, may be a veritable golden treasury in his anecdotal chats with the students about the doctors, patients, homes, and problem situations which arise almost daily in the round of very useful but possibly unobtrusive activity Thank heavens there are all sorts of personalities to be found in our medical schools The strength of the schools lies a great deal in this mixture of personalities, varying between the departmental specialist who loses his mind in a "heart case" to the general man who can gain the mind of the patient to his own heart and in doing so sees all round the "case and its whole situation" It is common for teachers in medical schools to have a phasic interest in some special aspects, but this may in no way impair the continuity of an all round enthusiasm

I hope that there is no absolute truth in the idea that "in the clinical and the scientific departments of medical schools the selection of staff on their research ability has ensured that they are manned entirely by specialists." I doubt if a medical school could survive on such unbalanced teaching personnel. Appointment should rightly be associated with ability within the humanities, and not infrequently anyway the "specialist" is basically a sound general physician or surgeon who has, after many years, tended to canalise his interests somewhat But not unwisely, in his dealing with undergraduates, he lets his mind flow in fields of knowledge, advice, and guidance well outside his so called specialty Specialism, worked properly into the tangle of medical education, can be a golden thread in the students' build up Over departmentalism must be avoided, it must definitely appear a reality to the student that what the administration may regard as tidy departmental isolation has, in fact, no effective separation either in teaching or the system of graduating examination In other words "specialisation" need not entail retreat from the central theme of Medicine Most undergraduates are potently attracted to those teachers who will engage them in a discussional attitude to the wide and open fields of medical and paramedical matters

It is certainly unwise for Dr Richards to assume that, whilst "the community supports universities primarily that they may teach all faculty members are principally interested in something other than teaching" A dualism of interest—teaching and research—is the proper province of the medical school No antagonisms or incompatibilities need arise out of these conditions Of course, general practitioners (by which I presume is meant domiciliary practitioners) can and must be increasingly brought into the picture They are already so in some medical schools, and their influence will grow We all know that training on sick people in hospitals is only one aspect of medical activity Training in the diagnosis of health and the ways of maintenance of health in the home, the factory, the school, or the street are other aspects worthy of teaching skill, and, in further answer to Dr Richards, there are, therefore, not a few senior people who in their teaching feel sure they are doing something of quite definite value to society I have no doubt that we can rest assured that many of us who have responsibilities in the appointment of teachers in medical schools do not fail to weigh all the merits of the candidates, and we do not put personality, general y, wide perspective, and an understanding of the graduates' real demands out of very high priority ese considerations

artment of Child Health
University of Bristol.

A V Neale

Obituary

CHRISTOPHER GRAHAM MILLER
B.M Oxfd

ristopher Miller, who died at Bradford on April 30, ie age of 24 received his early education at Clifton ge, and in 1944 he went up, as a scholar, to Balliol ge, Oxford, later graduating with second-class urs For his clinical studies he proceeded to the lon Hospital, from which he qualified last year he time of his death Miller was in his first hospital intment, and a senior colleague tells of the cientiousness and kindness which he brought to his as house-surgeon. His clinical notes, on which orked far into the night, were of a quality unusual in teaching hospitals, he felt keenly responsible is patients, and seldom left the hospital A friend knew Miller at Oxford writes

His first interest in medicine was humane and he combined this a deep Christian feeling He was one of an important p of students who kept his College together during the ult war years, his main special activity was in the ol Boys Club He was a delightful person to know vas shy, and his reserve took a little breaking through— most penetrating and wittiest remarks might be made st to himself—but this quietness was never uncomfortable he had many friends I felt that he would be an influence ood medicine and good life '

Births, Marriages, and Deaths

BIRTHS

ORE —On May 7, the wife of Dr P G Ashmore—a daughter
ERT —On May 14 in Guernsey the wife of Dr Edward Aubert —a daughter
CE SMITH.—On May 17 at Oxford the wife of Dr Roger Bryce-Smith—a son.
RDEN —On May 9 the wife of Dr Harold Dearden—a daughter
TON —On May 4 the wife of Dr Paul Denton—a son
INE.—On May 18 in London the wife of Dr John Devine —twin daughters
R —On May 13 in London the wife of Dr A G Farr—a son
SER.—On May 6 the wife of Dr Douglas Fraser—a son
ILTON —On May 9 at Llanelly the wife of Dr W S Hamilton —a son.
S —On May 11 at Hythe Kent the wife of Mr Roger Miles F R.C.S.—a son
NTREE —On May 14 at Grantham the wife of Dr J K. Rowntree—a son
LEY —On May 10 in London the wife of Mr B E C Stanley F.R.C.S —a daughter
TEHEAD —On May 13 in London the wife of Dr Michael Whitehead—a daughter

MARRIAGES

Belder—Hall.—On May 19 at Markbeech Kent Keith Roy John de Belder M.B. to Elizabeth Mary Hall
GLE—Berry —On May 17 at Heywood Lancs John Harvey Diggle M B. to Margaret Jean Berry S R.N
TCHER—Kent —On May 12 in Birmingham Joseph Henry Fletcher M B to Mary Kent M.B

DEATHS

ERSON —On May 10 at Cheltenham Frederick Thomas Anderson, M D Brux. F.R.C.S E aged 88
NERMAN —On May 13 at Stanhope co Durham James Bannerman M.B. Edin aged 77
Y —On May 12 Frederick William Bury M.D Dubl. aged 79
HAM.—On May 5 Sophia Graham M.B Lond D P.M
ENLEES —On May 16 in Edinburgh James Robertson Campbell Greenlees D.S O M A M.B. Camb aged 72
L.—On May 16 at Haslemere Surrey Robert William Basil Hall, K.C B. O B.E M R.C.S surgeon vice-admiral R.N retd
ES —On May 15 at Claygate Surrey Arthur Herbert Hayes M R.C P D P.M major R.A.M C retd
THCOTE.—On May 19 in London Reginald Saint Alban Heathcote M.A D M B.Sc Oxfd F R.C P aged 62
NSTON —On May 17 William Ellis Johnston M B. Aberd aged 45
DOX —On May 3 Rodger Frederick Maddox L.M.S.S.A aged 26
LER.—On April 30 in Bradford Yorks Christopher Graham Miller B.M Oxfd aged 24
ERVILLE LARGE —On May 1 William Collis Somerville-Large B.A M B. Dubl F.R.C.S I

Appointments

Bauerova Olga M D Bratislava D M R asst radiologist Bury and Rochdale hospitals Lancs

Belcher J R M.B M.S Lond F.R C.S consultant thoracic surgeon London Chest Hospital

Black Wallace M.B Lond F R C.S consultant surgeon ear nose and throat department Harrow Hospital

Courtney James L.R.C.P E, D.M.R E asst radiologist Burnley and district hospitals Lancs

Drummond R G M B Edin D.P H asst county M O.H and asst school M O Isle of Ely

Edmunds Vincent M D Lond M R C P asst physician Charing Cross Hospital annexe at Mount Vernon Hospital

Fisher, J A M D Belf M R C.P consultant physician Mid Ulster Hospital.

Green Dora M.R C.S D C.H asst county M O H and asst school M O Isle of Ely

Greener Joan M.B. Birm D.P H D.P.M consultant child psychiatrist Mapperley Hospital and child guidance centres Nottingham city and county

Hargreaves E A M.R.C.S D P.H asst county M O H. Colchester

Jones E R M.R C.S D P.M asst psychiatrist (S.H.M O) Cefn Coed Hospital Swansea

Kingdom L G M.A. M B. Camb F R.C.S. consultant ear nose and throat surgeon *Queen Mary's Hospital for Children* Carshalton Surrey

McArthur J B H M.B Lond M R C P.E asst chest physician (S.H.M O) Caernarvon and Anglesey Hospital Management Committee

McParland, M. F L.R.C.P I D C H D.P.H asst M O.H Preston Lancs

Mettam Elsie. M B. Manc D.M R D consultant radiologist Doncaster Royal Infirmary Victoria Hospital and Kilton Hospital Worksop Notts Fullerton Hospital Denaby Main Yorks and Retford and District Hospital and Rampton *Hospital Notts*

Park G D, M C M B. Glasg D P H M.O H Stirling

Salmon L F W M.B.E M.B M.S Lond F R.C.S consultant ear nose and throat surgeon St Helier group of hospitals Surrey

Smiley T B M B. Belf F R C.S consultant thoracic surgeon Northern Ireland hospitals

Wadsworth W V M B Manc M R C.P, D.P.M. deputy medical superintendent Cheadle Royal Mental Hospital Cheshire

Watson Kathleen M B Lond, D.A consultant anæsthetist Huddersfield group of hospitals

Williamson M S M.C M B. Durh M.R.C O G consultant obstetrician and gynæcologist Durham group of hospitals

Wilson Peter, F R.C.S E D O.M.S consultant in ophthalmology to Leeds Regional Hospital Board

Wishart James M.B. Glasg F R.F.P S F R C.S.E consultant in orthopædic surgery hospitals in Bradford A group with additional duties in Wakefield B and Ilkley and Otley groups of hospitals

Young Austen M B. Edin F R.C.S F.R.C.S.E consultant ear nose and throat surgeon Chesterfield Royal Hospital and United Sheffield Hospitals (Royal Infirmary unit) with duties at the Lodge Moor Isolation Hospital, Sheffield

Hospital for Sick Children Great Ormond Street London

Jackson Ruby M B. Glasg resident aural registrar
Roxburgh, R C M.B. Camb M.R.C.P D C H house-physician (senior house-officer grade)

Colonial Service

Anwyl W E M R.C.S. M O (surgical duties) Somaliland Protectorate
Baird, R B M.B. Edin M R C.P junior specialist (pathology) Nyasaland
Bland R H. O B.E M D Dubl asst director (leprosy contact) Nigeria.
Cannon D A M.B. Glasg D T.M & H asst director of laboratory services Nigeria
Christodoulides I J M D Athens district M O Cyprus
Comty J H M.B Lond. M.O Mauritius
Evans Thomas M.R C S D P.H. D T.M & H asst director of medical services Northern Rhodesia.
FitzPatrick J V M.B N U I M O North Borneo
Fowler A. F M.R C.S D T.M & H D.P H senior M O Tanganyika
Gerada A M.D Malta M.O (temporary) Nigeria
Graham H. P M.B. Durh M O Sarawak
Ingles R A L.R C.P E M.O Kenya
Mansfield H N M B Lond M R.C O G special grade M O Kenya
Mantwa S L. A M.D Edin F R C.S.E. D T.M.& H director of medical services Nigeria
Moodie A S M.B Glasg D P.H tuberculosis specialist Hong Kong
Rerrie J I M R C.S D P H senior M O (health) Jamaica
Ross C M M B. Belf D T.M senior leprosy officer, Nigeria
Shaw F O J M R C.S M O Kenya
Skomoroch Z W MED DIP Warsaw M O (temporary) General Hospital Barbados
Thomson K D B M.B Lond M O (temporary) Nigeria
Topham L J M.B. Birm M R C P M O (special grade) Nigeria
Trapl, H. M D Prague D T M. & H district M O (temporary) Leeward Islands
Wattley G H M D Brist M R.C.P D T.M & H M O grade A Trinidad
Whittaker L R M.R.C.S D C.H M O Kenya
Wilson W J S M.D Lond, M R C P D T.M & H medical specialist Jamaica

Notes and News

THE CASE FOR A MINISTER OF SOCIAL SERVICES

THE Minister of Health, divested of responsibility for housing, is no longer a member of the Cabinet, and earlier this year we suggested [1] that it was unlikely that the remodelled Ministry, now small, isolated, and junior, would have much bargaining strength either at the level of Cabinet committee decisions or in its relations with the Treasury The argument for appointing, or identifying, a member of the Cabinet responsible for the health and other social services has lately been expressed by Mr Aneurin Bevan, erstwhile Minister of Health and subsequently Minister of Labour Such a member, he reasons,[2] should be at least as influential as the Chancellor of the Exchequer "some way must be found to protect the social services from annual raids by the Chancellor of the Exchequer, whoever he may be It is all the more necessary to do this because a modern Chancellor must take in review the whole field of social income and expenditure in order to assess the deflationary or inflationary influences at work The expenditure on the social services is a standing invitation to a harassed Chancellor in search of reduced expenditure, or increased revenue, or both "

CHANGES IN THE POISONS LIST

THE following changes are made in the poisons list and rules under the Poisons List (Amendment) Order, 1951 (S I 1951 no 721), and the Poisons Rules, 1951 (S I 1951 no 722), which come into operation on June 1

Part 1 of the poisons list

(*a*) The item anti histamine substances is amended to include chlorcyclizine and promethazine

(*b*) The following substances are added gallamine, organic compounds of mercury which contain a methyl (CH_3) group directly linked to the mercury atom, and paramethadione

Part 2 of the poisons list

The entry 'organic compounds of mercury' is amended to read organic compounds of mercury except compounds which contain a methyl (CH_3) group directly linked to the mercury atom "

First schedule to the principal rules

(*a*) The item anti histamine substances is amended to include chlorcyclizine and promethazine

(*b*) The following substances are added gallamine and para methadione

(*c*) At the end of the item commencing with the word 'Amino alcohols' the following words are added and except procaine when contained in any preparation of which a substance to which the Penicillin Act 1947 applies is an ingredient or part'

Group 2 of the third schedule to the principal rules

(*a*) In the first column to the item commencing 'anti histamine substances there is added chlorcyclizine and promethazine

(*b*) To the second column of the item Phenols there is added para tertiary amyl phenol "

Fourth schedule to the principal rules

(*a*) The item anti histamine substances is amended to include chlorcyclizine and promethazine

(*b*) The following substances are added gallamine and para methadione

Ninth schedule to the principal rules

In the note to this schedule after the words organic compounds of mercury ' there are added the words 'except compounds which contain a methyl (CH_3) group directly linked to the mercury atom

SCULPTURE AT MENTAL HOSPITAL

THE value of art in the therapeutic programme of a hospital for nervous and mental disorders is now widely recognised Two recent books, *Art versus Illness*, by Adrian Hill, and *Art and Regeneration*, by Maria Petrie, have helped to explain and popularise the principles involved Most hospitals have concentrated on the graphic arts, and many have availed themselves of the services of the Council for Music in Hospitals Sculpture has had less attention, and the exhibition at the Basingstoke Museum, by patients from Park Prewett Hospital, will therefore be of interest This exhibition was opened on May 24 by Dr W S Maclay, senior commissioner of the Board of Control, and will remain open until June 9 Park Prewett was fortunate in obtaining the services, as instructor, of Eric Benfield, F R S A, author of *Purbeck Shop* and a sculptor of some distinction himself He has not forced his own ideas on patients, but has encouraged them to express their own fancies and imaginations, and he is always ready to advise on technique None of the exhibitors had had any previous experience in sculpture, and it was a pleasant surprise to discover the latent talent The 42 exhibits, in Bath stone, by sixteen patients, display a variety of subjects—some rather conventional, others such as ' Snake woman " and " Tree of Life," original and imaginative The bizarre is less in evidence than is usual in exhibitions of graphic work from mental hospitals, but there is something of the " primitive " in many of the exhibits As is true of graphic creations, the schizophrenic group of patients are the most generous contributors of the sixteen, twelve are classified amongst the schizophrenias—be it active or latent, or schizoid personality

HEALTH SERVICE ESTIMATES 1951-52

IN our correspondence columns on April 21 (p 912) Dr Harold Leeson asked what was the " other staff " whose wages and salaries, according to the hospital estimates, came to £21,144,000 In a written answer in the House of Commons on May 11 the Minister of Health explained that this entry relates to " a great variety of staff who cannot be classified in a small number of groups but about one half of the amount is for 'domestic staff' and another quarter for 'porters' using those terms in a broad sense "

ROYAL CANCER HOSPITAL CENTENARY

THE centenary of the Royal Cancer Hospital, London, was celebrated last week by a reception at the hospital and demonstrations in the Chester Beatty Research Institute

At the centenary dinner on May 17, Sir Edward Cripps, the chairman, read a message from the King congratulating the hospital on its great work during the 100 years of its existence and wishing it continued success Sir Henry Dale, O M, F R S, recalled how Dr William Marsden founded the hospital at Hollywood Road, West Brompton, after his wife died from cancer The hospital, which later moved to its present site in Fulham Road, was the first to receive patients without letters of recommendation from subscribers and also the first to deal solely with cancer Its founders had little encouragement from others, who did not altogether approve of a charitable hospital for one disease, but they did what they could with courageous enterprise, and their efforts were reflected in the magnificent record of the hospital in the years that followed Sir Henry thought it apt that the centenary should fall at the time when, in the Festival, the country was holding a public audit of its achievements during the last century Unhappily we had not seen that peaceful coöperation which the exhibition of 1851 was meant to inaugurate, and many of the scientific discoveries since made had been used for destruction, but it was comforting to reflect that many of the scientific advances made during the urgency of war had been adapted for humane use The Royal Cancer Hospital, he concluded, had much to be proud of in the past and great hopes for the future Lord Horder, consulting physician to the hospital, said that he spoke as the oldest member of the staff of the hospital, and he recalled some of the personalities with whom he had been associated during his work there The special hospitals had made immense contributions to medical knowledge despite the fact that their foundation had been discouraged He went on to ask for a change in the hospital's name, and suggested that it be called the " Royal Chelsea Hospital," with the subtitle " for the treatment of cancer and allied diseases " Proposing The Guests, Mr Oliver Lyttelton, president of the hospital, paid tribute to the work of the medical profession He was glad, he said, that research institutions had not come under the control of the National Health Service, for it was essential that research should be completely independent of Government control With departmental control there was a tendency to uniformity, and with uniformity often came mediocrity in no profession was uniformity more inappropriate than in medicine Mr Hilary Marquand, the Minister of Health, said that the Royal Cancer Hospital was an institution of which the country and Commonwealth could be proud The change of ownership that came with the National Health Service had brought no change in the purpose of the hospital's work He was glad to hear that a film was being prepared which would bring to the attention of the public the dangers of cancer the purpose of this film was not to terrify but to reassure and enable early diagnosis to be made Cancer was the deadliest of foes and a challenge to all those concerned in fighting it, and the hospital could be proud of its 100 years spent in attempting to overcome the disease

At the Chester Beatty Research Institute the demonstrations illustrated the contributions of the various sciences to cancer research In cytology the effect of radiation and various chemicals on cell structure was shown, and methods of cell study by means of ultraviolet micrography and microspectrography, phase contrast microscopy and cinemicrography, and electron micrography were exhibited Other demonstrations included the preservation of chicken tumour viruses by freeze drying electrophoretic diffusion studies, the biochemistry of tumours and of carcinogenic and radiomimetic substances, cytogenetic studies of chemical mutagens, spectroscopy of biologically important substances and the application of spectroscopy to cancer research, and methods of separation of commercial dyestuffs into fractions for chemical identification and biological testing in relation to occupational bladder tumours A selection of specimens illustrated the earlier history of experimental carcinogenesis, and in the institute library a selection of original papers from the institute was shown

---

[1] Leading article *Lancet* March 3 1951 p 513

[2] *Tribune* May 18 1951 p 5

ONE OF THE BETTER EXHIBITIONS

A NEAT pictorial epitome of progress in public health may now be seen at the London School of Hygiene and Tropical Medicine One of the study groups which are formed by the students in the D P H course has collected perhaps a couple of hundred photographs, drawings, and other exhibits, and has arranged them cleverly to show how past evils have been tackled and what has still to be done From cheering illustrations of improvement in the physical environment of children, we pass to a review of housing and town planning, an exposition of the Five Freedoms portraits of the founders of modern hygiene, and sections on tropical medicine and nutrition, including some telling facts and pictures from the Gambia, where Prof B S Platt s department has a field unit at work. Small but of a high standard, this exhibition is a fitting contribution by the school to the Festival of Britain The students responsible are Dr C G Burgess, Dr A. G Farr, Dr E H Lamb, and Dr D H Mackay—helped occasionally one suspects, by Prof James Mackintosh and other members of the school council, in whose name Dr Andrew Topping the dean, last week welcomed Mr Hilary Marquand the Minister of Health, as the first visitor

NATIONAL MORBIDITY INQUIRY

IN 1948 the Ministry of Health arranged for the collection of data about inpatients from selected hospitals for central analysis in accordance with the 1948 International List of Diseases, Injuries, and Causes of Death. From this limited trial it is clear according to the Ministry, that wider collection of data would yield results of value for the compilation of national morbidity statistics, the development of research, and the general planning of the National Health Service For these purposes it is not necessary to collect information on all hospital patients , and the Minister is therefore considering the introduction of a system of sampling The Ministry states (R H B [51]45) that it will shortly ask hospitals that have been taking part in the limited trial to comment on the transcription form now in use The aim is to introduce a revised form at the beginning of 1952, and to ask all hospitals to complete this form in respect of a sample of their patients Meanwhile hospitals taking part in the trial are asked to continue to do so on the present basis

RUSSIAN LONGEVITY

OLD comrades never die—to judge by a recent Russian survey on longevity [1] which showed that there are more than 30 000 people in the Soviet Union who are more than 100 years old. Neither do they fade away for Vassily Sergeivich Tishkin, now in his 145th year, worked 256 days on his collective farm last year, and on election day this winter walked to the voting booth himself while Makhmud Eivazov, who is 142 is a deputy of his local soviet, works on a collective farm, and regularly bathes in a mountain stream. Whereas in capitalist countries there are few examples of such persistence, conditions in the Soviet Union are stated to favour long life, and the Kharkov Institute of Biology is to publish a book called ' U S S R —Country of Longevity ' Which draws from the *New York Times* [2] the rejoinder that length of life in the Soviet Union is apt to be governed by capricious laws

---

Biochemica e Terapia Sperimentale and *Patologia Comparata della Tuberculosi* are now being published as a single journal entitled *Notiziario dell'Istituto Vaccinogeno Antitubercolare*, of which the first issue is dated January–March, 1951

University of Cambridge

In a congregation on May 12, the degree of bachelor of medicine and surgery was conferred on B E L Thompson

University of London

Prof P B Medawar, D SC , F.R.S , has been appointed to the Jodrell chair of zoology and comparative anatomy at University College from Oct 1 Dr Medawar has held the Mason chair of zoology in the University of Birmingham since 1947

University of Sheffield

Dr H E Harding, senior lecturer in pathology, has been appointed reader in pathology

University of Manchester

Dr C Fraser Brockington has been appointed professor of social and preventive medicine in succession to Dr Andrew Topping Dr Brockington will take up his duties in Manchester in August

Dr Brockington studied medicine at Cambridge and Guy's qualifying in 1927 In 1928 he obtained the D P H and two years later the degree of M D After holding resident appointments at the Hospital for Sick Children Great Ormond Street and at Brighton Infectious Diseases Hospital and Sanatorium in 1930 he became assistant county medical officer for Worcestershire After some years in private practice he returned to a public health appointment in West Sussex in 1936, going to Warwickshire as deputy medical officer of health in 1938 and becoming county M O H in 1942 In 1946 he received his present appointment as county M O H for the West Riding of Yorkshire and he has been lecturer in preventive medicine in the University of Leeds since 1948 He has published papers on epidemiology nutrition and social medicine

Royal College of Surgeons of England

At a meeting of the council on May 10, with Sir Cecil Wakeley, the president, in the chair, Mr R L Holt and Mr G Qvist were admitted to the court of examiners Mr A. H Harkness, (London Skin Hospital), Mr I W Magill (Westminster) Mr A O Parker (Cardiff), Surgeon Captain R W Higgins, R N , and Prof T Nicol (King s College) were admitted to the fellowship The Walker prize was presented to Prof Alexander Haddow (Chester Beatty Research Institute), and the Begley prize to Mr G L Howe (Middlesex)

Diplomas of membership were granted to those named in our report of the comitia of the Royal College of Physicians (*Lancet* May 5 1951 p 1023) The D O H was also granted to A J Watson, and the D P H to H L Wolfe

Royal College of Surgeons of Edinburgh

At a meeting on May 17 with Mr W Quarry Wood, the president in the chair, the following were admitted fellows

H A Beagley Anwar El Masry W T Gibbs R R Gilfillan P D Goatcher J M D Hay T A H Hurrell R M Jackson W H McGillivray I M. Maciver Murarimohan Mukherji, T J Noonan Gurdial Singh D B Skewes R G Townsend L W van Blerck J A M White

West London Medico-chirurgical Society

This society s annual banquet is to be held on Wednesday, June 6 at the Royal College of Surgeons, at 8 P M

Lebanon Hospital for Mental and Nervous Disorders

Addressing last Monday the annual meeting, in London, of the Lebanon Hospital for Mental and Nervous Disorders, Asfuriyeh the Earl of Feversham, the president, said that the hospital had done good work in a country where the need was great He welcomed the matron of the hospital, Miss Mary Morrissey who had just arrived from the Lebanon , and finally he proposed that Sir William Houstoun Boswall, formerly British Minister in Beirut, be elected a vice president Mr H Lyn Harris, chairman of the London committee, said that 1950 had been a year of great progress The hospital had been partly rebuilt new sanitary and medical equipment had been installed, and many improvements for the welfare of patients and staff had been made The chairman went on to speak of the energy and enthusiasm that Dr W M Ford Robertson, the medical director, had put into his work since taking up his post in February, 1950 The report of the medical director was read by Dr J C Sawle Thomas, chairman of the medical committee, who said that advances had been made in the medical teaching at the hospital under the new director who held the post of associate professor of psychiatry at the American University of Beirut It was hoped to start a neurosis centre at the Lebanon Hospital as soon as possible , and other schemes included the provision of scholarships to enable the best student nurses to come to Great Britain for further training

---

[1] New York Times, April 27 1951 p 4
[2] *Ibid* April 28 1951 p 6

Royal Sanitary Institute

Mr G. R. Oake, chairman of the Interdepartmental Committee on the Inspection of Meat, will discuss this committee's report in the Benjamin Ward Richardson lecture, to be delivered at the institute on Wednesday, June 20, at 2.30 P.M.

West London Hospital Medical School

Dr Leonard Colebrook, F.R.S., will deliver the fourth Alex Simpson Smith lecture on Tuesday, June 12 at 8.30 P.M., at 11, Chandos Street, W.1. Dr Colebrook is to speak on Outstanding Problems of Burns and Scalds. Application for tickets should be made to the dean of the school, London, W.6.

French Congress of Stomatology

This congress will be held in Paris at the Fondation Eastman from Oct. 8 to 13 under the chairmanship of Dr René Vincent. The organisers would especially welcome papers from British doctors who are interested in dental problems. Further particulars may be had from Dr Frez, secretary general of the congress, 12, rue Notre Dame des Champs, Paris, 6e.

Charges for Dentures and Spectacles

These charges, under the National Health Service Act, 1951, came into force last Monday, May 21 (see *Lancet*, April 28, 1951, p. 967). The charges are not applicable to patients who on that date were already undergoing dental treatment involving dentures, or to those for whom glasses were already on order.

Medicine and the Festival

The Festival scientific meetings organised jointly by the British Medical Association and the Royal Society of Medicine will be opened on Monday, June 4, at the Royal Society of Medicine, 1, Wimpole Street, London, W.1. The opening ceremony will be performed by the Earl of Athlone, chancellor of the University of London, accompanied by Princess Alice, chancellor of the University of the West Indies.

Conference on Electron Microscopy

The electron microscopy group of the Institute of Physics is holding a conference at St Andrews on June 19 and 20. The speakers will include Dr M. S. C. Birkbeck of the Chester Beatty Research Institute, Mr C. E. Challice, and Dr A. S. McFarlane of the National Institute for Medical Research. Further particulars may be had from the hon. secretary of the group, Mr F. W. Cuckow, M.SC., F.INST.P., Chester Beatty Research Institute, Royal Cancer Hospital, London, S.W.3.

Award of George Medal

The George Medal has been awarded to Squadron Leader T. C. L. Brown, M.B.

On the night of Dec. 20, 1950, Squadron Leader Brown was travelling as a passenger on a training flight from Singapore when a propeller blade broke loose. The blade cut through the fuselage and seriously injured the co-pilot, and within a few seconds the faulty engine fell out of the aircraft. Without regard to his own safety Squadron Leader Brown administered medical aid to the injured man, with whom he stayed until the aircraft crashed. He himself was seriously injured, and "there is no doubt," says the citation, "that he consciously risked his life in order to save that of the injured officer."

British Cardiac Society

The thirtieth annual meeting of this society was held in Glasgow on May 10, under the chairmanship of Dr J. H. Wright. A discussion on heart disorders of pulmonary origin was opened by Prof. J. McMichael, Dr A. J. Thomas, and Dr Paul Wood. Short communications, arranged by the secretary, Dr K. Shirley Smith, included papers on vector cardiography, clinical and cardiographic aspects of cardiac infarction, and electrokymography. Colour films illustrating movements of the valves of the heart and diaphragmatic flutter were shown.

Donor Eyes

The Southern Ophthalmological Society visited the corneo-plastic unit at the Queen Victoria Hospital, East Grinstead, on May 5, for a demonstration by Mr B. W. Rycroft of the operative technique of lamellar corneal grafting and dacryocystorhinostomy. He also showed cases illustrating optical, therapeutic, and cosmetic grafts, and he emphasised the urgent need for donor eyes. He invited the cooperation of the society, and of all ophthalmic surgeons, in the provision of donor material. A box for transport of the eye under suitable conditions would be sent in time for any case if notification were received by the unit in advance.

Société Nationale Française de Gastro-entérologie

The dates of this society's next meeting have been changed from June 16 and 17 to June 15 and 16.

Malaya's Need for Doctors

At the request of the Colonial Office the Ministry of Health has notified hospitals of the need for more doctors in Malaya. The Ministry's circular (R.H.B. [51]44) remarks: "The Government regard as an essential step in the re-establishment of law and order there, that full civil administration and social services should be introduced in each area as it becomes ready."

The 1949–50 issue of the collected papers of the Middlesex Hospital Medical School has now been published.

The title of the U.S. Public Health Service's monthly journal, hitherto known as the *Industrial Hygiene Newsletter*, has been changed to *Industrial Health Monthly*.

CORRIGENDUM: *Plasmosan in the Prevention and Treatment of Shock.*—The qualifications of Dr F. J. R. Stoneham, joint author of this article last week, are L.R.C.P., M.R.C.S., D.A.

Diary of the Week

MAY 27 TO JUNE 2

Monday, 28th

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, University Street, W.C.1
5.30 P.M. Prof. A. Fölling (Oslo): Oligophrenia Phenylpyrouvica. (First of two lectures.)

ROYAL EYE HOSPITAL, St George's Circus, S.E.1
5 P.M. Dr T. Rowland Hill: Ocular Palsies.

Tuesday, 29th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr J. B. Kinmonth: Surgical Physiology of Large Arteries with Particular Reference to Traumatic Spasm. (Arris and Gale lecture.)

UNIVERSITY OF LONDON
5.30 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Prof. Warren H. Cole (U.S.A.): Surgery of the Biliary System. (Last of two lectures.)

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL
5.30 P.M. Professor Fölling: Oligophrenia Phenylpyrouvica. (Last of two lectures.)

WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St Mary's Hospital Medical School, W.2
5 P.M. Dr G. Bousfield: Avoidance of Post-injection Paralyses. (Almroth Wright lecture.)

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W.C.2
5 P.M. Dr H. J. Wallace: Erythemato-squamous Eruptions.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, W.C.1
5.30 P.M. Mr H. H. Skeoch: Hormone Therapy in Ophthalmology with Cortisone and A.C.T.H.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Prof. P. E. Vernon, PH.D.: Investigations of Intelligence and its Measurement.

WEST END HOSPITAL FOR NERVOUS DISEASES, 73, Welbeck Street, W.1
2.30 P.M. Mr Joseph Minton: Ocular Manifestations of Nervous Disease.

Wednesday, 30th

INSTITUTE OF DERMATOLOGY
5 P.M. Dr R. W. Riddell: Medical Mycology—Superficial Mycotic Infections.

INSTITUTE OF OPHTHALMOLOGY
5.30 P.M. Mr J. D. Magor Cardell: Burns of the Eye.

ROYAL EYE HOSPITAL
5.30 P.M. Mr L. H. Savin: Common Plastic Operations and Orbital Surgery.

Thursday, 31st

ST GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, S.W.1
1.30 P.M. Dr M. A. Partridge: Psychiatry lecture-demonstration.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr J. L. Franklin: Seborrhœic Dermatoses.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S.E.5
3 P.M. Dr Jacques Le Beau (Paris): Neurosurgical Difficulties in Performing Limited Prefrontal Operations.

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Mr A. J. Slessor: Peripheral Nerve Injuries.

UNIVERSITY OF ST ANDREWS
5 P.M. (Medical School, Small's Wynd, Dundee.) Prof. W. Mercer: Surgery of the Chronic Hip.

Friday, 1st

ROYAL EYE HOSPITAL
5.30 P.M. Dr C. A. Keele: Advances in Pharmacology of the Eye.

Saturday, 2nd

BRITISH SOCIETY FOR RESEARCH ON AGEING
3 P.M. (Middlesex Hospital Medical School, W.1.) Annual Conference.

PHYSICAL EXERCISE*

ITS CLINICAL ASSOCIATIONS

SIR ADOLPHE ABRAHAMS
O.B.E., M.A., M.D. Camb., F.R.C.P.
CONSULTING PHYSICIAN TO WESTMINSTER HOSPITAL

The Pathology of Exercise

The ill effects that are with more or less justification attributable to exercise fall under two heads: those in which a grave lesion or a fatal collapse occurs during the performance, and those in which, as the result of repeated maximal or submaximal efforts, deterioration of some vital structure, especially the heart, is produced. To these may be added a number of minor disturbances, which are less serious but which act as a handicap and encourage advice in the hope of prevention.

When death occurs during the performance of physical exertion, two features are as a rule conspicuous: the triviality of the effort, or the discovery of some long pre-existing lesion which had never been suspected.

When no adequate cause for death is found post mortem, the presumption is the occurrence of an intense vagal inhibition in a strongly predisposed subject, especially of the more or less hypothetical thymico-lymphatic type. In this, narrowness of the aorta is a most consistent characteristic (Millar and Ross 1942). In the majority of deaths that occur during exercise, necropsy reveals disease of such magnitude as to make it almost unbelievable that the sufferer could have survived at all with moderate activity, still less the capacity for outstanding athleticism.

Jokl (1940a) has collected 67 examples comprehended under the category of acute fatal non-traumatic collapse during work and sport. The conditions discovered at necropsy included coronary arterial disease, aneurysm of the aorta, cerebral arterial disease, rupture of an aneurysm in a tuberculous cavity, and rupture of the aorta. One of his most striking examples may be described in detail.

During a strenuous game, the captain of the Transvaal rugby team, 32 years of age, collapsed and died. His previous athletic ability had earned him the title of the Iron Man of South African Football.

At necropsy the heart weighed 17 ounces. In the wall of the left ventricle were fibrotic patches. The coronaries exhibited widespread atheroma, the left branch being narrowed in three places. The aorta was extremely thin and soft. The left kidney was small with advanced hydronephrosis; the right kidney, the size of a walnut, was cystically degenerated. The thymus was conspicuously enlarged.

Young subjects may be afflicted with grave congenital lesions through which their survival is seriously jeopardised, yet remain completely free from distress until some precipitating factor—apparently most trivial—results in fatal collapse.

Lumsden (1946) records a remarkable case.

An Indian seaman, aged 25, reported to his medical officer with the complaint of dizziness. He had had six years' naval service with a clean medical history, and examination revealed no abnormal physical signs; the cardiac rate was 66 and rhythm regular. Having volunteered to demonstrate his disability by taking a short run of twenty yards, he fell unconscious and died immediately. Post-mortem examination showed an enormously dilated right atrium, a patent foramen ovale, and advanced atheroma of the ascending aorta which was thickened, hard, and inelastic.

The two following cases came under my own observation.

A soldier, aged 31, with three years' service was engaged in light physical training at 7.15 A.M. After a few minutes he collapsed and he was dead at 7.40 A.M. Necropsy showed slight coronary atheroma. The right ventricle weighed 19 ounces, the myocardium being almost completely replaced by fat. The wall of the left ventricle was thickened, and although of normal appearance, showed an early stage of the same patchy necrosis.

A young woman collapsed and died whilst skipping shortly after a meal. Necropsy revealed congenital absence of the left branch of the coronary artery. Presumably the gastro-coronary reflex caused a critical reduction of oxygen supply to a myocardium with insufficient reserve.

Many circumstances may produce a fatal vagal inhibition during very mild exercise. An unusual cause of death is reported by Lande et al. (1942).

During a football match a player sustained a slight collision and fell dead. It was discovered post mortem that a hydatid cyst on the inferior surface of the right lobe of the liver had ruptured into the abdominal cavity. Fatal allergic shock occurred from sudden intraperitoneal injection of its contents.

In 1884, a historical catastrophic lesion resulting directly from violent exercise occurred in a medical student.

Whilst representing Cambridge against Oxford in the 120 yards hurdles race, an event that he won in first-class time, he collapsed with severe pain in the back. Œdema of the legs and scrotum rapidly developed, with slowly progressing dilatation of the superficial veins of the abdominal wall and a high degree of albuminuria, all of which persisted for the remainder of his life—i.e., 25 years—during which he practised as a leading obstetrician. At necropsy the whole of the inferior vena cava below the hepatic veins was found to be converted into a flat impervious ribbon.

He had followed the not unusual practice of holding his breath for the whole or the greater part of the race—a kind of converse Valsalva phenomenon. Extreme distension of the inferior vena cava had led to localised rupture of the intima followed by forcible extravasation into the walls of the vein whilst exertion was still in progress—a dissecting varix in fact, homologous with a dissecting aneurysm of the aorta.

Sprinters are accustomed to hold their breath during their intense effort, in the belief that fixation of the thorax is an aid to locomotion. Hence provocation of the above lesion has been present on tens of thousands of occasions. Yet I can trace only one similar example of thrombophlebitis (Foster and Brouwer 1941).

The patient was a girl of 20, giving a gymnastic performance, and in her case the lesion was far less severe. Œdema of the legs and dilatation of the veins of the abdominal wall gradually disappeared, and after 11 months she was able to return, with very little inconvenience, to her occupation of games mistress.

This girl had undergone tonsillectomy shortly before her accident, and it is suggested that a temporary bacteriæmia was responsible for a weakening of the vessel wall, which yielded to the strain. The obstruction must have progressed slowly enough to permit the development of an adequate collateral circulation. In the case of the medical student, it is reasonable to postulate a predisposition to thrombosis. Shattock (1913), to whom we are indebted for a description of the necropsy, ascertained that a brother died with œdema of the lower part of the body following pressure on the inferior vena cava, and another brother from embolism of the pulmonary artery following thrombosis of a femoral vein. It is not unlikely that modern hæmatological investigations would have revealed a familial exalted coagulability of the blood—the reverse of hæmophilia.

The sudden sharp rise in blood pressure that occurs in violent exercise may be responsible for rupture of a congenital aneurysm which has provided no previous evidence of its existence.

EXERCISE AND INFECTION

The danger of taking exercise whilst suffering from a pyrexial illness has often been emphasised, and although the warning has usually been disregarded without subsequent ill effects, and the subject has enjoyed the impish satisfaction of proving the doctor wrong and wearing the crown of heroism, it is certain that the danger is by no means hypothetical or negligible

---

* The second Lumleian lecture for 1951 delivered before the Royal College of Physicians on April 12. The first lecture was published on May 26.

For at least one serious communicable disease, poliomyelitis, the predisposing influence of physical exercise has been demonstrated beyond doubt Experimental evidence that fatigue of exhausting exercise lowers resistance of the rhesus monkey to poliomyelitis virus has received clinical support (Levinson 1945) In the San Francisco epidemic of 1930, exhausting exercise preceded the onset of illness in 7 out of 60 patients In one case, after a febrile illness of two days, the patient was sufficiently improved to play in a football match Within a few hours the symptoms of poliomyelitis appeared with extensive paralysis terminating in death

A champion girl swimmer suffering for several days from what was thought to be a digestive disturbance competed, against medical advice, and died of poliomyelitis within thirty six hours

Of 107 boarders in a hostel who competed at an athletic meeting, 21 fell victims to infantile paralysis It appears that when paralytic symptoms establish themselves after physical strain, more particularly if combined with chilling, the polyneuritis is specially related to the muscles employed

The relation of exercise to tuberculosis is not so easy to establish Deaths of famous athletes from pulmonary lesions appear to supply persuasive evidence, but I have an impression that the tuberculous diathesis may be accompanied by a flair for athletics, and, if this is granted, cause and effect are not easily distinguished It must be remembered that athleticism is a peculiar quality, and that the magnificent physique as measured by anatomical standards and by performance is not necessarily the magnificent physique as measured by resistance to disease Apart from exercise as such, exposure to wet and cold, the not infrequent accompaniment of feats of endurance, may lower resistance to this infection

HEAT STROKE AND CRAMP

One danger of violent exercise which is not generally appreciated is that of heat stroke In violent exercise heat is generated, and up to a point with advantage Rise in temperature favours dissociation of hæmoglobin in the tissues and alters the velocity of chemical reactions and the rapidity of diffusion to an extent which increases significantly the rate of lactic acid re synthesis Concentration of blood spares the heart and increases the supply of oxygen to the tissues In the athlete these processes are developed during training, whilst the thermotaxic mechanism maintains a maximum efficiency What is the limit of physiological efficiency? I have myself developed a rectal temperature of 105 8° after running for an hour when the external temperature was 85° To continue for a longer period, as in the case of a marathon race with climatic conditions unfavourable to heat loss—a humid atmosphere and a following wind—might invite a serious danger

Neuroglobin separates out at 108°F, so the critical body temperature is probably a little below this One death occurred on the road during the marathon race at Stockholm in 1912 That more fatalities have not been recorded is a tribute to the capacity of the human body to adjust itself to emergencies, but the marathon race has so far been held only in countries where great heat is not to be expected Nevertheless I have always attempted to represent the danger, and to advise, as a reasonable precaution, that the hottest hours of the day should be avoided

When exhausting exercise is undertaken in circumstances conducive to heat stroke it is impossible to separate the symptoms caused by an accompanying hypoglycæmia I witnessed some alarming psychosomatic and profound metabolic disturbances in the cross country race at the Olympic Cross Country race in Paris in 1924, which took place during particularly humid heat It was interesting to see that the winner, Nurmi, finished completely free from distress, a striking tribute to the capacity possessed by the super athlete for adjustment of any kind

Curiously enough, muscular cramp, the result of salt depletion from profuse sweating, does not occur in marathon runners at least I have not encountered an example Yet I recall the employment some thirty years ago, by a really long distance runner, of a special lemonade which contained sugar and salt The sugar I accepted as a reasonable fuel, the salt I dismissed as a fad, but in the light of subsequent knowledge it would appear that he had empirically hit upon an essential requirement

The occurrence of cramp in lawn tennis players is presumably related to this biochemical factor, but there are clearly other less comprehended elements in cramp, as in swimmers Hyperventilation and excessive loss of carbon dioxide may play a part But, as is well known, cramps occur in circumstances when muscular exercise is in no way concerned

EXERCISE AND THE ABDOMEN

Since duodenal ulceration is by no means uncommon in athletes, surgeons have been at some pains to identify a causative factor in strenuous exercise They have naturally been drawn towards the mechanical side Over thirty years ago, David Wilkie explained the preponderance in males as dependent on a relatively high pylorus and lax duodenum subjecting the hepatoduodenal ligament to strain Fixity of the male duodenum he regarded as predisposing to kinking at the first duodenal angle, and, since regurgitation is impeded, to an unduly long exposure of its first part to acid chyme undiluted by bile or pancreatic juice

Arbuthnot Lane laid even greater emphasis on the mechanical hypothesis In athletic exercises the abdominal muscles are particularly concerned, and their powerful contractions, he pointed out, thrust the viscera into the pelvis The sagging of a full and heavy ileum results in a pull upon the duodenojejunal flexure, the next fixed point As a consequence the duodenum becomes distended, yields in its first (relatively mobile) part, and gives way on its convex surface

At the end of World War I I sat with Lane on medical boards, and on one occasion three young officers with duodenal ulcer were included Two had been runners and one an oarsman of some distinction, and these he regarded as support of his thesis So called psychosomatic medicine had not at that time attained its present day prominence, but even then I hazarded the possibility of a neurogenic responsibility, having regard to the highly emotional temperament that so often characterises the athlete—a point of view that the great surgeon received without enthusiasm

It is possible that the swing to the psychical side in the ætiology of peptic ulceration has been excessive, and that there may be room for a more respectful acceptance of the mechanical or anatomical factor

EXERCISE AND THE NERVOUS SYSTEM

Apart from this gastro intestinal relationship, a few further words will suffice regarding the Nervous System and violent exercise The central nervous system may be affected in any exhausting exercise, presumably from anoxia, but permanent injury does not occur

A paper published in 1876 contained the alarming pronouncement "If any psychologist will take the trouble to trace out the history of each of our prominent pedestrians, he will discover that a very large proportion of them have been subject to some form of madness" What mental or nervous disturbances the writer comprehended under "madness" is open to speculation He may have included fanaticism, infatuation, monomania, and the like, to which athletes are, in the eyes of the non athletic, only too prone So far as the inmates of mental homes afford a guide, there is certainly no indication of a disproportionate athletic contribution

Exercise as such has no particular bearing, but the circumstances of intense competition may have a considerable emotional reaction The continuous overflow of impulses to the muscles, the complex processes involved in coördinating skilled movements and focusing attention, the excitement, apprehension, and anxiety experienced especially by the leading exponents so prominent in the limelight—all of these suggest that the "strain" of exercise may have a reasonable meaning if applied to the nervous system Fatigue and excitement attending athletic competition represent special stimuli for neurotic subjects to lose control, and spectacular demonstrations of a hysterical character are not unknown at the end of a race

EXERCISE AND THE KIDNEY

Albuminuria, now universally accepted as a negligible sequel of exercise in children and adolescents, was at one time regarded as proof of kidney disease demanding complete cessation of activity and very considerable dietetic restrictions

Although Pavy had identified a condition he termed intermittent albuminuria, priority should be accorded to Clement Dukes and William Collier for their recognition of its innocence, and tribute paid to their courage for asserting, in the face of eminent opposition, that it necessitated no restrictions or prohibitions of any kind. Their bold uncompromising pronouncements rescued members of our profession from pitfalls, many boys and young men from unnecessary suffering, and parents from exaggerated anxiety and needless expense Dukes (1905) recognised the complete disappearance of albuminuria in men in whom he had discovered the condition when at school ten or fifteen years previously Collier (1906, 1907) extended his investigations, in particular to Oxford oarsmen, for albuminuria of exercise is intimately related to the pubertal or postural variety During the years of growth, the circulation, unstable from defective innervation of the blood vessels, allows serum albumin to transude through the over distended capillaries of the kidney In the recumbent position albumin disappears from the urine Its return on assuming the erect attitude is due to compression of the left renal vein against the aorta indeed cystoscopy may show that the left kidney alone is responsible In exercise, blood is diverted to situations where it is urgently required, and the kidney, which is very sensitive to oxygen want, is called upon to endure this deprivation In the vast majority of cases orthostatic albuminuria disappears in early adult life, and, as one would expect, the post exercise albuminuria which is universal in young subjects is inconspicuous in older athletes even after severe exercise, because the vasomotor system is more stabilised Since calcium metabolism appears to be concerned in the process, we see again the circumstances of growth, the demand of the bony tissues

I may cite two from a very large number of personal observations (Abrahams 1926)

> The urine of a man of 30 after the extreme effort of walking $8^1/_4$ miles in an hour, contained only 0 1% of albumin, a few hyaline and granular casts, but no blood Crystals of oxalates were identified Twelve hours later, no albumin was present
>
> The urine of another, after running half a mile in World's record time, showed an almost imperceptible trace of albumin precipitated in the cold by dilute acetic acid Oxalates again were present This would seem to support the neurogenic explanation of oxaluria
>
> In my own case, the average of a dozen examinations of urine after an hour's run has been the transient presence of protein 10 mg per 100 ml and 30 red blood corpuscles and 4 leucocytes per c.mm

March Hæmoglobinuria —This rare condition, in which exercise appears to be the essential causative factor, is in line with orthostatic albuminuria with a special constitutional element Gilligan and Altschule (1950) who have paid considerable attention to this condition, in recording its occurrence in a young woman, state that of the 76 previous examples one only, described by Vogt (1943), was encountered in a female It seems probable that so great a sex disparity is inadmissible, instances in females are more easily overlooked or, for obvious reasons, misinterpreted Exercise qua exercise is not solely responsible, for it has not occurred after the most vigorous cycling The erect attitude is a sine qua non (Watson and Fischer 1935) Syphilis and other causes of hæmolysis, especially chilling, must be excluded, as well as possible confusion with such a state of red urine as may follow ingestion of large quantities of beetroot

Blood examination reveals no clue to the peculiarity The fragility of the red cells is normal, although there is, of course, hæmoglobinæmia The blood loss is trivial it has been estimated as less than 16 ml.

The explanation would appear to be an abnormal vaso motor reflex occurring in exercise—a reflex which gives rise to increased blood supply to the liver and spleen and escape of abnormal amounts of hæmoglobin into the blood stream Lordosis of the spine is apparently an influence, and it is said that the condition can generally but not always be prevented by imposing kyphosis through the application of a plaster jacket

I have had no personal experience of any case in an athlete

The temporary *glycosuria,* not infrequent after exercise, is explained by the overflow of adrenaline It is, of course, negligible

STITCH

This term accurately applied is any sharp local twinge of pain , Shakspere uses it in this sense, and that great stylist Clifford Allbutt (1898) refers to the agonising stitch of pleurisy But in common usage the term is restricted to a pain occurring during exercise, usually in the infracostal region It may be severe enough to cause complete disablement in a track athlete, so we are often importuned for views as to its ætiology and advice for its prevention

For long it was generally held that stretching of the capsule of the spleen was the cause—naturally an unsatisfactory explanation for its occurrence on the right side of the body Moreover Barcroft showed that the spleen contracted during exercise

Capps (1941), in view of its relation to exertion, a full stomach, and exposure to cold as precipitating factors, and relief by rest, explained it on the grounds of ischæmia of the diaphragm, comparable to angina pectoris and intermittent claudication Some experiments by Conybeare (1932) on students at Guy's Hospital, in whom stitch was induced by taking exercise shortly after a meal, appeared to exonerate the diaphragm, since fluoroscopic observation showed that the movements were full and unimpaired despite the pain.

The most reasonable explanation is that it is of ligamentous origin Stitch occurs in those situations where the abdominal wall is least able to provide adequate support When violent jolting movements coincide repeatedly with relaxation of muscles maintaining an intra abdominal pressure and assisting in supporting the viscera, an intermittent tugging occurs on the ligaments supporting the stomach, liver, spleen, and bowel, in fact an acute physiological visceroptosis due to the erect attitude

Unhappily the ventilation of these scientific considerations does not appear to be of much practical value The advice to use a tight abdominal binder will naturally receive little gratitude That the stomach should be as empty as possible is a wise precaution which is not by any means always effective. In fact, it seems as if stitch results from a special anatomical predisposition that cannot be overcome.

The muscle pain that often follows exercise is a minor trauma or an aseptic tissue inflammation. It can be treated accordingly.

URTICARIA

Urticaria may follow exercise quite independently of raised body temperature. But when one recalls how urticaria can be induced by any sort of antigen, by emotional disturbances and mental states of every kind, by heat or by cold, it is not remarkable that exercise may be one if not the only factor responsible for an attack. And since permeability increases with vascular dilatation, a point will be reached when exudation occurs; so that it does not seem necessary to postulate the local liberation of histamine.

"ATHLETE'S HEART"

This term, if legitimately employed, would apply to a heart of superior contractility particularly efficient for the circulatory demands of athletic feats and of violent exercise generally. Instead, its habitual meaning can only be condemned as an unwarranted assumption of some permanent debilitating or deteriorating alteration resulting from an imposition of exceptional severity or from repeated more or less prolonged submaximal efforts. And embodied in such an idea is the presumption of what is known as "heart strain."

It is well known that when once a term gets into literature its eradication is almost impossible, in spite of failure to produce any positive evidence of its existence and even where there is conclusive proof that it does not occur and never did exist. Moreover the term "strained heart" is, especially in connection with athletics, socially acceptable. It carries with it no stigma; on the contrary some prestige accrues through an implication of heroism or martyrdom.

Two sources of fallacy appear to be responsible. First, a prejudiced expectation arising out of the very considerable circulatory demand and the failure to distinguish strain from stress. Secondly, a mistaken interpretation of the symptoms of participants during and after the feat of exertion.

Strain means a hurt or injury from excessive tension when the structure in question is stretched beyond its proper limits. The physiological dilatation of a healthy heart is of a temporary character, and no post-mortem evidence is available of any pathological change. The cases of so-called acute dilatation are almost always unrecognised paroxysmal tachycardia. The permanently enlarged and defective hearts encountered in hypertension and emphysema are in a different category. Either a toxic factor or a degenerative change in the heart muscle itself is present.

Stress may be rightly said to inflict further injury on a heart already damaged, and genuine strain of the muscular tissue may result with rupture of the muscle or a valve. But in all these cases evidence of disease is forthcoming, and it is not with such that investigation of the so-called athletic heart is concerned.

What is the clinical picture of distress in violent exertion? The subject gasps for breath. The face is pale with a pinched expression of suffering. The pulse is weak and rapid. Cold perspiration may be present. Nausea, vomiting, and even unconsciousness may occur. These are, to be sure, alarming to a solicitous onlooker; but they are not the features of cardiac failure, which are cyanosis, over-distended veins, an enlarged liver.

The exhaustion that ensues during or after an extreme effort may possibly be due to adrenal depletion or to an acute hypoglycæmia resulting not from exhaustion of carbohydrate depots but from disturbances in the regulating faculties of the vegetative systems. But the essential feature is vasomotor collapse from inability to integrate tasks beyond the body's scope. The body can deal with a variety of functional stresses if confronted with one at a time, but its resources of adaptation may be overtaxed if several are imposed simultaneously—e.g., malnutrition, circulatory stress, hypoglycæmia, infection, overheating, co-existing mental or physical fatigue, and menstruation, to mention a few of the most familiar. In other words, any instance of severe exhaustion in an athlete cannot be ascribed to physical stress alone but to the coexistence of any influence leading to generalised vascular dilatation, to which some subjects are constitutionally prone. Headache, precordial pain, nausea, vomiting, disorientation, collapse, and unconsciousness may be produced; yet these symptoms, however alarming, have no baleful significance. One recalls the historic marathon race in London in 1908 when the Italian, Dorando, staggered blindly into the Stadium, and, according to picturesque journalistic exaggeration, lay for a time between life and death. On the following day he had completely recovered and he subsequently ran a considerable number of marathon races.

It is not denied that such a state ought if possible to be avoided, but an appreciation of the true state of affairs transfers the lesion from the heart about which solicitude is usually mistakenly expressed. Even in a perfectly healthy subject undertaking strenuous exertion, sickness and other symptoms may result from cerebral anæmia, since on cessation of the exercise the pumping action of the leg muscles ceases, stagnation occurs, and the volume of blood returning to the right auricle is insufficient to maintain an adequate arterial blood-supply to the brain. Some very efficient athletes are prone to fainting and collapse through a general vagotonic reaction. I have often encountered this during so trivial an ordeal as taking the blood-pressure; another familiar example is the prick of a needle in a hypodermic injection or blood examination.

Adoption of the recumbent position, deep breathing, pressure on the abdomen, and flexion of the legs and arms will substantially reduce the symptoms and accelerate recovery.

At one time oxygen inhalations were a favourite therapeutic measure, and cylinders were kept in readiness on athletic grounds. But apart from a psychological effect, oxygen can have no restorative value, since the oxygen requirement falls below the oxygen income available from ordinary air. And a recovery from fatigue is limited by the rate of return of lactic acid into the muscles from the blood and inactive tissues which is not affected by oxygen.

The possibility of hypoglycæmia is an attractive explanation of the symptoms after long-continued exhausting exercise. This applies particularly not to comparatively short intense efforts, where the circulatory system bears the brunt, but to those of long duration. Gordon, Levine, and their fellow-workers (1925) found a close correlation between the physical condition of runners at the finish of a marathon race and the level of the blood-sugar. They advised an adequate carbohydrate ingestion before and during any such protracted and vigorous muscular effort (Levine and Gordon 1924). My observations upon leading British marathon runners have not shown any evidence of hypoglycæmia, nor have they found it desirable or practicable to take any form of nourishment during the race. Considered as a purely academic problem, what is the likelihood of hypoglycæmia developing? It is estimated that in a man weighing 60 kg—a reasonable average in a marathon runner—the liver weighs 1500 g. and contains 15% glycogen. The muscles constituting 40% of the body contribute 1.5% glycogen or, in all, 585 g. In a run of 2½ hours' duration at a speed demanding the inspiration of 3 litres of oxygen per minute, 560 g of carbohydrate would be consumed, and since in addition some fat is burnt, a margin should be available. It is doubtful therefore whether preparatory ingestion of sugar is necessary or advantageous, though it is at least harmless, but to suck glucose sweets during the race, as the American workers recommended, is not favoured by a practical athlete.

As a final word upon heart strain, an appeal to statistics may be pertinent. Notwithstanding the lack of positive evidence of any pathological change, an alternative hypothesis has been a sort of slowly progressive deterioration. Thus a writer on the subject of arteriosclerosis (Plesch 1932) asserted that athletes showed marked arterial degeneration by the age of 35 or 40 and that most of them die before 50. In the subsequent correspondence challenging the accuracy of this opinion, it appeared that his interpretation of athletes was big persons of excessive weight, stage acrobats, and others whose occupations had hazardous associations. In these, the physical element was trifling compared with nerve strain, the anxieties attending intermittent unemployment and hardships, together with the possible influence of syphilis and over indulgence in alcohol. To indict athleticism in such circumstances would be as illogical as to draw conclusions about the malevolent effects of high altitudes from the mortality rate in parachute testers.

In 1873, Morgan, the Manchester consulting physician, himself an oarsman of distinction, undertook the laborious investigation of the life histories of all who had rowed in the Universities' Boat Race between 1829 and 1869. In 1904, Meylan repeated the investigation in the case of Harvard oarsmen between 1832 and 1892. The results yielded a close correspondence, showing a life expectation nearly five years' longer than that of the selected risks in insurance tables. More recently Cooper and his colleagues (1937) found that of 100 oarsmen at Ormond College, Melbourne University, 17 had died from natural causes during the fifty years succeeding their athletic career. The expected mortality of men of the average age of 21 over the same period was, as quoted by the Australian Mutual Provident Society, 31·8%.

It may be objected that such subjects were exceptional material, and that notwithstanding their longevity it could not be denied that even this might have been longer had they abstained from strenuous exertion in their early life—an unanswerable argument.

No such organised inquiry has been extended to track athletes. My own observations enable me to submit many examples of octogenarians and a few nonagenarians who in their youth were outstanding runners and have enjoyed perfect health and present in their advanced age a condition that most men twenty years their junior could not surpass. No controls are available to permit comparisons between athletes who have continued to follow the hygienic life of active participants in sports and outdoor recreations, moderation in living, and scientific feeding, and those who live fast, overeat, drink heavily, and drive themselves to exhaustion especially with mental strain.

How is it possible to assess the causes of degenerative changes in a man who in his youth was a trained athlete and in later years carried heavy business or professional responsibilities? Regard, too, must be paid to the difference in temperament between the scholar of sedentary habit and the athlete whose ardent spirit and activity drive him into enterprises and risks, not free from dangers, which the scholar in his sheltered life is more likely to escape.

EXERCISE IN HEART DISEASE

Since some criticism is advanced of the prudence of undertaking strenuous exercise even in the case of the completely healthy, it might seem that no momentary difference of opinion is possible in subjects of admitted organic cardiac disease. And yet as clinicians we must not submit to summary decision. It is perhaps a natural conclusion that valvular disease of the heart is a crippling disorder that hampers efficiency and demands extreme care in the way of prohibiting exertion lest deterioration ensues. There is, however, ample evidence that valvular disease as such need impose no handicap so far as capacity for exertion is concerned.

I have seen a magnificent sprinter with a much enlarged left ventricle, the consequence of aortic regurgitation. The best middle distance runner of his generation had mitral disease. Jokl (1940b) has recorded the case of a man of 32, winner of 14 marathon races, whose heart lesion—aortic and mitral disease resulting from rheumatic fever at the age of 9—was discovered on routine examination. It is clear that circulatory disease even if so severe that it acutely threatens life may not at all impair physical efficiency, that disease of the aortic valve itself gives rise to no symptoms, that mitral stenosis will permit of full physical capability so long as the myocardium is healthy.

Admittedly the position of a practitioner is not a comfortable one when approached for advice on the extent of exertion permissible in a boy or girl with unmistakable valvular disease. To play for safety by complete prohibition may well be a policy in his own interest but one irreconcilable with his conscience. The responsibility of forbidding exercise may be as great as that which he is compelled to accept by inviting a certain risk. For the ill effects must be contemplated. No boy can gain the companionship to which he is entitled and which forms an essential element in his school life without the special associations of games and other forms of competitive exercise. To grow up with a belief in his physical inferiority is a serious blow to his character with an adverse influence upon his attitude to life. The danger of moral deterioration may be worse than physical injury unless those in authority can find efficient substitutes for exercise, and their task is far from easy. The practitioner will be influenced by the circumstances of each individual case and partly no doubt by his own prejudices.

Apart from athleticism what should be the attitude in general towards prohibition or limitation of exercise and the imposition of inactivity in subjects of cardiac disease? Just as rest of injured parts is the oldest and most valuable of all methods of treatment, this, like all other therapeutic measures, may be injudiciously or excessively applied. Emphasis upon rest and complete abstinence from activity is proper in the acute stage of cardiac disease and in convalescence, but is the traditional insistence upon continued or prolonged rest justifiable?

Infection has more to do with cardiac failure than strain upon or mechanical defect in the heart itself. In children with valvular disease, both congenital and acquired, there is generally an unwarranted fear of exercise; their exercise tolerance may be satisfactory as compared with normal children. If failure ensues it is due to relapsing rheumatism.

In the case of congestive failure the patient should be allowed out of bed as soon as severe dyspnœa at rest has subsided, although activity should, of course, be kept below the symptomatic threshold of pain and dyspnœa. As cardiac output is less in the sitting or erect posture than when recumbent, a little activity may actually be resting the heart. Restriction of activity reduces blood flow to a minimum and may favour the development of thrombi in the venous system or the arteries, and œdema of lungs. Infarction of the lungs and myocardium is often observed in patients subjected to unduly prolonged rest. Moreover cardiac neurosis is induced by insistence on excessive caution.

empty as possible is a wise precaution which is not by any means always effective In fact, it seems as if stitch results from a special anatomical predisposition that cannot be overcome

The muscle pain that often follows exercise is a minor trauma or an aseptic tissue inflammation It can be treated accordingly

URTICARIA

Urticaria may follow exercise quite independently of raised body temperature But when one recalls how urticaria can be induced by any sort of antigen, by emotional disturbances and mental states of every kind, by heat or by cold, it is not remarkable that exercise may be one if not the only factor responsible for an attack And since permeability increases with vascular dilatation, a point will be reached when exudation occurs, so that it does not seem necessary to postulate the local liberation of histamine

"ATHLETE'S HEART"

This term, if legitimately employed, would apply to a heart of superior contractility particularly efficient for the circulatory demands of athletic feats and of violent exercise generally Instead, its habitual meaning can only be condemned as an unwarranted assumption of some permanent debilitating or deteriorating alteration resulting from an imposition of exceptional severity or from repeated more or less prolonged submaximal efforts And embodied in such an idea is the presumption of what is known as "heart strain"

It is well known that when once a term gets into literature its eradication is almost impossible, in spite of failure to produce any positive evidence of its existence and even where there is conclusive proof that it does not occur and never did exist Moreover the term "strained heart" is, especially in connection with athletics, socially acceptable It carries with it no stigma on the contrary some prestige accrues through an implication of heroism or martyrdom

Two sources of fallacy appear to be responsible First, a prejudiced expectation arising out of the very considerable circulatory demand and the failure to distinguish strain from stress Secondly, a mistaken interpretation of the symptoms of participants during and after the feat of exertion

Strain means a hurt or injury from excessive tension when the structure in question is stretched beyond its proper limits The physiological dilatation of a healthy heart is of a temporary character, and no post mortem evidence is available of any pathological change The cases of so called acute dilatation are almost always unrecognised paroxysmal tachycardia The permanently enlarged and defective hearts encountered in hypertension and emphysema are in a different category Either a toxic factor or a degenerative change in the heart muscle itself is present

Stress may be rightly said to inflict further injury on a heart already damaged, and genuine strain of the muscular tissue may result with rupture of the muscle or a valve But in all these cases evidence of disease is forthcoming, and it is not with such that investigation of the so called athletic heart is concerned

What is the clinical picture of distress in violent exertion? The subject gasps for breath. The face is pale with a pinched expression of suffering The pulse is weak and rapid Cold perspiration may be present Nausea, vomiting, and even unconsciousness may occur These are, to be sure, alarming to a solicitous onlooker, but they are not the features of cardiac failure, which are cyanosis, over distended veins, an enlarged liver

The exhaustion that ensues during or after an extreme effort may possibly be due to adrenal depletion or to an acute hypoglycæmia resulting not from exhaustion of carbohydrate depots but from disturbances in the regulating faculties of the vegetative systems But the essential feature is vasomotor collapse from inability to integrate tasks beyond the body's scope The body can deal with a variety of functional stresses if confronted with one at a time, but its resources of adaptation may be overtaxed if several are imposed simultaneously—e g, malnutrition, circulatory stress, hypoglycæmia, infection, overheating, co existing mental or physical fatigue, and menstruation, to mention a few of the most familiar In other words, any instance of severe exhaustion in an athlete cannot be ascribed to physical stress alone but to the coexistence of any influence leading to generalised vascular dilatation, to which some subjects are constitutionally prone Headache, precordial pain, nausea, vomiting, disorientation, collapse, and unconsciousness may be produced, yet these symptoms, however alarming, have no baleful significance One recalls the historic marathon race in London in 1908 when the Italian, Dorando, staggered blindly into the Stadium, and, according to picturesque journalistic exaggeration, lay for a time between life and death On the following day he had completely recovered and he subsequently ran a considerable number of marathon races

It is not denied that such a state ought if possible to be avoided, but an appreciation of the true state of affairs transfers the lesion from the heart about which solicitude is usually mistakenly expressed Even in a perfectly healthy subject undertaking strenuous exertion, sickness and other symptoms may result from cerebral anæmia, since on cessation of the exercise the pumping action of the leg muscles ceases, stagnation occurs, and the volume of blood returning to the right auricle is insufficient to maintain an adequate arterial blood supply to the brain Some very efficient athletes are prone to fainting and collapse through a general vagotonic reaction I have often encountered this during so trivial an ordeal as taking the blood pressure, another familiar example is the prick of a needle in a hypodermic injection or blood examination

Adoption of the recumbent position, deep breathing, pressure on the abdomen, and flexion of the legs and arms will substantially reduce the symptoms and accelerate recovery

At one time oxygen inhalations were a favourite therapeutic measure, and cylinders were kept in readiness on athletic grounds But apart from a psychological effect, oxygen can have no restorative value, since the oxygen requirement falls below the oxygen income available from ordinary air And a recovery from fatigue is limited by the rate of return of lactic acid into the muscles from the blood and inactive tissues which is not affected by oxygen

The possibility of hypoglycæmia is an attractive explanation of the symptoms after long continued exhausting exercise This applies particularly not to comparatively short intense efforts, where the circulatory system bears the brunt, but to those of long duration. Gordon, Levine, and their fellow workers (1925) found a close correlation between the physical condition of runners at the finish of a marathon race and the level of the blood sugar They advised an adequate carbohydrate ingestion before and during any such protracted and vigorous muscular effort (Levine and Gordon 1924) My observations upon leading British marathon runners have not shown any evidence of hypoglycæmia, nor have they found it desirable or practicable to take any form of nourishment during the race Considered as a purely academic problem, what is the likelihood of hypoglycæmia developing? It is estimated that in a man weighing 60 kg—a reasonable average in a marathon runner—the liver weighs 1500 g and contains 15% glycogen The muscles constituting 40% of the body contribute 1 5% glycogen or, in all, 585 g In a run of 2½ hours' duration at a speed demanding the inspiration of 3 litres

Respiratory System and Smoking.—The condition of the patient's lungs and heart and his blood-pressure are assessed, and perhaps breathing exercises are instituted. Patients with bronchitis and asthma are operated on between April and October under local analgesia; 3 were so treated. As postoperative "chestiness" and cough are more common in habitual smokers, with consequent strain on the repair, such patients are advised to smoke but one cigarette or pipe after each meal.

Septic Foci.—Dental and nasal sepsis are eliminated.

Varicosities.—3 men were operated on for varicose veins and ulcers at the same time as the herniotomy. In 1 of them a sinus persisted in the hernia scar until he died three and a half years later, indicating the advisability of eliminating sepsis first and doing one operation at a time.

Double Herniæ.—The hernia was double in 36 men (18%). Since May, 1943, each hernia has been operated on separately, at an interval of ten days or more, the larger hernia being done first. The late Percival Cole suggested to me that the "yield" in the second hernia acts as a safety valve to the increased abdominal contents and wall rigidity following the reduction and herniorraphy. When both herniæ are closed simultaneously, the intra-abdominal contents may be increased and the abdominal wall rendered more rigid. Further, with a double herniotomy there is the risk of the second one becoming infected during the prolonged procedure.

ANALGESIA AND ANÆSTHESIA

As relaxation and absence of heaving and oozing are essential, and vomiting, coughing, and retention of urine afterwards are detrimental to cure, the choice of anæsthetic is all important.

Local analgesia (amethocaine 1 in 2000 with adrenaline 2 minims of 1 in 1000 per fluid oz.) is used in patients aged more than sixty-five; it is inserted through only two punctures, and a relaxed and bloodless field is assured. For the patient's comfort light anæsthesia is induced with thiopentone or with open ether; it is discontinued when the hernial sac has been removed. This combination is safe and consistently gives ideal conditions, with minimal postoperative disturbance.

Spinal Anæsthesia.—A low spinal anæsthetic (Dodd 1945) is good in patients aged up to sixty-five, but I lost a patient aged seventy-two immediately after the "spinal" was given. The blood-pressure should be recorded throughout the operation, for a gross fall may take place and need correction. My assistants say that they cannot estimate the blood-pressure with the finger-tips; it must be measured. 'Methedrine' (Dodd and Prescott 1943) is given to restore a low blood-pressure.

General anæsthesia alone is perfect in some patients, but in others it does not give the relaxed, quiet, and bloodless field which is essential. Tension and straining split the aponeurosis, even in young patients.

OPERATION

Suture Material.—Since 1929, interrupted linen thread sutures have been used—no. 50 for the sac neck and the detensioning suture between the rectus sheath and the pubic spine, and no. 90 for the remainder. It is so satisfactory that I am reluctant to change for floss silk (Maingot 1945), 'Nylon' (Moloney et al. 1948), or stainless steel wire (Abel and Hunt 1948).

External Oblique Aponeurosis.—After the skin and fat have been incised, the external oblique aponeurosis is cleaned down to the thigh, and upwards and inwards to the outer border of the rectus sheath and to the insertion of the upper and lower pillars of the external abdominal ring into the face of the pubic bone (the normal external ring is internal to and above the pubic spine). The upper parts of the adductor longus and pectineus muscles are uncovered to reveal the outlet of the femoral canal, and possibly an unnoticed femoral hernia. The external oblique aponeurosis is split from the apex of the external ring almost to the superior iliac spine. The two leaves are dissected freely up and down.

Dislocation of Spermatic Cord.—The spermatic cord or round ligament, with the surrounding fat, is wiped upwards from the shiny deep aspect of Poupart's ligament, from a point internal to the pubic spine. It is lifted on the finger from the posterior wall of the inguinal canal, for it may conceal a direct sac.

Division of Cremaster Muscle.—The cremaster is divided from the conjoined tendon and the internal oblique muscle at the internal abdominal ring. The branch to the spermatic cord from the deep epigastric artery at the internal ring is exposed and divided, a step which completely uncovers the inner edge of the internal inguinal ring in the transversalis fascia (fig. 1).

Division of Spermatic Vessels.—In 13 patients aged more than sixty-five the bulk of the spermatic cord was further lessened by dividing the spermatic vessels but not the vas deferens and its artery. 3 testes atrophied after this, but only 2% in the patients of Grace and Johnson (1937).

Orchidectomy.—In men over seventy, with poor tissues and a large hernia, the testis was removed and the inguinal canal abolished. When the need is plain, this is a useful step. A man aged fifty-five, weighing 22 stone, whose repair included this, has been cured for five years.

Lipoma of Spermatic Cord.—A considerable amount of extraperitoneal fat was excised in 22 herniæ to make the spermatic cord less. Fat, by burrowing through the internal abdominal ring or splits in the transversalis fascia, predisposes to another hernia.

Hernial Sac.—The sac, direct or indirect, or both, is transfixed and divided at the parietal peritoneum, and the fatty "shoulder" often found on the inner side of an oblique sac is removed. The bladder is separated from a direct sac. Three inguinal sacs, an internal direct, an external direct, and an indirect, have recently been excised from the same patient.

Digital Exploration of Peritoneal Cavity.—A finger is inserted through the opened sac into the peritoneal cavity, exploring for other sacs, femoral or direct (fig. 2). Maingot (1945) also advises this step. 3 people had three sacs (two inguinal and one femoral), and 36 had two. Failure to remove a second sac leads to a "recurrence."

Transversalis Fascia.—The restoration of transversalis fascia is considered vital to the cure. It is separately closed or reefed with interrupted stitches fitting it snugly round the spermatic cord to reconstitute the internal abdominal ring.

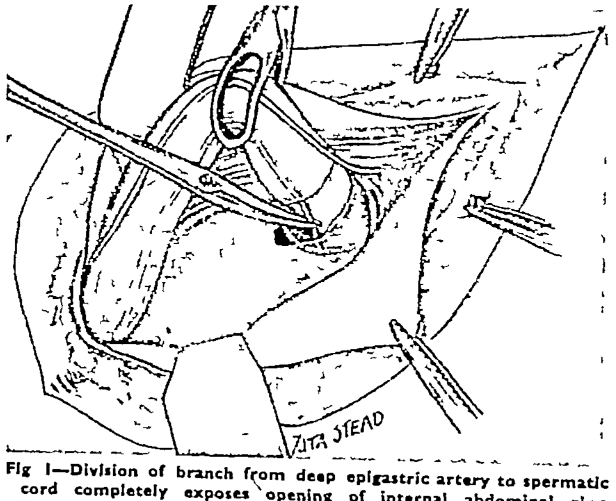


Fig. 1.—Division of branch from deep epigastric artery to spermatic cord completely exposes opening of internal abdominal ring in transversalis fascia.

John Hunter had what appears to have been myocardial infarction at the age of 45 Twelve years later he suffered from severe anginal attacks He died suddenly at the age of 65 At necropsy, extensive disease of the coronaries with calcification of the aortic valves and the scars of infarcts were found He lived, therefore, for twenty years after the onset of symptoms indicating serious heart disease Is one to assume that he would have lived longer if he had resigned himself to an invalid or semi invalid existence, and would his happiness have been increased or reduced by such a régime ?

James Mackenzie first experienced angina of effort in 1907 and symptoms of a myocardial infarct in 1908 At his death in 1925, extensive atheroma of the coronaries with several healed infarcts were found Thus he had led an active and useful life for seventeen years after his first infarct Was the great cardiologist a poor therapeutist in regard to his own case ?

REFERENCES

Abrahams, A (1926) *Brit med J* ii, 135
— (1946) *Lancet*, ii, 605
Allbutt C (1898) System of Medicine London, vol v, p 198
Blotner H (1945) *Arch intern Med* **75** 39
Bramwell J C Ellis R (1931) *Quart J Med* **24** 336
Campbell J M H Mitchell, G U Powell, A T W (1928) *Guy s Hosp Rep* **78** 279
Capps, R B (1941) *Arch intern Med* **68**, 94
Collier W (1906) *Trans med Soc Lond* **30** 75
— (1907) *Brit med J* i, 4
Conybeare E T (1932) *Guys' Hosp Gaz* p 165
Cooper, E L Sullivan J Hughes E (1937) *Med J Aust* i, 569
Dukes C (1905) *Brit med J* ii 848
Foltz E E, Ivy, A C, Barborka, C J (1942) *J Lab clin Med* **27**, 1396
Foster R C, Brouwer, S W (1941) *J Amer med Ass* **117** 2107
Gilligan, D R Altschule, M D (1950) *New Engl J Med* **243**, 944
Gordon B Levine S A, Kohn, L A (1925) *J Amer med Ass* **85** 508
Herriman G R (1925–26) *Proc Soc exp biol Med, N Y* **3**, 856
Jokl, E Melzer, L (1940a) *S Afr J med sci* **5**, 4
— Suzman M M (1940b) *J Amer med Ass* **114**, 467
Keys A, Henschel A F (1942) *J Nutrit* **23** 259
Lande P Courbin, J, Derville, P (1942) *J méd Bordeaux*, September, p 580
Lee R I (1915) *Boston med surg J* **173**, 499
Levine S A Gordon B (1924) *J Amer med Ass* **82** 1778
Levinson S O (1945) *Amer J Hyg* **42** 205
Levy R L Rousselot L M (1933) *Amer Heart J* **9**, 178
Lumsden, C E (1946) *Brit med J* ii 734
Meylan G L (1904) *Harvard Grad Mag* **12** 362 367 543
Millar W G, Ross T E (1942) *J Path Bact* **54**, 455
Morgan J E (1873) University Oars London
Plesch, J (1932) *Lancet* i, 385
Shakspere W Twelfth Night iii ii, 73
Shattock S G (1913) *Brit med J* i, 385
Tung C L (1934) *Amer Heart J* **10**, 79
Vogt H (1943) *Dtsch Arch klin Med* **191** 488
Watson E M, Fischer L C (1935) *Amer J clin Path* **5**, 151
Whittle, C H (1929) *Lancet*, i 1354

RADICAL CURE OF INGUINAL HERNIA IN THE ELDERLY

HAROLD DODD

Ch M Lpool, F R C S

SURGEON TO KING GEORGE HOSPITAL, ILFORD, THE ROYAL HOSPITAL, RICHMOND, AND THE ROYAL LONDON HOMŒOPATHIC HOSPITAL

IN young people herniæ often provoke feelings of inferiority and are sometimes used as a reason for avoiding heavy work In the elderly they are a common cause of capricious behaviour and reluctance to perform simple tasks, such as shopping, and they are responsible for much anxiety as well as inconvenience

The Registrar General reports 3305 deaths from hernia in England and Wales in 1948 Many of these must have followed an emergency operation, and might have been avoided by a well planned routine operation Such an operation can be performed successfully even in the elderly

Landers (1938) found that 1 in 4 industrial employees aged more than fifty were ruptured, a third of the herniæ being double, he believed that ruptures follow the middle age weakening of the supporting tissues He noted that 25% of hernial repairs fail

Gibson and Felter (1930) published very good results in 155 patients aged over fifty, the recurrence rate being 3 8%

Grace and Johnson (1937), writing on herniotomy in 1032 patients aged over fifty, found that the hernia was primary in 90% and recurrent in 10% Their mortality rate was 3% Their repair was of the Bassini type They tried to make a strong posterior wall of the inguinal canal by suturing the conjoined tendon with transversalis fascia or in a separate layer to the shelving edge of Poupart's ligament, especially in direct hernia The spermatic cord was usually transplanted, and in about half the cases the external oblique aponeurosis was sutured behind it When the hernia was recurrent, large, sliding, scrotal, irreducible, or uncontrollable by a truss, the spermatic vessels (not the vas) were divided, the recurrence rate was distinctly smaller after this than without it

25% of the primary herniæ and 34% of the recurrent herniæ recurred Grace and Johnson remark that these rates of 25% and 34% may discount the effectiveness of the procedure, but many patients had but a slight return, and the symptomatic results were excellent In 611 patients the recurrence rate was 21%, with indirect sac, with direct sacs 32%, and with direct and indirect sacs 35 8%, the average being 25 8%. After wound infection the recurrence rate was 40%

Grace and Johnson agree with Page (1934) and Mayo and Mayo (1937) that a simultaneous double herniotomy carried a higher recurrence rate (31 5%) than did unilateral herniotomy (19 5%) with an oblique sac it was 25 2%, and with a direct sac 37 2%

Sainburg (1950) reported 142 cases in patients between sixty and ninety eight years of age, 25 of these patients were unsuitable for operation, and 69 of the 117 operations were emergency ones He holds that circulatory diseases, bronchitis, obesity, enlarged prostate, renal failure, and cerebral thrombosis contra indicate operation Careful preoperative examination is therefore essential He used much the same method of repair as is described below He suggests that the spermatic cord should be resected because the testis will usually be nourished by its intact scrotal attachments, necrosis of the testis followed in only 2% of such resections Double herniotomies were done in two operations The patients were got up and about as soon as possible The infection rate was 6·5% A follow up of 56 patients seen from six months to five years after operation revealed 6 recurrences (10 7%) but, like those reported by Grace and Johnson (1937), they did not cause any symptoms In the emergency operations 11 of 69 patients died (15 9%), but in the other operations all the patients survived

I suggest that operation for all herniæ as soon as they are seen will save suffering and premature death of patients and inconvenience to patients' families and to our profession The results will be improved and our national efficiency increased individually and collectively

In September, 1938, I began operating on all hernia in patients aged more than one year of age On the rare occasions when operation was refused, a truss was ordered The results obtained since 1934 in 200 patients who were over fifty years old and treated by operation are presented here The age groups were as follow 50–60, 104, 60–70, 68, 70–80, 24, over 80, 4 There were 182 men and 18 women

PREOPERATIVE EXAMINATION

Poor Tissues—In elderly patients herniæ are often associated with some constitutional ailment The patient may be getting feebler and his muscles may be wasting, as in 22 (11%) of patients in my series Other patients are obese and flabby from lack of exercise, overeating, and excessive drinking, the muscles and aponeuroses being permeated with fat Rehabilitation is needed before and after operation, and at operation the use of small needles and fine sutures make good reconstructions possible, where thick sutures—e g, catgut—and large needles would split fragile tissues and render a cure unlikely

Rectum and Prostate—The rectum is examined to exclude carcinoma (found on 3 occasions) and enlarged prostate The urinary function is checked, for prostatectomy may be necessary 2 octogenarians were cured of herniæ after prostatectomy

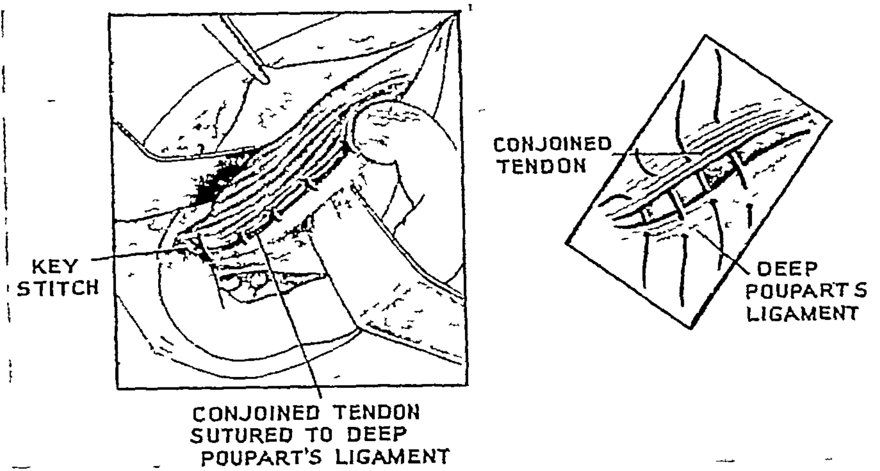


Fig 4—Stitches approximating conjoined tendon to deep Poupart's ligament (left) take up different bundles of fibres to spread strain (right)

appeared since the inguinal repair. A woman, aged fifty, who had been cured of an indirect left inguinal hernia and a left femoral hernia, was treated ten years later for a right inguinal hernia (direct and indirect) and a right femoral hernia. An inguinal hernia has appeared in 3 men after a femoral herniorraphy.

Hydrocele.—In 5 cases a hydrocele was treated at the same time as the hernia.

Recurrent Herniæ.—17 herniæ (8·5%) were recurrent, 1 was twice recurrent. All the patients continue cured. A recurrence indicates, but never contra-indicates, another operation.

Carcinoma of Rectum and Colostomy.—3 patients had carcinoma of the rectum, 2 of them with colostomies begged for operation because the hernia was troublesome. The repairs remained sound until the patients died after three and a half years and one year. The third patient reported with an enormous left inguinal hernia, and the rectal carcinoma was discovered on examination. The hernia was treated, and the neoplasm was resected six weeks later, but the patient died from this. A fourth man successfully withstood resection of a carcinoma of the rectum five years after the herniorraphy.

RESULTS

Postoperative Deaths.—3 men (1·5%) died soon after the operation: the first half an hour later from asphyxia, while unconscious and unattended for a short time; the second from a streptococcal infection in the second of bilateral herniæ treated at the same time, and a pulmonary embolus; and the third from a perforated diverticulum of the descending colon five days later.

Later Deaths.—There have been 19 deaths since the operation from causes apparently unrelated to the hernia. In all instances the relatives said that the hernia had been satisfactory. The repairs of 16 of these patients, seen from six weeks to four years before their death, were sound.

Untraced Patients.—It was impossible to trace 4 patients.

Examined Patients.—174 patients have been specially examined during 1949 and 1950, from fifteen years to eighteen months after operation.

Recurrences.—5 recurrences (3%) were found. If one man who was re-treated over five years ago is excluded, the rate is 2·4%. Of 78 persons seen whose repair was more than five years old, 4 had a recurrence at four, six, seven, and nine years later, giving a recurrence rate of 5·4%; excluding the re-repair it would be 4%. The details of these 5 recurrences are as follow:

(1) Man, aged 52, R.I.H. (direct), Bassini in 1937, recurred in 1941. In 1944 second operation, Bassini with a Tanner "slide" and exteriorisation of spermatic cord. In January, 1950, sound.

(2) Man, aged 59, L.I.H. (indirect), operation in 1939 (Bassini), reappeared in November, 1948; symptomless, wears a truss.

(3) Man, aged 64, D.I.H. (direct), operation in May, 1941, at one session. The second—i.e., the left—recurred in autumn, 1947; symptomless, truss unnecessary, repair declined.

(4) Man, aged 53, D.I.H. (indirect), operation in May, 1942, one session (Bassini), left second; small symptomless recurrence (left) in May, 1949; truss unnecessary; re-repaired in March, 1950, "internal direct" sac removed.

(5) Man, aged 84, D.I.H. (indirect), scrotocele, operation in April, 1948 (Bassini Tanner Halsted), at separate operations; in September, 1949 small right symptomless bulge.

It is said that a surgeon never sees his recurrences, but these were found by the follow-up examination. The patients had consulted no one.

Simultaneous Double Repair.—The danger of repairing a double hernia at one session is illustrated by the man who died from septicæmia and a pulmonary embolus that originated in the second hernia, and by 2 of the recurrences being in the second of double herniæ treated together. Of the 36 cases of double herniæ 24 were dealt with at separate operations, with 1 recurrence, and 12 were repaired at one operation, with 2 recurrences.

Five-year Results.—The cases followed up five or more years after operation may be analysed as follows:

	No. of cases
Patients operated on five or more years ago	93
Patients died from the operation	3
Patients died since the operation	9
Patients untraced	3
Patients seen over five years after the operation	78
Recurrence (one now cured over five years)	4
Five-year cures	96%

A patient, aged seventy-five at operation, worked as a rent collector until he was eighty. Several men over seventy years of age are still gainfully employed—e.g., a bus driver, aged seventy-three—and many are satisfyingly occupied by house and garden work.

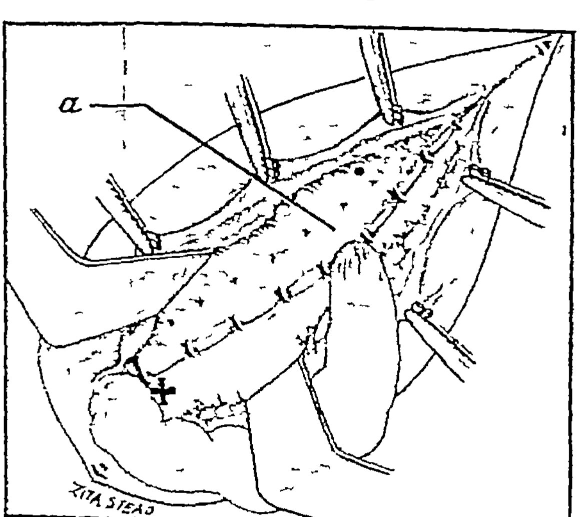


Fig. 5—Closure of external oblique aponeurosis by overlapping and new external ring well removed from pubic spine (+): a upper leaf of external oblique aponeurosis sutured to lower leaf by overlapping about $^1/_4$–$^1/_2$ in. behind the spermatic cord.

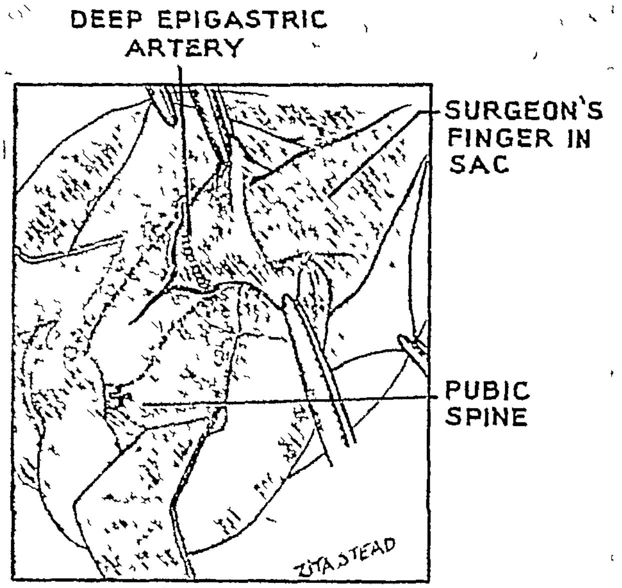


Fig 2—Surgeon's index finger exploring inferolaterally to pubic spine (+) for possible direct or femoral sacs

Tension in Conjoined Tendon Tanner Slide—The conjoined tendon varies in height above Poupart's ligament and in its muscular and aponeurotic substance Ordinarily it can easily be approximated to Poupart's ligament (fig 3B) after having been relaxed with a stout suture between the outer edge of the rectus sheath and the periosteum of the pubic spine

When the conjoined tendon is poor, Tanner's (1942) procedure is invaluable This consists in sharp dissection of the external oblique aponeurosis from the internal oblique to the midline of the abdominal wall A "hockey-stick" incision is made in the internal oblique aponeurosis, curving upwards and outwards from the symphysis pubis for 3 or 4 in to within $^1/_2$ or $^3/_4$ in of the outer border of the rectus muscle (fig 3A, B, and C) In this way an attenuated conjoined tendon can be readily sutured to Poupart's ligament from the detensioning stitch between the rectus sheath and the pubic spine The threads are inserted through different portions of conjoined tendon and of Poupart's ligament to avoid splitting their fibres (fig 4, right)

The "slide" incision exposes a crescentic area of pyramidalis and rectus muscles which fuses with the anterior rectus sheath No weakness of the part has been observed in the 102 patients submitted to this "slide" procedure

External Oblique Aponeurosis and Inguinal Canal—The upper leaf of the external oblique aponeurosis overlaps the lower for $^1/_4$ or $^3/_8$ in Its preliminary mobilisation permits the external ring to be made at, or even just inside, the pubic spine

Obliteration of Inguinal Canal—When the tissues are poor and the sac is direct, the external oblique aponeurosis is closed behind the spermatic cord, a new external ring is made just outside the internal ring, and the pillars of the original external ring are closed over the pubic spine (fig 5)

Fascial grafts taken from the external oblique aponeurosis closed the gap between the conjoined tendon and Poupart's ligament in 9 men Occasionally the edges of the graft were sutured, forming it into a sheet of aponeurosis With the Tanner slide, grafts are seldom needed, moreover, they tend to split the conjoined tendon and Poupart's ligament

Repair—The techniques used were as follow

(1) The original Bassini repair	104 cases
(2) Bassini method plus the Tanner "slide"	58
(3) Bassini, Tanner "slide," and exteriorisation of the spermatic cord (Halsted)	44
(4) Bassini with fascial graft	4
(5) Halsted operation, including 5 fascial grafts	26 ,,
(6) Division of spermatic vessels	13 ,,
(7) Excision of testicle	24 ,,

POSTOPERATIVE TREATMENT

Getting Up—Most patients got up in fourteen to twenty days Since 1944 they have stood up a day or two after the operation and returned home in twelve days, with no discouragements so far

Abdominal Supports—To avoid stretching of the lower abdominal wall, and therefore of its openings, obese and frail people have been fitted with no 1 Curtis abdominal belts

FINDINGS AT OPERATION

The types of hernia found at operation are shown in the accompanying table

Type of inguinal hernia	No of cases	No of indirect sacs	No of direct sacs	No of herniæ with both direct and indirect sacs
Unilateral	164 (*82%*)	122 (*74%*)	19 (*11 5%*)	23 (*14%*)
Bilateral	36 (*18%*)	46 (*64%*)	13 (*18%*)	13 (*18%*)
Total	200	168 (*71 2%*)	32 (*13 6%*)	36 (*15 3%*)

COMPLICATIONS

Retention of Urine—2 men (one over eighty) who had emergency operations for hernia developed persistent postoperative retention of urine, and prostatectomy was successfully performed

Atrophy of Testis—Although the results as regards hernia were good, the testis atrophied in 10 cases 7 after a Bassini repair, and 3 after division of the spermatic vessels For this reason care must be taken that the inguinal rings are not made too tight

Subsequent Other Herniæ—8 patients developed a hernia on the other side and an umbilical hernia Some have been treated

Femoral Herniæ—In 4 cases a femoral hernia was also present and treated, and in 3 cases a femoral hernia has

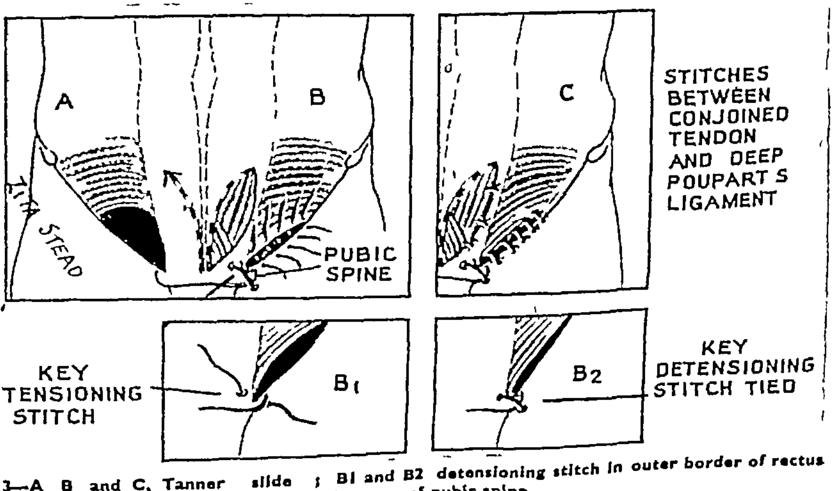

A
B
C
TILASTEAD
PUBIC SPINE
STITCHES BETWEEN CONJOINED TENDON AND DEEP POUPART'S LIGAMENT
KEY DETENSIONING STITCH
B1
B2
KEY DETENSIONING STITCH TIED

Fig 3—A B and C, Tanner slide; B1 and B2 detensioning stitch in outer border of rectus sheath and periosteum of pubic spine

spared much tribulation Constipation in the breast fed infant is in fact only one of many imaginary disorders in pædiatrics (Gordon 1951)

SUMMARY

1 The bowel rhythm was investigated in 1499 infants seen in infant welfare centres

2 In breast fed infants, in the first month, stools are frequent, often 4 or more a day, in the third, fourth, and fifth months, some 40% of such infants miss a day, and it is not uncommon for the delay to be a week, in the second six months of the first year, breast fed infants go regularly once or twice a day

3 In bottle fed infants the initial frequency is not so definite But it is exceptional for a bottle fed infant to miss a day, and should it do so, an organic lesion should be suspected

4 It is suggested that mistaken efforts to remedy the bowel infrequency of healthy breast fed infants is one of the main causes of habitual constipation in later life *As breast-feeding is diminishing, both in incidence* and duration, chronic constipation may be expected to become less of a problem There is indirect evidence that this is already happening

REFERENCES

Abdel Khalik A K Erfan H Askar A (1932) *Arch Dis Childh* 7 249
Brennemann J (1948) Practice of Pediatrics Hagerstown
Brown P W (1937) *Med Clin N Amer* 21 891
Chodak Gregory H H (1934) *J State Med* 42 632
Ellis R W B (1947) Child Health and Development London
Fukushima M (1930) *Orient J Dis Child* 7 38
Gesell A. Ilg F L (1943) Infant and Child in the Culture of To day London.
Gordon I (1942) *Arch Dis Childh* 17 139
— (1951) *Brit med J* i 611
Graham Stewart A ,(1928) *Practitioner* 121 183
Hurst A (1943) *Med Pr Circ* 210 375
— (1919) Constipation and Allied Intestinal Disorders London
Hutchison R (1933) *Postgrad med J* 9 457
Keith, A (1915) *West Lond med J* 20 150
Oldfield J (1943) *Med Pr Circ* 210 351
Pfaunder M. Schlossman A (1935) Diseases of Children Philadelphia and London
Smith R M (1930) *New Engl J Med* 202 802
Spock B (1947) Pocket Book of Baby and Child Care New York
Sunderman F W Boerner F (1949) Normal Values in Clinical Medicine Philadelphia and London.
Takai S (1935) *Tohoku J exp Med* 27 590
Watkins A C (1948) *Practitioner* 160 278
Williamson N B (1947) Handbook on Diseases of Children Edinburgh

OPHTHALMOSCOPIC DETECTION OF MICROFILARIA OF ONCHOCERCA VOLVULUS

J W R SARKIES
M.R C S, D O.M S

COLONEL, INDIAN MEDICAL SERVICE (RETIRED) TEMPORARY OPHTHALMOLOGIST, COLONIAL MEDICAL SERVICE

MANY workers have described the observation of microfilariæ in the aqueous humour of the eye with a slit lamp and corneal microscope Estrada (1942) published a series of 11 cases of onchocerciasis, in which he described microfilariæ seen in the vitreous humour with an ordinary ophthalmoscope, using lenses from plus 20 to plus 50 dioptres, the simplicity of this method is very attractive, especially under rural conditions It was decided therefore to compare results obtained by ophthalmoscopy and by slit lamp examination in native schoolchildren and industrial workers of the lower Volga district of the Gold Coast

It was found that microfilariæ could be seen in the aqueous humour with an ophthalmoscope incorporating a plus 20D to a plus 28D lens, held 3 5–5 0 cm from the centre of the anterior chamber—i e, at the focal distance of the lens used The whole of the pupillary area is illuminated by reflection from the fundus, and since the embryos are seen in silhouette, the margin of focus is greater than with a corneal microscope using direct illumination from a slit lamp For this reason the embryos can be recognised more rapidly and, in cases where they are scanty, are less likely to be missed with an ophthalmoscope In none of the cases in this series were microfilariæ seen in the vitreous humour with lenses of this power, nor were they seen with a plus 4D lens in the ophthalmoscope held at about 25 cm from the eye, although other small opacities in the vitreous could be seen in this way

All the persons were examined under a mydriatic, first with an ophthalmoscope and then with a slit lamp, a dark room was not available, but the examinations were made in a shady hut, a standard battery model Lister Morton ophthalmoscope being used The instrument is brought towards the eye, with the light directed on the optic disc (which in pigmented races gives an appreciably brighter reflex than does the rest of the fundus), until the pupillary margin of the iris comes clearly into focus At this point microfilariæ can be seen, if present, silhouetted against the illuminated pupil as tiny black threads swimming through the aqueous humour with a rippling motion, this motion is quite characteristic and differentiates microfilariæ from other opacities—e g, cells in the aqueous humour, threads of persistent pupillary membrane, and small particles floating in the lacrimal secretions on the anterior surface of the cornea A microfilaria can be brought into clear focus by moving the ophthalmoscope slightly backwards or forwards according to the position of the embryo in the anterior chamber

MICROFILARIÆ FOUND BY OPHTHALMOSCOPY AND WITH SLIT LAMP

—	School children	Industrial employees	Total
Total examined	111	204	315
Microfilariæ (Mf) in skin smears	38	150	188
Mf. seen by ophthalmoscopy alone	6	14	20
Mf seen by ophthalmoscopy and with slit lamp	4	30	34
Mf seen with slit lamp alone	0	1	1
Percentage of cases with positive skin smears showing Mf in aqueous humour	26	30	28 6

RESULTS

The results are given in the accompanying table The persons examined consisted of two groups, both highly selected in that they attended a normal school or earned their living under fairly competitive conditions, this probably explains the relatively low percentage of persons shown to have onchocerciasis by skin sweats who had microfilariæ in the eye Of the 55 with embryos in the aqueous humour these could be seen with an ophthalmoscope in 54, whereas with a slit lamp they were seen in only 35 In the solitary case diagnosed with the slit lamp alone, one embryo only was found, and it had attached itself to the posterior surface of the periphery of the cornea, outside the pupillary area

COMMENTS

There is no doubt that, if a minute search were made in every case with the slit lamp, microfilariæ would be seen even more often than with an ophthalmoscope Such a search is often precluded by fatigue and by lack of cooperation on the part of the patient Therefore, when the microfilariæ are scanty, ophthalmoscopy offers a greater chance of success In remote areas of Africa, where the disease is prevalent, the simplicity of the apparatus has obvious advantages, for the doctor

TABLE II—FREQUENCY OF MOTIONS IN 700 BOTTLE FED INFANTS

Month of age	No of infants in each frequency group								Total
	4 or more daily	3 daily	2 daily	1 daily	Every other day	Every 3rd day	Every 4th day	Less often	
1	24	13	32	18	2	0	0	0	89
2	11	16	34	27	2	0	0	0	90
3	4	10	47	31	0	0	0	0	92
4	5	11	32	23	0	0	0	0	71
5	1	11	41	20	0	0	0	0	73
6	1	5	31	26	0	0	0	0	63
7–9	2	7	71	57	0	0	0	0	137
10–12	1	4	28	51	1	0	0	0	85
									700

already becoming regular, and after six months most infants who were breast fed have one or two motions a day. Of the 16 infants in the breast fed series who missed four days or more, 9 usually went every five days, 1 every six, 4 every seven, 1 about eight, and 1 child missed twelve days without disturbance (table I). These last figures, depending as they do on mother's recollections over the previous weeks, can only be taken as approximate.

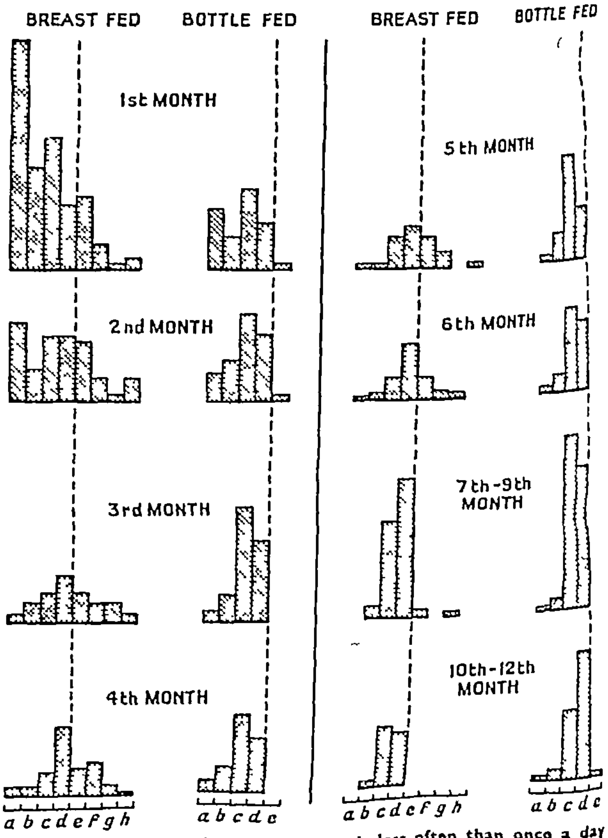
The bottle fed infants show a completely different picture (table II). Frequency in the first month does not appear to be so definite, but it is extremely rare for a bottle fed child to miss a day (although bottle fed infants are more constipated than breast fed in the sense that their stools are harder). In fact in the first two months only 4 out of 179 did not have a motion daily, and 3 of these 4 had symptoms suggestive of pyloric stenosis. It appears that if a bottle fed baby does not have a bowel movement daily an organic disorder should be suspected.

DISCUSSION

The most important feature of these figures is that 41% of healthy breast fed babies in the third, fourth, and fifth months do not have daily motions (see figure). In the past this has been regarded as abnormal by parents and the medical profession, and even today is probably so considered by most people. This being the case, the immediate reaction in the past has been to put the matter right. Generations of physicians have discoursed upon the advisability of inculcating good habits at an early age, and potting has become ritual. It needs no great imagination to prophesy the course of action of the mother of the breast fed child at ages three to five months, who pots her child three or more times a day, and finds that nothing happens for one or several days. She uses purgatives, laxatives, suppositories, enemata, and her little finger. This may be the starting point of the habitual use of purgatives, which became a weekly ritual in Victorian times but was already known in B C 800 to occur—as Hindu writings show (Brown 1937)—and was practised not long ago in 95% of the working classes in America (Chodak Gregory 1934). Many physicians have regarded this abuse of purgatives as the cause of constipation—Hurst (1943) among them, in a discussion of dyschezia. Is it possible that habitual constipation in the adult is thus the result of a misinterpretation of the physiology of the normal breast fed infant? If this be the case, constipation should be a diminishing disease, for breast feeding is diminishing not only in incidence but also in the length of time that the child is suckled (Gordon 1942). Furthermore, additions to the diet that make for regularity of bowel movement are introduced at a much earlier age than they were at three months by many pædiatricians, and even earlier in America. To find out if a disease such as constipation is diminishing is a task that would receive no encouragement from statisticians, for it is neither notifiable nor yet does it appear on death certificates or necropsy reports.

One thing is certain, the disease receives much less attention than it did in former years. Arthur Keith in 1915 stated that it was a "condition which causes nearly as much suffering as even a great war." Who would make this statement today? For the years 1928–32 inclusive there was an annual average of 56 references to constipation in the *Quarterly Cumulus Index Medicus*, in 1946 there were 19, in 1947 only 15, and in 1949 in *Excerpta Medica* only 11. Nobody will suggest that the volume of medical literature generally has diminished correspondingly in these years. Maybe the diminution of breast feeding, and the realisation that infrequency of motions in breast fed infants is normal, will eventually cause constipation to disappear as chlorosis has done. Thus will end an unhappy era in therapeutics, wherein something normal has been made a disease, and vast amounts have been written about its imaginary causes. Treatment, which varied from colectomy to psychotherapy, has included, not only roughage but a residue free diet (Smith 1930), not only increased fluids but diminished fluids (Oldfield 1943), and not only exercise but complete restriction of exercise achieved by three months in a spinal carriage (Graham Stewart 1928)!

If more talent and endeavour were spent on study of the normal infant, in say, well baby clinics, instead of being devoted to describing rare and exotic diseases, or to developing skilled operations such as colectomy for artificially promoted disorders, mankind would be



To the right of the dotted lines stools less often than once a day

a = 4 times a day or more
b = 3 times a day
c = twice a day
d = once daily
e = once every 2 days
f = once every 3 days
g = once every 4 days
h = once every 5 days or less often

out from both hilar regions to the lung periphery and largely confined to the mid zones (fig 4). The areas of increased density correspond with remarkable accuracy to the distribution of the radiation. The changes demonstrated on the film are roughly proportional to the dosage levels, being greatest where the dosage was highest.

The patient's condition rapidly became worse, and she died within twenty four hours.

Necropsy Findings.—An elderly obese woman showing no external abnormality. The pericardium was adherent externally to the mediastinal pleura but otherwise normal. The heart weighed 400 g and apart from right-sided dilatation, was normal. No other cardiovascular abnormality was detected. The right and left lungs weighed 1200 and 1125 g respectively, and both showed symmetrical contraction of the middle thirds spreading outwards from the hilum in a fan like manner (fig 5). These contracted areas were uniformly hard, greyish, airless, bloodless, and sharply demarcated from the apices and bases, which were œdematous and partially air-containing. The larynx, trachea, and bronchial tree appeared normal, and no evidence of neoplastic disease was detected in the lung or in the tracheobronchial lymph glands. The alimentary hepatic, biliary, lymphatic, urinary, endocrine, central nervous, and skeletal systems were normal.

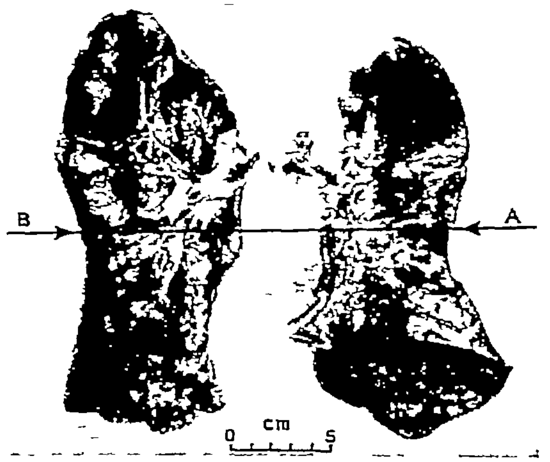


Fig 5—Half of each lung showing contraction of middle thirds.

Histology.—Paraffin and frozen sections were examined from every lobe of the lung and from various levels of the bronchial tree. Hæmatoxylin and eosin, van Gieson, and Weigert's stains for fibrous and elastic tissues, and Scharlach R for fat were used. All sections from the consolidated areas of both lungs showed complete obliteration of the alveolar pattern by cellular avascular granulation tissue composed of fibroblasts and large swollen macrophages with faintly granular but mostly clear cytoplasm in about equal numbers (fig 6). The macrophages were of special interest because their appearance in paraffin sections first suggested the possibility of their containing fat, which was subsequently confirmed in frozen sections stained with Scharlach R. The distribution of these lipoid macrophages was focal, the cells being arranged in clusters of up to 100 cells surrounded by fibroblasts with a scanty admixture of lipoid-containing cells. The mean size of these lipoid foci was similar to that of normal alveoli and their distribution strongly suggested that they occupied the spaces of pre-existing alveoli which the presence of fragmented elastic tissue in the periphery tended to confirm. The bronchial epithelium appeared normal, though the lumen contained a few lipoid macrophages. The fat present was mostly intracellular and varied from a few fine granules to large globules which occupied most of the cytoplasm distending the cell envelope and obscuring the nucleus of the macrophage (fig 7). The fat was anisotropic, rotating polarised light. A minority of the lipoid cells also contained granules of carbon thus establishing their phagocytic nature.

The apices and bases of both lungs showed œdema only.

No unequivocal evidence of carcinoma was detected in any of the numerous sections of lung. Sections of the heart kidneys, spleen, and lymph glands did not show any abnormality.

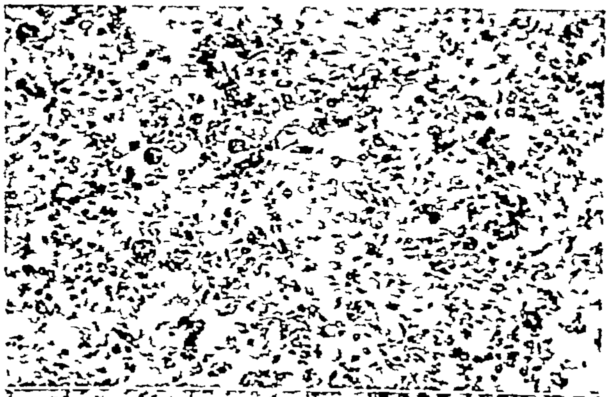
Anatomical diagnosis.—Lipoid pneumonia following radiotherapy for carcinoma of the lung.

DISCUSSION

The clinical picture of breathlessness, chest pain, and sometimes severe cough following some weeks or months after deep X ray therapy to the chest has already been noted many times, particularly in the United States (Groover et al. 1923, Warren and Spencer 1940, Fried and Goldberg 1940, Widmann 1942, Leach et al. 1942, Alexander 1944) and has previously been described as irradiation pneumonitis or irradiation pulmonary fibrosis. In many patients the disease does not run such a severe or fatal course as in the case recorded here.

The mechanism of symptom production has been studied in these cases by Leach (1943), who ascribes the dyspnœa, which is such a prominent feature, partly to the fibrosis, with compensatory emphysema of the unaffected lung, partly to a variable amount of fixation of the chest wall and partly to over-irritability of the Hering Brewer reflex. In our case, owing to the patient's grave condition, studies of abnormal physiology were impracticable.

Pathology.—The most conspicuous feature of the pulmonary consolidation was the intracellular lipoid, which was confined to the areas of both lungs which had been irradiated and which corresponded to the extent of the opacity shown by X rays. Inhalation of fatty material was excluded, so one must assume that the lipoid was endogenous. The demonstrable fat may then have been due to phanerosis and unmasking of lipoid substances normally present in pulmonary parenchyma and carcinoma, or to infiltration into injured cells rendered incapable of metabolising it. The presence of anisotropic fat capable of rotating polarised light identified it as cholesterol esters, which are normal constituents of all cells. It therefore seems that the fatty change was mainly, if not wholly, due to a degeneration liberating lipoid which was subsequently phagocytosed by macrophages, which accumulated in the alveolar



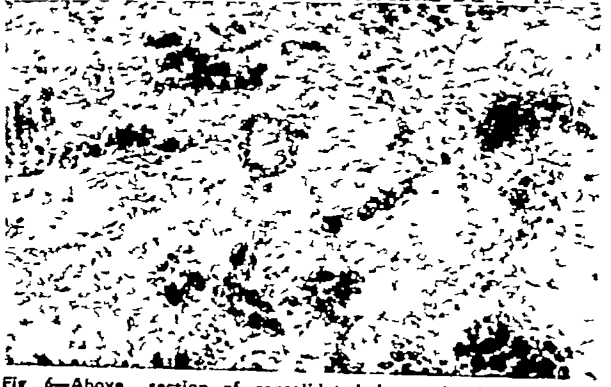


Fig 6—Above section of consolidated lung showing numerous macrophages filled with lipoid. (Hæmatoxylin and eosin.)
Fig 7—Below the same stained with Scharlach R., showing distribution of fat. (Both figs × 110.)

in such regions it provides a rapid means of diagnosing ocular involvement in the earliest stages

Certain limitations must be considered When the media are so opaque that the red reflex is abolished, microfilariæ cannot be seen by ophthalmoscopy Such conditions as cataract and plastic iritis occur in advanced onchocerciasis and give rise to gross opacities, at this stage, in endemic areas, the diagnosis can usually be made on clinical grounds, confirmed if necessary by conjunctival snipping When infestation of the eye is heavy, the pupils often do not dilate with mydriatics, in these cases the microfilariæ are usually sufficiently numerous to be seen with the smaller field available

For surveys of large numbers of people and for the preliminary selection of cases, ophthalmoscopy has considerable advantages For a more minute examination of the eye, however, it does not take the place of the slit lamp

I wish to acknowledge the advice and assistance of Dr M H Hughes, who has made clinical and laboratory investigations of most of the cases, and with whom I hope to elaborate the findings later My thanks are due to Dr R L Cheverton, director of medical services, Gold Coast, for permission to publish this report

REFERENCE

Estrada, A T (1942) *Amer J Ophthal* 25, 1145

LIPOID PNEUMONIA (NON-INHALATION) IN CARCINOMA OF THE LUNG TREATED BY RADIOTHERAPY

S J De Navasquez
M D Lond
READER IN PATHOLOGY IN THE UNIVERSITY OF LONDON

J R Trounce
M D Lond, M R C P
MEDICAL REGISTRAR, GUY'S HOSPITAL, LONDON

A B Wayte
M B Lond, D M R E
ASSISTANT SURGEON, RADIOTHERAPY DEPARTMENT GUY'S HOSPITAL, LONDON

Lipoid pneumonia is usually due to the inhalation of mineral or vegetable oil which irritates the pulmonary epithelium, causing fibrosis (Pinkerton 1928, Paterson 1938) Lipoid pneumonia arising without the inhalation of such oil has not yet been reported, and, although fibrosis in the lungs after irradiation has been fully described (Warren and Spencer 1940, Widmann 1942), the possibility of lipoid pneumonia resulting from irradiation seems to have been overlooked In the case described below lipoid consolidation of the lung was found after a pulmonary carcinoma had been treated by radiotherapy

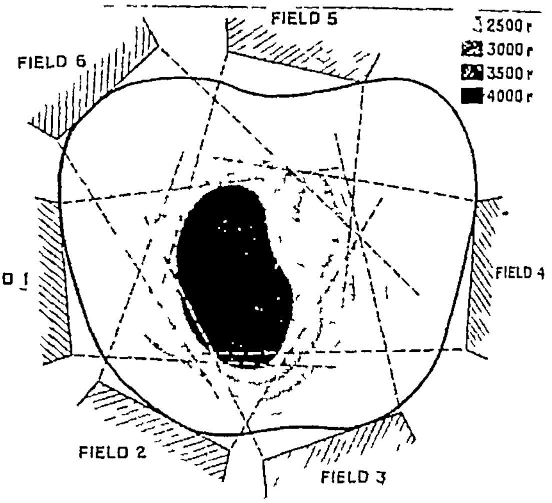


Fig 2—Fields of entry and dose distribution at level of tumour (A-B in fig 5)

CASE RECORD

A woman, aged 56, was admitted to Guy's Hospital under Dr Douthwaite in June, 1949, with two months' history of pain in the right upper chest with breathlessness and cough

On examination she had partial collapse of the right upper lobe, with a rounded mass in the right tracheobronchial angle (fig 1) Bronchoscopy showed that the right upper lobe bronchus was filled with new growth, which on section proved to be anaplastic oat-celled carcinoma

Treatment —She was given a course of deep X-ray therapy in July, 1949 Deep irradiation at 215 kV with Thoræus I filtration and a half value layer in copper of 1·85 mm was used Six fields of entry, each 10 × 10 cm, were arranged round the chest (fig 2) Two fields were treated each day with a surface dose of 350 r, a total dose to each field of 2800 r being given in twenty eight days This gave an aggregate tumour dose of about 4000 r units Fig 2 shows the approximtae dosage distribution within the thorax at the level of the tumour

Procaine penicillin 300,000 units was given daily throughout the course of radiotherapy in an attempt to control secondary infection and minimise the risk of lung gangrene

Progress —The patient's condition improved and fig 3 shows the radiological appearances ten weeks after the course of radiotherapy At the beginning of October, 1949, however, she again noticed increasing breathlessness, and this rapidly became worse She developed pain in the left side of her chest and was readmitted to Guy's in November, 1949

On readmission she was extremely dyspnœic and distressed Her temperature was 97°F, but her respirations 40 per minute Examination of the chest showed some impaired resonance at both bases, with harsh rhonchi and with a left-sided pleural rub Radiography revealed fairly dense shadows spreading

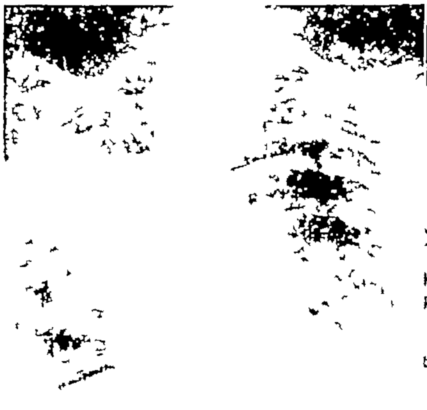


Fig 1—Radiograph showing opacity in right tracheobronchial angle with collapse of right upper lobe

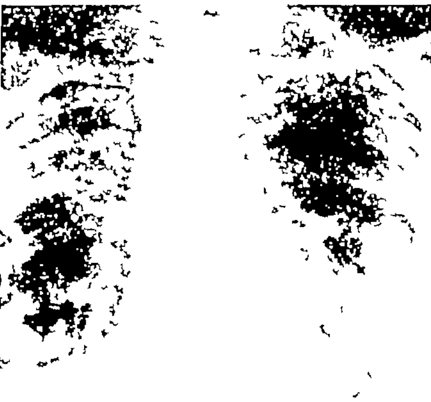


Fig 3—Radiograph ten weeks after radiotherapy, showing almost complete disappearance of shadows

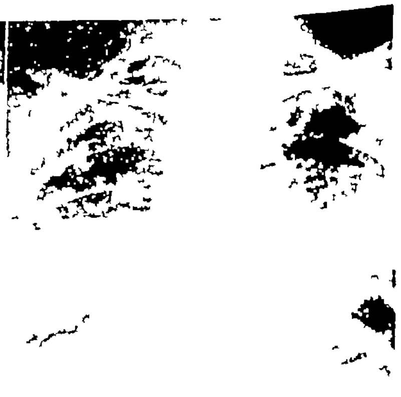


Fig 4—Radiograph ten weeks after that shown in fig 3 showing bilateral symmetrical shadows in middle thirds of lungs corresponding to areas irradiated.

CHANGES IN THE CEREBROSPINAL FLUID AFTER PNEUMO-ENCEPHALOGRAPHY

EDWIN R BICKERSTAFF
M.D Birm. M.R C.P
SENIOR REGISTRAR, DEPARTMENT OF NEUROLOGY, UNITED BIRMINGHAM HOSPITALS

In an earlier paper (Bickerstaff 1950) I reported changes in the cerebrospinal fluid (C.S.F) during pneumo-encephalography in 68 cases, and discussed the difficulties in finding an entirely satisfactory explanation for the mononuclear pleocytosis observed. These difficulties have not been resolved, though the number of cases examined in this way is now over 100

As most of the earlier workers on this subject (Hermann 1922, Weigeldt 1922, von Thurzo and Nagy 1923, Cestan and Riser 1924, Friedman et al. 1928, Jacobi 1930, Grant 1932, Eley and Vogt 1932, Kryspin-Exner 1932, Liberson 1933, von Storch 1936, Aird 1937, Newman 1937, Schwab and von Storch 1937, Levinson et al. 1939) had made their analyses on small numbers of cases in the hours or days following the pneumo-encephalography, and had recorded an almost exclusively polymorphonuclear pleocytosis, it was decided to re examine the C S.F in a large number of cases at carefully measured intervals following the first introduction of air, so as to compare these changes with those which take place during pneumo-encephalography, and to try to discover when the alteration in the type of cellular reaction took place

MATERIAL AND METHODS

The investigation was made pari passu with the routine work of this department A standard technique—alternate replacement of 5 ml. of C.S.F by the same amount of air—was used on each patient, and 80–100 ml. of air was introduced.

In 62 patients 3 ml. of C.S.F was removed at a second lumbar puncture done from 1 hour to 10 days after the first introduction of air, and the cells were counted within an hour

RESULTS

The cell counts are recorded in fig 1 An obvious difficulty in comparing figures is that each reading is taken from a different patient An attempt was made to examine at least two patients at each interval of time, and it was found that the same wide individual variations took place as were observed during pneumo encephalography (Bickerstaff 1950)

The cell count continued to rise after the introduction of air had been stopped, but only slightly for 2½–3 hours, after which it rose rapidly until 8–14 hours after pneumo-encephalography Very high figures were sometimes obtained—e.g , 3776 cells at 8 hours, 2560 cells at 9 hours, and 2840 cells at 14 hours The count thereafter began to fall, the rate varying from case to case but not reaching normal for at least 5 days

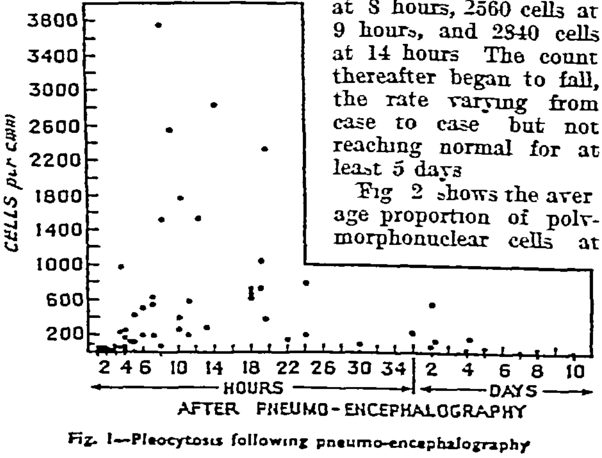


Fig. 1—Pleocytosis following pneumo-encephalography

Fig 2 shows the average proportion of polymorphonuclear cells at different times after pneumo encephalography, and, whereas during pneumo encephalography the pleocytosis had been almost entirely mononuclear, polymorphs now appeared in increasing numbers until by 6 hours they represented 90–97% of the total count, and remained in this proportion for a further 12 hours. Mononuclear cells then gradually began to reappear, but the polymorphs did not entirely disappear until 96 hours

The period of greatest subjective discomfort corresponded to the period of greatest polymorphonuclear reaction but did not necessarily bear any relation to the magnitude of the total cell count Patients with less than 200 cells per c mm sometimes suffered more severely than those with more than 2000 cells per c mm at the same interval after pneumo encephalography

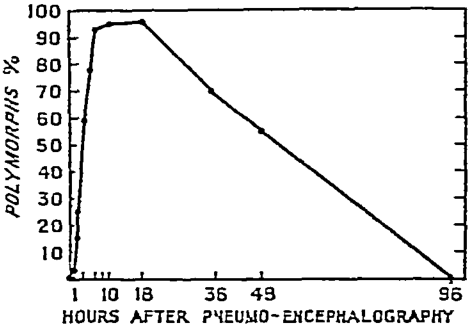


Fig 2—Proportion of polymorphs at different intervals after pneumo-encephalography

The biochemical changes were almost confined to the protein fractions The amount of sugar was either unchanged or increased by a few milligrammes at the height of the reaction The increase in protein, which had been found to follow the initial sharp fall during pneumo-encephalography, continued rather more rapidly, and readings of 75–100 mg were obtained at 2 or 3 hours and, with numerous individual variations, remained of this order until 22–24 hours, when they gradually fell, normal figures not being reached for 5 days There was not necessarily any direct relation between the amount of protein and the height of the cell count, and it remained raised in some cases after the cell count had begun to fall.

The tests for globulin became positive within 2 hours of the start and remained so until 24–36 hours

The diagnosis, the use of air or oxygen, time taken by pneumo-encephalography, and the height of the initial cell count did not influence the reaction, which appeared to depend on the length of time between the first introduction of air and the second examination of C.S.F

DISCUSSION

This investigation has shown that two distinct types of pleocytosis arise in the C.S.F in relation to pneumo-encephalography The first is seen during the actual procedure, it starts within the first few minutes and figures as high as 252 cells per c.mm may be reached in as short a period as 20 minutes It is almost entirely mononuclear, the magnitude of the rise being influenced by the height of the initial cell-count The second begins about 2½–3 hours after the first introduction of air, is more dramatic, is almost exclusively polymorphonuclear, and depends for its degree on the length of time before the fluid is re-examined, the greatest reaction being at 8–14 hours Mononuclears then reappear, but the C.S.F is neither cytologically nor biochemically normal for at least 5 days If different quantities of air are used, the cellular reaction is said to be proportional to the quantity of air (Schwab and von Storch 1937)

The pleocytosis after pneumo-encephalography is not so difficult to explain as the pleocytosis during pneumo-encephalography The later reaction is typical of an spaces and produced pneumonic consolidation The pneumonic consolidation was like that seen in lipoid pneumonia due to inhalation of oil, but differs both in the nature of the fat and in its pathogenesis

Studies are in progress to elucidate the mechanism of this phenomenon and its possible implications So far four consecutive examples of carcinoma of the lung which have not been irradiated have all shown the changes of lipoid pneumonia in the lobe affected by the tumour

SUMMARY

A case of primary carcinoma of the lung successfully treated by radiotherapy showed pneumonic consolidation due to fatty deposits (lipoid pneumonia) in the areas irradiated

Four consecutive examples of carcinoma of the lung which have not been irradiated have all shown similar changes

The fatty change is thought to be due to degeneration of the carcinoma and of the adjacent lung parenchyma, which is accelerated by deep radiotherapy

We are grateful to Dr A H Douthwaite for permission to publish this case

REFERENCES

Alexander T O (1944) *Bull Johns Hopk Hosp* 75 199
Fried J B Goldberg, H (1940) *Amer J Roentgenol* 43, 877
Groover T A, Christie A C, Merritt E A (1923) *Ibid*, 10 471
Leach J E (1943) *Ibid* 50 772
— Farrow J H, Foote F W jun, Wawro, N W (1942) *Ibid* 47, 740
Paterson J L H (1938) *J Path Bact* 46, 151
Pinkerton H (1928) *Arch Path* 5, 380
Warren S, Spencer J (1940) *Amer J Roentgenol* 43 682
Widmann B P (1942) *Ibid* 47 24

NEUROMUSCULAR INCOÖRDINATION OF SWALLOWING IN THE NEWBORN

J C Macaulay
M.D Lond, M R C P, D C H
FORMERLY HOUSE PHYSICIAN, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON

Success in the surgical treatment of congenital œsophageal atresia depends largely on early diagnosis Belsey and Donnison (1950), Donnelly (1950), Ladd (1944), and Ladd and Swenson (1947) have emphasised this and have described the clinical picture But a superficially similar syndrome, unassociated with gross anatomical defect, has not been described, and this should be considered in the differential diagnosis of œsophageal atresia or stenosis, as the following case shows

CASE RECORD

A full term illegitimate baby of healthy parents was delivered, under chloroform anæsthesia, with forceps, because of delay in the second stage of labour He weighed 7 lb 6 oz His colour was good, but there was excess of mucus in the upper respiratory passages At the first and all subsequent feeds in the maternity home he became cyanosed and 'bubbly," and vomited frequently He was treated in an oxygen tent with penicillin and sulphadiazine, but did not improve A Wassermann reaction was negative

On admission at the age of 10 days, to the Hospital for Sick Children, Great Ormond Street, under the care of Dr Wilfrid Sheldon, his weight was 7 lb 3 oz, temperature 98 6°F, pulse rate 132, and respirations 36 per min. There was moderate cyanosis The upper respiratory passages contained an excess of mucus, and breathing was irregular and rattling The cry was weak There was moderate indrawing of the lower intercostal spaces and suprasternal notch on inspiration The percussion note was resonant, and the breath sounds were vesicular, with many rhonchi and moist sounds throughout the chest, varying but not disappearing after coughing The heart sounds were normal No abnormality was noted in the abdomen. Reflexes and fontanelle tension were normal, and there was no neck stiffness There was a well marked cephalhæmatoma in the left parietal region of an otherwise normally shaped head

Investigations —In view of the previous history the possibility of congenital œsophageal atresia was at first entertained, particularly when swallowed iodised oil reached the bronchi, suggesting a tracheo œsophageal fistula The infant's stool, however, indicated that some milk had passed down the alimentary tract Accordingly, a stomach tube was passed and found to enter the stomach easily Iodised oil was next swallowed by the infant under radioscopy, whereupon it was seen that when the oil reached the pharynx it was first inhaled into the trachea and almost immediately afterwards coughed back into the pharynx and swallowed down the œsophagus This suggested that the swallowing mechanism was defective, to the extent that the infant could not shut off the larynx during deglutition, and therefore fluid was as likely to enter the larynx and trachea as to slip past into the œsophagus

Treatment —The baby was nursed upright Feeds of expressed breast milk, 3 oz three hourly, were given through a stomach tube until the power of swallowing returned Penicillin 50,000 units was injected intramuscularly twelve-hourly for ten days

Progress —Physical signs in the chest persisted for ten days, and cyanosis during tube feeds for a week Small amounts of milk were regurgitated even after tube feeds for the first five days of treatment The baby remained afebrile and gained weight satisfactorily

Further radioscopy a week later (at the age of 17 days) showed that the swallowing defect persisted, but four days later he had improved enough to take feeds by mouth

Laryngoscopy (Mr James Crooks) two weeks after admission (at the age of 24 days) showed no anatomical deformity of the larynx or the epiglottis The movements of the cords were irregular and incoördinated the left moved well, and the right poorly

The child was discharged from hospital sucking and swallowing normally There was no further vomiting, and subsequent progress was uneventful When seen at the age of 10 months he was a normal healthy child weighing 22 lb and could crawl and stand His voice was normal, and breathing regular A barium swallow did not show anything abnormal

DISCUSSION

Transient disorders of swallowing may occur in new born babies as a result of prematurity or of obstruction of the respiratory passages by mucus Persistence of regurgitation and inhalation of feeds, with cyanosis and dyspnœa, are almost always associated with gross anatomical defects In addition to organic lesions of the œsophagus, congenital abnormalities of the medulla and extreme cases of amyotonia congenita may produce a similar picture

In the case described here there was no evidence of any of these However, the swallowing defect, the irregular breathing, the weak cry and the incoordinated movements of the larynx, with subsequent recovery, point to a reversible lesion of the medulla—a temporary partial bulbar palsy There was no clinical evidence of an intracranial hæmorrhage, but possibly there had been some bruising and œdema of the medulla which subsequently disappeared A more likely explanation is that there was an immaturity of the bulbar centres, with a consequent failure of coordination of swallowing, laryngeal movements, and breathing This is supported by some careful observations of Peiper (1942), who investigated the temporary swallowing and breathing disturbances of newborn babies and concluded that they were due to immaturity of the medullary centres

It is a pleasure to record my indebtedness to Dr Wilfrid Sheldon for advice and permission to publish, and to Mr James Crooks for the laryngoscopy report

REFERENCES

Belsey R H R Donnison C P (1950) *Brit med J* ii 324
Donnelly B (1950) *Lancet* i 666
Ladd W E (1944) *New Engl J Med* 230 625.
— Swenson O (1947) *Ann Surg* 125 23
Peiper A (1942) *Mschr Kinderheilk* 90 37

ut had not then had dysentery or more than trivial ea

xamination his temperature was 101°F , he was very over and below the right lower ribs, though the liver ould not actually be felt , his right diaphragm was le but not raised on fluoroscopic examination , and cell count showed 20,000 leucocytes per c mm (poly 85%) These findings left little doubt that the patient ppuration affecting the liver

tment and Progress —Since it seemed probable that ection was amœbic, a course of emetine gr 1 daily for days was begun on the third day The patient appeared rove a little at first, the pain and tenderness diminish out, as he continued to have a swinging temperature g 101°F, a course of procaine penicillin 300,000 units was begun on the thirteenth day and continued for days, though it had no striking effect Because of the ent fever and tenderness, on the fourteenth day a was inserted into the right tenth interspace in the illary line, and superficially a few ml. of thin dark pus was aspirated Further needling revealed no more The pus contained gram positive cocci on the smear moderate growth of coagulase positive *Staphylococcus* on culture (sensitivity to penicillin not determined) mperature and pain gradually lessened after the aspira nd from about the twentieth day onwards the patient l well He was discharged on the thirty fourth

ow up —Since then he has remained perfectly well, from a little effort dyspnœa In June, 1949, September, January, 1950, June 1950, and December, 1950, he was screened, and on each occasion the right diaphragm was completely paralysed but not raised

DISCUSSION

In the present case, although the diagnosis of suppurative hepatitis seemed virtually certain, there was doubt about the ætiology Since hepatitis of this kind, developing as an apparently isolated manifestation, is nearly always amœbic, it seemed likely that amœbiasis with secondary infection was responsible The fact that the patient had been free from bowel symptoms while serving in the tropics does not contradict this hypothesis

This case, and others seen for short periods after amœbic hepatitis during the war, suggest that paralysis of the diaphragm may not be particularly rare It is easy to overlook this condition, an ordinary chest radiograph often revealing nothing amiss, screening is necessary for its detection A most striking way to demonstrate the paralysis under the X ray screen is by asking the patient to sniff The sound side of the diaphragm then descends, and the paralysed side simultaneously ascends

It is interesting to speculate whether the paralysis is muscular or nervous , but it is difficult to answer this question without necropsy material

REFERENCES

Isaac F (1945) *Radiology* 45 581
Ochsner A DeBakey M Murray S (1938) *Amer J Surg* 40 292

Medical Societies

ROYAL SOCIETY OF MEDICINE AND SOCIETY FOR ENDOCRINOLOGY

Adrenocorticotropic Hormone

E section of endocrinology of the Royal Society of cine and the Society for Endocrinology met on May nder the chairmanship of Dr F T G Prunty, to a symposium on A C T H

of F G YOUNG, F R S , discussed the evidence that are two pituitary gland principles that can affect drenal. These he called the " ascorbic acid factor " F), which is active in reducing the adrenal ascorbic content in hypophysectomised rats , and the enal-weight factor " (A W F), which increases the ht of the adrenal gland under similar conditions but not deplete its ascorbic acid The commercial lard preparation of A C T.H is rich in A A.F and ively poor in A W.F It is possible, however, to te a preparation of A C T H which is very rich in F and poor in A A F Although so far no preparation C T H has been entirely free of either factor, the of ascorbic acid depletion activity to adrenal ht activity in various preparations has varied from to 1 5000 or more, which is strongly in favour of existence of two separate principles If the pituitary d of a rat is removed, the adrenal gland atrophies ow one injects A W F , the adrenal gland shows a ral increase in size affecting all zones of the cortex distribution of lipoid granules, however, is normal ' large normal " picture is different from that luced by injections of A.A F , when the main result change in the distribution of lipoid granules (particu involving the zona fasciculata) If preparations C T H with mixed activity are stored, there is greater of A A.F than of A W F So far, the clinical applica- of the adrenal weight factor has not been elucidated here is now plenty of evidence that the activity of T H resides in a small peptide fraction of the main ein complex This peptide fraction can be removed acid hydrolysis as in the original experiments of Li his co workers or more simply by dialysation exchange column separation has shown clearly that T H consists mostly of a fast moving acid protein with small amounts of a slow moving basic peptide Hormone activity appears to reside entirely with the latter

Mr C J O R MORRIS, PH D , pointed out subsequently that A.W F as well as A A.F is separable by dialysis from the protein component It seems impossible that anything representing chemical combination in the ordinary stoicheiometric sense can exist between the protein and the peptide components The protein is, therefore, no more than a " carrier " which happens to be separated with the active principles Pituitary growth hormone, on the other hand, is not separable in this manner, and thus cannot be identical with A W.F , although commercial growth hormone usually contains A W.F Both A A.F and A W F can properly be spoken of as adrenal corticotropic hormone, and one must in future remember and allow for this dual nature of A C T H

METABOLIC REACTIONS

Dr PRUNTY reported some results of treatment of rheumatoid arthritis with A C T.H He showed that there is good correlation between the percentage fall in circulating eosinophils and the rise in urinary excretion of reducing steroids when A C T H is given, but no correlation when adrenaline is given The clinical activity of various batches of A C T H differs widely This is due partly to variation in the material, partly to variation in the responsiveness of the patient For any given batch and patient, the activity of A C T H is greatest when given by slow intravenous infusion, and least when given as a single daily dose Attempts to prolong the action of A C T.H by giving " depot " injections made up with polyvinylpyrrolidone have been unsuccessful

URINARY METABOLITES

Prof G F MARRIAN, F R S , discussed the methods of extraction and estimation of urinary steroids In the urine steroids occur free or conjugated Some conjugates are chloroform soluble, others are chloroform insoluble conjugates with glucuronic acid These are not normally extracted by current methods Methods of estimation of the conjugates involve acid hydrolysis, which itself may cause destruction of the free steroid Although standard methods of extraction and estimation acute irritation of the meninges, is accompanied by headache, vomiting, neck stiffness, and occasionally a very slight pyrexia, and is certainly due to the irritant properties of the air The same type of cytological change at the same intervals of time is present after ventriculography (Bickerstaff 1950) but is not so great as after pneumo encephalography, either because less air is used or because the increase in meningeal vascular permeability, thought to be produced by pneumo encephalography (Levinson et al 1939), is not present

Fleck and Stein (1951) are inclined to ascribe both stages of the pleocytosis to meningeal irritation If this is so, it is strange that the mononuclear pleocytosis does not occur during ventriculography

The return of the mononuclears from 20–24 hours onwards—still in much larger numbers than in normal C S F —finds a parallel in the work of Jackson (1949), who showed that, in experimental "aseptic hæmogenic meningitis," 24 hours after the introduction of the blood the perivascular spaces have become filled with lymphocytes, which then begin to reappear in the C S F Kubie and Schultz (1925) had noted similar results from artificially produced meningeal irritation, the initial polymorph response arising from the meninges, and the later mononuclear response from the perivascular spaces It seems likely that the same sequence of events occurs after pneumo encephalography, and it is noticeable that clinical signs of meningeal irritation are present during the period of polymorphonuclear reaction only It seems possible that the earliest changes of all—the mononuclear pleocytosis in the first few minutes—may also originate from the perivascular spaces

Two points of practical importance arise from this investigation First, no samples of C S F examined at any time from the first introduction of air to at least 5 days later can be considered representative of the usual composition of that patient's C S F , and, if further examination is required, it is wise to postpone it for 10 days or more

Secondly, there is, almost constantly, clear clinical evidence of meningeal irritation during the first 24 hours after pneumo encephalography This fact has been known for many years, indeed Bohn (1937) analysed 1000 cases in an attempt to discover some means of minimising the symptoms Nevertheless, at times it may be feared that infection has accidentally been introduced into the theca, a fear which may be increased when on examination of the C S F a brisk polymorph pleocytosis is discovered We have seen, however, that this is a constant phenomenon, there is very little rise of temperature, the sugar content of the fluid is, if anything, higher than normal, cultures are sterile, and the reaction settles spontaneously Re examination of the C S.F is not necessary, unless there is pyrexia, and the polymorph reaction is not an indication for the intrathecal introduction of antibiotics, unless pyrexia is accompanied by a low C S.F sugar level or a positive culture is obtained from the C S F

It has been impossible to forecast, as a result of this investigation, which patients are likely to have severe reactions, but it has been a most striking fact that those who underwent pneumo encephalography under general anæsthesia experienced very much less subjective discomfort in the following 24 hours, even though the cytological reaction was considerable

One of the remarkable features of this investigation has been the individual variations in cellular response both during and after pneumo encephalography, though a constant technique was used When one considers how differently different people may react to the same irritant stimulus, it is easy to understand the variations in mode of onset of such conditions as bacterial meningitis or poliomyelitis, when so many modifying factors may be at work

In conclusion it is repeated that no diagnostic significance can be attached to any of the different results, the same type of reaction with the same variations occurring in neurologically normal patients as in those with gross organic disease

SUMMARY

The cytology and biochemistry of the C S F was studied in 62 cases at intervals from 1 hour to 10 days after the start of pneumo encephalography

A brisk polymorph pleocytosis began at 2½–3 hours, reached a maximum at 8–14 hours, and did not return to normal for at least 5 days

The C S.F protein level rose steadily, reaching 100 mg per 100 ml after 3 hours and remaining at this level until 22–24 hours

The nature of the reaction and the practical applications of this knowledge are discussed

The ready coöperation of Dr J Rounthwaite, Dr C Woods, and Dr M Wilson, resident clinical pathologists at the Queen Elizabeth Hospital, who counted the cells, often at very inconvenient hours, is gratefully acknowledged, as is the help given successively by the house physicians to the neurological unit, and the permission granted by Prof. P C P Cloake and Dr G S Hall to make these investigations on their patients

REFERENCES

Aird R B (1937) *Arch Surg* 34 853
Bickerstaff, E R (1950) *Lancet* ii, 683
Bohn, S S (1937) *Bull neurol Inst N Y* 6 540
Cestan R , Riser, R (1924) *Bull Soc méd Hôp Paris* 48 953.
Eley R C Vogt E C (1932) *Amer J Roentgenol* 27 686
Fleck, L , Stein, W (1951) *Lancet* i 1126
Friedman E D , Snow W Kasanin J I (1928) *Arch Neurol Psychiat , Chicago*, 19 762
Grant F C (1932) *Ibid* 27 1310
Hermann G (1922) *Med Klin* 18, 1146
Jackson I J (1949) *Arch Neurol Psychiat Chicago*, 62, 57
Jacobi W (1930) *Dtsch Z Nervenheilk* 112 266
Kryspin Exner W (1932) *Psychiat Neurol Wschr* 34 509
Kubie L S Schultz G M (1925) *Johns Hopk Hosp Bull* 37 91
Levinson A Kaplan I Cohn, D J (1939) *J Lab clin. Med* 25 475
Liberson F (1933) *Amer J med Sci* 185, 478
Newman H W (1937) *J Amer med Ass* 108 461
Schwab, R S , von Storch T J C (1937) *New Engl J Med* 217, 21
von Storch T J C (1936) *Brain*, 59 250
von Thurzo E Nagy M (1923) *Dtsch Z Nervenheilk* 79 374
Welgeldt, W (1922) *Münch med Wschr* 69 1761

SUPPURATIVE HEPATITIS AND DIAPHRAGMATIC PARALYSIS

John W Todd
M D Lond , M R C P
CONSULTANT PHYSICIAN, FARNHAM HOSPITAL, SURREY

It has been widely recognised for many years that amœbic hepatitis can paralyse the diaphragm Ochsner et al (1938), for example, say "The characteristic roentgenological changes are elevation and immobility of the diaphragm, usually the right" It is also well known that the diaphragm does not recover as quickly as does the liver In the India Burma theatre during the late war it was often observed that many soldiers who had apparently fully recovered from amœbic hepatitis continued to have complete paralysis, and often considerable elevation, of the right side of the diaphragm during the remainder of their stay in hospital But I have only been able to find one reference to this matter in published reports—Isaac (1945) says "It will be found that, while clinical response to specific treatment may be dramatic, the X ray signs will be much slower in returning to normal" No one seems to have followed cases to determine how long the diaphragmatic paralysis persists This case record may therefore be of interest

CASE RECORD

A man, aged 23 was admitted to Farnham Hospital in February, 1949, with ten days' history of pain in the right side, fever, and malaise He had been in the Royal Navy and had served for eighteen months in the Far East until May, 3)

that œstrogens stimulate adrenal
hereas androgens inhibit it, probably
n on A C T H

ON TO PITUITARY GLAND

discussed the mechanism of adrenal
Increased secretion of adrenal cortical
o occur within minutes, possibly within
plication of stress such as the in-vivo
ion of histamine Adrenal cortical
t this response if given a few seconds
ine, but not if given with or after
ent on to describe experiments where
isolated perfused adrenal glands was
omatography, and showed that the
adrenal steroids is doubled within 20
dition of A C T H to the perfusate A
ence is found when the effluents from
nt animal origin are analysed

SUMMARY

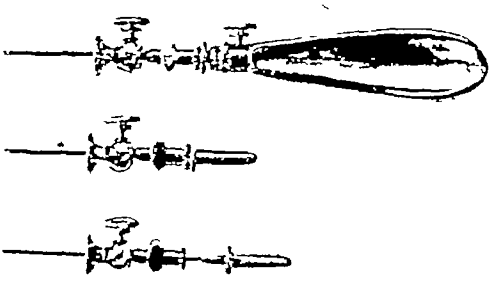
summing up the results of the con
t the amount of the peptide fraction
is active in causing adrenal ascorbic
eems to correlate well with the clinical
ations of A C T.H, with few exceptions
roneously spoken of as side-effects of
important These "side effects" are
ical as the antirheumatic effect Until
be regularly assayed in terms of all the
ects of A C T H, the road will not be
ing of synthetic compounds which may
action on the rheumatic state Mean
rtant to note that the specificity of the
C T H has not been fully established

New Inventions

UNIVERSAL NEEDLE FOR BONE-MARROW ASPIRATION

BONE-MARROW aspiration needles are now an essential
t of the clinical pathologist's equipment The needles
uld meet the following requirements

1) An adjustable guard, allowing for use in adults, a
dle length of not less than 2 5 cm
2) As short a distance as possible between the needle point
l syringe fitting so that the success of a puncture can be
ified quickly and marrow for films will enter the syringe
idly
3) A handle, to ensure steadiness and ease in the rotatory
vement usually employed in piercing the bone, a handle
especially helpful when piercing dense bone and the iliac
st
4) A variety of needles, all adaptable to the one handle,
use in adults children, or infants and allowing a narrower
dle than usual to be used on adults when it is likely that
ellular marrow will be entered—e g, in pernicious anæmia,
kæmias and certain neoplastic deposits



(5) The instrument must be sturdy, easily cleaned, re assembled, and sterilised, and conveniently transportable

After using the usual British, American, and Continental patterns I have not found one to fulfil all these requirements, but following the satisfactory use, some years ago, of the "Gimson" needle for bone-marrow transfusions in infants, my senior technologist and I have designed a new type of marrow-aspiration instrument which incorporates all the requirements (see figure) The main features are three needles, sizes 16, 17, and 18 S W G, each of which has its own stylet, the strengthened end of which will fit into a common handle, where it is held firmly in place with a side screw. When the marrow cavity is entered, the stylet, still fixed in the handle, is withdrawn and a 'Record' fitting syringe is attached to the top of the needle The reason for choosing these three needle sizes is that 16 S W G is the usual adult Salah type and 17 and 18 S W G, have been found suitable for children and infants The needle lengths are 3 5 cm. for the 16 S W G and 3 25 cm for the 17 and 18 S W G, and each is adjustable with a guard with a convex presenting surface

The instrument has been tried out extensively in the three sites usually chosen for marrow aspiration—sternum, iliac crest, and vertebral spine—and has been found very satisfactory From the patient's aspect it occasions the minimum of discomfort and "suction pain," *and the operator, especially the less experienced,* finds it safe and easy to manipulate in obtaining an adequate marrow sample The handle and three needles rest conveniently in a $7^{3}/_{4} \times 1^{1}/_{2}$ in boiling-tube for sterilisation and transportation

The instrument is made by Messrs S J Owen of 35, Northampton Square, London, E C 1, under the style of the "H-H [Hill-Howe] Universal Bone-marrow Aspiration Needle"

Hospital of St Cross
Rugby

R O HILL, M B Lond, D C P

Reviews of Books

Progress in Biophysics and Biophysical Chemistry

Editors J A V BUTLER, Chester Beatty Research Institute, Royal Cancer Hospital London, J T RANDALL, F.R.S, Wheatstone professor of physics in the University of London at King's College London Butterworth Springer 1950 Pp 279 50s

BIOCHEMISTRY we know, biophysics we know, and physical biochemistry we have heard of Is biophysical chemistry identical with the last-named, or is it a new product of the hybridisation of the sciences? If both terms refer to the application of physical chemistry to living, or sometime living, matter, it is unfair to couple the 'bio" with either ' physics" or "chemistry" "Physicochemical biology" is a possible solution. As further complication, J F Loutit's article on the Tolerance of Man for Radioactive Isotopes, though it comes from a radiobiological research unit, is clearly concerned with radiopharmacology and radiotoxicology However, nomenclature is the least of isotopic horrors, and Dr Loutit dilates amusingly on our exiguous knowledge of the tolerance dose of radium The catholicity of biophysics and ' biophysical chemistry" is shown by the circumstance that the articles come from laboratories devoted to colloid science, textile physics, physical chemistry, cell metabolism, cytology, radiobiology, medicine, and zoology All of these except one are in England

H Gutfreund contributes a usefully critical discussion of the measurement and results of measurement of the molecular constants of proteins paying particular attention to osmotic pressure The determination of the size and shape of protein molecules by measurements of the scattering of visible light and X rays is dealt with by G Oster K M. Rudall gives an enthusiastic account of the results and current interpretation of X ray studies of fibrous proteins, polysaccharides and polynucleotides M G M Pryor approaches the problem of muscular contraction from a different angle He leads through a thermodynamic treatment of the stretching of rubber and plastics, and model experiments with tendon, to the ' kinetic hypothesis in which muscle contraction is regarded as resulting may give reliable comparative results, they measure only a small fraction of the total steroid excretion Preliminary treatment of urine extracts with β glucuronidase causes non destructive hydrolysis of fractions previously unestimated, and the yield is increased as much as thirtyfold Much of the work done on urinary excretion of adrenal steroids must be regarded as empiric since it has not taken into account this large glucuronide conjugated fraction Preliminary results with the new technique show that all the steroid fractions estimated appear to come from the adrenal gland Furthermore, excretion of all fractions is increased in patients given ACTH

In addition, there is considerable doubt as to whether the type of steroid isolated is the only type secreted by the adrenal gland For example, seven 21 methyl steroids known to be of adrenal origin cannot be chemically assessed by current methods of estimation of urinary steroids Professor Marrian emphasised that there is as yet no method for the full quantitative analysis of all adrenal steroids and their metabolites If those workers who use present methods as a routine were to devote the same amount of time to developing improved methods, much greater progress would be made in this field

TISSUE REACTIONS

Prof G R **Cameron**, F.R S , spoke of the local tissue reactions during ACTH and 'Cortisone' therapy Most of the evidence suggests a local reduction of tissue œdema Pain, stiffness, and swelling of rheumatoid arthritis, for example, decreases during treatment, and this can be explained as the result of movement of œdema fluid from the affected area That this œdema removing effect is not of central origin is indicated by several findings, including the *local* relapse of tissues when hormones are withdrawn—e g , only those joints which have been affected by rheumatoid arthritis before treatment relapse afterwards Ebbing of œdema from diseased tissues was dramatically shown in serial photographs of nasal polyps treated with ACTH The effects of ACTH on the cellular reaction to injury, such as the healing of wounds, shows big species differences , in rats healing of experimental wounds is not inhibited, in guineapigs it is sometimes inhibited, and in rabbits it is always inhibited Nevertheless, all the evidence shows that the type of granulation tissue formed is qualitatively the same as normal granulation tissue It is the quantity and speed of its formation which is decreased

Professor Cameron reported some experiments on the alteration of capillary permeability by cortisone Rabbits that are injected intravenously with dyes of large molecular size retain the dye within the blood vessels If, however, the animal is injected with histamine or leucotaxin, or is roughly handled, the dye passes from the serum into the tissue spaces This effect is inhibited by cortisone He suggested that the local tissue action of cortisone may depend on the fact that it is surface active and may increase the resistance of the diseased cell surface to outside modifying influences Cortisone cannot, however, prevent the pulmonary œdema which follows the intravenous injection of ammonium compounds

In the subsequent discussion it was noted that these hormones had no effect on *normal* capillary permeability Dr E G L **Bywaters** said that the local effect of cortisone injected into rheumatoid granulation tissue is very little other than the production of a mild necrosis near the injected crystals This may well be due to the vehicle rather than the cortisone Dr G D **Kersley** mentioned that intra articular cortisone has been found to reduce the inflammatory reaction of a diseased joint to surgery He also pointed out that some of the effects of ACTH on capillary permeability may be due to contamination by posterior pituitary substances

ASSAY

Mr A S **Parkes**, D SC , F R S , mentioned some of the difficulties in the assay of ACTH In the intact animal any interference may cause the production of endogenous ACTH as part of a non specific response to stress This can be averted by removal of the pituitary, but for technical reasons only the rat can be successfully hypophysectomised as a routine Thus all work involving ACTH assay is for practical purposes limited to the rat, and this may have influenced previous experimental work In the hypophysectomised rat ACTH produces morphological, histological, and chemical changes, any of which might form the basis of an assay test Sayers and his co workers have used the depletion of ascorbic acid in the adrenal gland as their index of ACTH activity This test is sensitive and reliable and is now standard procedure Even so, several animals should be used for any one assay

A more elegant method of assay may be provided by perfusing hypophysectomised animals or isolated adrenal glands with ACTH and collecting the steroids secreted via a cannula in the adrenal vein There may also be a future for the assay of ACTH in intact animals after preliminary pituitary inhibition by large doses of desoxycorticosterone—a kind of physiological hypophysectomy Another test measures the effect of ACTH on the survival time of mice in a closed vessel This test depends on the fact that cortisone increases the resistance of mice to hypoxia ACTH is active in prolonging the survival of mice under these conditions. Unfortunately posterior pituitary extract has the same effect, and contamination of ACTH by this hormone has not been excluded

EFFECTS ON PERIPHERAL CIRCULATION

Dr J H **Kellgren** spoke of the reaction of the peripheral blood vessels to ACTH treatment In untreated rheumatoid arthritis the joints are warm and the fingers are cold Cold fingers also occur in scleroderma, in acrocyanosis, and in dermatomyositis This finger coldness is akin to that found in Raynaud's phenomenon, but greater in degree , a more or less continuous spasm of the arterioles in the fingers can only be relieved by considerable body heating However, if ACTH is given in these diseases there is flushing of the fingers and an increase in finger blood flow and temperature The increase is comparable to that noted in Raynaud's phenomenon treated by sympathectomy

In the subsequent discussion one speaker noted that where rheumatoid arthritis occurred only in one arm the increase in the peripheral circulation was greater in the fingers of the diseased arm than in those of the normal arm

PLASMA EXTRACTS

Miss **Delphine Parrott** reported experiments to determine the ACTH like activity of plasma extracts Circulating blood loses its ACTH like activity in a matter of minutes if stored without preservative , but if blood is taken straight into acetone reliable assays of the subsequent plasma extract can be made on hypophysectomised rats ACTH activity of the plasma is markedly increased in stress and in Cushing's syndrome, but is absent in Simmonds's disease The rapid decay of ACTH activity in stored blood suggests a circulating ACTH destroying enzyme

ACTH AND GONADS

Dr P M F **Bishop** quoted work suggesting that the gonads and their secretions have some relation to ACTH action ACTH cannot normally inhibit wound healing in adrenalectomised animals But if luteinising hormone is first given to adrenalectomised animals the power of ACTH to inhibit wound healing is restored Furthermore,

THE LANCET

ONDON SATURDAY, JUNE 2, 1951

Pneumoconiosis in Coalminers

agree that the high incidence of pneumoconiosis outh Wales coalminers constitutes a major em of preventive medicine and engineering ons differ, however, about the emphasis to be d on the various methods of protection Broadly ing, some authorities would concentrate on the ression and control of dust, while others favour dic medical examination It is clear that if suppression in the mines were adequate there d be no need for periodic medical examinations ed, the latter method, by which a miner can be n out of a dusty job when he has developed an stage of pneumoconiosis, is not prevention at it may mitigate, but does not prevent, the ts of dusty conditions In so far as it does gate them it is a valuable measure But there is al danger that, if too much emphasis is placed periodic medical examinations, the primary need dust suppression and control will be ignored

he case for compulsory periodic examination of lminers is well stated by members of the Pneumoiosis Research Unit of the Medical Research incil. Thus Dr CHARLES FLETCHER, director of unit, said in 1948 that "the sincerity of the ustry's and the Government's concern with the lth of coalminers will be judged by the speed and roughness with which such a system is instituted this country" [1], and in a recent article COCHRANE, ETCHER, GILSON, and HUGH JONES [2] again set out arguments in its favour The main advantages, they see them, are three In the first place it would ver the interval before safe dust levels are defined d effective dust suppression is achieved Secondly, would reveal the mines, seams, or districts where rly signs of the disease were still arising despite ist suppression, which would enable the engineers take appropriate action. Thirdly, if periodic amination were combined with routine dust studies representative pits it should be possible in time determine the level of dustiness which does not ive rise to cases of pneumoconiosis Dr FLETCHER nd his colleagues also restate the evidence that adiographic changes can be detected before much arm has been done and that at this stage removal rom exposure to dangerous dust will prevent the rogressive massive fibrosis which they say is the ause of serious disability In the first instance a ilot scheme would be necessary, and it might well tart, they think, in South Wales, since there "the neumoconiosis panels are already used by the men as an irregular system of periodic examination." But in their opinion the scheme should be kept separate from compensation issues, and the pneumoconiosis panels should stick to "their statutory function of assessing disability and its cause" The National Joint Pneumoconiosis Committee, on the other hand, thinks that an experimental scheme would be more likely to succeed if it was not linked directly with the X-ray and dust-environmental surveys which are being carried out by or under the auspices of the Pneumoconiosis Research Unit of the Medical Research Council Quoting the Committee's opinion in Parliament,[3] Mr HAROLD NEAL, parliamentary secretary to the Ministry of Fuel and Power, said that facilities for X-ray examinations are already extensive and that every miner who claims benefit is radiographed In the two years ended last December, about 31,000 X-ray films were used, and 10,000 miners were diagnosed as having pneumoconiosis All of these, whether they left coal mining or not, have to report periodically for re-examination by the pneumoconiosis medical board, and 'the increased confidence of the men in the advice of these Boards was shown by the fact that up to the end of 1950 about 5500 of the 10,000 cases diagnosed had remained at work in the industry" This confidence may be further enhanced by the new regulations, summarised on a later page, whereby the arrangements for men certified as having pneumoconiosis under the Workmen's Compensation Acts are brought into line with the arrangements for those certified under the more recent Industrial Injuries Act both groups, subject to initial and recurrent examination for fitness by a pneumoconiosis board, may now work in mines and may claim benefit for any worsening of their condition. Over many years the pneumoconiosis panels (formerly the silicosis and asbestosis medical board) have built up a considerable body of experience of industry and the pneumoconioses (not only in coal mining), and we should rather see their work and influence widened than narrowed by confining them more strictly to their "statutory" duties

MEIKLEJOHN,[4] with much knowledge of periodic medical examinations in this country and abroad, believes that the time is not yet ripe to establish a system for all coalminers In his John C Bridge lecture he suggested the advantages of such examinations, though theoretically attractive, are not manifest in practice The advantages usually mentioned are (1) reduction of pulmonary tuberculosis, (2) detection of early silicosis, (3) collection of evidence on conditions producing the disease, and (4) assistance in diagnosis by providing serial records As regards tuberculosis "as often as not the tuberculous workman is absent on the occasion of the medical board's visit and so escapes examination and suspension, no matter, for the incapacitating effects of the disease itself soon eliminate him from work" The examinations, says MEIKLEJOHN, have little value in providing evidence of conditions producing the disease because the necessary exposure is considerable, and usually men move, and working conditions change, too often This objection, however, is not wholly valid for coalmining, in which the conditions are fairly stable Early diagnosis of silicosis depends very largely on radiographic changes, and panels of experts may interpret technically satisfactory films with some accuracy (though unfortunately the standard of chest radiography is still not high enough) The early and consistent diagnosis of early simple pneumoconiosis in coalminers is much more difficult than the diagnosis from the liberation of a plasticiser (? adenosinetriphosphate) In a review entitled "Local Refractometry the Observation of Transparent Inhomogeneous Matter" J St L Philpot brings together methods used for observing inhomogeneities in one, two, and three dimensions, treating the observation of moving boundaries in solutions as well as techniques of microscopy One of the latter, phase contrast microscopy, is discussed by A F W Hughes in relation to biological research A Engström describes the use of soft X rays for the analysis of minute amounts of biological material, the density of cell structures as small as 1 μ in diameter can be measured and a number of chemical elements determined in the volume of a single mammalian cell Bioelectric potentials are discussed very thoroughly by E E Crane, who considers many things from the cell wall of an amœba to electric fishes which generate 6 kilowatts, he has a valuable section on bioelectric potentials in relation to secretory function

---

[1] Fletcher C M. *Brit med. J* 1948 1, 1015 1065

[2] Cochrane A L Fletcher, C M Gilson J C Hugh Jones, P *Brit J industr Med.* 1951 8, 53

[3] *Lancet* May 19 1951 p 1129

[4] Meiklejohn, A *Brit J industr Med.* 1950 7 105

This volume of critical reviews represents an important pioneering effort on which editors and authors are to be congratulated Further volumes to cover other aspects of the subject are promised, and they will be welcome

Infant Feeding and Feeding Difficulties

P R EVANS, M D, F R C P, director, department of child health, and children's physician, Guy's Hospital, physician, Hospital for Sick Children, Great Ormond Street, RONALD MAC KEITH, M R C P, assistant children's physician, Guy's Hospital London J & A Churchill 1951 Pp 255 12*s* 6*d*

THIS book reminds one of Mrs Beeton Wherever one opens it and reads in it for a quarter of an hour, it is informative, interesting, and attractive to read On the other hand it is difficult to imagine anyone reading it through If he did so, he would not easily derive from it a coherent practice of infant management, as the authors in the preface claim he should This is because the material, though full and up to date, does not seem digested, nor entirely self-consistent, and sometimes there is no summing-up of the evidence This is the case in the very important matter of whether natural feeding is really superior to artificial The evidence of Grulee's figures is given, and also Stevenson's argument that extra vitamin A abolishes the difference, but no balance is struck Occasionally (as though to compensate) there is a sweeping ex-cathedra statement without a word of supporting evidence, such as "If the mother is a child, breast feeding is undesirable" No definition of a "child" or "undesirability" is given

Such defects are not very important if a book is used as a work of reference Among its merits from that point of view are a host of small practical details such as the size of the cup to use for children and how to shape a teaspoon for infant-feeding These show great experience of the job and an uncommon appreciation of the difference that "wrinkles" can make to the doing of it One must also commend such a passage as "An adequate food supply is not the only thing the baby needs to grow happily The baby grows by breathing, exercising, feeding and feeling He needs fresh air, food, warmth, stimulation and security, which a loving mother will provide"

Über den Blutfarbstoffwechsel gesunder Säuglinge und Kinder

WILHELM KÜNZER Dozent an der Universität Würzburg Basle S Karger 1951 Pp 86 Sw Fr 11

THIS monograph deals with the fall of hæmoglobin during the first three months of postnatal life This fall has been attributed by different authors either to increased hæmolysis or to decreased regeneration of red cells Dr Künzer gives results of detailed studies of hæmoglobin levels, reticulocyte counts, blood-volume estimations, and quantitative estimations or urobilin and bilirubin in the fæces, and draws the conclusion that increased hæmolysis is responsible for the postnatal fall of hæmoglobin He attributes this to an increased vulnerability of fœtal hæmoglobin, which, as is well known, differs from the adult hæmoglobin in many ways Details of blood-pigment metabolism are discussed, and a useful method for the quantitative determination of bilirubin in the stools is described

The Chordates

HERBERT W RAND, PH D, associate professor of emeritus, Harvard University London H K 1950 Pp 862 45*s*

THIS lively and encyclopædic account of all the e logy, histology, morphology, comparative an (including its history), classification, and vert zoology that a student needs to know for an ho degree is profusely illustrated, and there is a gen supply of bold type, standing out like traffic light guide him This is no tome of dry description, author gets quickly down to rock-bottom prin and builds up from them Moreover he writes in clear English, the proofs have evidently been very fully read, and the index is satisfactory, but there not seem to be a single reference to any other work ex under the illustrations (which all seem to be borrow and in the account of the *history* of compara anatomy A paragraph *in the preface suggests* t this omission is deliberate, *because of the* diffic in indicating *appropriate collateral reading to* student

Design for Sanatoria

Report of the N A P T Architectural Committ London National Association for the Prevention Tuberculosis 1951 Pp 128 12*s* 6*d*

THREE years ago the National Association for th Prevention of Tuberculosis appointed a special committe to discuss the design and construction of sanatoria an chest hospitals of the future This committee of seventee included five medical superintendents, one sanatorium matron, a consulting architect, and two consultin engineers, and it was advised by eighteen othe specialists, including a radiologist, two pathologists, a pharmacist, a physiotherapist, three thoracic surgeons, one chest physician, and four clergymen. There may have been some ex patients among this galaxy of experts, but ex officio the patient was not represented. It is not surprising therefore that this volume, striving as it does with great success to reconcile the desiderata of all its contributors, should occasionally seem to overlook Absent Friends

The ideal sanatorium is envisaged as having 200–250 beds divided into wings, "houses," or ward units *of 30* beds, and as being destined to last for the next *30–50* years Many things are considered in detail the site and size of the sanatorium, the structure of its building, its windows, balconies, roofs, doors, fittings, heating, lighting, floor-covering, decoration and equipment of rooms, cleaning, garbage and sputum disposal, kitchen and food transport, dishwashing, laundry, chapel, and mortuary The *layout* is lavish, the pharmacists occupying 8 rooms, the pathologists 9 (though they may manage to jog along with 7, or even 6 if they can share their library with other bodies) Similarly surgeons, radiologists, physiotherapists, and occupational therapists all need a good deal of elbow room, and the administrative block must have offices to accommodate a clerical staff of twelve Some 80% of the patients, however, have a quarter of a bedroom each, and though there is a central hall for concerts and film shows, and an abutting library and quiet room (and if possible a separate television room), there is no mention of lounge common room, or small games department, or of any revolving shelter in the grounds whither a patient might repair for respite from his fellow men

Until large quantities of money and building materials become available, and large staffs, both nursing and domestic, can be coaxed into tuberculosis work this is likely to remain a sanatorium in the air Military hospitals can spring up almost overnight, and vast accommodation of one sort or another would be quickly forthcoming in the event of a savage epidemic of small pox, typhus, or some such *quick killing* disease, but towards tuberculosis we have been comparatively apathetic Why, it may be asked, not adapt existing buildings for the present emergency? A foreword warns us that this temptation should be resisted on grounds of running costs and efficiency Certainly nobody contemplating building a sanatorium can afford to miss reading this book, but who, having read it, could afford to build the sanatorium?

Fortunately for the schools, two new sources of help have appeared in December, 1950, the American Medical Association established a foundation with an initial appropriation of $500,000 to help the medical schools, and last week, in New York, another organisation was formed for the same purpose This organisation, the National Fund for Medical Education, is being sponsored by the medical profession, educational and scientific foundations, a group of university presidents, industry, agriculture, and organised labour, and its chairman is Mr Herbert Hoover Its objectives are to inform the public of the plight of the medical schools and to raise from private sources a minimum of $5 million annually for their benefit The Fund will be helped by the foundation set up by the A M.A , which has agreed to merge its funds with those of the new organisation All money collected will go to the schools because the costs of administration will be borne by twelve foundations

PANIC IN THE STREETS

THE possibility that an atomic attack on a modern city might cause widespread panic is exercising official brains, and in this country a Home Office working party is pursuing inquiries, partly by means of questionaries issued to the police about the estimated movements of population From the U S.A comes an article[1] reviewing the causation and prevention of panic and measures for its control.

Panic, says this article occurs when overmastering fear, especially of the unknown causes a group to lose its sense of solidarity and to disintegrate into a disorganised mass of individuals, whose behaviour may be antisocial and lacking in the essentials for individual self preservation Contributory factors are those lowering morale—tension, insecurity, rumours imitative behaviour due to heightened suggestibility, lack of previous information about the nature of the danger, and strong sensory stimuli such as noise To these might well be added such physical factors as hunger, fatigue exposure, and pain Preventive measures should be based on organisation to maintain essential services communications police and fire, rescue, first aid, and medical, sanitation, welfare, civil defence, including anti radiation or anti-chemical warfare, engineering and demolition and transport, both for maintaining the foregoing and to effect any necessary evacuation of survivors In general, the higher the standard of education and intelligence among a population, the less is the risk of panic reactions Cantril et al.[2] in their investigation of the famous mass panic following the Orson Welles *Invasion from Mars* broadcast in 1938, found that college graduates were more resistant to the general alarm than people who had been educated at grammar school, even so, 28% of the panic stricken sample interviewed were college graduates Specific information beforehand about a possible danger would help people by removing the unknown element in their fears Such information should be accompanied by allocation of active roles to members of the threatened community to give them a sense of increased solidarity They should be warned about spreading rumours and told how to deal with them, and instructed in the various physical and mental reactions that acute stress may evoke, so that they may better understand and tolerate such reactions in themselves and their fellows Methods of handling crowds, blocking routes of mass flight, and segregating panic reactors would be a matter for the civil authorities

The American workers recommend that psychiatric casualties should be dealt with, as far as possible, without removing the patient from his family or group setting The secondary gain of neurotic illness should be minimised and the suggestion of disability avoided. Screening of psychiatric casualties should be carried out at casualty-collecting points where sedation can be given and shock, exposure, and fatigue treated Psychotherapy should be brief, consisting of reassurance, support, and exhortation this should be enough for most patients, who would then be fit to return to the population Others would need to be evacuated, preferably to hospitals not far removed, for more intensive psychiatric care. The detail in which the latter is discussed and the comparatively ample facilities debated as makeshift measures, would bring a sardonic smile to the Asiatic face, for they call to mind MacCurdy's[3] remark that Westerners cannot face the prospect of misery "Except in the coldest of winter months, in the absence of available buildings, adequately heated tents will constitute acceptable facilities Folding canvas cots would be acceptable in lieu of beds"

For the average man, morale depends upon his feeling himself to be under the protection of some accustomed figure of authority, whether this be Providence, the Government, Mr Herbert Morrison's signature on a passport, or merely the shadowy "They" whom he alternately reckons on and reviles The solidarity of a group, according to Freud,[4] results from its members being identified with one another by virtue of their common emotional bonds with the "leader" If the leader or his surrogates are lost or demonstrably impotent to cope with the situation the group falls to pieces and the individual feels atomised and abandoned The external danger then becomes overwhelming because he is facing it in a state of agonising mental loneliness comparable only to the terror of a young child separated from his mother That all the individual members of a group do not get into this state of panic is presumably because the more fortunate of us, even if physically sundered from our leader figures, feel enough self confidence, through having taken them and their precepts into our moral being, to cope with whatever danger confronts us as we imagine what they would do ideally Paradoxically, it appears that the essence of a true democracy is for each one of its citizens to be able to slap himself on the chest and exclaim, in the words of le Roi Soleil "L'État, c'est Moi!"

PREVENTION OF TETANUS

TETANUS is not notifiable in England and Wales, but the General Register Office records that 48 males and 21 females died of the disease in 1948 Conybeare and Logan[5] have shown that the death rate among males is now about half what it was during the years 1931–40, while the female death rate has declined little Of the 36 children who died from this cause between 1938 and 1947, 29 were under a month old, most of these infants were males Three times as many fatal cases occur in rural areas as in Greater London and the large cities and the east and south west of the country suffer more than other regions.

Although the over all risk of tetanus is small, the disease is so distressing and the mortality so high that the question of when to give antitetanic serum must constantly be faced The decision usually depends on the extent, nature, and depth of injury, but Pratt[6] showed that of 56 Boston children who developed tetanus 80% had only minor injuries or superficial scratches. Unfortunately A.T.S may cause serum sickness or severe hypersensitivity reactions, so the practitioner's dilemma in treating minor injuries may be very real Since the of whom were vaccinated with BCG in 1935–37 A persistent high degree of tuberculin sensitivity was commoner among the unvaccinated than the vaccinated, but in certain areas the changes in skin sensitivity suggested that some of the vaccinated had undergone superimposed infection with virulent tubercle bacilli In one community the fluctuations and reversions from positive to negative were more common in both vaccinated and unvaccinated than in any of the other Agencies This waning of sensitivity was thought possibly to be related to climatic factors such as excessive sunlight, which might decrease the general reactivity of the skin In the U S A geographical variations in the pattern of tuberculin sensitivity have been observed before Palmer and his colleagues[7] noted that a low level of skin sensitivity was much more common in some of the southern States than elsewhere in the country, and they suggested that in these areas infection by acid fast bacilli other than the tubercle bacillus may account for some of the weak skin reactions to tuberculin It was in men from the south eastern States, too, that Michael and his colleagues[8] found among army personnel the highest incidence of sarcoidosis, in which tuberculin skin sensitivity is often low or absent

---

[1] Caldwell J M. Ranson S W Sacks J G *U.S Armed Forces med J* 1951 2 541

[2] Cantril H Gaudet H Hertzog H. Invasion from Mars. Princeton 1940

[3] MacCurdy J T Structure of Morale. London 1943 p 13

[4] Freud S Group Psychology and the Analysis of the Ego. London 1949

[5] Conybeare, E. T Logan W P D *Brit med J* March 10 1951 p 504

[6] Pratt, E. L *J Amer med Ass* 1945 129 1243

The work of Palmer and Meyer on familial factors in the response to BCG vaccination, and Aronson's indication of possible climatic factors in the intensity of the tuberculin skin reaction, are examples of what can be achieved when the artificial tuberculin infection produced by BCG is used both as a research tool and a prophylactic measure

---

[7] Palmer C F Petersen O S *Publ Hlth Rep*, *Wash* 1950 65 1 Palmer C E, Ferebee S H Petersen O S *Ibid* p 111

[8] Michael M, Cole R M Beeson P B, Olson B J *Amer Rev Tuberc* 1950 62 1403

Annotations

MEDICAL DISCIPLINARY COMMITTEE

Doctors have observed an ethical code since the time of Hippocrates or even earlier In this country the professional corporations from their foundation maintained discipline among their members, in 1578, for instance, the Incorporation of Barber Surgeons of Edinburgh forbade Duncan Hunter to exercise any surgery or barbercraft in the burgh under penalty of ten pounds (Scots) because he had employed an unqualified assistant In 1858 the Medical Act set up the General Medical Council to regulate medical education and enforce professional discipline, and at first all members were doctors The council, in the exercise of its disciplinary powers, was criticised on occasions, and as a result of the Axham case in 1926[1] lay members were introduced But whatever its faults the Council has served as a model for other professional organisations

It had for some years been felt that to take up the time of a large body of senior professional men to hear every case was wasteful, and under the Medical Act of 1950 a small committee of the council becomes the "court" of the profession The Law Society also has a small committee for this purpose, but the origin of discipline in this profession is the courts, from which it derives the tradition of a small body The Pharmaceutical Society has a disciplinary body, and the Royal College of Veterinary Surgeons, which has exercised disciplinary powers over veterinary surgeons since 1849, adopted the practice of a small committee under the Veterinary Act of 1949

The General Medical Council now has two committees concerned with disciplinary business The Penal Cases Committee, made statutory under the new Act, is a "court of first instance" in that it decides whether there is a *prima facie* case to be dealt with by the Medical Disciplinary Committee A complaint may prove to be too trivial, or a doctor who has had a first conviction recorded against him in a court of law may not have to be brought before the Disciplinary Committee unless he commits a further offence The members of one committee may not be members of the other, except for the president, who presides over both The Medical Disciplinary Committee consists of 18 members Cases are heard by 9 members, with a quorum of 5, unless it appears to the president that "there are circumstances requiring the presence of a greater number of members of the committee", this procedure was adopted in one of the cases at last week's session which presented unusual features When 9 members are sitting 1 lay member and 2 direct representatives must be invited to attend In their deliberations the committee is assisted by a legal assessor An important difference between the new committee and the council under the old procedure is that the committee has the power to cause the oath to be administered—a power which it exercised in every instance at its first penal session. The committee, like the council before it, is also responsible for striking dentists off the Dental Register Such cases are heard by the Dental Board, and if the board thinks that the dentist should have his name erased from the Register, a recommendation is made to the Medical Disciplinary Committee and may be challenged before that committee Possibly, when legislation is introduced to amend the Dental Acts the Medical Disciplinary Committee will no longer act in this way

One of the most celebrated cases against the General Medical Council, and the only one which went on appeal to the House of Lords, resulted in the ruling that the council had not made "due inquiry" because it refused to allow evidence not before the Divorce Court to be called The Medical Act, 1950, reverses the rule in the Spackman case Whether this will be an advantage to justice remains to be seen The chief criticism of the old procedure was that there was no appeal from an erasure Now any practitioner whose name is deleted from the Register may, under Section 20 of the 1950 Act, appeal to the Privy Council within twenty eight days

HELP FOR AMERICAN MEDICAL SCHOOLS

Medical schools in the United States are in serious financial difficulties As noted in our leading article last week, a committee set up by the Surgeon General of the U S Public Health Service has reported that, though research grants to medical schools almost quadrupled between 1941 and 1948, the funds for maintaining the schools themselves did not increase on anything like the same scale The inability of the schools to expand is one reason why only a third of the students who complete their premedical education can find places in them—and this at a time when, according to the Federal Government Reorganisation Commission,[1] the number of trained doctors is "woefully inadequate for the conduct of national defence, for the Federal hospitals, and for the needs of the people generally"

It is estimated that an additional $40 million a year is needed—$10 million for the public schools and $30 million for the private schools But, as the Surgeon General's committee points out, it is doubtful whether this extra money can be got from the existing sources

---

[1] See *Lancet* 1926 i 1116

[1] *New York Times* May 17, 1951 p 1

Special Articles

ADMINISTRATION OF DRUGS

HAZARDS AND PRECAUTIONS

W. TRILLWOOD
Ph.C.
CHIEF PHARMACIST, UNITED OXFORD HOSPITALS

IN handling drugs the nurse may be exposed to both unavoidable and avoidable risks.

As regards unavoidable risks, the strain on nursing staff has never been more intense; even in hospitals where there is no shortage of nurses, the intensity of work is maintained by the pressure of heavy waiting lists. Hospital authorities have repeatedly stated that in a general hospital taking acute cases the optimum bed-occupation is 85%; yet many hospitals are working at 90–95% and even higher levels. It does not seem to have been acknowledged that one possible source of errors is overwork.

Another risk is related to innovations in drug therapy. During the last decade the range of potent drugs in daily use has increased enormously. Ten years ago some of the potent drugs now in common use would have been rejected as too toxic; but new techniques of control have been evolved to make possible their use in therapeutics. There has, however, been no parallel evolution of safety precautions to protect the nurse from errors in administering these substances. Indeed, the nurse is at a particular disadvantage in that her knowledge of drugs and treatments is based on a syllabus outdated by at least fifteen years. She is, for example, required to have some knowledge of linseed poultices, cupping, blisters, and leeches; but officially she is not aware of the sulpha drugs and antibiotics. Nevertheless she is expected intelligently to administer these substances with whatever information she can gain from ward practice. In any event her training in materia medica is inadequate; and if she is to be kept abreast of developments the syllabus must be revised at short intervals. The nurse should, it seems, have a longer general course which would include the basic principles of prescription reading and of drug administration, storage, checking, control, and sources of information on the properties, dosage, and therapeutic effect of new drugs.

AVOIDABLE RISKS

Prescribing by Nurses.—There is a fairly widespread tendency for the hospital nurse to prescribe routine drugs. This is a practice for which she is not fitted; indeed, with certain drugs it is illegal. It would be wise to implement the standing order for ward sisters drawn up by the Royal College of Nursing which expressly states that the ward sister "shall on no account give medicines to patients without the written authority of the medical attendant."

Failure to Read a Label.—This is one of the richest sources of mishaps. Under this heading should be included the alteration of a label, or the re-labelling of a drug by the nurse; the administration of a drug from an unlabelled container; and the transfer of a drug into an unsuitable container (e.g., lysol into a lemonade bottle or, worse still, into a graduated medicine bottle). The dangers of these practices should be emphasised repeatedly, until as a routine the nurse reads, re-reads, and checks every drug label before and after use—until any container that is not labelled or is not clearly labelled, or whose contents are otherwise in doubt, is rejected or destroyed.

There is a special variant of this risk in the practice of measuring doses of drugs into a series of unlabelled gallipots or spoons. This procedure is usually carried out at the drug cupboard, wherever this happens to be. The nurse administering drugs is charged with a tray bearing the unlabelled gallipots or spoons, and is expected to remember which drug is for which patient, with no clue to the identity of the drugs apart from their colour and consistency. I suggest that the labelled medicine containers should be taken to the bedside and each drug measured, checked, and administered on the spot.

Administration of a Drug to the Wrong Patient.—This is fortunately rare, but the risk has to be seriously considered. Patients are impressed by the speed with which nurses learn to address them by name; and for day staff this knowledge is obviously the main safeguard; but for a night sister supervising several wards of sleeping or unconscious patients the safeguard is less certain. Name discs attached to the person of the patient would seem to be the only sure means of identification.

Failure of the Checking System.—This is the greatest source of potential danger. In his home the patient usually has direct access to the drugs prescribed for him; the drugs are dispensed in labelled containers so that, provided the patient can read and that he follows the directions, there is little risk of mishap. In hospital practice, however, the nurse intervenes as a third party. The law does not demand that any particular nurse—or indeed that any nurse at all—shall check another nurse before a drug is given. But it is a matter of common sense that the senior nurse available should check her colleague; and no nurse, however senior, should feel that her dignity is jeopardised in calling for a check.

In busy medical wards with many patients, some perhaps having several drugs at different intervals, it is difficult for the nurse to select the drugs to be given at any particular time. Usually this difficulty is overcome by means of a "medicine chart." The sister compiles a list of patients in her ward under time headings, and from the original prescription sheets she copies the name and dose of the drug prescribed. Thereafter this copy of the original documents becomes the chart by which all drugs are administered and checked. This procedure is extremely dangerous. First, a mistake in copying from the original prescription is perpetuated; indeed, when a fresh chart is prepared details are re-copied from the old one and any mistake is renewed. Then there is likely to be a time-lag in copying a new prescription or in changing an existing prescription on the chart. In a busy medical ward this is very liable to happen, and most sisters are aware of the danger. In fact every sister questioned by me in an investigation in the Oxford region admitted freely that prescriptions were sometimes written or altered without her knowledge. To counter this risk several different systems are used; the most precarious is that which depends on the doctor telling the sister that he has made a change of drug or dosage. Neither the sister nor the doctor seems to be alive to the risk of forgetting to tell, or of not remembering what was told. One can conceive of an adverse laboratory report necessitating an immediate reduction in dosage of a potent drug; but because of a misunderstanding between nurse and doctor the change is not copied for some time on to the "medicine chart" and the patient thus continues on the higher dosage.

PLAN FOR IMPROVED CHECKING SYSTEM

In formulating a new method for avoiding these risks, it is axiomatic that the original prescription should be the focal point of every checking system; and that no drug whatever should be administered by a nurse without direct reference to the original prescription each time a dose is given. A prescription, like a cheque, is an order in writing, and as such it needs no verbal instruction before being honoured. But it is also an order to the pharmacist, who will require the original document to prepare the drug; and if, for this or other reasons, the prescription is not on the ward when it is required direct

1914–18 war few have doubted the prophylactic value of ATS , the disease may still arise even after adequate doses,[7] but this seems to be very rare With massive infections of mice Taylor and Novak [8] found that local injection of procaine penicillin G was more effective than specific antitoxin in prophylaxis The bacilli are penicillin sensitive and it may be possible to achieve adequate concentrations at the site of production of toxin, but this would not obviate the need for ATS The main problem, however, is not the efficacy of ATS as a temporary cover but to ensure that those most liable to the disease shall be protected During the late war British troops were immunised with two doses of tetanus toxoid, and if wounded they received ATS as soon as possible after the injury as possible , American wounded received a boosting dose of toxoid in place of antitoxin There were very few cases of tetanus in either army An effort to secure similar protection among certain groups of civilians is being made in several countries, but the practical difficulties are great We have to remember that two doses of 1 ml. of toxoid are required, separated by an interval of at least six weeks, and that a third dose, 6–12 months later, should also be given Severe reactions to toxoid are now very rare, and it can be given subcutaneously without causing a local reaction In America, where toxoid is often combined with diphtheria prophylactic or pertussis vaccine, immunisation against tetanus is widely practised

Bigler [9] immunised 300 children and infants during 1938–39, and he found that with two injections of toxoid protective levels of antitoxin were not always obtained He recommends that a booster dose of toxoid should always be given no matter how short the interval between the initial injections and wounding Detectable amounts of antitoxin were present in the blood serum of all immunised children ten years after inoculation, and the response to a boosting dose occurred within 7 days There is little doubt that toxoid could prevent most, if not all, civilian cases of tetanus , and there certainly seems to be a case for offering it to school-children in rural areas, where the risk is greater than in the cities Conybeare and Logan suggest that this could be done when they receive their boosting dose of diphtheria prophylactic on entry into school.

RETINAL CHANGES IN AORTIC COARCTATION

A SIGN that may help in the diagnosis of coarctation of the aorta has lately been described by Granstrom [10] Of 40 patients with coarctation who were referred to him for routine fundus examination, 24 had increased tortuosity of the retinal arteries This tortuosity was often widespread but sometimes it was confined to isolated sectors In extreme instances it amounted to corkscrewing of the arterial loops, some of which were embedded in retinal tissue , in others it was less pronounced but "sufficient in degree to be characteristic" This abnormality was more usual in patients over the age of 25 and it was unaffected by operation for the coarctation Associated changes in arterial calibre and at the arteriovenous crossings were at the most slight , and hæmorrhages and exudates were entirely absent The veins (unlike those in congenital tortuosity of the retinal vessels) showed no undue tortuosity Granstrom associates this sign with the generalised coiling of the arteries of the upper half of the body often found in coarctation Since a certain amount of increased tortuosity is not uncommon in normal fundi it may be difficult to decide when the change is pathological Of Granstrom's 24 cases in which the sign was regarded as present, only 7 were classed as having "marked corkscrew tortuosity," while 17 had "slight but unmistakable changes" In assessing the sign much will obviously rest with the eye of the beholder

SICKNESS INSURANCE IN SWEDEN

SWEDEN was late among the European countries in adopting compulsory sickness insurance on a national scale In August, 1947, however, a comprehensive scheme applying to virtually all Swedish residents passed through parliament This was to have been brought into operation on July 1, 1951 , but, owing to financial difficulties, parliament decided last December to postpone the date

Under the scheme,[1] contributing members and their dependents are entitled to medical care with free choice of doctor and hospital Remuneration of both general practitioners and specialists is based on a scale of fees for services rendered , 75% of these costs is borne by the insurance societies, and the remainder by the insured persons themselves Doctors are not obliged, however, to restrict their fees to the amounts prescribed in the scale , they may charge, and the patients may pay, higher fees , but the patient is not entitled to recover from the insurance societies more than 75% of the fees on the official scale The doctors receive mileage payments, and the expenses necessarily incurred by insured persons in travelling to receive medical treatment are reimbursed when the cost exceeds 3 crowns (there are 14½ crowns to the pound sterling) The scheme provides a maternity benefit—a lump sum cash payment—and periodical cash payments to patients certified as incapable of work, the amount of the latter varying with the contributions paid Sickness payments, however, are granted only to people whose annual earnings exceed 600 crowns Others may insure for medical treatment only, and they pay a reduced contribution Sickness payments are not payable during the first three days of incapacity Medical supplies will be obtainable free or at reduced cost The benefits of the scheme do not include such forms of treatment as massage, electrotherapy, or therapeutic gymnastics , but insured people may become entitled to these as supplementary benefits through the voluntary insurance system, to which the State grants subsidies equal to 20% of the contribution income This voluntary system also provides supplementary sickness benefits in cash, but the total cash benefits of the compulsory and voluntary systems may in no case exceed the earnings of the insured person

The scheme will be administered locally by the existing sickness insurance societies, which are to be reorganised Each insured person is required to join a society in his district The societies are supervised and directed by the National Control Council, but they have a considerable measure of local autonomy The control council fixes the contributions payable to the insurance fund, and distributes the contribution income in due proportion among the societies The total cost of the compulsory scheme in the first year of operation will, it is estimated, be 237 million crowns The State will contribute 70% of this sum, the remainder being covered by the income from contributions Special legislation is to be introduced for universal free provision of hospital treatment Local authority hospitals will receive a State subsidy of 2 crowns per patient per day

REMUNERATION OF GENERAL PRACTITIONERS

AT a whole day meeting on May 24, the General Medical Services Committee considered the latest proposals from the Ministry of Health for adjusting the remuneration of general practitioners in the National Health Service The committee was not satisfied with these proposals , and it decided to send its observations to the Ministry, asking for an immediate reply

---

[7] Smith, E J R *Proc R Soc med* 1942 35 340

[8] Taylor, W I Novak M *Ann Surg* 1951 133 44

[9] Bigler J A *Amer J Dis Child* 1951 81 226

[10] Granström K O *Brit J Ophthal* 1951 35 143

[1] See *Bull int soc Security Ass* 1951 4 28

GENERAL MEDICAL COUNCIL

As we reported last week, the presidential address by Prof David Campbell opened the session of the General Medical Council on May 22 The Medical Disciplinary Committee, the body which in future will hear penal cases under the Medical Act, 1950, sat for the first time for the hearing of such cases on May 24, but there remained some cases postponed or adjourned from previous sittings which the whole council heard on the first day, after taking dental disciplinary cases

POSTPONED JUDGMENTS

The council did not see fit to direct the Registrar to erase from the Register the names of the following practitioners in respect of whom judgment had been postponed for one year *Thomas Dunbar* registered as of 63, Finlay Drive Glasgow, E 1, M.B. Glasg (1943), and *Peter Augustine Smyth*, registered as of 33, Lillie Road, London S W 6, M.B N U I (1927)

In May 1950 the Council postponed judgment for one year after having found *Garden Hepburn Sicapp*, registered as of 8, Bath Street, Stonehaven, Kincardineshire M B Aberd. (1928), proved to have been convicted on charges of being in charge of a car while under the influence of drink. After hearing that the practitioner had been convicted of a similar offence earlier this year and that his appeal against this conviction was to be heard in the *High Court of Justiciary in Edinburgh*, the council decided to postpone judgment further until its session in November, 1951

Judgment on *Joseph Kevin Conlan* registered as of 81, Strubbington Avenue, North End, Portsmouth, M.B Durh (1940) was in May, 1949, postponed for two years the practitioner to appear at the session in May 1951 and produce testimonials Dr Conlan was not present but a letter from him and enclosed testimonials were read. The President announced that the council had decided to await the further appearance of the practitioner in November 1951 when he would be expected to produce full and up to-date testimonials as to his conduct

NEW CASES

The President announced that the council had directed the Registrar to erase from the Register the name of *Stanislaw Gerlecki* provisionally registered as of flat 2, 132, Cromwell Road, London, S W 7, MED DIP Warsaw (1930) The case was heard in camera.

Gurdit Singh Malik, registered as of 1, Hailey Road, New Delhi India, M.B Lond. (19_7) was charged with having given an international certificate of inoculation against yellow fever for Mrs. Edill Sydney Smith, of 10, Wenger's Flat, New Delhi, when he had not inoculated her, this certificate being untrue, misleading and improper within the meaning of paragraph 1 of the Warning Notice The case was postponed at the November session to enable the practitioner to arrange to be legally represented. Dr Malik did not appear and was not represented. The council decided to hear the case in his absence

Mr F P Winterbotham, solicitor to the council, presenting the facts, explained that India had taken considerable precautions against the entry of yellow fever, and the issue of a false certificate would defeat the purpose of the government There was no date on the certificate, but it stated that it was not valid "for more than 4 years from the date of the last inoculation 15-6-48' It gave the origin and batch number of the vaccine as 'Haffkine no 426" It had been found that no such tube of batch no 426 had been used for yellow fever, it would seem, therefore, that the practitioner had made a false statement

A letter from the practitioner to the Registrar of the General Medical Council, which Mr Winterbotham read, stated that Mrs. Smith came to him first in January 1948, for a cholera injection as there was a scare of cholera in New Delhi 'She came back again in June, 1948, for cholera injection which was due as she was going back to Europe She had her necessary injections which were entered in the book of certificates supplied to her by Air India, Ltd" She already had a certificate for yellow fever inoculation, given to her by an army medical officer in 1947 Dr Malik explained to her that she was protected for four years and did not need another injection until 1951 But she insisted on having a certificate written in the book, as it would be more convenient for her to have all the certificates together 'Knowing that she was protected against the infection, I complied with her request, which I would never have done otherwise" Dr Malik's letter stated that he gave an explanation of the facts to the director-general of health services, government of India, and at his request produced the original certificate issued to Mrs Smith by the army medical officer "Thereafter I was given to understand that my explanation was accepted and no action was to be taken against me" He ended "I sincerely apologise for the indiscretion committed by me and I hope you will kindly be pleased to overlook my lapse"

Mr Winterbotham said that the government of India took a serious view of the case because Dr Malik was extending the immunity for a period beyond that to which it ought to extend after the inoculation on March 31 1947 A letter from the director-general of health services, India, further explained that Dr Malik's name was not borne on any provincial Medical Register in India, and therefore the matter came before the council.

After consideration in camera, the President announced that the council had found the facts alleged proved to their satisfaction, and, that in relation to the facts so proved, the practitioner had been guilty of infamous conduct in a professional respect They directed the Registrar to erase from the Register the name of *Gurdit Singh Malik*

COMMITTEE APPOINTMENTS

At its sitting on May 22, the council elected the following to form the Medical Disciplinary Committee

Members for England and Wales—Dr W Russell Brain, Prof R J Brocklehurst, Dr J A. Brown*, Dr O C Carter* Sir Henry Cohen Dr H Guy Dain*, Prof R B Green, Dr E A Gregg*, Lord Nathan†, Sir Cecil Wakeley

Scotland—Dr R W Craig*, Miss Florence Horsbrugh, Dr J A. Kerr Sir Sydney Smith

Ireland—Dr James Boyd, Dr Frank Kane*, Mr R A Stoney

*Direct representative †Lay member

The council elected the following to the Penal Cases Committee

England—Dr J P Hedley, Mr J B Hynd, Mr N E Waterfield.

Scotland—Mr Andrew Allison.

Ireland—Prof J M. O Connor

Under regulations approved by the council, members of the Medical Disciplinary Committee will hold office for one year, and will be eligible for re election The committee elected at the May sitting will, in future, hear cases in November and in the following May, and at any intervening session The president is an ex officio member of the committee

BUSINESS OF COUNCIL

Dr HEDLEY, presenting the report of the Finance Committee, said that there was a deficit on the accounts for 1950 of £3293 One of the largest items of expenditure (£2840) had been the cost of exceptional repair work and alteration of premises which was not recoverable from the War Damage Commission The result of the increase in registration fees from £5 to 11 guineas, which came into operation on Oct. 11, 1950, was already obvious, and Dr Hedley said that in the next year or two, when the amount spent on the repairs and improvements had been wiped out, the council would be comfortably off financially

Dr DAIN chairman of the Pharmacopœia Committee, reported that 40 094 copies of the *British Pharmacopœia* 1948 and 3721 copies of the *Addendum* 1951, had now been sold. The report of the British Pharmacopœia Commission stated that building repairs to the laboratory were now complete It was expected that chemical checking may not be possible It is at this point that the present system fails

Because a prescription may be required in two places at the same time, it follows that there must be at least two identical documents—the original and a facsimile—one to be used by the pharmacist, the other to be kept on the ward as a check for the nurse and for the information of the prescriber The "medicine chart" should be discarded, together with the usual individual prescription sheets Instead, each ward should have an interleaved prescription pad, on which drugs may be prescribed for any patient in the ward The pages of the pad are perforated so that five prescriptions appear on each leaf, the under side of each alternate leaf is coated with carbon black and is adhesive at one edge Automatically each prescription will appear as a facsimile on the perforated under leaf

The upper, original prescription slip is sent to the pharmacist and retained by him until the patient is discharged Then all the prescription slips issued for this patient, pasted in chronological order on to standard size sheets of paper will be returned to the ward for filing with the patient's case history Thus the original prescriptions with details of all the drugs supplied to each patient will be preserved for record purposes The pharmacist will not be aware of the cancellation of a drug therefore, to complete the record, the date of the cancellation should be noted on the original prescription when it is eventually returned for filing

The facsimile prescription is kept on the ward Each patient will have a printed prescription mount to which each facsimile prescription is affixed by means of the adhesive edge. Mounts are arranged in patient order for the convenience of the prescriber, the prescription sheets on the mounts are arranged in time order for the convenience of the nurse Sections on the prescription mount correspond to the usual medicine rounds so that the nurse administering drugs can readily pick out the drugs required for each patient This arrangement avoids the need to make a copy "medicine chart" The nurse uses the prescription mount every time a dose of medicine is administered When the patient is discharged his prescription mount bearing the facsimile prescription slips may be destroyed

By means of the prescription mount the prescriber has on one sheet of paper complete up to date details of all the drugs being administered to each patient If a drug is to be stopped, or the drug or dosage is to be changed, the prescriber cancels and dates the appropriate facsimile prescription slip and writes a new prescription if required Thus any change in treatment will be immediately effective without verbal instruction or confirmation It follows also that no drug will be administered without a written authority, and that unauthorised prescribing will be prevented

My thanks are due to Miss M J Marriott, hon secretary of the Association of Hospital Matrons for permission to use the report of the annual general meeting of hospital matrons, 1950 I should also like to thank the many members of the nursing staffs of hospitals in the Oxford region for their frank discussion of the nursing problems and practice

Specimen copies of the prescription pads and prescription mounts may be obtained from Messrs. Maestrom Ltd, Holly Lane, Birmingham, 24

PROVINCIAL TEACHING HOSPITALS

Boards of Governors

THE Minister of Health has made the following appointments, mainly to fill vacancies caused by the retirement in rotation of one third of the members, to the boards of governors of the ten provincial teaching hospitals in England and Wales Of 102 appointments, 78 are reappointments of retiring members, 3 appointments are still outstanding The names of medical members are shown in bold type

UNITED NEWCASTLE UPON TYNE HOSPITALS

Reappointed Robert Muckle, now appointed chairman, Viscount Allendale, C.B, M C Lord Eustace Percy, P C, Viscountess Ridley, J.P, Sir Walter Thompson, J P William Allen, Alderman P S Hancock, J.P, O B E, Mrs. I Horn, M B E

New member Prof B W Abrahart

UNITED LEEDS HOSPITALS

Reappointed Sir George Martin, K B E, J.P, chairman, Prof **Digby Chamberlain,** F R C S M R Hollings B CH.D J C Hunter, W L Lawton, C B E, J P the Rev Canon A S Reeve, W S Hill, W W Powell, Richard Wheater Alderman Joseph Wilkinson, J P

UNITED SHEFFIELD HOSPITALS

Reappointed A Ballard, chairman, **J L. A. Grout,** M.C, F F.R, Lieut Colonel N Gervis Pearson, D S O, M.C, G F Young, J V Bibby, D S O, W R S Stephenson

New members Miss Anne Wetherall D J Haggie; **J E Stacey,** F.R C O G Jack Ford, one appointment outstanding

UNITED CAMBRIDGE HOSPITALS

Reappointed Thomas Knox Shaw, M C, chairman, Mrs. H A Adrian Mrs E M Charvet, W M Francis, Alderman E T Halnan R H Parker, M C, Mrs Emily Parsons, **A. S H. Walford,** F R C S, T G P Spear

New member **Janet E Bottomley,** F R C S

UNITED OXFORD HOSPITALS

Reappointed Sir David Lindsay Keir, now appointed chairman, **E M Buzzard,** F R C.P, Prof **A. D Gardner,** F R C P Mrs G Hewitson, A W H Booth King, **J C Scott,** F R,C S, E A Smewin, **Janet Vaughan,** O.B.E, F.R C.P, Mrs M A Johnson.

New members **Gordon Scott,** M B the Rev John Lowe

UNITED BRISTOL HOSPITALS

Reappointed C C Clarke, chairman, Prof **R. J Brocklehurst,** D M, Prof **A V Neale,** F.R C.P G F Bullock, M.B.E, the Rev K L Parry

New members **J W E Snawdon,** M.B, M D.S. **W A. Jackman,** T D, F R C S E Miss G M Morgan W J Munslow, Philip Hopkins.

UNITED CARDIFF HOSPITALS

Reappointed G D Shepherd, M B E, J.P, chairman, Sir **David Rocyn-Jones,** C B E F R.C S E, J.P, Prof **G L Strachan,** F R C O G, Alderman the Rev W Degwel Thomas, Alderman Sydney Jones Alderman Mrs D M Rees, M P, Alderman R G Robinson, J.P, Ernest Tear, J.P, Sir Ivor Thomas

New members **J D Spillane,** F.R C.P one appointment outstanding Mr Lewis Lewis is appointed for the period ending March 31, 1952, vice Sir Willie Reardon Smith (deceased)

UNITED BIRMINGHAM HOSPITALS

Reappointed S F Burman, M.B E, chairman, C L Chatwin **A. L d'Abreu,** O B E, F R C S Alderman W L Dingley V W Grosvenor W H Newton, E A Norton, W J Simpson, T A Hamilton Baynes

New members Councillor A Shanks, M.C **R. P Scott Mason,** M C, F.R.C.S

UNITED MANCHESTER HOSPITALS

Reappointed C M Skinner, chairman, Percy Chadwick, J.P, T M Larrad Sir **Harry Platt,** F.R.C S Prof **W H Semple**, Prof **W I. C Morris,** F.R.C O G, James Sillavan

New members **F R Ferguson,** F R C P, Mrs C M Spafford, W J Curley, one appointment outstanding

UNITED LIVERPOOL HOSPITALS

Reappointed T Keeling M A, J P, chairman A N Denaro, M.B E, J P Prof **W M. Frazer** O.B E, M.D, Prof **T N A. Jeffcoate,** F.R C O G **J T Morrison,** O B.E., F R C.S; Prof E A. Owen

New members L H Buckley, J.P Mrs. J Bingham, J P, **B L. McFarland,** F R C S T J D Large, O B E

Miss Winifred Armit housekeeper to one of the old ladies on whom Dr Murray called on Sept. 12, said she noticed nothing wrong with him. He was a conscientious man, he looked after the old lady very well indeed and was always completely sober. Dr R G Miller told the committee that he had found Dr Murray an excellent assistant—conscientious, trustworthy, hard working, and very well liked by the patients. When he had completed his sentence Dr Miller would be willing, if the committee's decision allowed it to take Dr Murray back as an assistant, and, if he wanted to take a partner as a partner.

Mr Richards, in his address said that Dr Murray was no confirmed alcoholic. He was a quiet, unostentatious man, who took great care of his patients. This was an isolated incident, brought on by overwork. All the evidence was that the collision occurred on Dr Murray's side of the road. He had been strongly advised to appeal against the conviction, but had refused.

The committee decided that the Registrar should not be directed to erase Dr Murray's name from the Register.

CHARGE OF PROCURING DRUGS

Henry William Miles Williams registered as of Pantacelyn, Merthyr Mawr Road Bridgend, Glam. M.R.C.S (1923) appeared on a charge of having been convicted at Pontypridd Police Court on April 27, 1949 of six offences of unlawfully procuring drugs when he had been fined £15 for each offence, and costs of £10 10s and of being convicted at Porth Police Court, on Nov. 9 1950, of driving a car under the influence of drink or drugs, when he was fined £5 5s and £2 12s 6d costs and disqualified from holding a driving licence for 12 months and of driving a car in a dangerous manner for which he was fined £5 and had his driving licence endorsed. Mr C Morgan, instructed by Messrs. W R. Davies solicitors, on behalf of Dr Williams admitted the convictions which were proved.

Mr Winterbotham, dealing with the offences in 1949 said that during investigations in another matter the police noted that the name Edwards occurred frequently in the register of a chemist for morphine. Edwards was a patient of Dr Williams and it was evident said the police that he was the "messenger" for Dr Williams. There was no direct evidence that Dr Williams himself took the thirty ½ grain morphine sulphate tablets so obtained. After the conviction he signed an undertaking not to obtain dangerous drugs.

With regard to the second conviction, a police constable found Dr Williams in his car his pupils were dilated, and his speech thick. The police officer took a box of tablets, which were found to contain 'Sodium amytal.' Sodium amytal had been prescribed for Dr Williams by a psychiatrist. The chief constable pointed out that sodium amytal was not one of the drugs which Dr Williams had undertaken not to use.

Dr Williams in evidence, said that he served in the line from 1916 to 1918 until, at the age of 20 he was severely gassed with phosgene and mustard gas. After being in hospital for some time he was discharged from the Army. He qualified in medicine. He continued to suffer from the effects of the gassing. He had a slight intention tremor which became pronounced sometimes and prevented him from taking up surgery as he wished. He decided on general practice and joined Dr Clarke in 1937. During the late war the house in which he lived at Porth was destroyed by enemy action whilst he was inside. This seriously affected his health. At some time in the 1940's he started using morphine and obtained supplies through a patient he always paid for them. In 1948 he told Dr Clarke and as a result of the latter's advice went to a hospital as a voluntary patient. Since he had come out of hospital he had not used a dangerous drug. He had been advised to take sodium amytal during attacks of migraine he used no other drug. On Oct 5 1950, he had a bad attack of migraine and took sodium amytal. Dr Williams explained the circumstances which led to his conviction for driving whilst under the influence of drink or drugs on this occasion he had pleaded not guilty. Evidence had been given that a slight trace of sodium amytal was found in his urine and no evidence of alcohol.

In reply to the president Dr Williams said that he had been a partner of Dr Clarke's but after the first offence he had become an assistant. He had taken morphine for about three years he took quite an amount—as much as 3 grains. He was under treatment in hospital for six weeks. Asked by the president if he had severe withdrawal symptoms witness said he had not he had been under deep narcosis. He found the sodium amytal steadied him.

The vicar of Porth, the Rev. J. A. J. Jones said the people had a regard and affection for Dr Williams.

Dr Clarke said he was certain that since Dr Williams came out of hospital he had not taken morphine. The psychiatrist had recommended witness to give Dr Williams sodium amytal. Dr Williams had periodic attacks, and under sodium amytal got over them. In reply to the president, Dr Clarke said he had the impression that Dr Williams got periodic cravings for morphine but he was certain that he had taken none. He told Lord Nathan, a member of the committee, that there had been no complaints from patients about Dr Williams.

Mr Morgan pointed out that Dr Williams had obtained morphine for his own use and there was no question of any fraud on the health service. He had made heroic efforts and had conquered the habit.

The committee did not direct the Registrar to erase the practitioner's name from the Register.

CHARGES OF DRUNKENNESS

John Vincent Gill registered as of 3, St John's Park, Rosetta Belfast M.B Q.U. Belf (1944), was charged with having been convicted at Belfast in 1948 and in 1950 of driving a car under the influence of drink. The convictions were admitted and found proved. He was represented by Mr N Leigh Taylor.

In evidence Dr Gill stated that on the first occasion he had arranged for another practitioner to look after his practice, while he went to a party. He arranged for his wife to drive him home but she asked him to get the car out of the car-park it was while he was doing this that he was arrested. On the second occasion he was also arrested whilst parking the car, he was at that time worried that his wife might have another miscarriage. These were isolated incidents. Since the last conviction he had joined a total abstinence association connected with the Roman Catholic Church.

The committee postponed judgment for one year until May 1952.

Harold Stanley Groves, registered as of the Poplars Blagreaves Lane Littleover Derby M.R.C.S (1915) was summoned to appear on a charge of having been convicted on Oct 10 1949 at the Magistrates Court Derwent Street Derby of driving a car under the influence of drugs, when he was fined £30 and 6 guineas special costs and his licence was endorsed, and of being fined £20 and 7 guineas costs and disqualified from holding a licence for 12 months at the same court on Jan. 3, 1951 for being under the influence of drink to such an extent as to be incapable of having proper control of a motor car.

Dr Groves was not present. Dr D A. Skinner of Taylor Simpson and Morley solicitors, said that although he had advised his client to come he had said he did not feel equal to appearing before the committee. After consideration in camera, the president announced that the committee had decided to proceed with the case in the absence of the practitioner.

The offences were admitted and proved. Mr Winterbotham presented the facts. Mr Skinner said that on the first occasion the drug from the effects of which Dr Groves was suffering was chlorodyne which could be purchased by the public. The magistrates found a special reason why the statutory disqualification, following conviction of driving a car under the influence of drugs should not be imposed. Dr Groves at the time of the offence had been suffering from headache and diarrhœa. Dr Groves ceased practice in April, 1949 and was not engaged in a professional capacity at the time of the second offence. He had an unhappy life with his second wife and it was she who informed the police, who watched him go to his car and as soon as he got in, arrested him. The magistrates imposed a lesser fine on this occasion than they did for the first offence.

The committee postponed judgment for six months, the president saying they would wish to see Dr Groves in November.

James William Hay registered as of 51 Spencer Street Carlisle M.B Aberd. (1924) was charged with convictions of driving a car whilst under the influence of drink, of driving a car without due care, and of being found drunk the offences occurred in 1938 1946 1950 and 1951. The convictions were proved and admitted.

Mr P Strong of Messrs Wright Brown, and Strong, solicitors, said that Dr Hay had been having treatment with Antabuse at Crichton Royal Infirmary and had undertaken not to touch any alcohol in future.

The committee postponed judgment for one year, until May, 1952.

investigations would commence shortly on standards and tests for substances described in pharmacopœial monographs

Educational Business

The annual returns for examinations, presented to the council, showed that seven universities—Birmingham, Cambridge, Dublin, Manchester, Oxford, St Andrews, and Sheffield—and the Scottish and Irish Conjoint Boards held no examinations for diplomas in public health during 1950 Commenting on this, Dr R M F PICKEN said "This 'creeping paralysis' has been going on for years, the public health service has become less and less attractive" This trend had become more marked as a result of the National Health Service Act It was extremely difficult to get candidates to come forward for the D P H, because they felt that it was not worth their while to become medical officers of health The answer could not be found in the council The PRESIDENT remarked that the main source of candidates was London University, along with the English Conjoint Board and the National University of Ireland Dr PICKEN pointed out that a large number of the students at the London School of Hygiene and Tropical Medicine were not intending to enter the public health service in this country

The council adopted draft regulations under section 2 (i), (ii), and (iii) and Section 3 (iii) of the Medical Act, 1950, as to the experience to be required after qualification before full registration in the Medical Register These draft regulations, which are subject to approval by order of the Privy Council, provide that the applicant shall have been engaged in employment as a house officer for 12 months—6 months in medicine and 6 months in surgery Not more than 6 months in midwifery or more than 6 months in a health centre may be reckoned towards the completion of this 12 month period These regulations will not come into force until the "appointed day" under the Act, and the president reminded members of what he had said in his addresss about the council not being precipitate in the matter

The council considered replies from licensing bodies to a circular concerning the compilation by the council of a list of hospitals, &c, approved by these bodies for the purpose of section 2 of the Medical Act The PRESIDENT reported that all bodies seemed to agree on reciprocal approval, as far as hospitals were concerned All agreed to keep the list up to date if it was maintained by the council. Some universities proposed to approve hospitals in the Dominions and the U S A (the U S A had many vacant posts), and Colonial authorities might insist on the Colonial student returning to the Colony to work after qualification The president agreed that hospitals in the U S.A or the Dominions or Colonies so approved by licensing bodies should not be included in the list The list would follow, with modifications, the arrangement of the *Hospitals Directory*

The council discussed at length whether posts, as well as hospitals, should be included Professor GREEN opened by explaining why the University of Durham felt it was not possible to give complete reciprocity of posts, as opposed to approval of hospitals In the discussion it was suggested that the body which licensed the student should inform him of the type of appointments that it would approve, and, to meet the danger that two 6 month periods in two specialties might be taken, it was stated that specialist posts could be suitably marked, with an explanation that two such posts would not be acceptable, while one unmarked and one marked post would be Prof A P THOMSON read the note which the University of Birmingham was proposing to issue on the pass list, for guidance He also said that the director of studies would write to the student's chief within six weeks of his appointment, and if he received an unsatisfactory report would visit both chief and student (for things could be unsatisfactory because of the chief as well as because of the student), in this way any difficulties could be overcome early, instead of the student completing his 6 months and then finding himself with an unsatisfactory report The discussion concluded with Professor GREEN saying he saw no objection to a comprehensive list, so long as there was no suggestion that any combination of posts in that list would be accepted by any particular licensing body

The council discussed further educational business in camera

The session was concluded on May 23

Medical Disciplinary Committee

The Medical Disciplinary Committee met on May 24 and 25

This committee now exercises the disciplinary functions of the council, and it accepted the recommendation of the Penal Cases Committee that as from May 22, 1951, the Warning Notice should be issued, with such variations as the circumstances might require, by the Medical Disciplinary Committee, in lieu of the council.

The question of the application of paragraph 6 of the Warning Notice, which deals with advertising and canvassing, to sound broadcasting and to television is to be discussed by representatives of the British Medical Association and members of the Medical Disciplinary Committee and the Penal Cases Committee, acting jointly, since in the normal course both committees would be concerned with any reconsideration of the Warning Notice.

The annual report of the council of the B M.A for 1950–51 "noted with concern the laudatory references sometimes made to medical practitioners in announcements regarding forthcoming television programmes and also in actual performances" The council considered that "the increasing departure from anonymity and the references to appointments, experience, and achievements in the medical field are a possible source of danger to the individual concerned and contrary to the best traditions of the profession"

Correspondence read at the meeting of the committee said that the B M.A would submit a memorandum on the subject

RESTORATIONS TO REGISTER

The committee directed the Registrar to restore to the Register the names of *John Matthew Campbell*, *Bernard Drummond Hendy*, and *Vincent Blumhardt Nesfield* Under the new procedure these cases were considered in camera, and the result announced to the applicant when strangers had been readmitted

MANSLAUGHTER CHARGE

James Joseph Murray, registered as of Clooneyquin, Castlerea, co Roscommon, L.M R C.P and R C S Irel (1941) was charged with having been convicted of manslaughter at Chester Assizes on Oct 30, 1950 when he was sentenced to 3 years' imprisonment and disqualified from holding a driving licence for 10 years The conviction was admitted and proved Dr Murray was represented by Mr Norman Richards.

Mr Winterbotham, presenting the facts, said that in the evening of Sept 12, 1950, Dr Murray's car ran head on into a motorcyclist, who was killed, the accident happened on Dr Murray's right side of the road That morning Dr Murray had got up early, complaining of a headache He had some whisky and went back to bed, another doctor looked after the practice Dr Murray got up in the afternoon to see some elderly ladies about whom he was worried, and afterwards went to some public houses Evidence was given by doctors who examined him after the accident that he was, in their opinion, under the influence of drink, although he performed many of the tests satisfactorily Dr Murray in evidence had stated that he could not say what had happened at the accident

Miss Bessy Barret, a certified midwife, said that Dr Murray had been working very hard for two weeks previous to the accident he had given up his half days to do maternity cases. On Sept 12 she saw him in the morning and at midday, when in her opinion he was sober There was never any suggestion of drink taking while she had been working with him professionally He was a most conscientious doctor

In England Now

Running Commentary by Peripatetic Correspondents

HE action of the Marylebone authorities in refurnish-
the Baker Street apartments of Mr Sherlock Holmes
et another example of civic patronage Mr Holmes
rted the borough many years ago and has since
ained in retirement in Sussex His one incursion
the realms of scientific detection during recent
s was his elucidation of the problem of the Lion's
e Yet he is honoured by the district which he
ned, while another Baker Street inhabitant, Mr
on Blake, is completely ignored Without those
antages enjoyed by Holmes, Mr Blake exposes evil-
s twice a month He has no Dr Watson to give him
ap diagnosis but relies on his own prodigious memory
rovide medical information Take for example his
se of The Hollywood Contract " in which a young
an was recently persuaded to impersonate a leading
star But for the acumen of Mr Blake, this remark-
fraud might be continuing still Blake, believing
actress to have been murdered, paid a visit to her
age where he found a mat with an ominous stain on
If the stain proved to be human blood the case would
closed Without hesitation, he commanded his
stant, Tinker, to take the mat back to his laboratories
re, as he explained, a quick Wassermann test would
blish its identity So far as is known, he was
nously unacquainted with the actress, so we can
marvel at his brilliance in realising that such a
would be specific In comparison, Sherlock Holmes
ears a mere charlatan. Why then should Holmes
ive the honour due to Baker Street's greater son ?

* * *

often have to refer to tables and charts relating
ace area to body-weight Only nurses and others
have to wash patients all over have any idea of the
e variation there is in people's surface area For
ance, a frail woman of 5 ft 2 in. may have a surface
of 14 sq ft , whereas your well-upholstered 6 ft
n's surface will cover 22 sq ft or more In the
mary way, even in our student days, we doctors
ly try our hand at giving human beings a rub down ,
grooming a horse brings home to one what surface
a really means I don't know how many square feet
re are on a 14-hand or 15-hand horse, but to the
ateur groom its area seems about the same as a tennis
rt s. What must it be like to rub down an elephant ?
m told on reliable authority that it about reaches the
it of human endurance and that a machine has
refore been devised for doing the job easily and
editiously
Couldn't we have a smaller model to mechanise bed-
hs ? "Only over the ward-sister's dead body, you
l say But I am not so sure , there has been a big
nge in the sister's outlook on manual labour in the
t twenty years. The scarcity of nurses certainly has
nething to do with it Even sister-tutors no longer
k on hard labour as an essential part of a probationer's
ining So I fancy everybody in the ward would wel-
ne my Robot Bed-bather especially the patients,
en they found that it couldn't have cold hands because
hadn't any hands at all.

* * *

see that doctors visiting London during the Festival
advised to use public transport rather than a car
ause of the difficulties confronting motorists in the
tropolis. What with traffic-blocks, local variations
the enforcement of parking rules and pedestrian
sing places and the certainty that there won't
a vacant place to park the car within a mile of one's
tination it isn't worth while using a private car
short journeys in London—unless of course one has
hauffeur and or a shiny new Jaguar of vast publicity
ue
One solution is to ride a bicycle As students we all
l them and became expert at riding them through
ffic in any weather I learnt a lot of tips from a
ckney errand-boy in the next bed when I was warded
h an appendix His main advice was 'Wherever
yer gets, Guv, stick onter yer bike like bleedin' glue and yer won't get nipped—see ? " "Nip" was a favourite word of his with a wide range of meanings It covered such eventualities as being fatally crushed between two buses or (and this seemed to him worse than death) being taken up by the police for the minor offences he committed from time to time

My early training came in useful last week when I had to get my son's bicycle from Liverpool Street Station to Charing Cross. With the foolish pride of middle age I was tempted to take a taxi, but it was a fine day so I decided to chance a ride Believe it or *not*—and it was in the evening rush-hour—I did the journey in 12 minutes dead, without chasing the amber or any other of the motorist's time-saving tricks And I did *not* get nipped

I shall not be surprised to see our doctor sons returning to the habits of our doctor fathers, unencumbered by their coat tails and the need for keeping up appearances And those who must have publicity will no doubt appear on the latest Rolls Corgi motor scooter

* * *

Whatever you do, don't follow my example and arrive in Canada on July 1 Having spent 2 days "doing New York," you will arrive, footsore but blithe, in the great university city at 9 A.M. So high are your spirits that you will merely laugh at battered suitcases, once proudly locked, now, after one short night on the C.N.R , battered string-bound wrecks. You will mother them towards a taxi and sink back, thinking smugly how impressed your chief will be at your prompt appearance on a Saturday

Settled in your room, two of your only three dollars gone to the taxi-driver, you will walk briskly to the hospital, looking we trust the epitome of that rather tiresome soul, the Competent Woman Doctor The long hot empty streets will puzzle you, the shuttered silent shops perplex you, and the ominous words on the bank ' Closed for Dominion Day, July 1 " petrify you. Reaching the hospital you will hear, "Oh, no, I'm afraid he's not here—he's at his log cabin. No, I'm afraid he isn't either, he's on vacation. No, she's gone to Niagara for the weekend," and then, more coldly, ' I'm sorry, we can't cash any traveller's cheques till Monday , you see, it's Dominion Day " You will totter away, clutching your one remaining dollar, to spend a solitary and hungry week-end Your useless cheques make but eloquent testimony to the joyful news *Canada is a Dominion.*

No , not on July 1

* * *

Professors of medicine are fond of emphasising the importance of taking an accurate and complete history They tell us that it is of greater value than the physical examination. Indeed so impressed are they with its advantage that they sometimes prefer to interrogate the patient concealed behind a screen. To this admonition and exhortation we lesser mortals react—perhaps with respect and admiration perhaps with less respectful tolerance of senile idiosyncrasy , perhaps with impatience at pomposity and a longing to see the experts trying to practise their leisuredly methods in our crowded surgeries or outpatient departments. And yet

A well-covered matron appeared with an introduction from Dr X She had lost 2 stone in the past two months and he would be glad of investigations to ascertain the cause We undertook the weary time-consuming procedure of proving negatives, at the end of which we asked the patient if she could think of anything that might be responsible. 'Well," she replied "I went to Dr X two months ago because I was over-weight, and he put me on a diet

* * *

A few years ago I was out walking one evening when I lost the path in a wood After a few minutes' meandering, I saw two cigarettes burning through the trees, and after a moment's hesitation called out "Excuse me, but is there a path near here ? " No answer A further call also produced no response, and beginning to feel annoyed I walked over—to find two glow-worms Next day I checked up with Ishihara, and that was how I found I had a beautiful red-green blindness believe to be of limited value Primarily the interest of the G P is the whole person integrated in the social background, and not in any part of that person In any case, no labour is saved by such a breakdown, and most of the routine work of the G P does not lend itself readily to a breakdown on the lines of the division of clinical material which is possible in a hospital

Two exceptions to this are found in the work of the general practitioner obstetrician and the general practitioner physician

That midwifery properly comes within the province of the family doctor we have no doubt, but we are certain, too, that it can remain there only if the other responsibilities of the G P are small enough to enable him to devote a large part of his time to maternal care We find that to deal with 120 cases per annum within the group, the G.P obstetrician's list of patients under the General Medical Service must not exceed 1200, and that he must give four afternoons per week to maternity clinics Ideally these would be carried out at a centre which had adequate accommodation for the teaching of exercises and relaxation, for films, talks, discussions, and a mother's club All normal deliveries are carried out by the midwives, and the G.P obstetrician, working in the closest cooperation with them, must be available for advice and for emergencies such as suturing the perineum, postpartum resuscitation, and difficulties in labour

It is our view that the only major operative procedure that should be carried out in domiciliary practice is the application of forceps when the head is on the perineum, with another doctor present as anæsthetist All other operative procedures belong to the hospital obstetrician

The G.P physician must be a family doctor who, by training and experience, is of consultant physician status His function is discussed below

Any member of the group who, because of special experience, wishes to run a particular clinic—e g, in dermatology—is of course encouraged But each member is primarily a general practitioner with his own list of patients for whom he takes full and continuous responsibility A patient normally has access to other group members only through his own doctor, except that a duty rota is in operation and he may have to call upon the doctor on duty when his own is off duty

THE DISPOSAL OF ORGANIC ILLNESS

The G P can dispose of major organic illness in three ways he can treat the patient in the home with the help of the district nurse, the home help service, and the domiciliary consultant service, he can refer the patient to a general hospital, or he can admit the patient to a G P hospital In a G.P hospital the practitioner can assume complete responsibility for the case, or, if he is working within a group, he can attend to the patient under the surveillance of the G P physician, or he can hand over to the G.P physician entire responsibility for the patient while he is in hospital

Cases admitted to a G P hospital should be freely accessible to all members of a group practice, and the problems they present should be fully discussed at the routine meetings of the group The main responsibility of the G.P physician is to familiarise himself with the work done by his colleagues to ensure that their standards of diagnosis and treatment do not fall below those of general hospitals To be able to do this, it is essential that the G P physician has access to a general hospital, and he should hold a post of clinical assistant there

This arrangement successfully ends the problem of the isolation of the G P from his colleagues in hospital, and eliminates what has been a regrettable feature of the work of cottage hospitals in the past—namely, that in some cases the standard of treatment has fallen below that of general hospitals This is particularly the case in major operative surgery We can see no place for the G P surgeon, and, apart from minor surgery, we refer all surgical cases to a general hospital

On the other hand, we have found that with a group practice including a G P physician and a cottage hospital, the G P is fully able to treat the majority of medical cases that he meets in his practice without having to request admission to a general hospital, or make use of the domiciliary consultant service This continuous care by the G P of patients who have serious organic illness, enormously increases the interest of his work and encourages him to maintain and improve his standards of practice

FUTURE DEVELOPMENT

Rationalising the work of the practitioner can enhance his ability to deal with many conditions which are customarily referred elsewhere, and it can also have the purpose of giving him time to conduct research into the problems that confront his practice He should not compete with his colleagues in hospital and laboratory in the investigation of the obscure and technical, but he is in a unique situation to study the relation between disease and social factors, and can make a contribution in the understanding of the problems of childhood and psychoneurosis Solutions evolved in general practice will always have a wider field of applicability than those dependent on some special institution or apparatus[1]

A group of G P s such as we have described is better placed for undertaking such work than is the G P working in isolation

CONCLUSION

The maintenance of high standards in medicine, particularly in general practice, depends primarily on personnel and not on buildings and equipment The development of the health services during the past forty years has seen the springing up of many services ancillary to that of the family doctor and mostly intended to compensate for the deficiencies of general practice The result has been that the practitioner has lost a large part of his responsibilities and the family doctor is now far from being the pivot of the preventive and curative services An end will be put to the curtailment of the functions of the G P only when his standards can be raised We suggest that in present circumstances this can best be achieved by developing group practice and encouraging the hospital registrar to enter this field—a field which will give ample scope for the application of the skill which he has obtained in his long training and which will enable him to continue to do work which is professionally satisfying

The introduction of the National Health Service has seen great improvement in the hospital services but there has been no parallel improvement in the general practitioner service The most urgent need at the moment is for a body, equivalent to the regional hospital board which will take upon itself the responsibility for the planned development and improvement of general practice pronouncements, whether of confirmation or refutation, after early and thorough investigation of a claim, would prevent much wasteful expenditure of time, money, and materials

---

[1] From its very nature virus research, like bacteriology in general, has tended in the past to concentrate on medical and veterinary problems It will probably always be carried on against a background of its significance for medicine But if one looks around the medical scene in North America or Australia, the most important current change he sees is the rapidly diminishing importance of infectious disease The fever hospitals are vanishing or being turned to other uses With full use of the knowledge we already possess, the effective control of every important infectious disease, with the one outstanding exception of poliomyelitis, is possible

"Today the most intellectually exciting aspects of virology are not directly concerned with medicine As I see it, the main interest of the virus to biology now is the possibility of using it as a probe in the study of the structure and functioning of the cell it infects '—Prof F M BURNET, F R.S, *Scientific American*, May 1951, p 51

Cowley Road Hospital
Oxford
P D BEDFORD

DRUGS IN AMŒBIASIS

SIR,—In your leading article last week, I notice two separate quotations implying that "cyst passers" or "carriers" of *Entamœba histolytica* are now usually looked on as chronic cases of amœbiasis, and it is not quite clear whether or not you agree with this conclusion

Surveys of sections of the population of this country which have been made at different times show a carrier-rate ranging from 1 6 to 3 4%, and it is probable that these figures would be higher if repeated tests were done This means that at a conservative estimate between 1 million and 2 million of the inhabitants of Great Britain harbour *E histolytica* in their bowel. Is it seriously suggested that we have this enormous number of cases of chronic amœbic dysentery in our midst?

Welcome Laboratories of
Tropical Medicine
London N W 1
J S K BOYD

OFFICE MANNERS

SIR,—I should like to congratulate Brigadier Hardy Roberts on his article of May 19 It is full of that clear common sense which is the hallmark of the good administrator I hope that he will one day write a second article on the methods of dealing with the difficult case—for example, the member of the board or medical staff who cannot see any other point of view than his own

As a former "man at the Ministry" who has sampled Brigadier Hardy Roberts's persuasive hospitality, I can foresee that if this custom spreads some future Minister of Health may have to consider the reintroduction of the ancient Local Government Board rule for general inspectors It was to the effect that officers of the Ministry must never accept hospitality when visiting institutions in their official capacity!

Department of Human Ecology,
University of Cambridge
A LESLIE BANKS

LONDON SCHOOL OF HYGIENE ASSOCIATION

SIR,—A School Association has been formed, membership of which is open to all students who have followed a complete recognised course of instruction in the school There is a nominal entrance fee of 2*s* 6*d*, but no annual subscription Members are entitled to receive every year a copy of the annual report and any notices connected with the association It is hoped to arrange an annual "open day" and possibly an annual dinner A special association tie has been designed, which is obtainable at a cost of 17*s* 6*d*

I hope that all past students will join the association and maintain as close contact as they can with the school and staff Applications, together with the entrance fee of 2*s* 6*d*, should be sent to Miss K M Shaw, personal assistant to the dean

London School of Hygiene and
Tropical Medicine
Keppel Street London W C.1
ANDREW TOPPING

METHÆMOGLOBINÆMIA

SIR,—In your annotation of May 12, you say that "the newer sulphonamides do not cause methæmoglobinæmia" This prompts us to record some observations from the Premature Baby Unit at Hammersmith Hospital.

In the last few months we have seen five examples of methæmoglobinæmia in premature infants to whom sulphamezathine had been administered This type of cyanosis may sometimes be wrongly attributed to some other more serious complication, especially as it seems particularly prone to occur in the premature infant The blueness usually disappears within 48 hours or so of stopping the drug Two typical case histories are as follow

CASE 1—Birth weight 3 lb 10 oz Aged 16 days developed purulent blister on scalp Sulphamezathine 0 25 g first dose, and thereafter 0 125 g 6 hourly Diffuse cyanosis noted on 4th day of treatment, methæmoglobin 12% in venous blood sample, as determined by a Klett spectrocomparator Cyanosis disappeared within 48 hours of discontinuing the drug

CASE 2—Birth weight 3 lb 12½ oz Pustular eruption appeared on the neck on the 3rd day of life Sulphamezathine 0 125 g 6 hourly Generalised slaty cyanosis noted on 3rd day of treatment Venous blood sample showed 11% methæmoglobin Treatment continued for 7 days, 3 days later all cyanosis had disappeared

Institute of Child Health,
University of London
TREVOR MANN
DONOUGH O'BRIEN

Medicine and the Law

Finding of Negligence against Doctor and Hospital

IN Wood *v* Thurston and the Governors of Charing Cross Hospital (reported in the *Times* of May 25) Mr Justice Pritchard awarded damages for negligence against Dr Thurston and against the hospital as his employers, assessing them at £350 under the Law Reform (Miscellaneous Provisions) Act, 1934, and £3200 under the Fatal Accidents Acts

The facts were unusual Mr John Wood, manager of the accounts department of a bank, visited two public houses with friends between 7 P M and 9 P M in August, 1948 Subsequently the party, walking westwards along the Strand, found a stationary lorry in their way as they came to cross Bedford Street Instead of walking round behind the lorry, Mr Wood elected to crawl on all fours under it As he did so, the lorry began to move, one of its rear wheels pinned him to the ground, but he was freed before the wheel went completely over him After lying down on the pavement for a while, Mr Wood went with his friends to the casualty department of Charing Cross Hospital He arrived, according to the learned judge's finding, intoxicated but not drunk, he insisted that there was nothing wrong with him and he explained what had happened with the lorry, Dr Thurston examined him, treated him, as the records showed, for nose bleeding, and found no evidence of bone injury (which the judge held meant no bone injury to the nose) The patient was then allowed to travel home, a distance of 11 miles, in a taxi cab Early next morning he was admitted to the West Middlesex Hospital, where he died at 7 A M Necropsy disclosed a fractured collar bone, fractured ribs (9 on each side), and severely congested lungs Death was attributed to shock consequent on these injuries. The widow's allegations of negligence consisted in the doctor's failure to diagnose the injuries and in the fact that the patient was allowed to make the taxi cab journey when not in a fit state to travel Dr Thurston, who denied liability, admitted the failure of diagnosis but pointed out that Mr Wood, being intoxicated, could give no accurate account of his accident and that the patient's reactions to pain were dulled by alcohol Mr Wood, he said, repeatedly stated that there was nothing the matter with him and that he wanted to go home In examining the patient he had (amongst other things) pressed his chest from side to side and from front to back and had examined the skull for signs of injury Mr Wood had shown no signs of shock or pain, there was no crepitus, sweating, pallor, or abnormality

Mr Justice Pritchard said he thought the examination had been less careful than the circumstances required It had been contended that the intoxication would deceive a doctor, he thought the story of the man having been under a moving lorry and having been touched by the wheel made greater care necessary in the examination The use of a stethoscope would almost certainly have revealed the patient's true condition As regards the taxi cab journey, whether the cause of death was shock

Ireland Mental Health Act of 1948 has already introduced radical reforms, and that in this country active preparation of a new Mental Deficiency Act has been in progress for some time.

In view of this, we feel that the pamphlet has served no useful purpose but has caused unnecessary distress to relatives of patients in mental deficiency hospitals.

E. D. TAYLAR
A. SHAPIRO
B. W. RICHARDS
J. H. WATKIN

Harperbury Hospital, Shenley
near St. Albans and Leavesden
Hospital near Watford

DIURETIC EFFECT OF VITAMIN B$_{12}$

SIR,—Barnard and Weitzner[1] reported that single injections of 45–75 µg. of vitamin B$_{12}$ caused unequivocal increase in urinary output in 12 of 16 patients with normal blood pictures. They speculated on the mechanism of this action and suggested further clinical trials. Such a claim warrants further investigation, for œdema is too common, and too often unresponsive to treatment, for the present remedies to be viewed with complacency.

I have investigated this claim in 37 patients with normal blood pictures, comprising the following five groups:

1. 2 normal adults (1 woman, aged 32, and 1 man, aged 35).
2. 2 women, aged 54 and 58, with chronic nephritis. Both had generalised œdema with hypertension and nitrogen retention, the blood-urea values being above 120 mg. per 100 ml.

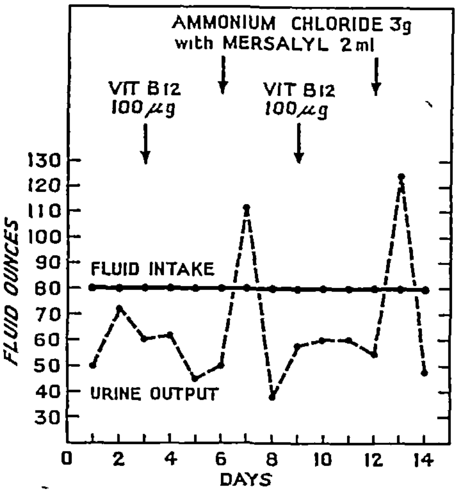


Fig 1

3. 1 man, aged 58, with the nephrotic syndrome due to Ellis's type II nephritis. His blood-pressure and blood-urea level were normal at the time of the test, but his plasma-protein level was very low at 4 g. per 100 ml., and there was extreme generalised œdema.
4. 30 patients in congestive heart-failure with generalised œdema (14 men and 16 women, all over 48 years of age). In many cases the ætiology was mixed, but the main factor was considered to be arteriosclerotic coronary disease in 20 cases (3 with rheumatic mitral stenosis and 3 with calcareous aortic stenosis), essential hypertension in 5, cor pulmonale in 3, thyrotoxicosis in 1, and syphilitic aortic incompetence in 1.
5. 2 men, aged 52 and 60, with generalised œdema due to cirrhosis of the liver.

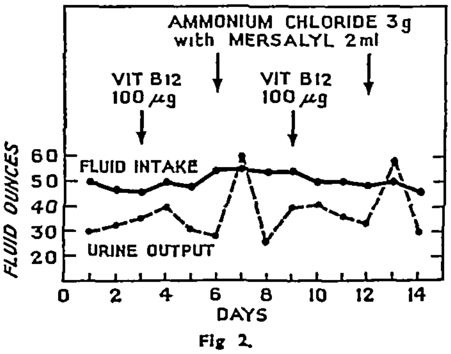


Fig 2.

The simple low-sodium diet described by Bedford[2] was carefully maintained for the 14-day trial period. This diet provides not more than 650 mg. of sodium per day and allows a free intake of fluid. The fluid intake and the urinary output, from 6 A.M. one day to 6 A.M. the next, were measured and recorded daily. Fluid lost via the bowel, skin, and lungs was not taken into account, but no patient had vomiting or diarrhœa during the trials. Daily weighing was impracticable owing to shortage of staff.

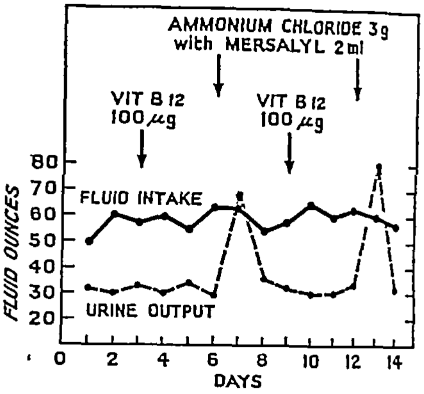


Fig 3.

The vitamin B$_{12}$ was tested against a mercurial diuretic, as follows:

After 3 days on the low-sodium diet, 5 ml. of 'Cytamen' (Glaxo), equivalent to 100 µg. of vitamin B$_{12}$, was injected intramuscularly at 6 A.M. 3 days later 3 g. of ammonium chloride was given by mouth at night followed at 6 A.M. the next morning by 2 ml. of mersalylum B.P. intramuscularly. After another 3 days the whole experiment was repeated.

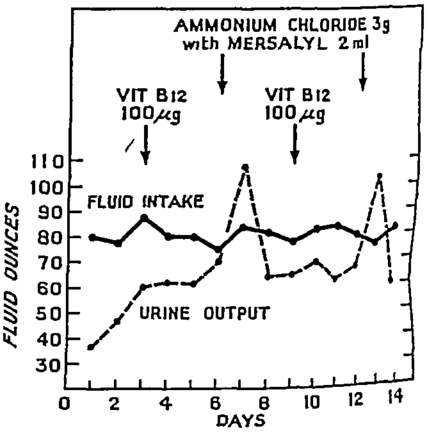


Fig 4

Figs 1–5 show the responses of the five groups of subjects. In no case was a significant increase (arbitrarily defined as output exceeding intake) observed following the administration of vitamin B$_{12}$, whereas in all cases the mercurial compound produced a diuresis, although this was occasionally within the normal range for the patient.

I conclude therefore that vitamin B$_{12}$ has no significant diuretic effect on subjects with normal blood pictures, and thus has no place in the management of generalised œdema. (The diuretic effect of vitamin B$_{12}$ on patients with blood disease is not considered here.)

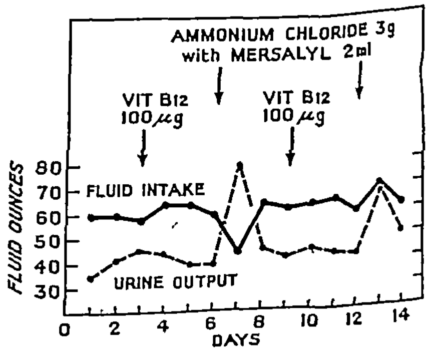


Fig 5

The establishment of a Therapeutic Trials Committee in this country is long overdue, for authoritative

---

1. Barnard, R. D., Weitzner, H. A. *Lancet*, 1949, ii, 717.
2. Bedford, P. D. *Ibid*, 1950, ii, 823.

play an important part in the affairs of the university and the British community in Cairo He devoted his leisure to acquiring an extensive knowledge of the antiquities of Egypt, a superb collection of photographs illustrative of this subject, and a number of private pieces of rarity and value In this strenuous and fruitful hobby he was assisted by his wife Viola, youngest daughter of Osbert Salvin, F R.S , who was an artist of no small ability They had married in 1913 She predeceased him in 1947, leaving a son who is a doctor

Returning to Britain in 1933, after receiving the Order of the Nile and being admitted a member of the Royal College of Physicians in 1932, he was appointed as independent lecturer, and subsequently professor of *pharmacology at Cardiff* There he expanded the department, playing an ever-increasing part in the affairs of the school of medicine, of the college in relation to the school of pharmacy, and of the university as a whole He continued the series of painstaking researches which led to a number of valuable contributions to his specialty, and wrote the articles on chemotherapy for the *Medical Annual* from 1937 to 1946 He was elected fellow of the Royal College of Physicians in 1937

In 1948 he married Amy, youngest daughter of the late R G Howson, of Stoke-on-Trent, who survives him.

J D P G writes "A man of taste, wit, and learning, widely read in classical and English literature, familiar with the byeways of France which he visited annually, discriminating in his praise or censure of a book, a wine, or a picture, skilled in working with metals or with woods, amiable, generous, and loyal, Heathcote was a lovable character His knowledge of his specialty was profound, and he laboured to achieve a synthesis between the pharmacist, the pharmacologist, and the clinician. As a teacher he was approachable, considerate, and helpful, never obscure or pedestrian He inspired a remarkable warmth of feeling in a whole generation of Welsh students and in his colleagues.'

JAMES ROBERTSON CAMPBELL GREENLEES

D.S O, M.A., M.B Camb

As we briefly announced last week, Dr J R C Greenlees, formerly headmaster of Loretto School, and latterly chairman of the South Eastern Regional Hospital Board for Scotland, died in Edinburgh on May 16, at the age of 72

Born at Glasgow on Dec 14, 1878, he was educated at Loretto, where he distinguished himself as a rugby player After qualifying he returned in 1908 to Glasgow, where he took appointments at the Western Infirmary and the Royal Hospital for Sick Children On the outbreak of war in 1914, he immediately volunteered, and for his services he was appointed D S O and created a chevalier of the Legion of Honour

He went to Loretto as headmaster in 1926 without previous experience of teaching, but under his leadership the school's reputation for scholarship and excellence in games was enhanced Because of the late war he deferred his retirement until 1945 He became chairman of the South Eastern Regional Hospital Board in 1947, and in 1948 he was appointed surgeon to the Royal Company of Archers

H A R writes "To make a name in the two professions of medicine and teaching, to have a distinguished record in the first world war, to have played rugby for Scotland seven times after a delicate childhood, is an unusual combination of achievements these are the highlights of Dr Greenlees s career It has been said that during his headmastership of Loretto emphasis was placed on the development of character, and it is in his qualities of sincerity, disinterestedness, and simple faith that the explanation may be found

"I cannot speak for his place in medicine as a general practitioner and children s physician in Glasgow Nothing much could be learned from Dr Greenlees himself, as most of his reminiscences consisted of humorous stories against himself Certainly, however, this period gave him a sympathy with the young general practitioner struggling to make a career in his chosen field. It may be said that Dr Greenlees was fortunate in his background and upbringing Be that as it may, he typified the outlook of 'noblesse oblige,' and regarded his advantages in life as a means which enabled him in fuller measure to serve the community He never ceased to be a physician even when a headmaster On his return more directly to the field of medicine as chairman of the Royal Hospital for Sick Children, Edinburgh his influence did much to weld this hospital—governing body, medical staff, and others—into one team His delight in this work was the close association it gave him with children—an association he regretted losing when he undertook work in a wider field as chairman of the South Eastern Regional Hospital Board, Scotland.

'Dr Greenlees threw himself, heart and soul, into the creation of the new hospital service—work he once described as 'more than an experience, an adventure.' He had definite views on most matters and was perhaps a little impatient with the intricacies of committee systems and the like His great strength was his obvious sincerity and disinterestedness and his great charm was that he granted such qualities to those who opposed him, and always insisted that they should be fairly heard

"He was keenly interested in the development of medicine He typified the high ideals of the true physician, and it is perhaps for his insistence that such ideals should be maintained in the turmoil of this revolutionary period in medicine that he will always be remembered In a new organisation, such as the hospital service it is easy for the machine to take hold of the individual The greatest contribution by men like Dr Greenlees to any organisation is that they give it a soul."

In 1922 Dr Greenlees married Allison Hope, daughter of Sir John Cargill, and they had a son and a daughter

---

Appointments

AIDIN A R M D Dubl. D T.M. D C.P consultant pathologist Worthing and Chichester hospital groups

BEAT J R. M D St. And medical superintendent (psychiatrist) Guernsey Mental Hospital

CHOPPING P T M B. Lond D.M R consultant radiotherapist, hospitals in western part of East Anglian region and United Cambridge Hospitals

CREERY R D G M D Belf D C.H *medical registrar* Southmead Hospital Bristol

CUNNINGHAM, R C. M.B Glasg D.P.H D.P.M. deputy medical superintendent (S.H.M O grade) Meanwood Park Hospital, Leeds

DALY B G M.B Edin. asst psychiatrist Towers Mental Hospital, Leicester

DENNISON D J M B Lond asst county M O South west Kent area

EDDY H D M C B.M Oxfd clinical assistant in neurology West Cornwall clinical area.

EGAN T O T M.D N U I D P.M *asst. psychiatrist* Saxondale Hospital *Radcliffe on Trent, Notts*

FAWCITT J B M.R C.S. D.M.R.D consultant radiologist Barrow and Furness group of hospitals

GROOM, W A L.M.S.S.A., D.A asst anæsthetist Fulham and Kensington group of hospitals

HAMILTON MAX M D Lond. D P M asst. psychiatrist Springfields Hospital London

HENRY L S M B. Durh F R.C.S E clinical assistant, ear nose, and throat department Trowbridge and District Hospital Wilts

JARVIS MARY M B Sheff asst. pathologist, Blackburn Royal Infirmary

LUTWYCHE URSULA M D *Camb* M R.C.P D C H senior registrar, Willesden chest clinic and tuberculosis unit Central Middlesex Hospital

McCALLUM D I M C M D Edin. M R.C.P.E D.P.H consultant dermatologist Nottingham skin clinic.

MONRO A B M.D Edin., D.P.M physician-superintendent and consultant psychiatrist Long Grove Hospital Epsom Surrey

NORMAN A P M.B.E M.D Camb M R.C.P asst. pædiatrician, Queen Charlotte s Maternity Hospital, London.

PEEL, E L M B M.Sc Manc. asst pathologist Stepping Hill Hospital Stockport Cheshire

REISS J L M.D Lwow D O.M.S. S H.M O ophthalmic department, Hampstead General Hospital London.

*SIMONS E L. M B. Camb. consultant pathologist Goole, Howden and Selby and Pontefract and Castleford hospital groups Yorks

SWITHINBANK J M. M D Lpool M.R.C.P consultant physician, Merthyr and Aberdare hospitals group

TYSER P A M.D Lond D P.H *district* M O.H Cambs (except Cambridge) deputy county M O and deputy school M.O Cambs

Local Treasury M O

FIELDSEND A B M.B. Leeds Willerby Hessle Anlaby Kirk Ella and Swanland (Hull)
GARRARD NORMAN M.A. M.B. Camb Liskeard Cornwall
HARDIE W G M.B Edin Crook co Durham.
HENDERSON I R. M B. Edin. D OBST Braemar Aberdeenshire
McVITIE G E. M B Edin. Keswick Cumberland
MORRISON D N B M B. Glasg Kemnay Aberdeenshire.
ROSS K A M B. Aberd Southborough Kent
STEWART R S M.B Edin. Dundee

*Amended notice

or the leakage of air into the pleural cavity on account of the fracture of the ribs, the judge thought death would probably not have occurred if the patient had been kept immobile at once He added some consolatory remarks for the benefit of the defendant doctor There were very few professional men who had not made mistakes in the early stages of their careers

Public Health

Retrospect and Prospect in Poliomyelitis

THE World Health Organisation has made a brave attempt to survey the world trends of poliomyelitis in 1950 [1] This suffers considerably from lack of population figures to convert crude incidence to case-rates, and a little from differences in code of all countries only England and Wales group encephalitis and myelitis together That there should be no information at all from the U S S R or China is not surprising, but one wonders what prevents the inclusion of reports from Abyssinia, Bolivia, British Honduras, Egypt, Eritrea, India, Somaliland, or the Sudan

For most countries the case-incidence and deaths in 1949 and 1950 are compared with the medians for the period 1942–48 From these figures the countries can be divided into four groups

1 Incidence much higher than median in both 1949 and 1950, Australia, Belgian Congo, England and Wales, France, Mexico, U S.A.

2 Incidence much above median in 1949 and much below in 1950 Canada Iceland, Mauritius

3 Incidence much above median in 1950 only Denmark, Northern Ireland, Norway, Scotland, Spain.

4 Incidence about median in both 1949 and 1950 Belgium, Federal German Republic, Finland, Ireland, Italy, Sweden, Switzerland.

For some countries the yearly incidence since 1938 is also given, and a broader view of present trends is thus possible If the total incidence during the last six years is divided by the total for the six preceding years the following ratios are obtained Netherlands 0 36, Switzerland 0 66, Italy 0 89, Denmark 1 03, Norway 1 2, Sweden 1 3, Finland 1 41, Ireland 1 43, France 2 03, Canada 2 28, U S A 2 5, Austria 3 15, Scotland 5 2, England and Wales 5 7, Belgian Congo 6 1, Australia 10 3, Union of South Africa 13 5, Iceland 113, Mauritius 850 The remarkably wide range is probably a measure of the present lack of equilibrium between virus and man The virus almost certainly has no natural host other than man, climate is no bar to its activity, and thus wherever man lives the virus may live too As long, therefore, as poliomyelitis remains unpreventable it will continue to be a world problem, and statistical observations of this kind will continue to have great interest

Employment of Pneumoconiotic Miners

Men suspended under the Workmen's Compensation Acts because of pneumoconiosis or silicosis, unaccompanied by tuberculosis, may now take up employment in the coal-mining industry if they are passed by a pneumoconiosis medical board as fit to do so The scheme, which is voluntary, does not apply to men suspended for tuberculosis, pneumoconiosis accompanied by tuberculosis, or silicosis accompanied by tuberculosis

By Regulations [2] which come into operation on June 4, men passed as fit who take up work underground, or in a surface job involving the working or handling of any minerals taken out of the mine, will be able to claim a modified disablement pension under the Industrial Injuries Scheme if their condition gets worse They will be examined by a pneumoconiosis medical board before entering employment and will in any case be called up for further examination from time to time The amount of any disablement pension will be based on the difference between the assessment of disablement given at the first examination and any increased assessment given at a later examination after taking up work The men may also be able to qualify for special hardship allowance, unemployability supplement, constant attendance allowances, and hospital treatment allowance

Applications by suspended men to take up work in the coal-mining industry should be made on the form attached to leaflet N I 61, which gives further information and can be obtained at local National Insurance offices.

Public-health Salaries

Committee C of the Medical Whitley Council recommend to local authorities the following arrangements in applying the new (award) salary scales [1] to doctors who started duty in a first or new appointment on or after Oct 1, 1950

1 Doctors who started duty after Sept 30 1950, but before the date of the first award of the Industrial Court (Dec 8, 1950) should have the new salary scales applied to them in the same way as to doctors in post on Sept 30, 1950 —i e, as laid down in section III of appendix B to M.D C circular no 2

2 Doctors who started duty on or after Dec 8, 1950, but before April 1, 1951, should be dealt with as follows (*a*) for the period from the date of taking up duty to March 31, 1951, they should receive the salary at which they were appointed, (*b*) from April 1, 1951, onwards they should receive in full the new salary payable under the award, (*c*) increments should be paid as laid down in clause iii of section III of appendix B to M D C circular no 2

3 Doctors starting duty on or after April 1, 1951, should be paid the new (award) salary in full from the date of taking up duty

4 Where arrangements more favourable to the officer than (1) and (2) above have already been adopted by the authority those arrangements should remain in force

Statistics for Eire in 1950

In Eire the birth-rate during 1950, according to the registrar general,[2] was 21 0 per 1000 population—0 4 below the rate for 1949 The death-rate—12 0 per 1000 population—was 0 1 below the rate for 1949 The death-rate for all forms of tuberculosis was 0 8 per 1000 population (respiratory 0 6, other forms 0 2) compared with 0 9 (0 7, 0 2) in the previous year Deaths from puerperal causes amounted to 1 1 per 1000 births registered, compared with 1 6 for 1949 Infant mortality, which in 1949 was 51 per 1000 births registered, fell in 1950 to 45—the lowest ever recorded

Obituary

REGINALD ST ALBAN HEATHCOTE

M.A, D.M, B.Sc. Oxfd, F R.C.P

Prof R St A Heathcote, first incumbent of the chair of pharmacology in the Welsh National School of Medicine, Cardiff, died in London on May 19, in his 63rd year

Born in 1888, he was the youngest son of the Rev G Vyvyan Heathcote, of West Deeping, Lincolnshire He gave early evidence of his extraordinary powers of memory and academic brilliance and was admitted as a scholar of Winchester this early promise was not belied, he passed to New College, Oxford, again as a scholar, and in 1911 to University College Hospital as the first holder of the Theodore Williams scholarship He qualified in 1913, spent some years in the R.A M C during the war of 1914–18, and completed his service as a Surgeon Lieutenant-Commander R N V R After the war he returned to Oxford and was enabled to pursue those studies which had early appealed to him, joining the staff of the department of pharmacology and graduating D M in 1919 and B SC in 1922

It was in this year that Heathcote was appointed professor of pharmacology in the University of Cairo, proceeding to Egypt at the age of 34 to develop and expand his department, to train and encourage local students who might ultimately take his place, and to considered to have been substantially delayed by infection in 1 or 2% of cases. There were no acute major post-operative infections. Investigation of the infected cases generally showed that every aspect of the treatment—toilet, excision, suture, and dressing—had been bad; and that the dresser was already known for indifferent work.

---

[1] *Epidemiol vital Statist Rep* 1951, 4 no 1

[2] National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment (no 3) Regulations 1951 S I 1951 no 918 H M Stationery Office 2*d*

[1] See *Lancet* 1950 ii 918 *Ibid* Jan 6 1951 p 58 *Ibid* May 26 1951 p 1176

[2] Quarterly Return of the Marriages Births, and Deaths registered during the December Quarter 1950 and Yearly Summary 1950 Government Publications Sale Office 3/4 College Street Dublin Pp 78 6*d*

For traumatic amputations the most commonly used method of closure was by a thin split skin graft; but composite ear grafts, palmar and thenar flaps, resuture of the amputated part, and proximal amputation were also done. The 55 cases treated by simple split skin graft healed in an average of 24·1 days (range 10–40 days); in the more complicated types of repair (by flap or composite graft) the average time of healing for traumatic amputations was 30–40 days. A personal follow-up of 60 of these traumatic amputations showed that all were back at their old work except one, a boy aged 14, whose mother refused to let him run the risk of another similar accident. Only 2 scars were tender to pressure, 5 showed some adherence of the stump to the underlying bed, and in more than 20 the stump was noticeable either because of loss of length and contour or because of the yellow colour of the graft.

CONCLUSION

These results and healing rates (10–20 days for finger lacerations, and 10–40 days for traumatic amputations of the finger tip) can be improved; but they can be held to justify the continuance of this work by dressers under the conditions of accommodation, equipment, time, and teaching described.

It would be impossible to assess accurately the value of work in this theatre in the training of dressers. During their clinical period the dressers at Guy's Hospital have two appointments, each for three months, in which they do turns of duty in the surgery. But the best work in the accident theatre is not always done by the senior dressers; what matters is the aptitude and keenness of each dresser. In any group of dressers about a quarter have technical ability and are keen to increase their operative experience; they make the most of the opportunity the accident theatre provides. About an equal number are the reverse; they have no liking for the operative side of surgery and will often persuade friends on duty with them at the time to undertake their operations. The remaining 50%, however, seem to welcome the opportunity of sitting down quietly in a well-serviced room and getting ahead with a detailed and comprehensible technical job. Every doctor ought to be able to treat these common minor open injuries by modern techniques; it is in such an outpatient accident theatre that the dresser gets his best training in this work; but I feel that if he wishes he can obtain further important training there. He can become familiar with the use of the light instruments which have been designed for handling and repair of delicate tissues, and which will be useful in many of his general surgical operations. I like to think that in this theatre the dresser can also learn an attitude of mind to soft-tissue injuries which may be called that of a “biological dressmaker,” in that he can learn to regard every wound as an individual tailoring job needing a planned repair, and not the application of a standard treatment.

There are other reasons to justify the reorganisation and the initial expense in providing such services. In every aspect of its work a teaching hospital should provide standards which the students take with them when they leave. Casualty departments have for too long been the “black holes” of their respective hospitals. They have been departments where, on the grounds of the numbers of patients to be treated and the apparent rarity of serious complications, work has been done which contradicts every maxim of good surgery both in practice and in principle, violating not only the rules for the control of infection but also every other concept on which good surgery depends. These departments have also often been a prodigious source of unsupervised waste of material and of medical time to the hospital, and in man-hours and disability to the State. The general provision of facilities such as those described above, in addition to its beneficial effect on teaching, could also prove both a local and a national economy.

We have a special debt to acknowledge to the department of medical art, Guy's Hospital, and the constant help that Mr. E. Engel has given us in the provision of photographs for teaching purposes.

SIGNIFICANCE OF CONVULSIONS IN CHILDREN WITH PURULENT MENINGITIS

CHRISTOPHER OUNSTED
M.A., B.M. Oxfd, D.C.H.
PÆDIATRIC RESEARCH ASSISTANT, OXFORD REGIONAL HOSPITAL BOARD

EFFICIENT chemotherapy has dramatically reduced the mortality from purulent meningitis. Swift and complete elimination of the infecting organism usually leads to permanent cure. Nevertheless, purulent meningitis still carries a definite mortality, particularly in younger children. The report to the Department of Health for Scotland (1944) on meningococcal meningitis showed that mortality in children aged less than one year was still 28·3%, whereas in young adults it was only 2·6%. Pneumococcal meningitis still carries a grave prognosis, even when the most thorough treatment is given. Jackson (1950) reported 24 fully treated cases with 7 deaths (mortality 29%). Jackson comments that the cause of death in these patients was not obvious.

Severe epileptiform convulsions are a common complication of purulent meningitis in childhood and may be partly responsible for the maintenance of the mortality. Their prophylaxis and treatment may play an important rôle in determining the outcome of the meningitis. Hippocrates, born about 460 B.C., commented on the grave significance of convulsions during brain fever, and Rilliet and Barthez (1884) said of these seizures: “Elles sont remarkables alors par leur intensité; elles se répètent coup sur coup jusqu' à la mort.” At the beginning of the penicillin era the Oxford workers emphasised the dangers of status epilepticus in infants with pneumococcal meningitis in these words: “Fits are as dangerous to the infant as the toxæmia of the infection, and their prevention or control is imperative” (Smith et al. 1946).

MATERIAL

This report concerns 90 consecutive cases of purulent meningitis admitted to the children's departments of the United Oxford Hospitals between November, 1946, and March, 1950, which received the chemotherapy appropriate for the infecting organism. Children who did not receive the appropriate chemotherapy, and children with tuberculous and non-bacterial meningitis were excluded.

The causal organisms were meningococcus (56 cases), *Hæmophilus influenzæ* (17 cases), pneumococcus (11 cases), β-hæmolytic streptococcus (2 cases), *Staphylococcus aureus* (1 case), *Staph. albus* (1 case), *Bact. coli* (1 case), and *Bact. paracoli* (1 case).

The results were assessed in terms of the immediate outcome of the acute illness as “cured” or “failed.” Failure was recorded only when the child died or was left with gross cerebral damage; all other children were classified as “cures.” This division takes no account, therefore, of residual lesions apart from cerebral damage or of cerebral lesions too small for immediate clinical detection. Similarly, a child was recorded as having had a fit only when a clear record of convulsive seizure was made in the notes. It follows that the

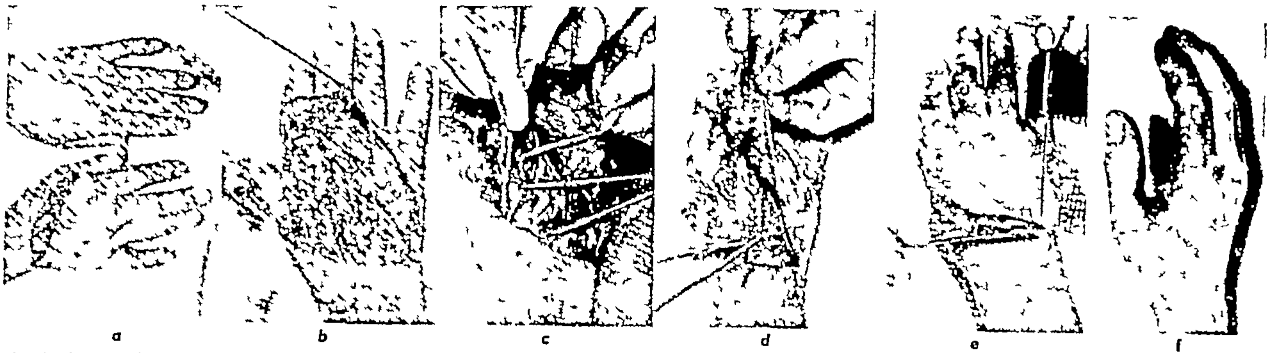


Fig 4—Some of the photographs displayed on the wall of the preparation room for the guidance of dressers *a*, avulsion of flap from dorsum of hand *b* exploration of wound after injection of local analgesic *c*, undermining with no 15 blade *d*, conversion of devitalised portion of flap into free skin graft by removal of deep surface fat, *e*, closure using Gillies's needle-holder, Gillies's hooks, and fine silk sutures, *f* results at first dressing at end of a week

A uniform system of documentation, including diagrams of the lesion, is used in all cases These records are periodically analysed, and the results made available to dressers Special care is taken to make certain that any adverse result seen in the postoperative stage is immediately brought to the attention of the dresser who did the job, such cases are made the subject of a thorough inquiry

OPERATIONS

The dressers are taught the policy of the surgery, which is that every open wound, however small, should be given a full dress surgical treatment, and that, if the full thickness of the skin has been divided, simple application of a dressing is inadequate care The chart on the wall of the theatre describes the steps taken in operating on all open wounds as follow

(1) *Toilet*, primary and secondary, with 1% cetrimide
(2) *Local analgesia* (*precautions to be taken in digital blocks*, use of ring tourniquet)
(3) *Exploration* and determination of anatomical extent of lesion
(4) *Excision* and/or debridement
(5) *Hæmostasis*
(6) *Closure* by approximation with or without undermining, by free graft, or by flaps, local or distant
(7) Aftercare

The primary toilet with 1% cetrimide is done, in hand and digital injuries, by the patient himself, wearing a mask and using a nail brush and nail file

We believe that a ring block analgesia with 2% procaine is safe, provided no adrenaline is added Over 3000 ring blocks have been given to date without complication

Our teaching is that all wounds, except those due to crush injuries, should have a minimal marginal excision to provide non bevelled non contaminated edges which can be accurately apposed After the wound has been excised these lacerations are accurately closed Crush injuries of the digits, on the other hand, are treated by debridement—i e, toilet and excision only of devitalised and grossly soiled tissues Suture in these cases is limited to that necessary for maintaining flaps in anatomical position The exploration and excision of digital wounds is done under a tourniquet, which is released when the latter is complete The finger is next elevated and compressed with dry gauze for 2–5 minutes Spurting vessels are clipped and twisted, if they still spurt they are ligatured Ligature material coarser than 3/0 catgut or 4/0 silk is never used in the hand If a general ooze still continues to obscure the field the tourniquet is reapplied, closure completed, the tourniquet released, and manual pressure applied over the dressing for 2–5 minutes In closure avoidance of tension and tentage is emphasised This generally means undermining with a no 15 blade while the edges are steadied with a Gillies tissue hook Tentage is avoided in the deeper wounds by a layered closure, using 3/0 catgut sutures with the knot tied on the deep surface of the flap 4/0 interrupted silks are used for skin suture, each edge is transfixed separately, the sutures are 3 or 4 mm apart, with bites of tissue 3 or 4 mm in width and depth Free grafts are generally of thin split skin, cut from the forearm with a Blair blade Full thickness grafts and local thenar and palmar flaps are cut to an accurate pattern of the defect, great attention is paid to the repair of the secondary defects in these operations

The dressing of a finger must be snug and secure with the finger semiflexed It is mainly of dry gauze kept in position with strips of zinc oxide strapping and minimal bandage We have found 'Nylon' derivative to be the best intimate dressing for lacerations This is a flexible transparent membrane that does not injure the tissues and is permeable to water vapour but impermeable to water If it cannot be obtained, tulle gras, with as little grease as possible is used

The patient is seen on the day after operation, if the dressing is in place and comfortable, he is not seen again for a week, and then most of the sutures are removed

The programme outlined above may be held to be too elaborate for some of the injuries to which it is applied, but its routine use has two advantages (1) a uniform standard of quick quiet healing can be obtained for all finger injuries treated, and (2) full advantage is taken of the training in technique that such repairs can provide

MATERIAL AND RESULTS

Nearly 3000 repairs a year are done in the outpatient accident theatre at Guy's Hospital A little under 50% of these are open digital injuries The range of work undertaken in the outpatient accident theatre covers all open injuries of digits, with and without tissue loss, including traumatic amputations, divisions of extensor tendon, and injuries of digital nerves, but excluding the repair of flexor tendons divided within the fibrous theca

Results in two series analysed are given here † The first series comprises 357 consecutive open digital injuries treated in three months in 1948 and including compound fractures, traumatic amputations, and injuries of extensor tendons During this period no case of isolated digital injury was admitted to the wards The second series is of 118 traumatic amputations of the finger tip treated in fifteen months The average healing time of the 357 open digital injuries was 10 2 days for lacerations without tissue loss, 18 6 days for crush injuries without tissue loss, and 15 3 days for the whole series of 357, including those with tissue loss fracture, and tendon and nerve injury The criterion of healing was that the wound was free from scab and dressing In this series healing was

---

† These form the subject of a separate detailed report written with Dr D C Douchar and to be published later

TABLE VI—RELATION BETWEEN FAILURES AND PHENOBARBITONE

—	Cures	Failures	Total
Phenobarbitone given	42	7 (*14%*)	49
Phenobarbitone not given	14	10 (*42%*)	24
Total	56	17	73

χ^2_1 (Yates's method) = 5 315) P is less than 0 05

and that there is in this group a parallel reduction in the incidence of convulsions (table VII) In the group treated with phenobarbitone the failure rate was 14%, and 10% had convulsions after admission to hospital, in the group not treated with phenobarbitone the failure rate was 42%, and 33% of the children had convulsions in hospital (tables VI and VII)

There seems, then, to have been a downward trend in the incidence both of seizures and of failures following the introduction of prophylaxis with phenobarbitone

Status Epilepticus

Status epilepticus was diagnosed when a series of seizures occurred in which the coma of one seizure merged with the acute phase of the next Status epilepticus developed in 8 patients, of whom 7 died The causal organisms in these children were meningococcus (4 cases), pneumococcus (3 cases), and β hæmolytic streptococcus (1 case) Only 1 of these children had been given prophylactic phenobarbitone before the onset of the first seizure

Phenobarbitone, paraldehyde, and chloral were used in various combinations to treat the established status epilepticus in the 7 fatal cases The solitary survivor was treated with intramuscular sodium iso amyl ethyl barbiturate ('Sodium amytal'), but this child, alive twelve months later, is mentally deficient

TABLE VII—RELATION BETWEEN FITS AND PHENOBARBITONE

—	No fits in phase II	Fits in phase II	Total
Phenobarbitone	44	5 (*10%*)	49
No phenobarbitone	16	8	24
Total	60	13	73

χ^2_1 (Yates's method) = 4 414 P is less than 0 05

The ages of these 8 children ranged from five weeks to two and a half years, average twelve months, and it was considered that all the 8 cases were failures. Nearly half the failures in the group aged less than four years were therefore associated with status epilepticus

Delayed Sequelæ

Of the 72 children discharged as 'cured," 65 were followed up as outpatients The shortest period of study was six months None of the children who escaped seizures have yet developed signs of permanent cerebral damage Of the 12 "cures" who had had multiple seizures in the acute phase, 1 has since developed recurrent convulsions and 1 other has severe mental defect If these children are classified as failures, the argument that multiple seizures are dangerous is correspondingly strengthened. Thus 17 of the 20 failures had multiple fits and 17 of the 27 children with multiple fits did not recover completely

DISCUSSION

Prognosis

The findings of this survey show that, in cases of purulent meningitis in childhood receiving adequate chemotherapy, there is a close association between the occurrence of fits and the outcome of the disease Bloor (1950) made a follow-up study of a series of children treated for *H influenzæ* meningitis, and found that convulsions were the only prognostic signs of value He found that the generally accepted criteria of severity in the acute phase bore little relation to the ultimate results, but, of those cases classified as failures, convulsions had occurred in 71%, whereas among the cured children the incidence of convulsions in the acute phase was 18% In Jackson's (1950) series of cases of pneumococcal meningitis convulsions occurred in the great majority of the fatal cases There is, to my mind, little doubt that seizures are prognostic signs of great importance in this group of diseases

It may be noticed, in passing, that the prognostic significance of convulsions is not peculiar to meningitis in childhood A similar relationship was found in infants with pneumonia (Dr V Smallpeice, personal communication)

Diagnosis

Attention has been drawn to the difficulties that attend the diagnosis of meningitis in early childhood (Jackson 1950, Smith 1951) Physical signs are often unreliable, and this is particularly true when the child has just had a fit Seizures occurred in nearly half the younger children in this series and are therefore themselves diagnostic signs of some importance Early, and hence successful, treatment of purulent meningitis depends on the prompt identification of the causal organism in a specimen of cerebrospinal fluid It follows that any small child who has had an *unexplained* febrile seizure should be admitted to hospital, and that, unless some definite contra-indication exists, a lumbar puncture should be done without delay By following this rule 4 hitherto unsuspected cases of purulent meningitis have been diagnosed in our department in the last three months

Prophylaxis

Phenobarbitone as prophylaxis is given on a weight/age dosage (Ounsted 1949) A flexible schedule of dosage is used because children who have already had a fit are likely to require, weight for weight, a greater quantity of drug For a child aged one year, weighing 24 lb, who is gravely ill, an initial dose of gr $^1/_2$ of soluble phenobarbitone may be given by intramuscular injection Gr. $^1/_4$ six-hourly may be given thereafter for the next thirty six hours, by mouth or by injection, and then gr $^1/_4$ thrice daily for the remainder of the acute phase of the illness

It is an advantage if the initial injection can be given by the family doctor, before the child is subjected to the strain of a long ambulance journey, 4 children in this series had convulsions during their journey from home to hospital.

Toxic effects from phenobarbitone in this dosage are, in my experience, almost unknown, nor have I seen any evidence of masking of the physical signs

Treatment

The treatment of convulsions and status epilepticus is unsatisfactory in small children with purulent meningitis The usual sedative drugs, such as chloral, phenobarbitone, and inhalant anæsthetics, are in our experience valueless Whitty and Taylor (1949) have shown that paraldehyde by the intramuscular and intravenous routes is highly effective in controlling status epilepticus It has, however, certain disadvantages when used for the treatment of gravely ill infants. Intravenous infusions in these children are often difficult and may be dangerous Intramuscular injections may take half an hour to have effect—a time lag of greater danger in convulsing infants than in the older person The children in this series in whom status epilepticus was treated with paraldehyde did not survive Search for a possible alternative for use in this particular group seemed reasonable

TABLE I—RELATIONSHIP BETWEEN FITS AND FAILURE OF TREATMENT

—	Cures	Failures	Total
No fits	51 (*96 2%*)	2 (*3 8%*)	53
Fits	21 (*56 8%*)	16 (*43 2%*)	37
Total	72	18	90

χ^2_1 (Yates s method) = 18 81 P is less than 0 001

incidence of fits given in this survey is the lowest true convulsion rate, whereas the incidence of cures is the highest probable cure rate

RESULTS

In the series as a whole, 18 children died or were left with gross cerebral damage, an immediate failure rate of 20%

Table I shows the over all incidence of convulsions in failed and cured groups It will be seen that 37 children (41%) had fits in the course of their illnesses In this group of children with fits the failure rate was 43%, whereas in the group free from fits the failure rate was 4% The value for χ^2 on the absolute figures is 16 56, and the difference is therefore of high statistical significance

Single and Multiple Fits

Table II sets out the series divided into those with no fits, those with a solitary fit, and those with multiple fits It will be seen that the treatment failed in 3 8% of children who had no fits, 10 0% of children with only one fit, and 55 5% of children with multiple fits The prognostic march is clear

TABLE II—RELATION BETWEEN INCIDENCE OF FITS AND FAILURES

—	Cures	Failures	Total
No fits	51	2 (*3 8%*)	53
1 fit only	9	1 (*10 0%*)	10
Multiple fits	12	15 (*55 5%*)	27
Total	72	18	90

Age

The tendency to seizures in febrile diseases of all types is much greater in children aged less than four years than in older patients (Lennox 1949, Bridge 1949) Table III shows the series divided into those older and those younger than four years There were 17 children aged more than four years, and of these 2 (12%) had fits, of the 73 children aged less than four years 35 (48%) had fits Age is clearly a factor in the convulsions provoked by meningitis as in the other febrile convulsions of childhood

In table IV only the children aged less than four years are considered The average age of this group of children was thirteen months The relationship between failure and the occurrence of seizures is essentially that found in the group as a whole The following points emerge from the table

(i) Half the children aged less than 4 years had fits

(ii) Only 1 of the 17 failures escaped convulsions

(iii) 37 of the 56 cured cases escaped convulsions

(iv) Of the total of 38 who escaped convulsions 37 (97% were cured

TABLE III—RELATION BETWEEN FITS AND AGE

Age	Fits	No fits	Total
More than 4 yr	2 (*11 8%*)	15 (*88 2%*)	17
Less than 4 yr	35 (*47 9%*)	38 (*52 1%*)	73
Total	37	53	90

χ^2_1 (Yates s method) = 6 037 P is less than 0 05

The value of χ^2 on table IV is 18 93, the differences are therefore of high significance

Early and Late Fits

Convulsions may occur at any time during meningitis in childhood Inspection of the records of the present cases suggested that seizures occurring after the institution of hospital treatment were more ominous than those limited to the early days of the disease* To examine this point more closely the illnesses of the 37 children with fits were divided into two phases Phase I was the time from the onset of symptoms to the time when the child's admission to hospital and initial examination were complete, phase II covered the remainder of the illness

TABLE IV—RELATION BETWEEN FITS AND FAILURES IN CHILDREN AGED LESS THAN FOUR YEARS

—	Cures	Failures	Total
No fits	37	1	38
Fits	19	16	35
Total	56	17	73

χ^2_1 (Yates's method) = 16 73 P is less than 0 001

Table V sets out the figures 24 children had fits only in phase I and had no further attacks while in hospital, in this group 18 out of 24 (75%) were cured 13 children had convulsions during phase II, in this group, in contrast, only 3 out of 13 (23%) were cured Thus it seems that the fits of the second phase carry the graver prognosis However, the possibilities of prophylaxis and treatment are greater in the second phase, since the child is under controlled conditions in hospital.

Phenobarbitone Prophylaxis

During the years covered by this survey the practice of giving phenobarbitone as a routine prophylaxis against convulsions was gradually introduced into our department

Among the 73 children in the series aged less than four years, 49 were given phenobarbitone as a routine throughout the acute phase of their disease and 24 had no such prophylaxis It must be emphasised that these two groups were not planned as deliberate controls and that, therefore, any conclusions drawn from tables VI and VII must be tentative In the most recent cases a larger proportion of patients were given phenobarbitone, compared with the earlier part of the series On the other hand, inspection of the records showed that children who had had convulsions before admission were more often given phenobarbitone than those who had not, and more likely to have further fits than those who had not had fits before admission These facts may weight the figures slightly against the group treated with phenobarbitone

TABLE V—RELATION OF FAILURES TO TIME OF ONSET OF FITS

—	Cures	Failures	Total
Fits before admission only	18	6	24
Fits after admission	3	10	13
Total	21	16	37

χ^2_1 (Yates s method) = 7 268 P is less than 0 01

It will be seen that the cure-rate is decidedly higher in the group treated with phenobarbitone (table VI)

---

* Hippocrates stated in his 25th aphorism It is better that a fever should follow a convulsion than that a convulsion should follow a fever

HYALURONIDASE

ASSAY AND ADMINISTRATION

D G EVANS
Sc, Ph.D Manc
READER IN
ICAL BACTERIOLOGY

F T PERKINS
M.Sc, Ph.D Manc
ASSISTANT LECTURER IN
CHEMICAL BACTERIOLOGY

WILFRID GAISFORD
M D Lond, M.Sc Manc, F.R C.P
PROFESSOR OF CHILD HEALTH AND PÆDIATRICS

UNIVERSITY OF MANCHESTER

N the two years since Gaisford and Evans (1949) orted on the use of hyaluronidase as an aid to parenal administration of fluid to infants and children, s enzyme has been widely used, but its efficacy has ned We discuss here some of the possible reasons for variation and suggest methods for improving the ults

The first and most important cause of these differences the uncertain potency of the preparation used, which ay vary within wide limits The second is the technique administration A third is failure to recognise the mitations of hyaluronidase

METHOD OF ASSAY

One of the clinical difficulties in judging the potency any particular specimen of hyaluronidase is that ccess or failure of absorption is evident only after jection A reliable method of assay in terms of a suitable andard is essential to ensure that the preparation used active and the dosage adequate Standardisation of yaluronidase by its method of preparation—e g, from estis or semen—is unwise and becomes unnecessary if a eliable assay is available

The potency of hyaluronidase preparations may be etermined by examining their diffusing activity in the kin, their action on hyaluronic acid, or their ability to ecapsulate streptococci (McClean 1942, 1943, Kass and eastone 1944, Fulton et al. 1948) A new method has been devised (Burnet 1948) which depends on the diminution in the viscosity of synovial fluid which hyaluronidase effects This has been called the ACRA test (acid, Congo red, and alcohol are used in the indicator system) A modification of the test has been described by Oakley and Warrack (1951)

We have investigated the ACRA test, using horse synovial fluid, for its value in assaying the potency of bull testicular hyaluronidase preparations Two methods of assay have been studied In the first, preparations of hyaluronidase were titrated to determine the minimal reacting dose and, in the second preparations were titrated to determine the dose which was just neutralised by a standard amount of antihyaluronidase

Determination of Minimal Reacting Dose

Each sample of horse synovial fluid was first titrated to determine the most suitable dilution to use Serial dilutions in borate buffer (Glenny et al. 1928) were incubated at 37°C for half an hour and then cooled at 4°C for ten minutes, when 0 2 ml. of 2% aqueous solution of Congo red was mixed with 0 75 ml. of each dilution With each mixture a drop from a Pasteur pipette was allowed to fall gently into a petri dish filled to a depth of 5 mm with acidified aqueous alcohol (1 ml. conc HCl + 100 ml 70% alcohol), and the minimal concentration of synovial fluid which gave a coherent blue globule was determined Six times the minimal concentration was chosen as the indicating dose in the hyaluronidase activity tests, so that excess of substrate was ensured

In testing the potency of hyaluronidase preparations a series of dilutions of hyaluronidase in borate buffer was made, and to 0 5 ml. of each dilution six indicating doses of synovial fluid in 0 25 ml. were added The mixtures were incubated at 37°C in a water bath for half an hour and cooled at 4°C for ten minutes To each mixture 0 2 ml. of 2% aqueous solution of Congo red was added, and with a Pasteur pipette drops of each mixture were allowed to fall gently into acidified alcohol

With those mixtures containing an insufficient concentration of hyaluronidase to affect the viscosity of the synovial fluid the drop remained as a coherent blue globule, but with those containing hyaluronidase in sufficient concentration to reduce the viscosity the drop diffused into the acid alcohol and stained blue The minimal dilution of hyaluronidase which gave a definite diffuse spread was taken as the end-point and referred to as the minimal spreading dose (M S.D)

Various preparations of hyaluronidase were titrated by this method at 25% differences between the dilutions, different samples of synovial fluid being used A typical set of results is given in table I As was expected, different end points were obtained with the different samples of synovial fluid for any one preparation of hyaluronidase, but the order of increasing activity of the preparations was the same with each sample of synovial fluid—i e, H2, H1, H3, H4 The ratios of the activities, however, were not always the same, and because of this the potency of any one preparation, if assayed in terms of a standard hyaluronidase, would vary in different tests The difficulties involved in determining with a high degree of accuracy the minimal reacting dose of enzymes or toxins are well known because end points in such tests are not sharply defined It was because of these considerations that the neutralisation method was investigated.

TABLE I—POTENCY OF HYALURONIDASE PREPARATIONS, WITH DIFFERENT SAMPLES OF SYNOVIAL FLUID ASSAYED BY DETERMINING MINIMAL REACTING DOSE (M.S.D)

Preparation of hyaluronidase	Titres (M.S D) with four samples of synovial fluid			
	SF1	SF2	SF3	SF4
H1	1/100	1/80	1/400	1/400
H2	1/25	1/16	1/100	1/100
H3	1/2000	1/1000	1/4000	1/4000
H4	1/6500	1/6500	1/7000	1/7500

Determination of Neutralised Dose

Antisera to bull testicular hyaluronidase were prepared in rabbits by giving weekly injections of hyaluronidase for six months The earlier injections were given subcutaneously and the later ones intravenously, and each dose contained about 5000–6000 M S D The antisera were tested for neutralising potency by determining the lowest dilutions which neutralised the activity of 20 M S D of hyaluronidase The most potent antiserum prepared was such that 1 ml neutralised almost 32,000 M.S D of enzyme

In testing the potency of hyaluronidase preparations a high titred antiserum was chosen and given the arbitrary value of 800 units per ml. Determinations were made of the dilution of hyaluronidase neutralised by 1 unit of antihyaluronidase, and the potency was expressed in terms of the number of units required to neutralise 1 ml of undiluted preparation A series of dilutions of hyaluronidase was made, and to 0 25 ml of each dilution 0 25 ml. of 1/200 dilution of antiserum (1 unit) was added, and the mixtures were left at room temperature for an hour to allow neutralisation to occur The appropriate dilution of synovial fluid (six indicating doses in 0 25 ml) was then added, and the mixtures were incubated at 37°C for half an hour, followed by cooling at 4°C, when 0 2 ml of Congo red solution was added, and drops of each mixture were tested in acidified alcohol. The end-

There was thus little evidence of cross infection in this virtually closed community, though the investigation was necessarily limited

Sensitivity tests were done on the 21 potentially pathogenic organisms isolated during these studies, the findings are shown in table IV Tube tests were made, doubling dilutions of each antibiotic in broth being infected with standard inocula from 7 hour broth cultures of the organisms The results were read by visual estimation of turbidity after overnight (sixteen hours) incubation Controls consisted of an Oxford staphylococcus and a local strain of β hæmolytic streptococcus

"Penicillin sensitive" strains all showed sensitivity equal to or greater than that of the Oxford staphylococcus, "penicillin resistant" strains were more than sixteen times as resistant as the Oxford staphylococcus (all of the 6 resistant staphylococci tested were penicillinase producers) "Streptomycin sensitive" strains were sensitive to 16 μg per ml or less, 2 strains, shown in parentheses in the "resistant" column of the table, resisted 16 μg but were inhibited by 32 μg per ml, and the remaining "resistant" organism resisted 32 μg but was sensitive to 64 μg per ml "Chloramphenicol sensitive" strains were all inhibited by 13 μg per ml or less, "resistant" strains both resisted 25 μg but were sensitive to 50 μg per ml "Aureomycin sensitive" strains were all sensitive to 2 μg per ml or less, the 3 gram negative strains graded as "? resistant" resisted 6 25 μg but were inhibited by 12 5 μg per ml of aureomycin under the conditions of the test

These tests with aureomycin are of uncertain significance, but the sensitivity tests do suggest that most of the potentially pathogenic organisms isolated from the patients and their environment were sensitive to the antibiotics used

DISCUSSION

The outstanding value to the smallpox patient of previous successful vaccination is again illustrated in this small outbreak Variations in response to infection, as shown by the length of the incubation period, the severity of prodromal illness, and the extent of the rash, are presumably individual manifestations depending on the rapidity and adequacy of the immune response in both vaccinated and unvaccinated persons In this epidemic, though such factors as the degree of exposure, age, and state of nutrition were similar in all the fatal cases in adults, no two of these patients presented identical pictures Individual variations in antibody levels have been found by Collier and Schonfeld (1950) to be correlated with severity and mortality in smallpox The equivalent severity of the prodromal stages in both vaccinated and unvaccinated groups suggests that, until the stage of secondary viræmia is initiated, there is little individual difference in response to infection by variola virus, if clinical smallpox is to be the outcome The subsequent course probably depends on the degree to which circulating antibodies neutralise virus liberated into the blood stream from internal sites of multiplication When neutralising antibodies are present in high titre, viræmic spread cannot occur, and no rash will appear, when they are moderate in amount, antibody neutralisation reduces the amount of active virus disseminated, and further modification of the disease results from additional antibody production by a host already trained to produce it Collier and Schonfeld (1950) found a more rapid rise in antibody level in vaccinated than in most unvaccinated persons In a non immune host with no basal antibody the course of smallpox will depend on the balance between the speed of multiplication and spread of the virus and the inherent ability of the host to produce antibody Delayed or inadequate immune response allows virus to invade and damage such a high proportion of the host's cells as to impair vital functions and cause death

The effects of the antibiotics used in treatment were disappointing inasmuch as they exerted no effect on the expected mortality Nevertheless clinical and bacteriological observations showed that secondary bacterial invasion of the skin lesions was minimised, so that no "pustular" stage and no classical "secondary fever" was seen Abacterial necrosis was followed by liquefaction of the cells involved in the lesions, the formation of bullæ, and desquamation of large areas of skin The distressing respiratory symptoms suggested that similar changes might be occurring in the trachea and smaller air-passages The continuance of pyrexia in at least two typically confluent cases might well be explained by loss of active skin surface How much the toxæmia resulting from extensive skin damage contributed to death is uncertain, for myocarditis had already developed in the earlier stages The nature of the cardiac damage is not known, but it may well have been due to virus invasion The inability of antibiotic therapy to influence the virus pathology of the disease might be related to failure to administer these preparations before viræmic spread and widespread cellular invasion had occurred, but there is no evidence at present to suggest that variola virus is susceptible to any antibiotic yet known (Eaton 1950)

In view of the obvious cardiac damage, it was our impression that the utmost attention should be paid to the problem of how best to nurse smallpox patients in future epidemics, so that such complications may be minimised Supportive measures—e g, early blood transfusions and, in some cases, administration of 'Eucortone' and vitamin K—may be advantageous, especially in females, because hæmorrhage and toxæmia rapidly cause weakness which may be fatal, as in the present series Dixon (1948) remarked that the "blunderbuss" therapy advocated by Boeck (1946) did not seem to be beneficial, yet the severe case is in such a serious state that all possibly effective measures are called for

The value of laboratory examinations in diagnosis was again demonstrated The primary case in this epidemic was considered to be chickenpox on what still seem, in retrospect, the most convincing clinical grounds, and yet the application of appropriate diagnostic techniques, as discussed by MacCallum et al (1950), would have revealed the true nature of this illness in time for protective vaccination a week or so earlier than was the case It seems reasonable to suggest that facilities for prompt laboratory investigation of cases in which there is the faintest possibility of smallpox—e g, in recent arrivals in this country from any infected region—should be available in all areas

SUMMARY

Some of the important clinical aspects of smallpox (variola major) are described, from a study of 17 patients

Attention is directed to the importance of cardiac damage in severe cases

Antibiotics had no effect on the virus, but greatly modified secondary bacterial infection of the skin lesions

We wish to thank Prof A W Downie for his assistance in the virus studies, and Dr R E O Williams for phage typing the staphylococci

REFERENCES

Boeck V H F (1946) *Bull U.S Army med Dep* 6 45 cited by Dixon (1948)
Collier W A, Schönfeld J K (1950) *Med J Aust* ii 303
Dixon C W (1948) *J Hyg Camb* 46 351
Downie A W McCarthy K Macdonald A (1950) *Lancet* ii, 513
Dunlop D, Davidson L S P McNee J W (1949) Textbook of Medical Treatment Edinburgh
Eaton M D (1950) *Ann Rev Microbiol* 4 223
Laidlaw S I A Horne W A (1950) *Med Offr* 83 187
MacCallum F O McPherson C A Johnstone D F (1950) *Lancet* ii 514
Ricketts T F Byles J B (1908) Diagnosis of Small pox London
Riley I D Arnold G C (1950) *Lancet* ii 504

SUMMARY

A method is described by which the potency of testicular or seminal hyaluronidase, prepared for therapeutic purposes, may be assayed by determining the quantity neutralised by a standard amount of specific antihyaluronidase

The clinical indications and methods of using the enzyme are outlined

We wish to thank Dr C L Oakley and Miss G H Warrack, of the Wellcome Research Laboratories, for helpful advice and for many samples of synovial fluid, and Dr D Riding, of the Evans Biological Institute, Dr F Fletcher, of Bengers Ltd, and Dr F A. Robinson, of Allen & Hanburys Ltd, for the hyaluronidase preparations

REFERENCES

Burnet F M. (1948) *Aust J exp Biol med. Sci* 26 71

Fulton, J K. Marcus S Robinson W D (1948) *Proc Soc exp Biol, N Y* 69, 258

Gaisford W Evans D G (1949) *Lancet* ii 505

Glenny A T Pope C G Waddington H. (1928) *J Path Bact* 31 133

Kass E H Seastone C V (1944) *J exp Med* 79 319

McClean D (1942) *J Path Bact* 54 284

— (1943) *Biochem J* 37 169

— Hale C W (1941) *Ibid* 35 159

Oakley C L Warrack G H (1951) *J Path Bact.* 63 45

CONCENTRATION OF PENICILLIN IN THE LUNGS

EFFECTS OF TWO PENICILLIN ESTERS IN CHRONIC PULMONARY INFECTIONS

A G S HEATHCOTE
M.R C S
SENIOR REGISTRAR IN PATHOLOGY

E NASSAU
M.D Vienna
PATHOLOGIST

HAREFIELD HOSPITAL MIDDLESEX

As a rule penicillin administered systemically does not reach the sputum in effective concentrations, and for this reason the scope of penicillin therapy in chronic pulmonary infections has been limited We have, however, been investigating two new penicillin derivatives which Prof. K A Jensen and other workers (1950) in Copenhagen had found to be excreted to an unusual extent through the lungs

This valuable property was discovered by Jensen and his colleagues in the course of their search for new insoluble penicillin compounds having a "depot" action like that of procaine penicillin, a dose of which injected intramuscularly gradually releases penicillin into the blood stream They found that an ester of penicillin—benzylpenicillin diethylaminoethylester hydriodide (L G 1)—gave a satisfactory depot effect, though equal doses of procaine penicillin usually produced higher blood penicillin levels for longer periods When they came to investigate the fate of L G 1 in the tissues of laboratory animals, however, they observed that the penicillin level produced in the lungs by equal intramuscular doses was several times higher with L G 1 than with either sodium penicillin or procaine penicillin Preliminary observations in man confirmed this peculiarity of L G 1 and seemed to justify the hope that it would prove more effective than other penicillin preparations in the treatment of pulmonary infections

MATERIALS AND METHODS

L G 1 is a white crystalline powder, said to be soluble in water at room temperature only to the extent of 1 part in 96, so that a saturated solution would be equivalent to about 10,000 units per ml. It was supplied in the form of a dry powder, to be prepared for injection by adding sterile water and shaking, so producing a suspension which could easily be injected intramuscularly

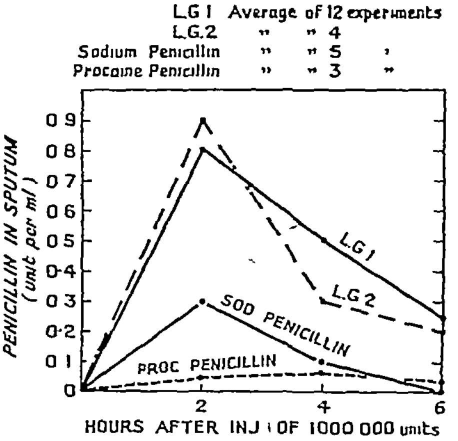


Fig 1—Penicillin levels in sputum after intramuscular doses of 1,000 000 units of penicillin in form of L.G 1 L.G.2 sodium penicillin or procaine penicillin in same patient.

We have also studied the hydrochloride of benzylpenicillin diethylaminoethylester (L G 2), which is much more soluble in water than L G 1

Patients with chronic non tuberculous pulmonary conditions were selected for treatment To avoid difficulties arising from the admixture of saliva with the sputum, only patients producing copious sputum—i e, cases of bronchiectasis, lung abscess, and suppurative pneumonitis—were chosen for the trial. Patients who had not received chemotherapy for a long time, if at all, were preferred

Since the standard dosage of crystalline sodium penicillin at Harefield Hospital is 1,000,000 units every 12 hours, L G 1 and L.G.2 were given in the same dosage Other patients received procaine penicillin in aqueous suspension, or sodium penicillin in aqueous solution

In some experiments specimens of sputum were obtained at 2, 4, and 6 hours after the injection and assayed for penicillin In other experiments the sputum was collected over the 24 hours, measured, homogenised, and assayed. Before treatment a 24 hour specimen was measured and examined bacteriologically Bacteriological examinations were also made during and after treatment The penicillin compounds were always given intramuscularly The course of treatment with L G 1 and L.G 2 lasted 1 week in each case

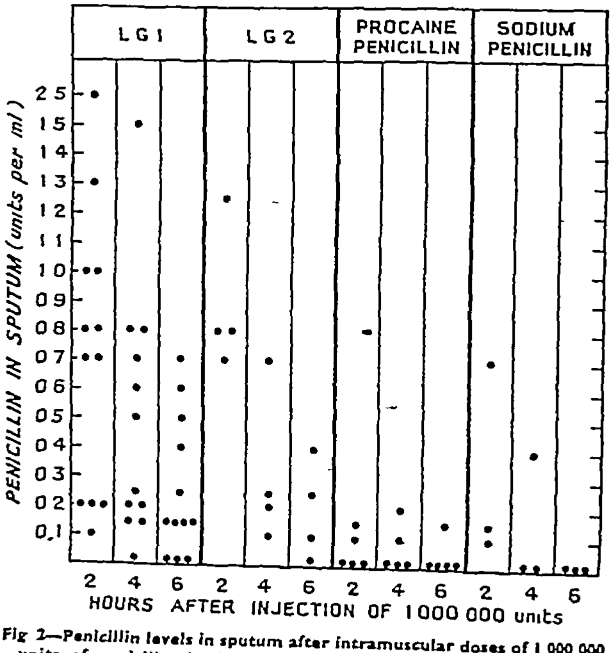


Fig 2—Penicillin levels in sputum after intramuscular doses of 1 000 000 units of penicillin in form of L.G 1 L.G.2 sodium penicillin or procaine penicillin in different patients.

TABLE II—POTENCY OF HYALURONIDASE PREPARATIONS, WITH DIFFERENT SAMPLES OF SYNOVIAL FLUID, ASSAYED BY NEUTRALISATION WITH ANTISERA

Preparation of hyaluronidase	Potency with three samples of synovial fluid		
	SF8	SF9	SF10
H1	16 (1/4)	18 (1/4·5)	16 (1/4)
H4	500 (1/125)	500 (1/125)	600 (1/150)
H5	56 (1/14)	48 (1/12)	48 (1/12)
H6	44 (1/11)	40 (1/10)	40 (1/10)
H7	56 (1/14)	48 (1/12)	48 (1/12)

The potency of a preparation is expressed in terms of the number of arbitrary units of antihyaluronidase required to neutralise 1 ml of the undiluted preparation. The dilutions of hyaluronidase (0·25 ml volume) at which the end point occurred with 1 unit of antihyaluronidase are given in parentheses.

point in this titration was read as the most concentrated dilution of hyaluronidase that was completely neutralised by antiserum and thus gave a coherent globule.

Results are given (table II) showing the potency of five different preparations of hyaluronidase when tested by this method with three samples of synovial fluid. Titrations were made with hyaluronidase dilutions which differed by 10–20%. It was evident that this test could, with different samples of synovial fluid, not only arrange the enzyme preparations in the same order of activity but also give potency values which agreed very closely. The end points were well defined and easier to read than those obtained in determining the minimal reacting dose.

Diffusing Activity in Skin

The examination of the diffusing activity in the skin is not a satisfactory method of determining quantitatively the potency of hyaluronidase preparations (McClean and Hale 1941). Since, however, the material was to be used for increasing the permeability of tissues to injected fluids, it was considered desirable to ascertain whether there was a correlation between diffusion in the skin and the ACRA test.

Diffusing activity of hyaluronidase preparations was tested by injecting intradermally 0·2 ml of each of a series of tenfold dilutions into depilated guineapigs. The end point was taken as that dilution giving a bleb which had entirely disappeared in ten minutes.

The activity of five hyaluronidase preparations was examined by the skin test in parallel with the ACRA test.

TABLE III—RELATION BETWEEN SKIN TEST AND ACRA TEST

Preparation of hyaluronidase	Skin test highest dilution producing diffusion	ACRA test M.S.D. with synovial fluid S14
H1	10^{-2}	1/120
H2	10^{-1}	1/50
H4	10^{-4}	1/6500
H5	10^{-3}	1/600
H6	10^{-3}	1/500

The results (table III) showed that the preparations fell into the same order of activity by both tests.

METHOD OF ADMINISTRATION

As regards the method of administration, the only modification suggested is a simplification of that described originally. All that is needed is a standard blood transfusion bottle and "giving" set.

With the intravenous needle attached to the set, the rate of flow is such that a two way set, as originally used, is unnecessary. The needle may be inserted in the midline above the umbilicus and directed downwards, or it may be inserted laterally just above or below the umbilicus and directed medially. The anterior abdominal wall has proved the most effective site for subcutaneous injection; the absorptive area is greater, there is less risk of sepsis, and there is less discomfort. The rate of flow after the injection of the hyaluronidase should be a continuous stream through the regulator, and it should be possible to give 100–300 ml of fluid within five minutes. The quicker the fluid is given, the more efficacious has hyaluronidase proved. It is of much less value in drip infusions.

Various techniques have been recommended. The hyaluronidase may be injected into the skin first, either intradermally or subcutaneously, and the fluid given through that site, or it may be dissolved in the infusing solution; or the solution may be injected first and the hyaluronidase added, in concentrated solution, after 2 or 3 ml have been injected. This last method has given the best results. The hyaluronidase powder is dissolved in sterile water and drawn up into a 1 ml syringe. When the flow of fluid to be injected (saline solution, saline glucose solution, or plasma) has started, the hyaluronidase is injected rapidly into the rubber tubing just above the needle inserted into the skin. The fluid injected should be cool; heat diminishes the activity of hyaluronidase. Hyaluronidase does not retain its potency long in solution; it is therefore necessary for it to be freshly dissolved to obtain the best results. The amount of diluent is of secondary importance; 0·5–1·0 ml of sterile water is usually adequate.

The conditions in which hyaluronidase has proved of particular value are severe dehydration fever in the newborn, pyloric stenosis (preoperatively when dehydration is only moderate and the general condition is good), and gastro enteritis. For any infant who is vomiting and unable to retain sufficient fluid, and when intravenous injection is technically difficult, this method of subcutaneous absorption affords a simple alternative route for fluid administration. *However, it must be emphasised that any seriously ill, toxic, and dehydrated infant who needs parenteral fluid will need it intravenously.* The value of hyaluronidase in such cases is that it minimises the number of intravenous infusions necessary. Often only one is required; thereafter subcutaneous injection will suffice till oral feeding can be resumed.

Hyaluronidase has also proved of value in pyelography in newborn and young infants in whom intravenous injection may offer considerable difficulties. Intramuscular injection of dye does not produce very satisfactory results. Any means of successful subcutaneous injection is therefore of value. The time taken for absorption of sufficient dye to give a reasonable picture is longer than in the case of intravenous injection, but this is compensated for by the fact that the injection can be given in the ward or nursery and the infant taken down to the X ray department twenty minutes later. This minimises the time spent in the X ray department. For a newborn infant 5 ml of diodone, mixed with 10 ml of sterile water in a 20 ml syringe, are usually adequate. It is important that the solution should be heated as little as possible. One end of a piece of rubber tubing (part of a catheter is suitable) 2 or 3 inches long is attached to the nozzle of the syringe, and an intravenous needle is attached to the other end of the rubber. The needle is inserted into the subcutaneous tissue of the anterior abdominal wall in the region of McBurney's point and directed outwards. About 1 ml of the dye solution is injected, and then the hyaluronidase, freshly dissolved in 0·5 ml of water, is injected into the rubber tubing. The rest of the dye is then injected fairly rapidly and the needle withdrawn from the skin. Exposures are made thirty minutes after the injection and thereafter as indicated. The injection is best timed to be given shortly before a feed is due—i.e., usually four hours after any fluid has been given. The feed may then be offered in the radiological department while the exposures are being made. This may make the procedure much easier and quieter and lead to the production of better films.

symptoms suggestive of water retention after continuous infusion for five days; in addition, after the treatment he had an attack of asthma, the intensity of which gradually decreased after forty-eight hours. The majority of the infusions were followed by local thrombosis of the vein segment utilised, but many of these veins recanalised rapidly. This is a serious drawback to the method. In view of this thrombotic tendency, it was thought inadvisable to use a glucose solution as the carrying medium. In two patients extravenous leakage resulted in a red painful swelling lasting 1–4 days.

CASE-SUMMARIES

Case 1.—A man, aged 72, with psoriatic arthropathy for the past five years, preceded by localised psoriasis for thirteen years.

Severe generalised rheumatoid arthritis involving all joints except the hip and spine. Psoriatic plaques covering the feet, legs, groins, abdominal wall, back, hands, forearms, and scalp. Nails showed typical thickening. Splenomegaly and generalised adenopathy were noted.

Treatment.—A.C.T.H. intravenously in a total dosage of 225 mg. as follows:

1. A.C.T.H. 25 mg. in 1 pint 0·18% NaCl over eight hours on alternate days; 5 infusions.
2. A.C.T.H. 50 mg. in 1 pint 0·18% NaCl over eight hours; 3 infusions.

Result.—Marked improvement. All joints became non-tender and painless on movement, and the stiffness greatly decreased. Raising the hands behind the head became possible. The psoriasis largely faded, residual areas showing only skin staining without thickening or scaling; and the splenomegaly and adenopathy disappeared. After the second infusion the patient could write letters, though he had been unable to do so for over a year. The erythrocyte sedimentation rate fell from 38 mm. in the first hour (Westergren) to 5 mm. by the third infusion. The right-hand grip improved from 88 mm. Hg to 170 mm. Hg during the course. One week after treatment was stopped the psoriasis was relapsing, but the arthropathy remained improved.

Case 2.—A man, aged 27, with Boeck's sarcoidosis following erythema nodosum in May, 1950.

Lacrymal and parotid glands enlarged. No significant lymphatic adenopathy, but liver and spleen easily felt. Radiograph of chest showed typical reticulation with moderate hilar adenopathy. Diagnosis confirmed by liver biopsy.

Treatment.—A.C.T.H. in total dosage of 700 mg.—250 mg. intravenously and 450 mg. intramuscularly—as follows:

1. A.C.T.H. 25 mg. intravenously in 1 pint 0·18% NaCl over eight hours; 1 infusion.
2. A.C.T.H. 25 mg. by intramuscular injection six-hourly for three days.
3. A.C.T.H. 25 mg. intravenously in 1 pint 0·18% NaCl over eight hours on alternate days; 9 infusions.
4. A.C.T.H. 25 mg. by intramuscular injection twice daily for three days.

Result.—After the first infusion, within twenty-four hours the spleen became impalpable and the lacrymal and parotid glands greatly diminished. Forty-eight hours later the spleen was again palpable. Two weeks later A.C.T.H. 25 mg. six-hourly by intramuscular injection was started. After three days there was no noticeable clinical change. Resumption of intravenous administration was quickly followed by the spleen becoming impalpable, diminution in the size of the liver, and flattening of the facial swellings.

Case 3.—A man, aged 53, with rheumatoid arthritis for the past ten years, and severe crippling since November, 1950.

Generalised arthropathy involving particularly the right knee-joint, with extreme joint tenderness, painful movement, and limitation of extension by 30°. Radiographs confirmed the diagnosis by showing generalised osteoporosis and typical joint changes.

Treatment.—A.C.T.H. in a total dosage of 1200 mg.—200 mg. intravenously and 1 g. intramuscularly—as follows:

1. A.C.T.H. 25 mg. by intramuscular injection six-hourly for ten days.
2. A.C.T.H. 50 mg. intravenously in 1 pint 0·18% NaCl over eight hours on alternate days; 4 infusions.

Result.—After four weeks' bed rest, physiotherapy, and repeated blood transfusion, the patient's condition was improving slightly and gradually. It was decided to use A.C.T.H. in an attempt to straighten the right knee-joint. The gradual improvement previously noticed continued with intramuscular injection of A.C.T.H., and extension of the knee became possible to within 10° of the normal. There was, however, no appreciable alteration of the pain and tenderness in the joints, and he was still unable to walk. After an interval of two weeks intravenous administration was begun. Walking became relatively painless after the second infusion and continued to improve. The other affected joints became almost entirely pain-free. There was no further improvement in the range of movement of the knee-joint, probably because of adhesions.

Case 4.—A man, aged 26, with bilateral iridocyclitis which had progressed since November, 1949. In January, 1951, found to have generalised adenopathy, enlarged liver, and radiographic changes suggesting pulmonary sarcoidosis. Mild asthmatic attacks since childhood, ceasing at onset of iridocyclitis in 1949.

Previous treatment had included 'Cortisone' 25 mg. by intramuscular injection daily for ten days, and streptomycin 50 g. concurrently with subconjunctival cortisone. Both had led to slight improvement.

Treatment.—A.C.T.H. in total dosage of 950 mg.—700 mg. intravenously and 250 mg. intramuscularly—as follows:

1. A.C.T.H. 25 mg. intravenously in 1 pint 0·18% NaCl over eight hours on alternate days; 8 infusions.
2. A.C.T.H. 12·5 mg. by intramuscular injection six-hourly for three days, followed by 25 mg. twice daily for two days.
3. A.C.T.H. 500 mg. intravenously in 0·18% NaCl over five days.

Results.—Ophthalmologist's report (Mr. Goldsmith) as follows:

Before treatment: old punctate keratitis in both eyes, moderate number of inflammatory cells in the aqueous. Many vitreous opacities in both eyes. Fundi not visible in any part. Vision: rt. 3/60, lt. counting fingers at 1 metre.

After first course of A.C.T.H.: anterior segment as before. Vitreous very much clearer. Small spots of healed choroiditis visible in both eyes at the periphery. Discs not seen. Vision: rt. 4/60, lt. no change.

After third course of A.C.T.H.: still old punctate keratitis. Cells in anterior chamber present but much fewer. Many small spots probably of choroidoretinitis scattered over whole fundus of both eyes. Both discs now quite clearly seen with no abnormality. Vision: rt. 6/60, lt. 1/36.

These were the first views obtainable of the fundi for over a year.

CONCLUSION

A.C.T.H. intravenously produces a more pronounced effect than a similar dose intramuscularly. Patients having A.C.T.H. by both routes volunteered the information that there was a remarkable difference in their symptoms while on the intravenous therapy. The average dosage intravenously was 50 mg. on alternate days, compared with 25 mg. every six hours intramuscularly, thus reducing the cost to a quarter. All patients demonstrated the usual effects of A.C.T.H., including a fall in eosinophils and an immediate increase in appetite, weight, and sense of well-being.

A.C.T.H. intravenously has no apparent harmful effect apart from the local venous thrombosis already mentioned. If this treatment is continued for a long time the normal complications of A.C.T.H. therapy are presumably possible. Four more patients are at the moment under treatment by this method without any further complications.

Our thanks are due to Dr. H. L. Marriott and Mr. A. J. B. Goldsmith for permission to publish details of cases under their care; to Dr. A. B. H. Hicks of Crookes Laboratories for his encouragement and assistance; and to Crookes Laboratories, Ltd., for their generous supplies of A.C.T.H.

A. M. JELLIFFE
M.D. Lond., M.R.C.P.
P. B. STEWART
M.B. Lond.
G. E. BEAUMONT
D.M. Oxfd, F.R.C.P.

The Middlesex Hospital,
London.

to determine, if possible, whether growth response was inhibited only while the organism was exposed to hyperthermia Tubes with pH 6.52 needed 168 hours' hyperthermia for complete inhibition of growth response, tubes with pH 6.98 showed complete inhibition of growth response at 120 hours, and tubes with pH 7.32 or more showed no appreciable growth response at any time (figs 3 and 4)

To differentiate inhibition of growth response from destruction of the organism to the extent that it could no longer be subcultured inoculation on Sabouraud's agar was made from each tube in this group at the end of the experiment The results of such cultures suggested that the length of the period of hyperthermia necessary to destroy C neoformans varied with the pH of the medium

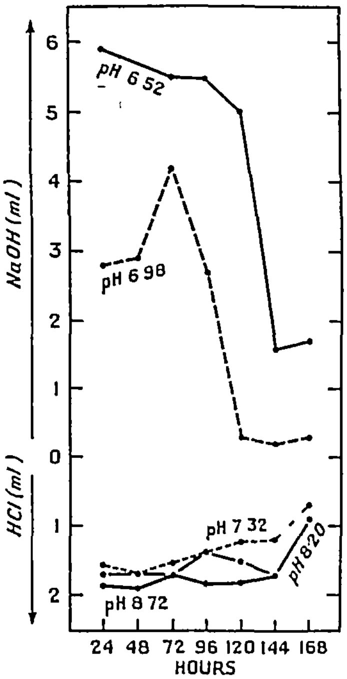


Fig 3—Effect of pH plus hyperthermia on acidometric growth response of *C neoformans* as determined 17 days after hyperthermia had ended

pH of medium	*Earliest hour at which culture showed no growth*
6.52	144
6.98	144
7.32	120
8.20	72
8.72	48

DISCUSSION

The most commonly used medium for culturing fungi is Sabouraud's agar Sabouraud's agar, which has a pH of 5.5–6 (Zinsser and Bayne Jones 1939), is preferable to other more commonly used laboratory media (pH 7.2–7.8) for the purpose of culturing fungi, because the acid reaction tends to inhibit the growth of associated bacteria (Whitby 1944), and because fungi seem to grow better on such an acid medium If an acid medium enhanced the growth of fungi, an alkaline medium might proportionately inhibit their growth This rationale led, five years ago at this clinic to the conception of alkalinisation as a means of treating patients with torula meningitis Three clinical cases of torulosis of the central nervous system were treated at the University Hospital with large quantities of alkalinising substances, and the results were published by Mosberg and Arnold (1950)

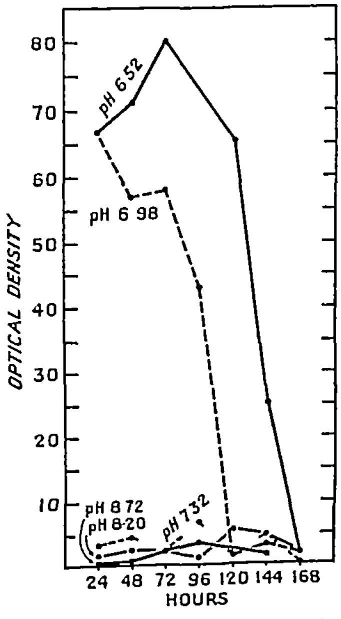


Fig 4—Effect of pH plus hyperthermia on colorimetric growth response of *C. neoformans* as determined 17 days after hyperthermia had ended

Crone et al (1937), using a 48 hour dextrose agar culture of torula suspended in 10 ml of peptone broth, pH 7.2, found that *C neoformans* was killed by heating in a water bath for 42 minutes at 50°C At 60°C it was killed in less than 5 minutes Since these temperatures were too high to be of value clinically, fever was not used therapeutically for torulosis in man Later, however, it was found that the growth of *C neoformans* could be inhibited at temperatures low enough to warrant clinical consideration if these temperatures were maintained long enough (Cox and Tolhurst 1944) A. M Kligman (unpublished experiments) has demonstrated that, with cultures of *C neoformans*, macroscopic growth is no longer visible and subculturing is impossible after five days' exposure to 40°C, three days' to 41°C, and two days' to 42°C

These facts suggest that human torulosis of the central nervous system should be treated by a combination of hyperthermia and alkalinisation

SUMMARY

pH seems to be an important factor in the growth of *Cryptococcus neoformans*

Long periods of hyperthermia seem to inhibit the growth of *C neoformans*

The length of the period of hyperthermia required to inhibit the growth of, or to kill, *C neoformans* varies with the pH of the culture medium

This work was done with the help of a grant from the Hoffberger Neurosurgical Fund

REFERENCES

Cox L B, Tolhurst J C (1944) Human Torulosis. Melbourne.
Crone J T, DeGroat A F, Wahlin, J G (1937) *Amer J Path* 13 863
Mosberg, W H Arnold, J G (1950) *Ann. intern Med* 32 1153
Schmidt, E G, Alvarez DeChoudens J A McElvain, N F, Beardsley, J, Tawab, S A. A (1950) *Arch Biochem* 26, 15
Von Hansemann D (1906) *Verh dtsch path Ges.* 9, 21
Whitby, L E H (1944) Medical Bacteriology 4th ed London
Zinsser H Bayne Jones S (1939) A Textbook of Bacteriology 8th ed New York and London

---

Preliminary Communication

A C T H BY INTRAVENOUS INFUSION

In order to enhance the effectiveness of A C T H therapy, a trial is being made of intravenous infusion of the hormone over periods varying from six hours to several days Hitherto the results have been remarkably gratifying Advantages that may be expected from the adoption of this route of administration are twofold (1) reasonably continuous stimulation of the adrenal glands, and (2) a considerable economy in cost

Theoretical objections to this technique are that it may cause hypertensive effects owing to contamination of the A C T H with posterior pituitary extracts, and that it may produce protein shock In no patient so far treated have these effects been observed, and it is likely that any anaphylactic effect would be counteracted by the presence of the A C T H No case in this series has been treated for longer than one month by the intravenous route, and eventual sensitisation is a possibility

MODE OF ADMINISTRATION

Infusions of 25 or 50 mg of A C T H in 1/2 or 1 pint of 0.18% sodium chloride solution were given over six to twelve hours (usually eight hours) on alternate days One patient received a continuous infusion of 500 mg of A C T H in 0.18% NaCl over five days

COMPLICATIONS

No significant rise in blood pressure or pulse rate was noticed during the infusions Case 4 developed mild

THE LANCET

LONDON SATURDAY, JUNE 9, 1951

Teaching the Teacher

THE art and practice of medical teaching is a perennial subject for discussion Professional educationists are rather fond of pointing out that university teachers rarely receive any systematic instruction in exposition and rhetoric, instead they are chosen on the basis of scholarship, ability in original research, technical competence—that is, almost every quality other than those explicit in the titles professor and lecturer While this is in the main true it does not necessarily follow that they are, as a group, bad teachers Every medical school has all sorts ranging from the almost incoherent, who fail dismally to hold the attention of a class, to the gifted few whose formal lectures and clinical classes are effortless masterpieces of dramatic art

It is doubtful if there is any close correlation between teaching ability, high critical faculty, and intellectual brilliance One of the most dangerous faults in medical teaching is that the forceful and persuasive teacher may impart to his material an entirely spurious veneer of precision and finality He may take a mass of unverified observations and a series of ingenious but fanciful hypotheses, add a "hunch" or two, and present the mixture with such emphasis and apparent logic as to make it sound like a divine revelation. This is the cardinal sin of certitude which held the minds of men in bondage in the Mediæval Age of scholasticism—a heresy which still persists and which should be fought with the vigilance and vigour of the Inquisition. In the past clinical teachers particularly offended in this respect, because many of them had insufficient or no experience of the discipline of scientific research and because the conditions of successful consultant practice so often require a pretence of omniscience that at last even the pretender is deceived At the other extreme is the teacher so oppressed by the doubts and uncertainties which beset most aspects of the theory and practice of medicine that his discourses, instead of stimulating and challenging his pupils, plunge them into a mist of confusion To steer a successful course between the Scylla of certainty and the Charybdis of confusion is the highest art of university teaching Most would agree that the aim of medical teaching is not only to instruct but to educate, in the sense that Lord MORLEY meant when he defined an educated man as one who knew when a proposition had been proved and when it had not If medical schools fail to provide such education, then doctors will be at a grave disadvantage in the community of professional men, indeed such schools will forfeit their claim to be parts of universities and will become merely technical colleges

Apart from these lofty considerations there is much that demands discussion and improvement the place of the theoretical lecture, the value of the tutorial system, the place of the young teacher, the use of visual aids, the clinico pathological conference—these and many other broad topics are important On the practical side a more systematic effort should be made to improve the standard of delivery There are still too many medical teachers who are inaudible, who bury their noses in their notes, who address their boots, the blackboard, the ceiling—anything but their audience—whose discourse is a sea of "ehs" and "ahs" with islands of words, who, while they may rise to the special occasion of a communication before a society, are casual, slovenly, and even unpunctual in their routine delivery We welcome therefore the announcement that the Postgraduate Medical School of London is holding a two day conference on medical teaching later this month Teachers from many medical schools are being invited, and there is a full programme ranging over many aspects The discussion of each subject will be introduced by a half-hour talk from one of a group of experienced teachers This enterprise cannot fail to do much good, the only drawback will be that, as with all reform movements, the preaching will in the main be to the converted

A Useful Vasodilator

ONE of the first drugs found to produce vasodilatation by autonomic blockade was 2 benzyl-4,5 imidazoline hydrochloride ('Priscol,' 'Priscoline') Chemically, this resembles both the sympathicomimetic amines and histamine, and it has an extremely complicated pharmacological action. In 1939, HARTMANN and ISLER[1] established experimentally that priscol lowered blood pressure and caused dilatation of the conjunctival capillaries Two years later AHLQUIST and his colleagues[2] found that it acted chiefly as a sympatheticomimetic agent, producing vasodilatation of the peripheral and coronary vessels and increasing cardiac output, and evoking histamine-like and parasympatheticomimetic effects Finally, they showed that it had an adrenolytic and a selective sympatheticomimetic antipressor action, potentiating sympatheticomimetic vasodilatator impulses

In man the effects of priscol on the circulation were studied by GRIMSON and his associates,[3] who found that the drug produced vasodilatation in the limbs when injected intravenously and to a lesser extent when administered orally In two of three patients investigated the cardiac output was unaltered, while in the third an initial high output was reduced to normal. In hypertensives large doses (100–200 mg) intravenously lowered the blood-pressure, but the results of sustained treatment were disappointing That the drug had a direct peripheral action was suggested by an increase in skin temperature in sympathectomised limbs, one side-effect was "goose flesh," which appeared even after sympathetic denervation In peripheral vascular disease the results were encouraging, but did not equal those of sympathectomy LYNN,[4] investigating the action of priscol on occlusive vascular disease and vasospastic

---

[1] Hartmann M. Isler H *Arch exp Path Pharmak.* 1939 192 141

[2] Ahlquist R. P Huggins R A. Wordbury R A. *J Pharmacol.* 1947 89 271

[3] Grimson K. S Reardon, M. J Marzoni, F A., Hendrix, J P *Ann Surg* 1948 127 968

[4] Lynn R B *Lancet* 1950 ii 676

Reviews of Books

A Manual of Artificial Radioisotope Therapy

Editor P F HAHN, Cancer Research Laboratories, Meharry Medical College, Nashville, Tennessee New York Academic Press 1951 Pp 310 $6 80

IN planning this survey by a group of authors, Dr Hahn has emphasised the developing scope of radio-isotope therapy by including more chapters on general principles than on particular forms of treatment The book includes some admirable sections—*for example*, on dosimetry by Edith H Quimby, on equipment by R L Weiland, on health physics by K Z Morgan, and on the value of autoradiography by C P Leblond and J Gross, and Hahn's examination of the general factors governing the present and future employment of isotopes in therapy is particularly helpful The established forms of therapy are discussed separately, with sections on radiophosphorus, on radio-iodine for thyroid carcinoma and hyperthyroidism, and on colloidal radio-isotopes given by infiltration and intravenously No detailed consideration is given to the external use of phosphorus, intraperitoneal colloidal isotopes, intravesical cavity radiation, or the possibilities of intravenous colloids for lung embolisation and therapy One difficulty facing the compiler of any textbook on this subject at the present stage is that it tends to be either very general or very particular, without enough attention to the tentative and developing fields of work which cannot be clearly defined or assessed In some ways Dr Hahn has escaped this difficulty, although possibly his analysis of the general scope of radio-isotope treatment might have been more usefully based on body areas and on functions than on a list of the chemical elements Some chapters, notably that on the treatment of hyperthyroidism, also give a good account of the uncertain state of present practice and of future possibilities The discussion, in several sections, of purely diagnostic applications may seem inappropriate, but this is justified where treatment depends largely on such applications It is perhaps early to look for a comprehensive account of radio-isotope therapy with broad perspectives, and Dr Hahn's book gives an excellent, if slightly disjointed, picture of the present state

Incontinence in Old People

JOHN C BROCKLEHURST, M D, *major*, R A M C, *formerly* Christine Hansen Research Fellow in the University of Glasgow Edinburgh E & S Livingstone 1951 Pp 187 30*s*

THE value of this monograph lies both in the light it throws on one of the more distressing disabilities of old age and also in its emphasis on a physiological approach and the need for research into predisposing and precipitating factors The subject is dealt with clearly and comprehensively in three separate sections, which are amply illustrated with diagrams and photographs

Part I consists in a critical review of previous reports The anatomy and physiology of the bladder and rectum, the mechanism of normal and abnormal micturition, and the causes of senile urinary incontinence are described in detail, and the effect of drugs on the bladder and rectum is discussed

Part II, dealing with the ætiology of incontinence in old people, describes a study of the bladder, rectum, and anal sphincter in senile incontinent patients By cystometry on a series of incontinent patients the author has confirmed the previous finding that the cause of urinary incontinence in old people is over activity of the bladder mechanism due to interplay of various factors He emphasises that of these factors impairment of the cortical inhibitory function is the most important Not everyone, however, would agree that a chronic urinary infection has little bearing on the disability, and most clinicians might maintain that the elimination of such an infection, if present, would contribute to the relief of the incontinence From a similar investigation of rectal function, by means of a rectometer, the author concludes that the rectum in senile incontinent patients is more than usually excitable

Part III concerns the management of incontinence in old people From the point of view of treatment these patients are divided into two groups—those who can coöperate, and those who cannot For the former group, the author rightly suggests that re education in inhibitory control and symptomatic treatment of local conditions is the proper mode of attack As to the latter group, he holds that the problem becomes one largely of efficient drainage, and he describes the use of a moulded bed in the *management* of incontinence Others might not agree that in the uncoöperative patient incontinence is entirely irremediable, and it might be argued that the stimulus to regain bladder control is removed by an appliance which not only tacitly encourages the patient in her incontinence but also largely immobilises her Only practical experience will show how far such an appliance should supersede careful *nursing* and *mobilisation*, which may still be preferable even for the mentally confused and uncoöperative

Recent Progress in Psychiatry

Editor C W J H FLEMING, M R.C S London J & A Churchill 1950 Pp 711 Price 50*s*

SEVEN years have elapsed since this volume's forerunner was published It contains a wealth of material including eighty pages of references, variously grouped But though psychiatrists will value this book for reference, he would be a remarkable man who could sit down and read any of the articles offhand As a display of knowledge and energy the book is magnificent, but there is little evidence of selection *in* the *feast* of material so lavishly supplied The shorter articles, rather than the more erudite, will carry most conviction to the average psychiatrist

Lecture Notes on Emergency Diagnosis

HANNS L BAUR, professor of internal medicine, University of Munich Oxford Blackwell Scientific Publications 1951 Pp 68 6*s*

This little book is designed for the medical student and contains much valuable information presented from the physiological standpoint Diagnosis is approached by careful reasoning and not by a series of lists of causes and a feat of memory There is much that may appear *almost unnecessarily* simple but which will give the student a sound basis on which to build his clinical judgment There are in all seven chapters, dealing with such subjects as the facies, the skin, disorders of breathing, coma, fits, and the like There is no index as such, and the book is intended to be read through rather than used as a book of reference A few minor difficulties in translation do not prevent it being pleasantly readable

A Medical History of Persia and the Eastern Caliphate

From the earliest times until the year A.D 1932 CYRIL ELGOOD, M D, F R C P, late physician to H.B.M. Legation, Teherán, Persia London Cambridge University Press 1951 Pp 614 50*s*

To read Dr Elgood's preface is to form some idea of the difficulty of the task he has undertaken In the earliest period up to the Islamic conquest, the material is scanty and written in the ancient Persian tongue, which few can read The author, if he is here often compelled to substitute a sketch of the history of the Persian State for a history of its medicine, at least makes it interesting, as when he writes of the treatment of the *captured Roman* emperor, the aged Valerian, by the reigning monarch who, whenever he rode abroad, mounted by means of a foot placed on the neck of a Roman emperor But with the coming of the Arabs Dr Elgood is *able to* hold our attention by his intimate knowledge of Arabic medicine The final period, after the arrival of the East India *Company* in the reign of James I, makes easier reading for most of us It demonstrates again, and in another field, how great is the contribution of medicine in the spreading of Western civilisation

Dr Elgood writes well of his difficult subject, but since it is admittedly difficult one could wish that he had adopted the example of the history textbook, prefacing his chapters by something of a synopsis and introducing those tables of dates, of *dynasties*, and of the succession of eminent physicians, which might make it *all* a little easier to comprehend Dates repeatedly placed in an outstanding position, like maps (of which there are none), are a great help in *following* an intricate presentation of events.

internecine dispute on the function of a particular hospital without asking our people to return to an *outmoded* method of finance?

Though this brave, if misguided, enterprise at Kingston may well succeed, we should not overestimate its significance; for though private money may be forthcoming for isolated endeavours of this sort, it will never again be found for a comprehensive hospital service. Beyond the neighbourhood of Kingston the effect can only be to make people glance uncertainly back at the years up to 1948. Yet this country is deeply—*and*, we believe, wisely—committed to the National Health Service. Those who recognise this should seek to remedy defects through the boards and committees within the service—and none can assert that here medical opinion has no outlet—or through the strong professional bodies outside the service. Any who encourage their neighbours to step back to 1948 are themselves out of step with the times.

Annotations

COTTON-WOOL

THE latest edition of the *Drug Tariff* (for April) includes for the first time a detailed specification for "hospital quality" cotton-wool. Hitherto the National Health Service has recognised only the *B.P.C.* standard, which is perhaps unnecessarily high for some surgical purposes, such as colostomy dressings, where no harm is done by airborne flecks of wool. The pharmacist must still supply a *B.P.C.* wool unless "hospital quality" is specifically ordered on the prescription, but doctors are asked by the Ministry to order this as often as they can, partly to save the Service's money but also because of the scarcity of raw cotton suitable for making *B.P.C.* wool. The difference in price is appreciable—*B.P.C.* 8s. 5d.; "hospital" 7s. 5d.—and the absorptive powers of the two are about the same. The main differences in the specifications are that the "hospital" wool need be only reasonably free from pieces of thread, whereas the *B.P.C.* insists on unqualified freedom; a little more fibre-dust and other foreign matter is allowed in the "hospital" specification; and the average staple fibre can be $^1/_4$ inch shorter in the "hospital" wool. The *B.P.C.* demands "appreciable resistance when pulled," whereas the specification for "hospital" quality does not mention resistance; this probably explains why patients who do their own dressings usually say the *B.P.C.* wool goes further and is less trouble to use. They also say that the wool interleaved with paper seems more economical than the more usual form in which the roll is apt to become an amorphous lump. It might be worth while to interleave both "hospital" and *B.P.C.* qualities, perhaps reducing their thickness at the same time. Otherwise a general change to a short fibre wool may add to the cost instead of saving money.

The reasons[1] for the rise in price are multiple and complex. When the pound was devalued in September, 1949, the price of raw cotton in England was bound to rise. But before devaluation had exerted its full effect, many countries began to lay in stocks of cotton for rearmament, because war had broken out in Korea. Then the Indian government banned the export of raw cotton, and Pakistan reduced its supplies to Britain. The British maker of *B.P.C.* cotton-wool, which is a mixture of the high and medium grades of Indian cotton, now found the higher grade unobtainable, the only alternative being Turkish cotton about equivalent to the Indian medium grade. Inferior cotton wool is made from low-grade cotton mixed with "linters" (cotton-waste), and the prices of raw cotton are controlled but that of cotton-waste is not—hence we are faced with the anomalous position that the price of inferior cotton-wools is rapidly approaching that of the better qualities. Similar difficulties are facing the manufacturers of lint, gauze, and bandages, who before the war used only American cotton, but now, owing to the shortage of dollars, must buy Egyptian yarns of unnecessarily high grade and corresponding high cost. There seems little hope of improvement in the cotton position for some time; but it is possible that rayon dressings[2] will help to ease the shortage.

This would have been a good time to erase for ever the unfortunate term "hospital quality," meaning "inferior quality." There was a time when hospitals were expected to make do with the cheapest sorts of dressings, whether wool, lint, gauze, or bandages. Obviously there is a place in hospital practice for two qualities of such materials; but that is no reason for calling only the worse of the two by their name. A more colourless terminology, such as "standard quality" for what is now hospital, and "super quality" for the present *B.P.C.*, would surely be preferable.

ALCOHOL AND THE MOTORIST

THE attitude of the peoples of different countries to drunken motorists seems to correspond roughly with their philosophy of life. In Scandinavia the attitude is keenly efficient, while in the sun-touched south it is one of live and let live. An international conference held last year[3] made it clear that laws against intoxication while driving vary from extreme severity to a laxity almost approaching indifference.

In Scandinavia the problem of alcohol and traffic is widely depicted on posters as a "dangerous crossing" between the car and the bottle, and legislation to discourage this transition is severe, well defined, and ruthlessly applied. On the other hand, in such countries as Italy, Spain, Portugal, and the Argentine penalties are not heavy; in Spain there was until last year no legislation against this offence, and driving licences were withdrawn only in extreme cases. The various statutory measures are precautionary, punitive (deterrent or corrective), and educational. Precautionary measures consist mainly in care in the issue of driving licences. Of punitive measures the most usual is withdrawal of the driving licence: this step is taken even in Spain if the motorist drives "in an acute alcoholic state." In Belgium there is legal provision for withdrawing the right to drive (no system of driving licences has ever been in force) and impounding the vehicle; these punishments are said to be of greater deterrent value than fines or imprisonment. Most authorities impose fines for the first offence and imprisonment for the second or subsequent offences; but in Denmark, Norway, Finland, and Iceland imprisonment is the rule even for a first offence except under extenuating circumstances. In Finland a drunken driver can be imprisoned for 8 years if found guilty of homicide, and for 6 years if the accident results in bodily injury. The Italian law betrays a certain sympathy for the drunken driver, for "no person is liable who has committed a crime deprived of the power of comprehension and will due to intoxication derived from fortuity or inevitable accident." (Punishment is, however, augmented when intoxication is premeditated in order to commit a crime or create an alibi, *or if the* crime is committed in a state of "habitual drunkenness.") The value of educational and propagandist measures was generally acknowledged at the conference. In Sweden the Union of Temperance Drivers carried out a vigorous conditions, by means of venous occlusion plethysmography, found that intravenous injection caused pronounced vasodilatation in the skin of the extremities, and that intra arterial injection doubled the calf blood flow and increased the flow through the foot to a still greater extent Intra arterial injection after acute arterial embolism produced pronounced, vasodilatation, and increased the foot flow threefold in the sympathectomised limb, but intermittent claudication was not relieved in any of eight cases of occlusive arteritis DOUTHWAITE and FINNEGAN[5] found that priscol acted powerfully upon the smaller arteries and arterioles of the fingers and toes, and had a more lasting action than other vasodilators when given by mouth Unlike LYNN, they found that intermittent claudication was relieved, and in twelve out of twenty-four cases of occlusive disease night pain was abolished They suggested that the value of priscol was likely to be greatest in Raynaud's disease, but that it should also be tried in peripheral arteriosclerotic disorders They advised against its use in hypertension, since doses large enough to lower the blood-pressure produced alarming side effects, these occurred even with smaller doses which did not affect the pressure at all IGLAUER and his co-workers[6] reported that priscol did not affect cardiac output Lately GOODWIN and KAPLAN[7] have shown that in occlusive peripheral vascular disease oral administration of priscol reduced the calf toe temperature difference and shortened the circulation-rate in the lower limbs Numbness, coldness, and rest pain were much reduced or abolished, and of ten patients with claudication nine claimed that its severity lessened After the drug was withdrawn, however, the findings were little different from those before administration was started Side-effects were slight, and the drug was administered to patients with anginal pain and ischæmic heart disease without untoward incident ZURROW and his associates[8] noted that priscol increased gastric acidity

---

[1] Crabtree, R. *Pharm. J.* 1951, 166, 53.

[2] Fairburn, J. W., Whittet, T. D. *Ibid*, p. 161.

[3] Proceedings of the First International Conference on Alcohol and Traffic, 1950. Stockholm: Kugelbergs Boktryckeri. 1951. Pp. 336. 15 Sw. Kr.

The evidence thus suggests that priscol is an effective peripheral vasodilator, acting mainly on the skin vessels There can be no doubt that it is a powerful sympatholytic agent, capable of acting directly on the denervated vessel wall It is unlikely to prove of any value in the treatment of hypertension, but, especially owing to the absence of serious side effects, it should find a place in the treatment of peripheral vascular disorders It should, however, not be given intravenously to patients with recent coronary occlusion or myocardial infarction In acute arterial occlusion the intra arterial injection of priscol is probably not only as effective as paravertebral procaine block, but also safer and more certain in its action Intravenous injection of the drug, by indicating the capacity of vessels to dilate, may be useful when sympathectomy is being considered Of perhaps greater importance is the ability of priscol given by mouth to produce peripheral vasodilatation without serious side effects Probably all patients with vasospastic disorders should have such treatment before sympathectomy is decided on, and the drug may also be given after operation to supplement the effects of surgery In occlusive peripheral arteritis the value of priscol is less well established, but despite the discouraging results quoted by LYNN it seems to be of definite, if limited, value when given by mouth It offers ambulant patients a reasonable chance of some improvement in peripheral circulation, without sympathectomy Long term studies may show that its action is more ephemeral than is at present hoped, but certainly this drug presents new possibilities in a group of disorders whose treatment is commonly almost as disheartening to the physician as to the patient

The Wrong Way

THE controversy that has raged for months over the proposed conversion of Kingston Victoria Hospital from a general-practitioner hospital to a gynæcological unit has reached an abrupt climax with the closure of the hospital and the announcement by the displaced doctors and others of a scheme to open a voluntary hospital in the neighbourhood Alternative accommodation is being provided by the regional hospital board, and some thirty practitioners have already signified their willingness to work there, but others, holding that the accommodation is inadequate, will have nothing to do with this arrangement Instead they plan, as we note in our news columns this week, to collect a fund of some £50,000 to purchase, adapt, and equip a house as a hospital with 15–20 beds, and to cover the costs for the first two years

The sponsors of this enterprise must have weighed the difficulties Structurally the proposed hospital can offer little more than countless other large houses already adapted as nursing-homes, and, like most small nursing-homes, it is likely to prove too small to run efficiently and yet with proper economy in nursing and other staff Furthermore, for such a small unit to have its own radiological and pathological departments would be an extravagance, yet without these departments it might have to depend on the good will of institutions in the National Health Service Unlike most of us the sponsors may count money the least of their worries for the appeal will draw together those of us—and they are many—who always want to back the little man against the big, as well as some of those who hold that the general practitioner has been roughly handled by the regional hospital boards, those who resent the breach of a long tradition at the hospital, and, of course, those who would not be disappointed to see the National Health Service fail General practitioners throughout the country have ground for resenting their gradual displacement from hospitals which they once staffed, but is this reason enough for asking the public to return to the discarded method of charitable support? Does not the Kingston appeal indeed show up some of the weaknesses of the old method? This appeal is being placed before the public in an area where the need is less than in other parts of the country A new hospital of this type might better be started in an area where the general practitioner *has no contact* with hospitals, no hospital beds of his own, no access to diagnostic departments, and little say on advisory committees But in Kingston the practitioner can have all of these, if he wishes And in any event should not the profession be able to settle this for tasks of this kind, under magnifications up to ×200, that Barer and Saunders Singer [2] have devised their new low-power microdissector This works on pantograph principles, but the family failing, an incurable backlash, has been overcome by spring loading, and accurate counter-weighting ensures that the instrument will "stay put" when the operator takes his hands from the controls In the present model the dissecting instrument will follow every movement of the operating handle, but at a reduction of 4 1, so the average shaky hand will not wobble the tip of the tool more than about 25 µ

---

[5] Douthwaite, A H Finnegan T R W *Brit med J* 1950 1 869

[6] Iglauer A Kaufman, J Herwitz G K *Amer J Med* 1951 10 515

[7] Goodwin J F Kaplan S *Brit med J* May 19 1951 p 1102

[8] Zurrow H B Henreld P H Fischer I Saland G *N Y St J Med* 1951 51, 1038

THE ADOLESCENT DELINQUENT BOY

THE juvenile delinquent is much in the news, partly because of the disquieting rise during the past ten years in the number of young persons found guilty of indictable offences, and partly because new methods of handling those offenders arouse heated controversy The publication by the British Medical Association of a booklet [3] on the subject is therefore timely, it embodies the report of a joint committee of the B.M.A and the Magistrates' Association with three coöpted members, under the chairmanship of Dr Doris Odlum, and is intended to complement a report on the unstable delinquent girl [4] published in 1946

The new publication deals with boys between the ages of 13 and 17 who are delinquents, truants, or beyond control. It outlines various factors affecting adolescent delinquents their home circumstances and the character of their parents, including the problems of broken homes, illegitimacy and adoption, intelligence and education (the latter may suffer severely in the truant), employment difficulties use of friends and leisure, deficient money sense, lack of religious values, level of physical health, and the effects of the cinema The powers of courts in dealing with the juvenile offender are summarised, and the last section contains the committee's recommendations for dealing with the problems discussed Of these recommendations perhaps the most noteworthy are early detection of ill treatment or neglect of the child, and his removal from harm as soon as possible under the provisions of the Children's Act, 1948, greater provision of educational facilities for the educationally subnormal child (last March the Minister of Education stated that in England and Wales there are known to be 28,000 requiring such provision, but only 15,000 can be dealt with) greater coöperation between the leaders of youth organisations and parents, and the encouragement of boys to join clubs while still at school, special placement in industry of more backward boys measures to educate future parents both by pre marital advice and by social and psychiatric services to deal with marital disharmony increasing the police force in order to deter the potential delinquent, special methods for dealing with the persistent absconder, and early recognition of the delinquent who is unlikely to respond to any form of treatment

While undeniably the causes of delinquency are many and various it is regrettable that the report, though usefully summarising a wide range of opinions, gives an over all impression of superficiality It never really faces up to the enigma it propounds in its opening paragraph "a very great number of boys who have the same characteristics or the same environment as those described here do not become delinquents" This problem of "differential response" as Reckless [5] terms it or "susceptibility" to use the phrase of Carr Saunders et al.,[6] was comprehensively discussed by Bowlby,[7] who quotes the findings of Burt, Aichorn, Healy and Bronner, and Stott Bowlby's own work [8] [9] led him to conclude that two factors are especially significant in the history of the persistent delinquent (1) prolonged separation of the child from its mother or mother substitute during the first five years of life, and (2) the child being more or less unwanted by parents whose main attitude towards it is hostile, critical, and punitive

That the attitude of society towards the delinquent and his often irresponsible parents is also mainly hostile, critical, and punitive remains a large ingredient in this chronic social problem Dissemination of information, as in the present report, is likely to help by arousing public interest and sympathy for the delinquent, but, apart from deeper understanding of the underlying reasons for his having "fallen among thieves," we are apt, like the Priest and the Levite, to view his predicament impersonally from the other side of the road.

A DANISH ANATOMIST

THE eponyms which haunted our anatomy years linger on when nothing remains of that prodigious feat of memory but astonishment that we ever achieved it Yet though the mature practitioner may brighten momentarily at the words "Stensen's duct" he is apt to look blank again if asked who Stensen was In the introduction to a new Danish edition of *A Dissertation on the Anatomy of the Brain*,[10] Prof Edv Gotfredsen describes Nicolaus Steno, or Niels Steensen, as one of the outstanding scholars of the 17th century, equally well known as anatomist, geologist, and Catholic theologian He was born at Copenhagen in 1638, and Thomas Bartholin, another famous Danish anatomist, discoverer of the lymphatic vessels, was among his teachers Steensen's contemporaries held a number of beliefs based on opinion rather than investigation Thus Thomas Wharton, who, in 1656, gave his name to another salivary duct, held that tears originated in the brain, and that milk came from the chyle, not the blood Steensen was the first to assert that all glandular secretions, including milk, are derived from the blood He discovered not only the parotid duct which bears his name, but the minute ducts of the lacrimal gland, moreover he described the lacrimal apparatus fully, and recognised that tears are simply a liquid for the irrigation of the eye He also demonstrated the existence of the buccal glands and of the cerumen secreting glands of the ear His work on the structure of muscle ran directly counter to opinion at the time Galen's view that the tendons were principally responsible for movement held the field, and the fleshy part of the muscle was conceived as mere packing material through which ran contractile fibrils from the tendons Steensen demonstrated that muscle tissue was made up of contractile fibrils, and that the tendons were merely anchoring cords and he also showed—nearly a hundred years before von Haller—that muscle contracts as a result of a direct stimulus He described the muscles of the tongue and the œsophagus, and the levatores costarum but most remarkable of all, at a time when even Harvey regarded the heart as the altar of the body where the blood was made liquid anew and impregnated with vital spirits, Steensen was able to state, as a result of his careful examination, that the heart was made of nothing else but muscle He observed the ovarian follicles before de Graaf published his account of them, and the lymphatic plaques in the small intestine in the same year as Peyer, and he published the first account of campaign in 1949, with mass meetings, lectures, films, and other methods, which resulted in a reduction in injuries and deaths and in the number of intoxicated drivers A mutual insurance company for non drinkers, established in 1933, now has a claim rate 37 08% lower than the average of other companies

---

[2] Barer R Saunders Singer A E *J sci Instrum* 1951 28 65

[3] The Adolescent Delinquent Boy Published by the British Medical Association B.M.A House Tavistock Square London W C 1 1951. Pp 32 3*d*

[4] The Unstable Delinquent Girl London 1946

[5] Reckless, W C Etiology of Delinquent and Criminal Behaviour Social Science Research Council Bulletin no 50 New York 1943

[6] Saunders A. M. C Mannheim, H. Rhodes E C Young Offenders. Cambridge 1943

[7] Why Delinquency? The Case for Operational Research London 1949

[8] Bowlby J Influence of Early Environment in Development of Neurosis and Neurotic Character *Int J Psycho-Analysis* 1940 21 154

[9] Bowlby J Forty four Juvenile Thieves Their Characters and Home Life. London 1946

[10] Discours de Monsieur Stenon sur L Anatomie du Cerveau. Copenhagen Nyt Nordisk Forlag Arnold Busck. 1950 Pp 50

A British representative held that, since alcohol is a narcotic interfering with judgment and self criticism, even when taken as "half a glass of pale ale," there is only one safe rule not to drink for a given number of hours before driving Swedish representatives contended that only with an alcohol blood level above 0 02–0 04% will driving efficiency be impaired In Scandinavia, Czechoslovakia, and South Africa blood tests are compulsory for determining intoxication Swedish pharmacologists have found that ordinary clinical examination gives uniformly positive findings only with a high blood-alcohol level, below 0 15–0 2% some people "pass" a clinical examination even though far from sober Road tests showed that the threshold for impairment of performance was at a blood alcohol level of 0 035–0 04% In most countries guilt depends, not on intoxication alone, but on the influence of this condition on ability to drive safely Norwegian law, however, does not consider this ability at all A blood level of 0 05% is regarded as proof that the driver is under the influence of liquor, and imprisonment is then almost automatic In Sweden there is usually no punishment unless the concentration exceeds 0 08%, with a concentration of 0 08–0 15% the culprit is usually fined, but a concentration of over 0 15% almost always involves imprisonment

SAFER CHILDBIRTH IN NEWCASTLE

"How to make the best of an old building" would make a good subject for an Ideal Hospital Exhibition in these lean years The Princess Mary Maternity Hospital at Newcastle upon Tyne is the teaching centre for obstetrics of the University of Durham At the outbreak of war it was transferred from the original building beside the Tyne to an orphanage on the outskirts of the city, an ugly, ill planned, two storeyed Victorian building, with winding stone corridors, awkward stairs, and very few small rooms The wards are large, and the sluices and kitchens inconveniently placed at varying distances along the corridors There are no staff rooms on the wards, and nowhere to receive relatives or friends This awkward place had to serve a parish of 3000 square miles in Northumberland and Durham, with a population of over 2 million Well over 2000 children are born there yearly Yet, despite the drawbacks of the building, the medical and nursing team have been able to establish and maintain a high and rising standard of pædiatric practice, accounts of which are now being presented in a series of pædiatric reports introduced by Prof E Farquhar Murray as chairman of the medical staff and Sir James Spence as pædiatric physician Those for 1946 and 1947 have so far appeared, they have been compiled by Dr Donald Court from the observations recorded by the pædiatric registrar, who had the day-to day care of all the infants born, and they supplement, by lucid narrative and attractive diagrams, the detailed figures given in the annual medical reports Indeed, both in scope and in production, they are a model for those who seek to interest other people in their work

In 1946, besides the registrar, the medical staff included 2 house surgeons, a resident obstetric officer, a non resident first assistant, 3 visiting obstetricians, and the professor of obstetrics of Durham University, on the nursing side, besides the matron, assistant matron, and sister tutor, there were 15 midwives, 20 State registered nurses working for the C.M B, and 21 untrained girls taking the eighteen months' midwifery course Medical students conducted 1080 of the 2352 births, pupil midwives 734, and the medical staff 538 Of the 2189 children born living, 2088 went home alive and well, and 85% of them were breast-fed when they left hospital. Breast feeding is taught assiduously, and even those babies who had to be fed artificially usually received the feed as a complement after the breast Only 1 4% of mature and 24% of premature infants were entirely artificially fed, and in 1947 (when confinements numbered 2369) the figure for premature infants had fallen to 21% Infections were taken very seriously, for in the first six months of 1944 infections had caused the death of 47 infants All unnecessary routine nursing procedures—such as test weighing—were therefore restricted, the babies were placed in cots beside their mothers' beds and not transferred to the nursery unless they were exceptionally noisy, they were even changed in their cots The pædiatrician watched the children and started chemotherapy as soon as any infection developed The result was that in the 30 months from July, 1944, to December, 1946, only 67 babies were seriously infected, 20 died—a fall in mortality from 50 to 4 per 1000 live births In 1946 itself only 6 children died of infection, and in 1947 only 3—a further reduction in the mortality from this cause to 1 4 per 1000 live births

The main causes of stillbirth were maternal disease (including toxæmia of pregnancy), birth injury, and fœtal malformations, in 1946 the rate was 69 per 1000 births The neonatal death rate was 46 per 1000 live births, and prematurity was the greatest predisposing cause In 1947 the stillbirth rate was 63 and the neonatal death rate 26 The annual medical reports for 1946 and 1947—prepared by Mr Hugh Arthur and Mr E L Nicholson, who joined the hospital staff at the end of 1946—show that part of this improvement was due to a falling mortality from breech delivery and forceps delivery, and in persistent occipitoposterior positions. These figures, however, relate to a hospital in which the "emergencies" are high, accounting in recent years for a quarter of the total admissions Only 281, or 12%, of the 1947 births were premature, but this small group included over a third of the fœtal and nearly half the early neonatal deaths Only half the infants weighing less than $3^1/_2$ lb survived, and the report comments that had some incubators and more nurses been available probably three quarters of them could have been saved Prevention of premature labour would be even more desirable, and this is a subject, as Dr Court points out, for much closer study

A LOW POWER MICROMANIPULATOR

In the past, laboratory operations under the low power microscope, such as the dissection of small embryos or the selection of minute crystals, have been done freehand, on the principle of What the Eye Can See the Hand Can Follow With one of the high power micromanipulators previously discussed in these columns,[1] or the Singer model which is British made, it is possible to pick out a single bacterium or remove the nucleus from a tissue cell, these instruments are intended for manipulating objects between (say) 0 5 µ and 50 µ in diameter, the main emphasis of their design being on precision rather than mobility or speed The freehand technique is probably as convenient as any for dealing with objects down to diameters of about 0 5 mm, the difficulties arise between this size and 50 µ, where a high power manipulator is essential Anyone who attempts the more tedious manœuvres of this order of magnitude, like sorting diatoms, pollen grains, or mould spores, without some mechanical aid, soon begins to develop an intention tremor, usually of about 0 1 mm in amplitude, and this tends to be at its worst at critical moments—nothing tires the hand more quickly than movements of a few microns on which the whole experiment hangs It is

---

[1] *Lancet* March 3, 1951 p 510

Special Articles

HOSPITAL SCHOOLS

J. HYWEL WILLIAMS

HEADMASTER, WELBURN HALL SPECIAL SCHOOL, KIRBYMOORSIDE, YORKS; FORMERLY OF CANADIAN RED CROSS MEMORIAL HOSPITAL SPECIAL SCHOOL,* TAPLOW, BUCKS

PROVISIONS for the education of chronically sick children were conceived in the minds of the liberal reformers of the latter part of the 19th century. The establishment of day and residential schools for cripples who were no longer receiving active medical treatment was followed by the introduction of schooling in a number of special hospitals treating chronic conditions in children of school age. Since that time, about a hundred hospital special schools have been established.

There are now several types of schools for physically handicapped children. The hospital school differs from most of the others in that it offers a supplementary rather than a primary service, and school work is necessarily subordinated to the need of the children for active medical treatment. These differences decide in some measure the function of the school, and certainly have considerable influence on the teaching techniques which can be used effectively in it.

The policy followed in any particular school must be directed partly by the function of the hospital it serves. Where treatment may last some years, the teacher faces problems quite different from those met by a teacher whose pupils will be returning to their ordinary schools in a few months. The first may well be influenced by the fact that the patient will finally need sheltered employment; while her colleague knows that her patient must be able to take his place with his contemporaries when he goes back to his ordinary school. Any analysis of the function of hospital schools must therefore be limited to a few general principles; and these will be modified by local conditions affecting individual schools.

RESTORING CONFIDENCE

The child admitted to school in a hospital is generally educationally backward; his standard of performance is not compatible with his intelligence quotient. He often has a history of irregular attendance or even long absences from school. Even where attendance has been regular until his current illness there will be a break between his last attendance at school and his admission to hospital. It must be remembered, too, that the child admitted to hospital is not immediately admitted to the hospital school. The time lag here depends, of course, on his medical condition and the amount of active treatment he receives. The break may often extend over several terms. The child will then have lost much of what he had previously learned, and with it his confidence in his ability to learn. Because he is ill, he will be emotionally disturbed to an extent depending partly on his medical condition and partly on his own natural emotional make up.

The teacher has the immediate task of restoring his confidence, by helping him to recover his original standards of performance. Some subjects of the curriculum, such as arithmetic, lend themselves to measurable standards more easily than others, and it is usually through these basic subjects that the teacher makes her first approach. Confidence is restored by achievement, and the teacher should be able to grade the work so that the child experiences this sense of achievement to the full.

It often happens that the child has been educationally retarded for a long period before his admission to hospital, and has lost hope of ever keeping up in formal subjects. But he clutches firmly to his one achievement, whether it be his ability with a paint brush, with craft tools, or with a musical instrument. Usually his strength lies in subjects that do not impose the arbitrary standards of number and reading—subjects where a result need be neither "right nor wrong," but just "a good attempt"; and where there is scope for interpretation rather than accuracy. Such a child can be led along the line of his interests, and through them can make his contribution to his contemporary group, besides gaining the satisfaction that comes from achievement.

Brian was such a case. He was admitted to the hospital school at the age of 12, having attended school for just a year since arriving at school age. He had spent much of his time in hospital, and more of it at home, being nursed by his grandmother. When he was admitted to hospital school he was illiterate and could not do simple sums. His physical condition (he was a case of Still's disease) restricted movement. But despite all his handicaps, he had one skill to his credit: he wrote with a neat hand. From this he gained considerable pleasure, and he spent much of his time copying out what were to him, at first, meaningless words.

He was then asked to write a story. At first reluctant, he ultimately agreed to make the attempt, on condition that the teacher corrected the spelling errors in the original and allowed him to copy out the story in his book. He will never reach any high standard of authorship; but he is beginning to write coherently and now, after 12 months' interrupted hospital education, he is writing and illustrating his own book. He can also read and is engrossed in his current interest—what he calls symbolic art. "You don't paint a thing how it looks sir; you paint it as you think it ought to look," was the comment he offered when I asked him what he was trying to do.

The children admitted to a hospital ward come from all types of school: there are pupils from grammar schools, and those who are educationally subnormal; children from Home Office establishments, and children from preparatory schools; pupils working for School Certificate, and those who are struggling with the beginnings of number and reading. The work is further complicated in nearly half our hospital schools by the fact that the children are not distributed according to age. The approach of the teacher must, therefore, be to the individual; wide age ranges and differing standards demand individual teaching, particularly in the basic subjects.

But the child is also a member of the ward community and should be encouraged to make his contribution to its life. The teacher must be able to design group activities which will give scope to the interests and abilities of her pupils, and lead to pride in personal achievement and in the satisfaction of making a useful contribution to the group. Nearly three quarters of the children attending hospital schools return to their homes, and to ordinary schools. There they are expected to take their place in a competitive community; and the hospital teacher must see that educationally, at least, they will be able to do so.

THE WORKING BACKGROUND

The pioneers in the education of the sick child were moved by pity; they were disturbed by the conditions under which crippled children were allowed to exist. Today we are asked to regard such children as perfectly normal and to treat them as such. There is something of truth in both these attitudes, but they both carry attendant risks. Sentimentality towards the sick child can create an emotional disturbance which might not otherwise have developed; yet if we treat the patient as a perfectly normal child suffering from a local condition we may well fail to recognise a disturbance which already exists.

The doctor can achieve some of his results without the willing cooperation of his patient; but the teacher can achieve nothing unless the child is fully cooperative. She cannot impose the sanctions of the normal school: there can be no detention after school hours, no corporal

---

* Special Unit for the Study and Care of Juvenile Rheumatism.

"Fallot's tetrad" nearly two hundred years before Fallot was born

The new Danish edition of his dissertation on the brain contains not only a facsimile of the original treatise, as it was delivered to the French Assembly in M Thevenot's house in 1665, but also the English translation, made by Dr G Douglas in 1733, which was incorporated in James Winslow's "Anatomical Exposition of the Structure of the Human Body" It is a beautifully scientific work, confessing ignorance, refuting unfounded assertions, proposing investigations, suggesting experiments Especially he pressed the need for careful dissection

> "As the Brain is a Machine, we must not flatter our selves that we can discover the contrivance of it by any other means than are made use of for knowing other Machines and we have no way left but to take it to pieces, and to consider what every part is capable of in a separated and an united state"
>
> And again "This method of Dissection makes indeed but a very small Shaw, and a Man cannot well display his Learning at the same time that he acknowledges his Ignorance but as for my own part I much rather choose to own what I do not know, than to impose upon my Hearers, ancient Opinions, which will some time or other be demonstrated to be false"

Steensen's achievements in geology were hardly less remarkable than his contributions to anatomy, and indeed geologists regard him as the founder of their science His remarkable mind, however, had still another field to explore In 1667 he was converted from the Lutheran faith, in which he had grown up, to Roman Catholicism, and in 1675 he gave up all his scientific studies and entered the priesthood He quickly rose to a bishopric, and became apostolic legate for Northern Germany and Scandinavia, but his natural austerity led him to forsake these honours, and he died a plain priest, in great poverty He is buried at Florence in San Lorenzo, the church of the Medici

CONTROL OF TINEA CAPITIS

THE rational treatment of ringworm of the scalp depends on identifying the responsible fungus, its dissemination can be prevented only if the local human and animal nidi of infection are found and eliminated *Microsporon audouini* is the commonest infecting organism, accounting for most school and institutional epidemics *M canis*, in which the kitten and not the puppy is usually the host, is a less common cause, it gives rise to sporadic cases in which infection becomes attenuated by child to child transmission and eventually dies out, unless enhanced by infection of an animal host, after 4–6 human transfers in series In some country communities trichophyton infections, usually acquired from calves and occasionally from horses, are a further cause of tinea capitis Of 1004 cases examined in Northern Ireland by Beare and Cheeseman[1] 957 were small spore infections, in 806 the organism was *M audouini*, and in 85 *M canis*, while in 66 the organism was undetermined There were 43 trichophyton infections, 1 of favus, and 3 kerions *M audouini* is essentially the fungus of epidemic ringworm, so these figures from a limited district may be misleading Walker,[2] in a three year survey of the dermatophytes in Great Britain, examined material from 2015 cases of tinea capitis and isolated *M audouini* in 1427, *M canis* in 505, *M gypseum* in 2, and various trichophyta in 81

In identifying infections with small spores Wood's light is indispensable, in some cases of tinea capitis, particularly of long standing, naked eye examination may show little or no abnormality, whereas examination with Wood's light reveals extensive areas of infection When spontaneous cure is taking place the fluorescence becomes less brilliant The nature of a miscrosporon infection is not readily determined without culture, but Beare and Cheeseman describe six points of differentiation which have enabled them to make a correct forecast of the culture findings in 97% of cases These six points are (1) the tendency of *M audouini* to affect specific areas of a city, and of *M canis* infection to arise sporadically, (2) the tendency of *M canis* to cause more severe reactions than *M audouini* (though sometimes there may be little or no reaction), (3) *M canis* infections when examined under Wood's light lose their brilliance and after a few weeks appear dull green, whereas *M audouini* fluorescence remains brilliant for some months, (4) visible changes in the lesions are more rapid with *M canis* than with *M audouini*, (5) a history of skin disease in a kitten in the house is far more common with *M canis* than with *M audouini* infections, and (6) associated tinea corporis is much more common with *M canis* scalp infections than with *M audouini* infections Early identification of the fungus is important because *M audouini* infections usually call for X ray epilation, whereas *M canis* can often be dealt with successfully by local applications

X ray expilation by the Kienbock Adamson technique is still the best method of dealing with *M audouini*, persisting *M canis*, and *Trichyphyton sulphureum* infections, for children between 1 and 3 years of age this may have to be carried out under general anæsthesia In infants under 1 year of age spontaneous cure is common, no matter what the organism, so that local application of fungicides may suffice Local epilation is inadvisable because of the risk of subsequent infection of non epilated areas, and because the resulting appearance is no better than when total epilation is carried out Beare and Cheeseman found that salicyl anilide in carbowax was ineffective, failure resulting in 7 out of 13 patients treated, and contact dermatitis in 3, in 1 patient severe folliculitis developed and led to gross scarring Among 23 patients treated with salicyl anilide in pentaglycol there were 14 failures Manual epilation is a necessary accompaniment of local fungicidal applications, and the whole process is not only tedious but depends for success largely on the intelligent cooperation of parents Nevertheless, Barlow and his associates[3] reported eventual cure in 64 8% of 261 cases of *M audouini* infection treated with local applications, in an average time of 10 weeks In their hands cuprammonium hydroxide in carbowax gave the best results (39 cures and 3 failures)

When local fungicidal applications fail it is because of their inability to penetrate into the hair shafts, their influence being confined to the epidermis and the follicles In these circumstances their only virtue is in lessening the spread of infection on the scalp and to other children, until folliculitis and scarring, or natural spontaneous shedding of affected hairs, takes place meanwhile absence from school is prolonged and the sense of uncertainty maintained Fungicides are much more likely to succeed in *M canis* than in *M audouini* infections, probably because in the former they set up a folliculitis more easily and it is this inflammatory reaction and subsequent shedding of the affected hairs that leads to disinfection For trichophyton infections other than *T sulphureum* Beare and Cheeseman recommend boric starch poultices, manual epilation, and Whitfield's ointment, and they emphasise the importance of strenuous efforts to eliminate or at least reduce the cattle ringworm at present prevalent in some parts of the country, in an attempt to prevent these human infections

---

SIR THOMAS WATTS, M D, a former M.P for the Withington division of Manchester, died at Southport on June 3, at the age of 82 For many years he was in practice at Hyde, Cheshire xcept those which do not come under the definition of rugs for National Health Service purposes The committee also listed the proprietary preparations which ught be prescribed under the health service

---

[1] Beare J M Cheeseman L A *Brit J Derm* 1951 63 165
[2] Walker J *Ibid* 1950 62 239
[3] Barlow A J E Chattaway F W, Whewell C S *Ibid* p 251

HEALTH CENTRES

A committee of the council has set out a plan for the ong term development of health centres, and has uggested ways of obtaining immediately some of the dvantages that health centres are intended to provide The committee proposes that all centres should provide general medical and some local health authority services, nd that some centres should provide dental services or more than one area , pharmaceutical services would also be provided where necessary The centres should erve 15,000–20,000 people living within half a mile of the entre Because of the common fear of infection, tuberculosis clinics should not be held at health centres unless there are separate entrances and waiting rooms It is suggested that accommodation should be provided for 4–8 doctors, who should be encouraged to work in financial partnership Doctors would pay for the use of the premises, but dentists who receive a fixed salary from the executive council should not be required to do so Centres are regarded as suitable for the instruction of trainee assistants and medical students, but the committee is not in favour of encouraging permanent assistantships

ADVISORY COMMITTEES

Medical —This committee has been particularly concerned with economy in prescribing In conjunction with the standing nursing advisory committee it reviewed methods of controlling infection in hospitals and ways of improving children's hospitals Following a report by the World Health Organisation, the committee advised the Minister that prohibiting the use of heroin in the United Kingdom would be justified if international agreement were reached to prohibit the sale and manufacture of heroin throughout the world , but that heroin addiction was not a serious problem in this country The committee also considered the use of ' Cortisone the treatment of cosmetic disabilities in the National Health Service and certain detailed points in the economical use of drugs and dressings in hospitals

Dental —This committee has been concerned with problems of coöperation between authorities providing dental services , the employment of dental hygienists and the use of certain dental materials and drugs in the general dental service

Pharmaceutical —The committee has reviewed the questions of pharmaceutical man power pharmaceutical manufacture and research in hospitals, standardisation of accommodation and equipment, and the provision of a central syringe sterilisation service

Nursing —This committee has reported on methods of obtaining and collating information regarding approved nursing techniques methods of disseminating this information to hospitals and nurses and the techniques to be recommended In conjunction with the medical advisory committee the committee advised the Minister on cross infection in hospitals and, in conjunction with the tuberculosis advisory committee considered the precautions necessary to safeguard nurses from tuberculosis

Maternity —This committee continued to study the place of the maternity unit in the hospital service and decided that special attention should be given to the care of premature infants and to sick and injured babies throughout the country

Mental health —The standing committee on mental health recommended to the Minister methods of reducing the shortage of nurses in mental hospitals and mental deficiency institutions

Cancer and radiotherapy —The committee again considered the question of cancer publicity and revised a previous recommendation to remove the implication that local health authorities should omit any reference to cancer in their general health propaganda The revised recommendation reads It is undesirable at the present time for any cancer publicity to be carried out by the Minister directly to the general public " The council later expressed the view that no publicity should be carried out by any central Government organisation directly to the general public

CHARLES HASTINGS MEMORIAL FESTIVAL

MEMBERS of the medical profession assembled in Worcester on Wednesday, May 30 in brilliant sunshine, to commemorate the founder of the British Medical Association, Sir Charles Hastings Doctors in academic robes, entering the Cathedral by the west door from the terrace overlooking the river Severn, took part in the special service, conducted by the Dean, the Very Reverend W E Beck, during which Sir Henry Cohen, president of the association, laid a wreath by the Hastings memorial window

In his address the Bishop of Worcester, the Right Reverend W Wilson Cash spoke of the part that religion had played in the life of Hastings He grew up in an age of great reformers and so was never satisfied with things as he found them He had to improve and perfect All his actions were governed by his faith in God, while in his many activities he proved himself a man of courage, devoted to duty The Bishop referred to the importance of voluntary service in our national life, and said that *long before the* phrase " Welfare State " was coined, *the* medical profession, under the leadership of men such as Hastings, was introducing it on this voluntary basis

At a luncheon, under the chairmanship of Dr. W D Steel, in the beautiful banqueting-room of the Guildhall, Admiral Sir William Tennant, Lord-Lieutenant of the county and city of Worcester, proposed the toast of the British Medical Association , and Dr J A Brown, chairman of the Representative Body, replied Dr E A Gregg, chairman of council, proposed the health of the guests , and the mayor of Worcester, Alderman W H Norton, replied to the toast

The Charles Hastings memorial lecture was delivered by Dr W H McMenemey, who said that a keen sense of responsibility may have developed in Hastings from the time when his father met with an accident and was rendered incapable of managing his affairs , Hastings was then only twelve years old In his career as house surgeon at the Worcester Royal Infirmary he showed his organising ability, while at Edinburgh his powers of leadership became evident early on when he became president of the Royal Medical Society On his return to Worcester as physician to the infirmary, in 1818, he was elected president of the Worcestershire Medical Society—a body which may have been instituted by Hastings during his temporary sojourn in Worcestershire for reasons of health in 1816 A medical society had, however, existed in Worcester since 1799, the year when Dr A P Wilson Philip left Winchester to settle in Worcester Wilson Philip made a considerable impression on young Hastings and influenced him both in his experimental work, for which he seems to have had a real flair, and in his relationships with the governors of the infirmary The Worcestershire Medical Society continued in existence until Hastings became preoccupied with the more important Provincial Association Nevertheless, the local society was important in its day and petitioned both Houses of Parliament prior to Henry Warburton's second and successful attempt to regulate the practice of anatomy

If the stage was set for the establishment of a medical association in 1832 the success of the Worcester enterprise is attributable, said Dr McMenemey, to the personality, the enthusiasm, and the industry of Hastings, to his ability to persuade men to work together, and to his farsightedness in deciding to publish annual transactions and later a journal, both of which helped to weld the members together Moreover, his ideals were cast high and made a universal appeal " We take our Pole Star to be the alleviation of human suffering," Hastings once said The success of the association was remarkable Its annual meeting was christened the Parliament of the profession by the *Morning Herald* in 1838, and in 1851 punishment, no cancelled half day holidays, even the traditional "impot" is banned by the conditions of ward routine Moreover, there is no single authority on the ward The doctor, the sister and the teacher are all authorities, while even ward maids not uncommonly weigh in with their own interpretation of discipline

The teacher needs, therefore, to tap all sources of information that will help her to obtain a comprehensive picture of the child She should be told about the limitations imposed by the child's physical condition, she should consult the almoner on his social background, and the sister on his out of school activities and interests The child's ordinary school should be asked about previous standards of work Above all, the teacher must appreciate that on first admission to hospital, the child is emotionally disturbed He has left his home and his normal associations and has entered a world which, in the first instance at least, can hold nothing but fear for him

It might be true to say that the teacher is the first ordinary contact that the child makes in hospital. Certainly, he has met an occasional nurse at a school medical inspection, and he will have had some experience of doctors But the teacher is an essential and accepted part of his normal everyday life, she brings into the ward something of the world outside the hospital, something of his old school, his friends, and a routine he can understand She thus begins with advantages which can be used to help him to make happy relationships with his new friends in the ward

Because the teacher is interested primarily in children, rather than in medicine or nursing, she should be able to detect causes of disruption or unhappiness in the ward She should be able to suggest out of school activities, and suitable literature for the ward library She has a contribution, to make to the child's happiness while he is a patient, by introducing a diversity of interests she can lead him away from thoughts of illness and thus prevent those unhappy states of mind which are common to chronic patients of all ages

The story has been told of the sick child who said he was glad they had introduced a school in his hospital, because "we now have something we can have a holiday from" This might be read as an indictment of the school, but I prefer to see it as the child's desire for the normal life of school and holidays, work and play and all the factors which contributed to the life which he has, temporarily at least, left behind him The ward routine of washings and bedpans and treatment must in time pall on the dullest mind and the least inspired personality Often the child may be ill yet not feel ill, and anything which destroys the frustration created by months in bed must have some value At least the child can have a holiday from school there is no holiday from the ward until he goes home

The growing cooperation of doctors and nurses has done much to ease the work of the hospital school-teacher during recent years This surely, is a recognition of the fact that the child's social life in hospital is not without importance[1] It is an attitude which acknowledges too, that a temporary physical illness should not result in a permanent educational deficiency

---

[1] Maclennan B W *Lancet*, 1949, ii 209

' it was not possible under the terms of the Act to institute any system whereby a patient pays according to his means and thus to have a stake in treatment commensurate with his income The impetus to recovery, which in neurosis is difficult to maintain with some patients even under ideal medical conditions, was under these circumstances sometimes hopelessly damaged In my view the offer of free treatment to neurotic patients by the National Health Service needs review, it is of doubtful benefit to all and a tragic disservice to some "—Dr T F MAIN, medical director of the Cassel Hospital for Functional Nervous Disorders, in his report for 1948–50

CENTRAL HEALTH SERVICES COUNCIL

DURING 1950 the National Health Service was settling down, and the report for that year by the Central Health Services Council[1] reflects the decrease in the number of major problems since its first report[2] was written

TUBERCULOSIS

The standing tuberculosis advisory committee suggested schemes to provide more beds for tuberculous patients, and for recruiting more nurses, and action has already been taken on many of these recommendations The committee also advised the Minister that hostels, under medical supervision, should be provided for chronic infectious patients who are able to get about, and that night sanatoria should be established for patients who are likely to recover and who are able to work Sheltered employment for disabled tuberculous persons, on the lines of the 'Remploy' scheme of the Ministry of Labour and National Service, is advocated, in addition to the village settlements which already serve this purpose Other recommendations include the establishment of clinics for treating rarer types of tuberculosis, and special centres for children suffering from, or susceptible to, tuberculosis In accepting the committee's report the council drew attention to the importance of the general practitioner in any comprehensive plan for the diagnosis, treatment, and reablement of the tuberculous, and also emphasised that all nurses, whether or not engaged in tuberculosis work, should be tuberculin tested and that negative reactors should be offered B C G vaccination

HOSPITAL ADMINISTRATION

The present structure of external hospital administration was examined by a special committee, which concluded that it was unnecessary at this time to make radical alterations Nevertheless, the present groupings and areas are not to be regarded as sacrosanct, and after further administrative experience the present groupings and areas should be reviewed The Minister was finally advised that area committees of regional boards should be abolished in due course, or regional areas redrawn to avoid the need for these committees. In special circumstances a regional board should be allowed to administer a convalescent home or other ancillary unit in an area controlled by another board It was suggested that capital allocations to boards should be spread over more than one year, and that hospital management committees should be given money for small capital works The Minister was reminded that it was desirable to appoint at least one general practitioner and one medical officer of health to each regional board

A committee has now been appointed to report on internal administration in individual hospitals, with particular reference to (1) finance, staff, and supplies, (2) administration in relation to the different types of hospitals, and (3) the extent to which administrative duties should be undertaken by medical and nursing staff

PRESCRIBING

A joint committee was set up with the Scottish Health Services Council to consider whether general practitioners should prescribe drugs of doubtful value or of unethical character, or unnecessarily expensive brands of standard drugs The committee recommended that there should be no absolute restriction on the prescribing by a general practitioner of any drug which, in his opinion, is necessary for the treatment of his patient, and that he could freely prescribe all drugs and preparations described in the *British Pharmacopœia*, the *British Pharmaceutical Codex*, and the *National Formulary*,

---

[1] Report of the Central Health Services Council for the Year ended Dec 31 1950 *H.M Stationery Office* Pp 47 1s 6d

[2] See *Lancet* 1950 ii 106

TABLE III—PROPORTIONAL MORTALITY OF SINGLE AND MARRIED WOMEN IN 1948

Status	Age group (yr)													
	16–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75 or more	Total
Single	36	40	27	18	21	28	35	45	55	72	100	137	386	1000
Married														
Actual	1	12	25	27	35	45	63	83	102	127	149	152	179	1000
Adjusted	30	34	20	14	16	23	35	44	57	83	121	158	365	1000

TABLE IV—NUMBER OF MARRIED AND SINGLE WOMEN RECORDING A MONTH'S SICKNESS EXPERIENCE IN 1948

Civil state	Age group (yr)										
	16–24	25–34	35–44	45–54	55–64	65–74	75 or more	Total	16–44	45–64	65 or more
Married											
Numbers	2016	6427	6522	4949	3196	1501	361	24972	14965	8145	1862
% of group	8 1	25 7	26 1	19 8	12 8	6 0	1 5	(100)	59 9	32 6	7 5
Single											
Numbers	3138	1455	893	931	767	565	261	8010	5486	1698	826
% of group	39 2	18 1	11 1	11 6	9 8	7 0	3 2	(100)	68 5	21 2	10 3

compared with married women under the age of 45 At 20–24 the rate for single is 25% above that for married women, and at 25–34 it is 42% higher Probably the group of single women aged 16–44 is biased by containing a number who have remained single because they are tuberculous Moreover, the chance of dying in child birth, which formerly constituted a grave threat to married women under the age of 45, has been greatly reduced, chiefly owing to the control of sepsis with sulphanilamides The mortality-rate of women in or associated with pregnancy and childbearing fell from 3 80 per 1000 live and still births in 1934 to 1 02 in 1947 in cases without abortion while the rate for cases with abortion declined from 0 82 to 0 16 Suicide and accidental deaths are two other causes in which the death-rates for single women under 45 are higher than those for the married As regards suicide, perhaps the neurotic disposition which finds an outlet in suicide may also have prevented marriage As regards accidents, a number of deaths would be due to accidents either at work or on the journey to and from the place of employment At 45–64 single women had higher rates than did married women for respiratory tuberculosis pneumonia, peptic ulcer, suicide and accidental deaths, but married women's rates showed a substantial excess over those of single women for diabetes, cerebrovascular lesions, arteriosclerosis, and nephritis

TABLE V—ACTUAL AND EXPECTED AGE DISTRIBUTIONS OF MARRIED AND SINGLE WOMEN RECORDING A MONTH'S SICKNESS EXPERIENCE

Age group (yr)	Married			Single		
	Actual	Expected	Difference	Actual	Expected	Difference
16–24	2016	1760	+256	3138	3473	−335
25–34	6427	5905	+522	1455	1225	−230
35–44	6522	6354	−168	893	981	− 88
45–54	4949	5196	−247	931	882	− 49
55–64	3196	3577	−381	767	680	− 87
65–74	1501	1764	−263	565	502	+ 63
75 or more	361	416	− 55	261	267	− 6
Total	24 972	24 972		8010	8010	

In table III the adjusted mortality among married women is based on the number of deaths which would have occurred among married women had their age distribution been the same as that of the single Owing to the difference in death rates, 10 3% of the deaths of single women occur at ages under 30 compared with an adjusted rate of 8 4% among married-women A quarter of the single women's deaths take place before the age of 55, whereas 21 6% of married women's deaths would occur before that time if their age-distribution was the same as that of the single women

The Social Survey interviewed in each month of 1948 a sample of about 3000 people aged 16 or more, to obtain their sickness experience during the two months preceding the interview Hence in the course of a year about 70,000 persons recorded a month's sickness experience During 1948, 24,972 of these were married and 8010 single women (table IV) Their age distribution is shown in table V, and is compared with an expected distribution based on the age distribution of the two classes in the general population

For married women $\chi^2 = 186\ 53$ when $n = 5$, hence P is less than 0 001 For single women $\chi^2 = 103\ 43$ when $n = 5$, hence P is less than 0 001 The age-distribution of both the married and the single women whose sickness experience was recorded therefore differs significantly from that among the general population In the discussion which follows three principal age-groups are considered 16–44, 45–64, and 65 or more, but, since the age distributions of the two classes differ, two rates have been calculated for single women—the actual rate, and that which would obtain if the age-distributions were comparable

TABLE VI—NUMBER REPORTING NO ILLNESS OR INJURY DURING JANUARY–DECEMBER 1948 PER 100 MARRIED AND SINGLE WOMEN INTERVIEWED

Month of experience	Age-group (yr)								
	16–44			45–64			65 or more		
	Married	Single		Married	Single		Married	Single	
		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted
January	32	45	39	25	23	23	13	21	23
February	32	41	38	25	20	20	20	13	12
March	33	41	38	26	28	27	22	13	12
April	36	44	38	26	27	26	19	9	10
May	36	42	38	25	31	31	19	13	14
June	36	47	42	24	27	23	18	29	30
July	36	46	42	25	28	26	14	30	32
August	37	45	44	23	33	34	15	16	18
September	35	43	40	21	30	30	18	18	18
October	30	40	35	19	25	26	14	11	11
November	29	37	36	20	24	25	15	5	4
December	26	36	33	19	21	22	15	12	12
Aggregate for whole year	33	42	39	23	26	26	17	16	17

Dr John Ayrton Paris, president of the Royal College of Physicians, told them that it was for them and for them alone to determine what should be the future state of the profession The lifelong interest of Hastings, however, was the welfare of the provincial practitioner, and it was not until the Provincial Medical Association had been in existence for twenty four years that he agreed to the wish of the majority to change in the title the word "Provincial" to "British"—an amendment first proposed in these columns some years earlier[1] Dr McMenemey's lecture was illustrated by lantern slides, which included a number of portraits of those early pioneers of the association who assisted Hastings i project

In the famous boardroom of the Worcester Infir wherein the inaugural meeting was held, visitors sa exhibition of records illustrating the work of Has including several of his publications

The British Medical Association, and particularl Worcester and Bromsgrove division, is to be congratu on this first Charles Hastings Festival, so happily ciding with the Festival of Britain Their decisi commemorate the founder every few years in a Se of rededication to the objects of the association is n a happy one

---

[1] Leading article *Lancet* 1832, ii 574

Public Health

DEATH-RATES AND SICKNESS-RATES OF MARRIED AND SINGLE WOMEN IN 1948

EILEEN M BROOKE
M Sc Lond
STATISTICIAN, GENERAL REGISTER OFFICE, LONDON

A COMPARISON has been made of the death rates and sickness rates of married and single women, based on the Registrar General's returns of death and the Survey of Sickness figures derived from monthly interviews held by the Central Office of Information on behalf of the General Register Office Widows and divorcees have been excluded from the analysis for two main reasons First, the group of single women may contain a number whose celibacy is due to bad health and poor physique, and whose sickness rate would therefore be above the average It would not be practicable to include the widowed and divorced with this group, since no such sanction has applied in their case Alternatively, since some single or divorced women, especially in the lower age groups, might be in a worse position economically than married women, with consequent repercussions on their health, it would be inadvisable to include them with the married group That age specific death rates are not greatly influenced by the inclusion of the widowed and divorced with either the single or married groups except at the higher ages is illustrated by table I

The lower age limit in the table has been set at 16 years because for National Insurance purposes this is the age at which working life is presumed to begin, the same lower limit has been taken in the Survey of Sickness The death rates of single women are higher than those of the married in all quinquennial age-g under 60 At ages under 45 the ratio (1 34) of the for single to that for married women is lowest at 20–24, whereas at ages 25–34 single women have a slightly more than 50% higher than that of the ma At ages from 45–64 the rate for single exceeds tha married women, but less markedly, the ratio va between 1 00 and 1 19 Unfortunately there i information more recent than that obtained at 1931 census to show which individual causes of d are mainly responsible for the excess

TABLE I—DEATH RATES PER 10,000 WOMEN BY MARITAL S IN 1948

Age group (yr)	Single	Married	Ratio of single to married	Single widowed and divorced	Marr widow an divor
16–19	11 9	8 5	1 40	11 9	8
20–24	17 3	12 9	1 34	17 4	13
25–29	23 4	15 0	1 56	23 9	15
30–34	25 4	16 2	1 57	25 9	16
35–39	28 0	19 0	1 47	28 6	19
40–44	36 2	26 0	1 39	36 8	26
45–49	47 1	40 7	1 16	48 9	41
50–54	73 5	61 9	1 19	73 5	63
55–59	101 3	90 9	1 11	103 4	94
60–64	145 5	145 0	1 00	161 7	153
65–69	233 1	246 8	0 94	241 0	245 6
70–74	398 5	398 6	1 00	433 3	491
75 or more	939 5	771 2	1 22	1047 1	1002

Table II shows for certain principal causes the de rates per 100,000 married and single women in diffe age groups, based on the mortality experience of the y 1930–32 Respiratory tuberculosis seems to be a p minent cause of the high death rate among single

TABLE II—DEATH-RATES PER 100,000 MARRIED AND SINGLE WOMEN AT DIFFERENT AGE GROUPS IN 1930–3

Cause of death	Status	Age-group (yr)						
		16–19	20–24	25–34	35–44	45–54	55–64	65–69	70 or
Respiratory tuberculosis	M	102	105	87	66	49	42	34	25
	S	103	126	124	83	57	44	42	27
Diabetes	M		2	3	4	13	52	108	138
	S	*	2	4	6	9	24	41	66
Diseases of blood and blood forming organs	M	3	3	5	7	14	28	44	41
	S	3	3	5	8	16	26	31	40
Cerebrovascular lesions arteriosclerosis	M			2	9	56	186	470	1145
	S	*	*	2	11	45	108	460	1439
Bronchitis	M	1	1	2	4	13	46	133	410
	S	2	2	3	6	14	44	100	550
Pneumonia	M	15	15	16	25	32	64	123	233
	S	11	9	14	27	44	81	136	297
Asthma	M	1	0	1	2	4	9	16	23
	S	0	1	2	3	5	13	12	23
Total respiratory disease	M	17	17	21	35	53	126	287	732
	S	14	14	20	39	68	146	257	933
Peptic ulcer	M	1	1	2	3	9	12	17	17
	S	1	1	2	5	11	16	22	23
Nephritis	M	4	7	9	18	40	86	160	239
	S	7	8	9	17	36	74	128	247
Suicide	M	3	4	6	9	13	15	13	10
	S	3	5	9	12	18	20	15	11
Accident	M	4	6	5	6	11	22	43	106
	S	10	11	9	10	18	33	59	219

* Blanks in this table denote that for the cause age-status group concerned less than 20 deaths were recorded

ays a doctor's certificate is not required, there may be tendency on the part of single women to forget to eport minor illnesses, where they would remember an ccasion on which they had consulted a doctor They nay also show a greater tendency to disregard minor nd symptomatic illnesses, and to continue at work n spite of feeling ill, so as to avoid the financial loss onsequent on obtaining a doctor's certificate and being way from work for a week In this connection it is well nown that, among piece workers who combine to orm a team, each member will make great efforts to void being away because of the monetary loss to the others Further, in 1948 married women may have had preponderance of minor complaints connected with child bearing and fatigue due to queueing, carrying heavy shopping baskets, and inability to obtain domestic help The inception rates of minor and ill defined illnesses show a fairly definite seasonal trend (see figure)

If all illnesses be considered, instead of only those starting or recurring during a certain period, it is found that in each quarter of 1948 the rates for married women in the age group 16–44 were from $1\frac{1}{4}$ to $1\frac{1}{3}$ times greater than those for single women, and, even when the variation in age structure between the two groups is allowed for, the married still show much higher rates than do the single women (table VIII) In the age group 45–64 single women had a higher rate in the first quarter and married women in the remaining nine months, while for ages over 65 married women had higher rates than single during the six months April September Taken over the whole year, there is very little difference between the rates for single and married women at ages 65 or more

TABLE IX—DAYS OF INCAPACITY AND NUMBERS OF MEDICAL CONSULTATIONS PER 100 MARRIED AND SINGLE WOMEN INTERVIEWED

Month of experience	Days of incapacity during month						No of medical consultations in month					
	Aged 16–44		Aged 45–64		Aged 65 or more		Aged 16–44		Aged 45–64		Aged 65 or more	
	M	S	M	S	M	S	M	S	M	S	M	S
January	78	79	100	175	245	114	34	33	46	60	57	30
February	80	54	95	192	254	144	38	28	49	65	70	37
March	57	61	73	109	169	127	36	28	55	44	50	62
April	59	70	43	72	99	57	32	31	37	39	55	43
May	63	71	48	72	124	76	31	30	39	58	62	30
June	52	61	56	83	115	68	33	29	48	43	49	15
July	72	65	88	85	139	167	37	23	50	35	79	59
August	57	72	69	37	145	161	29	28	43	26	54	69
September	48	68	85	86	130	104	32	34	54	31	47	53
October	73	82	119	200	190	77	40	28	65	45	58	47
November	87	79	120	151	399	280	37	31	61	64	76	76
December	82	91	150	140	377	444	46	29	49	65	96	70
Aggregate for whole year	67	71	89	114	196	155	36	29	50	47	63	49

Table IX shows the days of incapacity and numbers of medical consultations for each hundred married and single women Although at 16–44 married women had higher prevalence rates than did single women, the

TABLE X—PREVALENCE RATES PER 10,000 MARRIED OR SINGLE WOMEN FOR CERTAIN CAUSES

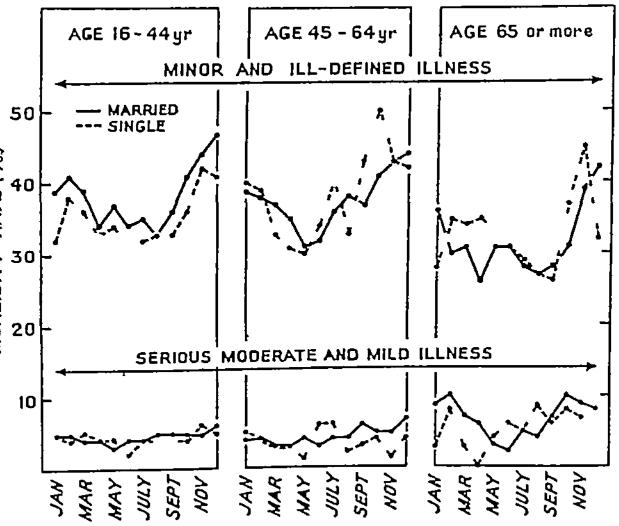
Disease group	Period	Aged 16–44		Aged 45–64		Aged 65 or more		Disease group	Aged 16–44		Aged 45–64		Aged 65 or more	
		M	S	M	S	M	S		M	S	M	S	M	S
Colds and influenza	Jan.–Mar	1876	2041	1516	1644	1274	1982	Veins	316	186	515	658	562	415
	April–June	1032	1087	730	828	959	914		495	169	618	411	388	152
	July–Sept.	1047	1097	825	1167	815	986		467	145	458	412	622	282
	Oct–Dec	2304	2319	1938	1774	1354	1457		461	92	614	253	519	452
	Jan.–Dec	1576	1650	1258	1278	1096	1344		436	148	539	424	521	327
Respiratory diseases	Jan–Mar	1108	771	951	1397	1166	1336	Anæmias	146	178	110	192	108	—
	April–June	927	947	958	1364	1592	1371		182	191	167	43	20	102
	July–Sept.	860	792	777	664	708	1174		184	122	87	69	64	47
	Oct–Dec	1041	872	952	991	1196	1608		185	64	129	69	—	352
	Jan.–Dec	984	846	909	1095	1171	1368		174	139	123	88	48	121
Mouth and teeth	Jan.–Mar	699	600	325	219	151	138	Skin and cellular tissue	341	385	455	274	410	369
	April–June	613	602	350	368	122	51		377	661	370	346	592	609
	July–Sept	694	693	405	458	236	—		238	472	343	320	365	423
	Oct.–Dec	818	808	486	207	248	201		286	539	324	346	609	503
	Jan.–Dec	708	676	393	318	188	97		309	514	372	324	494	472
Acute sore throat	Jan–Mar	129	143	15	55	43	—	Genito urinary and venereal	149	71	165	219	367	277
	April–June	116	81	66	—	20	—		121	44	127	65	122	305
	July–Sept.	83	99	43	23	64	47		104	53	116	183	236	47
	Oct–Dec	96	163	38	115	—	101		182	57	219	69	68	—
	Jan–Dec	106	122	41	47	32	36		140	57	157	130	199	157
Ear and mastoid	Jan–Mar	138	128	250	493	367	1014	Gastro intestinal	39	50	70	82	43	—
	April–June	165	242	253	476	469	1421		47	44	117	43	41	—
	July–Sept	227	213	333	458	751	1220		32	23	96	—	64	141
	Oct–Dec	172	128	414	415	497	1206		39	43	90	23	90	50
	Jan–Dec	176	177	314	459	521	1211		37	40	93	35	59	48
Rheumatism all forms	Jan–Mar	1240	650	2727	2301	3801	4240	Nervous	2577	1663	3147	3781	3801	3825
	April–June	1089	800	2798	2576	3551	3553		2759	1953	3132	2836	3408	2690
	July–Sept	1124	640	2798	2975	3755	3192		2411	1561	3145	3021	3154	1972
	Oct–Dec	1375	787	3105	2995	3634	3769		2724	1567	2933	2742	3341	3467
	Jan.–Dec	1210	720	2859	2727	3684	3692		2619	1686	3088	3063	3426	2990
Eye affections	Jan–Mar	358	236	615	932	1253	1521	Ill defined symptoms	3427	2413	3502	2712	3240	3041
	April–June	366	204	755	584	735	1218		3345	2320	4252	2771	3959	3553
	July–Sept	454	404	873	641	901	892		3423	2262	4472	4096	4237	2911
	Oct.–Dec.	494	397	981	876	1106	1407		3459	2241	4033	2696	3747	3317
	Jan.–Dec	420	324	809	748	994	1259		3415	2310	4068	3080	3797	3196
Heart and arteries	Jan–Mar	256	221	675	548	1253	1382	Injuries	105	128	115	27	259	230
	April–June	182	110	557	519	1306	1878		77	103	142	173	122	102
	July–Sept.	134	107	656	778	1631	1408		120	137	154	114	86	94
	Oct.–Dec	309	333	667	507	1151	1508		81	99	133	69	158	201
	Jan–Dec	221	195	640	589	1337	1538		96	117	136	100	156	157

TABLE VII—MORBIDITY-RATES PER 100 MARRIED AND SINGLE WOMEN FOR ILLNESS STARTING OR RECURRING IN EACH MONTH, DISTINGUISHING MINOR AND ILL-DEFINED COMPLAINTS

Month	Serious, moderate, and mild									Minor and ill defined								
	Aged 16–44			Aged 45–64			Aged 65 or more			Aged 16–44			Aged 45–64			Aged 65 or more		
	M	S		M	S		M	S		M	S		M	S		M	S	
		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted
January	5	5	9	4	5	9	9	3	8	39	32	34	39	40	40	36	28	46
February	5	4	3	4	4	4	10	8	8	41	38	37	38	39	39	30	35	38
March	4	5	4	3	3	3	7	3	3	39	36	37	37	33	34	31	34	34
April	4	4	4	3	3	3	6	—	—	34	33	37	35	31	33	26	35	35
May	3	4	5	4	1	1	3	4	4	37	34	37	31	30	30	31	33	31
June	4	2	2	3	6	6	2	6	6	34	32	34	32	34	34	31	31	30
July	4	4	5	4	6	6	5	5	4	35	32	33	36	40	39	28	29	27
August	5	4	7	4	2	2	4	9	10	33	33	32	38	33	33	27	27	24
September	5	4	3	6	3	3	7	6	6	36	33	34	37	43	43	28	26	27
October	5	4	2	5	4	4	10	8	8	41	36	38	41	50	51	31	37	38
November	5	6	4	5	1	1	9	7	8	44	42	41	43	43	43	39	45	47
December	6	5	5	7	4	5	8	10	9	47	41	43	44	42	42	42	32	36
Aggregate for whole year	5	5	4	4	4	4	7	6	6	39	35	37	38	38	38	32	32	33

Table VI shows that for each month of the year, in the age group 16–44, proportionately more single than married women reported freedom from any illness or injury The excess in the percentage number of single over married women who were sickness free varied between 13 in January and 6 in May If the adjusted numbers for single women be considered, they still exceed the numbers of married women who reported no illness or injury In the age group 45–64 a higher proportion of single than married women reported freedom from sickness except in January and February At ages over 65 there was no significant difference between the two groups, but the seasonal range was greater in the case of single women, the successive quarterly proportions being 16, 17, 21, and 9%, compared with 18, 19, 16, and 15% among the married On the whole there was more freedom from sickness during April to September than during the remaining six months, at all ages and in both classes

Table VII shows the inception rates for new and recurrent illnesses reported for each month, a recurrent illness in this context being an attack which occurs not less than a week after the subsidence of a previous attack of the same malady Distinction is made in this table between (1) serious, moderate, and mild illnesses, all of which generally produce three or more days' incapacity, and (2) minor and ill defined illnesses, of which the former are diagnostic entities generally causing incapacity lasting less than three days and the latter are complaints listed in numbers 773 and 780–795 of the International Classification of Diseases, 1948 Where serious, moderate, and mild illnesses are concerned, there is little difference between the inception rates for married and single women, and if the figures be aggregated over the year, the percentage rates in the age groups 16–44 and 45–64 show no difference between the two classes There is a slight variation between them from month to month, but in none of the three age groups is there a very striking seasonal pattern of variation



Monthly inception-rates of new and recurrent illnesses per 100 married and single women

TABLE VIII—PREVALENCE RATES (TOTAL ILLNESSES PER 100 MARRIED OR SINGLE WOMEN)

Season	Aged 16–44			Aged 45–64			Aged 65 or more			Aged 16–44	Aged 45–64	Aged 65 or more
	M	Single		M	Single		M	Single		M/S	M/S	M/S
		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted			
Jan –Mar	145	109	124	170	181	181	209	221	217	1 33	0 94	0 95
April–June	136	110	132	176	152	152	203	202	197	1 24	1 16	1 00
July–Sept	131	102	112	181	173	172	204	180	174	1 28	1 05	1 13
Oct –Dec	155	118	122	201	162	160	229	236	237	1 31	1 24	0 97
Aggregate for whole year	142	110	122	182	166	166	211	210	206	1 29	1 10	1 00

When minor and ill defined illnesses are considered, married women in the age group 16–44 show a consistently higher inception rate month by month than do single women If the figures for the year be aggregated, married women in this age group have an inception rate of 39%, compared with an adjusted rate of 37% among single women, the difference between the two percentages is significant, but not highly so (Difference = 1 98, 2S E = 1 66) The inception rates for minor illnesses in this group are 30 5% for married and 29 5% for single women, those for ill defined and symptomatic diagnoses are 8 2% and 5 7% respectively At 45–64 and over the age of 65 there are no consistent differences between the combined rates for minor and ill defined illness in the single and married

One explanation of the difference between the two classes at 16–44 may be that a greater proportion of single than married women in this age group is working, and, since for an absence from work of less than three days a doctor's certificate is not required, there may be a tendency on the part of single women to forget to report minor illnesses, where they would remember an occasion on which they had consulted a doctor They may also show a greater tendency to disregard minor and symptomatic illnesses, and to continue at work in spite of feeling ill, so as to avoid the financial loss consequent on obtaining a doctor's certificate and being away from work for a week In this connection it is well known that, among piece-workers who combine to form a team, each member will make great efforts to avoid being away because of the monetary loss to the others Further, in 1948 married women may have had a preponderance of minor complaints connected with child bearing and fatigue due to queueing, carrying heavy shopping baskets, and inability to obtain domestic help The inception rates of minor and ill defined illnesses show a fairly definite seasonal trend (see figure)

If all illnesses be considered, instead of only those starting or recurring during a certain period, it is found that in each quarter of 1948 the rates for married women in the age group 16–44 were from 1¼ to 1⅓ times greater than those for single women, and, even when the variation in age structure between the two groups is allowed for, the married still show much higher rates than do the single women (table VIII) In the age group 45–64 single women had a higher rate in the first quarter and married women in the remaining nine months, while for ages over 65 married women had higher rates than single during the six months April September Taken over the whole year, there is very little difference between the rates for single and married women at ages 65 or more

Table IX shows the days of incapacity and numbers of medical consultations for each hundred married and single women Although at 16–44 married women had higher prevalence rates than did single women, the

TABLE IX—DAYS OF INCAPACITY AND NUMBERS OF MEDICAL CONSULTATIONS PER 100 MARRIED AND SINGLE WOMEN INTERVIEWED

Month of experience	Days of incapacity during month						No of medical consultations in month					
	Aged 16–44		Aged 45–64		Aged 65 or more		Aged 16–44		Aged 45–64		Aged 65 or more	
	M	S	M	S	M	S	M	S	M	S	M	S
January	78	79	100	175	245	114	34	33	46	60	57	30
February	80	54	95	192	254	144	38	28	49	65	70	37
March	57	61	73	109	169	127	36	28	55	44	50	62
April	59	70	43	72	99	57	32	31	37	39	55	43
May	63	71	48	72	124	76	31	30	39	58	62	30
June	52	61	56	82	115	68	33	29	48	43	49	15
July	72	65	88	85	139	167	37	23	50	35	79	59
August	57	72	69	37	145	161	29	28	43	26	54	69
September	48	66	85	86	130	104	32	34	54	31	47	53
October	73	82	119	200	190	77	40	28	65	45	58	47
November	87	79	120	151	399	280	37	31	61	64	76	76
December	82	91	159	140	377	444	46	29	49	65	96	70
Aggregate for whole year	67	71	89	114	196	155	36	29	50	47	63	49

TABLE X—PREVALENCE-RATES PER 10,000 MARRIED OR SINGLE WOMEN FOR CERTAIN CAUSES

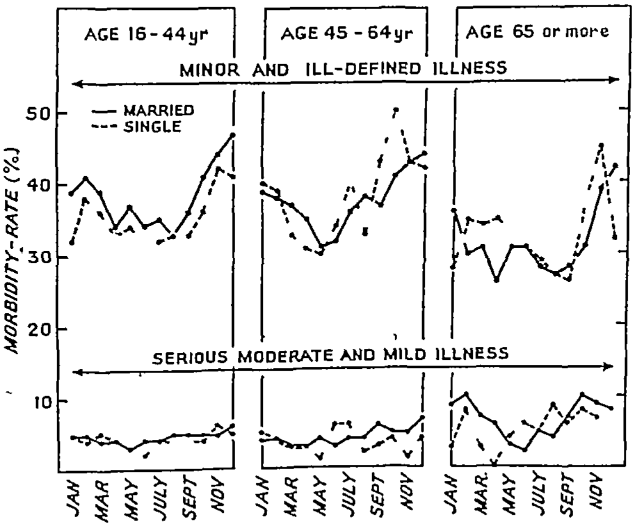
Disease group	Period	Aged 16–44		Aged 45–64		Aged 65 or more		Disease group	Aged 16–44		Aged 45–64		Aged 65 or more	
		M	S	M	S	M	S		M	S	M	S	M	S
Colds and influenza	Jan –Mar	1876	2041	1516	1644	1274	1982	Veins	316	186	515	658	562	415
	April–June	1032	1087	730	628	959	914		495	169	618	411	388	152
	July–Sept.	1047	1097	825	1167	815	986		467	145	458	412	622	282
	Oct.–Dec.	2304	2319	1938	1774	1354	1457		461	92	614	253	519	452
	Jan –Dec.	1576	1650	1258	1278	1036	1344		436	148	539	424	521	327
Respiratory diseases	Jan –Mar	1108	771	951	1397	1166	1336	Anæmias	146	178	110	192	108	—
	April–June	927	947	958	1364	1592	1371		182	191	167	43	20	102
	July–Sept.	860	792	777	664	708	1174		184	122	87	69	64	47
	Oct.–Dec	1041	872	952	991	1196	1608		185	64	129	69	—	352
	Jan.–Dec	934	846	909	1095	1171	1368		174	139	123	88	48	121
Mouth and teeth	Jan –Mar	699	600	325	219	151	138	Skin and cellular tissue	341	385	455	274	410	369
	April–June	613	602	350	368	122	51		377	661	370	346	592	609
	July–Sept.	694	693	405	458	236	—		238	472	348	320	365	423
	Oct –Dec	818	808	486	207	248	201		286	539	324	346	609	503
	Jan –Dec	708	676	393	318	188	97		309	514	372	324	494	472
Acute sore throat	Jan –Mar	129	143	15	55	43	—	Genito urinary and venereal	149	71	165	219	367	277
	April–June	116	81	66	—	20	—		121	44	127	65	122	305
	July–Sept.	83	99	43	23	64	47		104	53	116	183	236	47
	Oct –Dec.	96	163	38	115	—	101		182	57	219	69	68	—
	Jan –Dec	106	122	41	47	32	36		140	57	157	130	199	157
Ear and mastoid	Jan –Mar	138	128	250	493	367	1014	Gastro intestinal	39	50	70	82	43	—
	April–June	165	242	253	478	469	1421		47	44	117	43	41	—
	July–Sept	227	213	333	458	751	1220		32	23	96	—	64	141
	Oct –Dec.	172	128	414	415	497	1206		39	43	90	23	90	50
	Jan.–Dec	176	177	314	459	521	1211		37	40	93	35	59	48
Rheumatism all forms	Jan –Mar	1240	650	2727	2301	3801	4240	Nervous	2577	1663	3147	3781	3801	3825
	April–June	1059	800	2798	2576	3551	3553		2759	1953	3132	2836	3408	2690
	July–Sept	1124	640	2798	2975	3755	3192		2411	1561	3145	3021	3154	1972
	Oct –Dec	1375	787	3105	2995	3634	3769		2724	1567	2933	2742	3341	3467
	Jan.–Dec	1210	720	2859	2727	3684	3692		2619	1686	3088	3062	3426	2990
Eye affections	Jan.–Mar	358	236	615	932	1253	1521	Ill defined symptoms	3427	2413	3502	2712	3240	3041
	April–June	366	264	755	584	735	1218		3345	2320	4252	2771	3959	3553
	July–Sept.	454	404	873	641	901	892		3423	2262	4472	4096	4227	2911
	Oct.–Dec.	494	397	981	876	1106	1407		3459	2241	4033	2696	3747	3317
	Jan.–Dec.	420	324	809	748	994	1259		3415	2310	4068	3080	3797	3196
Heart and arteries	Jan –Mar	256	221	675	548	1253	1382	Injuries	105	128	115	27	259	230
	April–June	182	110	557	519	1306	1878		77	103	142	173	122	102
	July–Sept.	134	107	656	778	1631	1408		120	137	154	114	86	94
	Oct.–Dec	309	333	667	507	1151	1508		81	99	133	69	158	201
	Jan –Dec.	221	195	640	589	1337	1538		96	117	136	100	156	157

TABLE VII—MORBIDITY-RATES PER 100 MARRIED AND SINGLE WOMEN FOR ILLNESS STARTING OR RECURRING IN EACH MONTH, DISTINGUISHING MINOR AND ILL-DEFINED COMPLAINTS

Month	Serious, moderate, and mild									Minor and ill defined								
	Aged 16–44			Aged 45–64			Aged 65 or more			Aged 16–44			Aged 45–64			Aged 65 or more		
	M	S		M	S		M	S		M	S		M	S		M	S	
		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted
January	5	5	9	4	5	9	9	3	8	39	32	34	39	40	40	36	28	46
February	5	4	3	4	4	4	10	8	8	41	38	37	38	39	39	30	35	38
March	4	5	4	3	3	3	7	3	3	39	36	37	37	33	34	31	34	34
April	4	4	4	3	3	3	6	—	—	34	33	37	35	31	33	26	35	35
May	3	4	5	4	1	1	3	4	4	37	34	37	31	30	30	31	33	31
June	4	2	2	3	6	6	2	6	6	34	32	34	32	34	34	31	31	30
July	4	4	5	4	6	6	5	5	4	35	32	33	36	40	39	28	29	27
August	5	4	7	4	2	2	4	9	10	33	33	32	38	33	33	27	27	24
September	5	4	3	6	3	3	7	6	6	36	33	34	37	43	43	28	26	27
October	5	4	2	5	4	4	10	8	8	41	36	38	41	50	51	31	37	38
November	5	6	4	5	1	1	9	7	8	44	42	41	43	43	43	39	45	47
December	6	5	5	7	4	5	8	10	9	47	41	43	44	42	42	43	32	36
Aggregate for whole year	5	5	4	4	4	4	7	6	6	39	35	37	38	38	38	32	32	33

Table vi shows that for each month of the year, in the age group 16–44, proportionately more single than married women reported freedom from any illness or injury The excess in the percentage number of single over married women who were sickness free varied between 13 in January and 6 in May If the adjusted numbers for single women be considered, they still exceed the numbers of married women who reported no illness or injury In the age group 45–64 a higher proportion of single than married women reported freedom from sickness except in January and February At ages over 65 there was no significant difference between the two groups, but the seasonal range was greater in the case of single women, the successive quarterly proportions being 16, 17, 21, and 9%, compared with 18, 19, 16, and 15% among the married On the whole there was more freedom from sickness during April to September than during the remaining six months, at all ages and in both classes

Table vii shows the inception rates for new and recurrent illnesses reported for each month, a recurrent illness in this context being an attack which occurs not less than a week after the subsidence of a previous attack of the same malady Distinction is made in this table between (1) serious, moderate, and mild illnesses, all of which generally produce three or more days' incapacity, and (2) minor and ill defined illnesses, of which the former are diagnostic entities generally causing incapacity lasting less than three days and the latter are complaints listed in numbers 773 and 780–795 of the International Classification of Diseases, 1948 Where serious, moderate, and mild illnesses are concerned, there is little difference between the inception rates for married and single women, and if the figures be aggregated over the year, the percentage rates in the age groups 16–44 and 45–64 show no difference between the two classes There is a slight variation between them from month to month, but in none of the three age groups is there a very striking seasonal pattern of variation



Monthly inception-rates of new and recurrent illnesses per 100 married and single women

TABLE VIII—PREVALENCE RATES (TOTAL ILLNESSES PER 100 MARRIED OR SINGLE WOMEN)

Season	Aged 16–44			Aged 45–64			Aged 65 or more			Aged 16–44	Aged 45–64	Aged 65 or more
	M	Single		M	Single		M	Single		M/S	M/S	M/S
		Actual	Adjusted		Actual	Adjusted		Actual	Adjusted			
Jan –Mar	145	109	124	170	181	181	209	221	217	1 33	0 94	0 95
April–June	136	110	132	176	152	152	203	202	197	1 24	1 16	1 00
July–Sept	131	102	112	181	173	172	204	180	174	1 28	1 05	1 13
Oct –Dec	155	118	122	201	162	160	229	236	237	1 31	1 24	0 97
Aggregate for whole year	142	110	122	182	166	166	211	210	206	1 29	1 10	1 00

When minor and ill defined illnesses are considered, married women in the age group 16–44 show a consistently higher inception rate month by month than do single women If the figures for the year be aggregated, married women in this age group have an inception rate of 39%, compared with an adjusted rate of 37% among single women, the difference between the two percentages is significant, but not highly so (Difference = 1 98, 2S E = 1 66) The inception rates for minor illnesses in this group are 30 5% for married and 29 5% for single women, those for ill defined and symptomatic diagnoses are 8 2% and 5 7% respectively At 45–64 and over the age of 65 there are no consistent differences between the combined rates for minor and ill defined illness in the single and married

One explanation of the difference between the two classes at 16–44 may be that a greater proportion of single than married women in this age group is working, and, since for an absence from work of less than three veins, with the Bateman needle, is the best all round route for really severe cases. An additional reason is that these cases may need chemotherapy,[1] in addition to plasma[2] and amino-acids, by the intravenous route, often maintained for a week or longer; scalp veins are unsuitable for this purpose.

Sound technique should ensure an almost invisible scar as was found to be the rule in our patients, whose subsequent physical and mental development, to our surprise, was higher than the average. By fixing a sterile cotton-wool filter to the air inlet, sepsis is effectively eliminated; alternatively, merthiolate (1 : 20,000) can be added to the drip fluid. It is a salutary lesson to examine bacteriologically the last few ml. of each infusion solution, especially when plasma is added. When chemotherapy is given during the period of intravenous administration these measures may be dispensed with; but they represent the better practice, as the commonly found organisms—coliforms, staphylococci, &c.—may be drug resistant.

London, N.W.3 WILLIAM GUNN.

THE MEDRESCO HEARING-AID

SIR,—Several conclusions not mentioned by Mr. Gray and Miss Cartwright can be reached from their article of May 26. One is that the number of hours' use per day of the 'Medresco' aid is well below the original estimate. Another is that the first aim of design—namely, to make speech understood—has only been partially achieved. Doubtless there is a direct connection between these two facts.

According to table II of the report 55·3% of the patients interviewed used their aids for less than four hours per day during the previous week. Only about 60% of the patients who went shopping or out of doors used the aid on these occasions. The actual position is probably even worse, for most patients would be on the defensive when being questioned and would be likely to exaggerate the daily use. Making allowances for these factors the figures compare reasonably well with the estimates from other sources that two thirds of the medresco aids issued receive little use after the first few weeks.

The article mentions that patients complain greatly of the size and weight of the batteries and that only 65% are able to repeat all the words from a list reproduced at 3 ft. from the instrument. Surely this is a simple test, and the poor results achieved must mean that little benefit is derived from the aid in group conversation, in meetings, and at the theatre.

Gray and Cartwright state that half the patients are from households where the weekly income of the head is £5 per week or less. It is these patients who in general, need the greatest help; they are usually on the receiving end of speech, nor are they able to ask their superiors to repeat what has been said. Their instruments must be convenient and inconspicuous if they are not to be handicapped by their deafness. They cannot possibly derive sufficient benefit from an aid that weighs nearly 2 lb. in its lighter form, has a low degree of speech intelligibility, and is handed out at the rate of 2000 per week. Would it not be better to confine the scheme to patients in real need and to give them the best available hearing aid and careful guidance in rehabilitation?

Good commercial hearing aids can offer many advantages that are not available in the medresco. Most hearing aid manufacturers make a range of instruments and earphones giving several variations of tone. Maximum power output can be varied with the type of instrument and through provision of automatic volume compression. These aids weigh about 5 oz. and are robust and convenient in use. Great attention is paid to individual fitting. Patients are seen after one week and frequently during the first few months to check the fitting and to receive *further guidance*. Service is usually on a while-you-wait basis and postal service, and batteries are supplied in 24 hours.

The cost of use of a good commercial hearing aid is easily calculated. The figures below are based on a daily average use of 4·9 hours, as for the medresco. They ignore part exchange allowance on the old aid and interest on capital employed.

	Per week *s.*	 *d.*
Battery use at ½*d.* per hour	2	2
Service on a subscription basis at £2 10*s.* per annum	1	0
Two earphone cord replacements at 6*s.* 6*d.* each	0	3
Cost of aid at £25 every five years	2	0
Total cost of aid and maintenance	5	5

These figures suggest that there is little justification for continuing so extravagant a scheme as the wholesale manufacture and distribution of the medresco aid, bearing in mind how little it contributes to complete hearing rehabilitation. The aid is so bulky and heavy that it is inconvenient in use and is left at home, while the degree of speech intelligibility is comparatively low and does not justify the bother of carrying it about. There is little attempt at education in the use of the aid; indeed this would be impossible with a distribution of 2000 per week.

Would it not be better at this juncture to devise a Government scheme to give the greatest benefit where it is most needed, and to withdraw it entirely from those who make so little use of it or who can afford to pay for a commercial aid? Surely 5*s.* 5*d.* per week is within the reach of most people, many of whom could increase their earnings through the use of a good instrument. How much better it would be for the deaf if the hearing aid industry and the Ministry of Health could coöperate in fitting and service, leaving the Medical Research Council and the Post Office to provide a background of fundamental research.

Amplivox Ltd.,
London, W.1. A. EDWIN STEVENS
Governing Director.

SICKLE-CELL ANÆMIA IN GREECE

SIR,—Professor Choremis and his colleagues, in their article of May 26, bring evidence for the existence of the sickle cell trait amongst the inhabitants of Petromagoula. The fact that the individuals showing sicklæmia were also anæmic does not, however, justify a diagnosis of sickle cell anæmia—i.e., of an anæmia caused by sickle cell hæmolysis. Anæmia, a high serum bilirubin, and an enlarged spleen are findings not unexpected near "a swamp which was dried out by an English company a few years ago," a location which "comprised one of the most malaria stricken areas of Greece." Jaundice, abdominal pain ("crises"), joint pain, pyrexia, and an enlarged spleen—all are common to both malarial and sickle cell anæmia. If the parasites are not discovered the only means of differentiation is the response to antimalarial treatment.

Ultimate positive proof for the existence of a sickle cell anæmia involves an exchange transfusion demonstrating the abnormally short lifespan of the patient's red cells. This is, of course, impracticable in the field. In the few cases of sickle cell anæmia which I was able to find in Uganda—where the rarity of the disease contrasts strangely with the high incidence of the trait—it was noteworthy that the red cells showed an increased resistance to hypotonic salt solutions (only partial hæmolysis in 0·28% sodium chloride[1]). This lowered red cell fragility differentiated sickle cell anæmia from malarial and other hæmolytic anæmias where the fragility is usually raised.

Department of Pathology,
St. Bartholomew's Hospital, London, E.C.1. H. LEHMANN.

---

[1] Burns, E., Gunn, W. *Brit. med. J.* 1944, ii, 178.
[2] Alexander, M. B., Elser, Y. *Ibid*, p. 425.

[1] Lehmann, H., Milne, A. H. *E. Afr. med. J.* 1949, 26, 247.

Letters to the Editor

PNEUMOCONIOSIS IN COALMINERS

SIR,—We welcome your leading article last week, which gives a timely reminder to the world of medicine of the importance of this disease and of some of the proposals that are being made for its control

You appear, however, to contrast those who wish to prevent pneumoconiosis by dust suppression with those who wish to see periodic examinations used for its control, and you imply that we fall only into the latter group This implication is mistaken , there is no antithesis between the two methods of approach The final proof of the adequacy of dust suppression must be biological, and, we think, a system of periodic examinations is the best way of achieving it Without such examinations the excellent work now being done to suppress dust must lack the test of its efficiency which the engineers seek[1] Without medical evidence it will be impossible to establish safe levels of dustiness in the pits

Your article suggests to us that there are still some misunderstandings about the nature of coalworkers' pneumoconiosis We maintain that radiological signs of coalworkers' pneumoconiosis appear before the condition can in any way be described as a disease, and that even advanced *simple* pneumoconiosis is seldom a cause of serious disability Therefore, if men were advised to work in less dusty conditions before they have developed sufficient simple pneumoconiosis to become liable to massive fibrosis (not *after* they have developed this degree of simple pneumoconiosis, as you state), then they should be saved from the most serious disabling effects of the disease Massive fibrosis may advance independently of further dust exposure and does cause severe disability These facts enable radiological examination to be used for evaluating the adequacy of dust suppression, and at the same time to control a scheme of prophylactic medicine by warning miners of the necessity to reduce their dust exposure when they have reached a certain stage of simple pneumoconiosis It should be stressed that these facts contrast with the evidence available about silicosis A workman may leave a silicotic risk with a normal radiograph and develop severe silicosis later,[2] thus rendering prophylactic medicine by the use of radiology far less effective

In spite of what Meiklejohn says, we believe that our scheme is perfectly practicable It is confined to radiological examination because we know of no evidence to suggest that clinical examinations can assist in determining the prognosis in simple pneumoconiosis, whereas we have good evidence about the prognostic value of radiology We have considerable experience suggesting that the statement about "mass psychosomatic disorder" is a gross exaggeration All medical examinations run a small risk of producing some neuroses, but if periodic radiological examinations are well administered the risks will be negligible Indeed, there is evidence from other industries that they improve morale and aid recruitment A pilot scheme of examining miners at 20 representative pits which we have proposed would show how the men would react to examinations and whether an extension to the whole industry would really be as difficult as Meiklejohn's timid estimates suggest

You ask what test could be applied to doctors to prove their ability to diagnose early simple pneumoconiosis in radiographs in the absence of pathological confirmation A simple and valid test would be to see whether the doctors could distinguish the radiographs of men who had had dust exposure from those of men who had not A doctor who diagnoses pneumoconiosis from the film of a man without any history of exposure to dust and fails to diagnose it where his more experienced colleagues can do so confidently and correctly, should surely be regarded as insufficiently expert to undertake this work This type of study should gradually convince the doubting "chest physicians," whom you quote, that there are radiographic signs truly characteristic of dust exposure

While we agree with you that the Pneumoconiosis Medical Panels have the confidence of the men, the evidence which you quote for this confidence, given by Mr Harold Neal in the House of Commons, might equally be taken as evidence of economic pressure in South Wales[3] We agree that a widening of the work of the Pneumoconiosis Panels would be a possible way of providing periodic examinations, but we would rather see preventive medicine separated from compensation

You quote Meiklejohn's suggestion that the employers should provide certificates of fitness for the working places You do not say on what basis this certificate is to be granted On the basis of an arbitrary level of dustiness without any medical justification ? Surely it should be based on the demonstration by periodic examinations that the men working in these places are not developing any evidence of pulmonary abnormality

Space does not allow for detailed comment on some other points for instance, the accuracy of early radiological diagnosis of silicosis has never been determined and there is reason to believe that it would be similar to that of pneumoconiosis , again, the value of pre-employment radiographs is very limited unless followed by periodic examinations later

At present, the National Coal Board are spending large sums of money on dust suppression Your fear that emphasis on periodic medical examination will lead to such effort being "ignored" is surely rather absurd, and we claim that such examinations would lead to a more efficient direction of the engineering work

Your article suggests that to prevent pneumoconiosis the engineers should get on with the job of dust suppression unassisted by medical study We consider it unfortunate that you should advocate a policy contrary to the established practice—the full cooperation of doctor and engineer We want to see them working hand in hand to ensure the eradication of this serious disease from British coalmines

Medical Research Council
Pneumoconiosis Research Unit
Llandough Hospital
Penarth Glam

A L COCHRANE
C M FLETCHER
J C GILSON
P HUGH JONES

INTRAVENOUS FLUID THERAPY IN *CHILDREN*

SIR,—It would be unfortunate if Dr Mann's statement last week that cutting down is a "bad procedure" were accepted at its face value Experience has shown that in really malignant infantile gastro enteritis cases it is the best life saving measure , these are not comparable to the prevalent mild types responding to a single drip, many of which would recover equally well without parenteral fluid

The use of warmth, oxygen (in a tent), and oral Hartmann's solution (without glucose) can convert an ill, even a dehydrated and shocked, patient into a recovering one in a matter of hours continuance of vomiting and profuse diarrhœa after admission, however, are indications for intravenous fluid therapy I have used the subcutaneous and intramuscular routes (with and without hyaluronidase), the peritoneal cavity, the longitudinal sinus, and scalp veins in turn and at the same periods, and have come to the conclusion that the limb veins, with the Bateman needle, is the best all round route for really severe cases An additional reason is that these cases may need chemotherapy,[1] in addition to plasma [2] and amino acids, by the intravenous route, often maintained for a week or longer, scalp veins are unsuitable for this purpose

---

[1] Hudson A Warner C C Proceedings of the South Western Society of Mining Engineers March 17 1951 (in the press)

[2] McQuitty M Cuddihy B MacIntish C A Adams G T *Canad med Ass J* 1950 63 69

[3] Hugh Jones P Fletcher C M Med Res Coun Lond memorandum no 25 1951 H M Stationery Office

Sound technique should ensure an almost invisible scar as was found to be the rule in our patients, whose subsequent physical and mental development, to our surprise, was higher than the average By fixing a sterile cotton wool filter to the air inlet, sepsis is effectively eliminated, alternatively, merthiolate (1 20,000) can be added to the drip fluid It is a salutary lesson to examine bacteriologically the last few ml of each infusion solution, especially when plasma is added When chemotherapy is given during the period of intravenous administration these measures may be dispensed with, but they represent the better practice, as the commonly found organisms—coliforms, staphylococci, &c—may be drug resistant

London N W 3 WILLIAM GUNN

THE MEDRESCO HEARING-AID

SIR,—Several conclusions not mentioned by Mr Gray and Miss Cartwright can be reached from their article of May 26 One is that the number of hours' use per day of the 'Medresco' aid is well below the original estimate Another is that the first aim of design—namely, to make speech understood—has only been partially achieved Doubtless there is a direct connection between these two facts

According to table II of the report 55 3% of the patients interviewed used their aids for less than four hours per day during the previous week Only about 60% of the patients who went shopping or out of doors used the aid on these occasions The actual position is probably even worse, for most patients would be on the defensive when being questioned and would be likely to exaggerate the daily use Making allowances for these factors the figures compare reasonably well with the estimates from other sources that two thirds of the medresco aids issued receive little use after the first few weeks

The article mentions that patients complain greatly of the size and weight of the batteries and that only 65% are able to repeat all the words from a list reproduced at 3 ft from the instrument Surely this is a simple test, and the poor results achieved must mean that little benefit is derived from the aid in group conversation, in meetings, and at the theatre

Gray and Cartwright state that half the patients are from households where the weekly income of the head is £5 per week or less It is these patients who, in general, need the greatest help, they are usually on the receiving end of speech, nor are they able to ask their superiors to repeat what has been said Their instruments must be convenient and inconspicuous if they are not to be handicapped by their deafness They cannot possibly derive sufficient benefit from an aid that weighs nearly 2 lb in its lighter form, has a low degree of speech intelligibility, and is handed out at the rate of 2000 per week Would it not be better to confine the scheme to patients in real need and to give them the best available hearing aid and careful guidance in rehabilitation?

Good commercial hearing aids can offer many advantages that are not available in the medresco Most hearing aid manufacturers make a range of instruments and earphones giving several variations of tone. Maximum power output can be varied with the type of instrument and through provision of automatic volume compression These aids weigh about 5 oz and are robust and convenient in use Great attention is paid to individual fitting Patients are seen after one week and frequently during the first few months to check the fitting and to receive further guidance Service is usually on a while you wait basis and postal service, and batteries are supplied in 24 hours

The cost of use of a good commercial hearing aid is easily calculated The figures below are based on a daily average use of 4 9 hours, as for the medresco They ignore part exchange allowance on the old aid and interest on capital employed

	Per week	
	s	*d*
Battery use at ½*d* per hour	2	2
Service on a subscription basis at £2 10*s* per annum	1	0
Two earphone cord replacements at 6*s* 6*d* each	0	3
Cost of aid at £25 every five years	2	0
Total cost of aid and maintenance	5	5

These figures suggest that there is little justification for continuing so extravagant a scheme as the wholesale manufacture and distribution of the medresco aid, bearing in mind how little it contributes to complete hearing rehabilitation The aid is so bulky and heavy that it is inconvenient in use and is left at home, while the degree of speech intelligibility is comparatively low and does not justify the bother of carrying it about There is little attempt at education in the use of the aid, indeed this would be impossible with a distribution of 2000 per week

Would it not be better at this juncture to devise a Government scheme to give the greatest benefit where it is most needed, and to withdraw it entirely from those who make so little use of it or who can afford to pay for a commercial aid? Surely 5*s* 5*d* per week is within the reach of most people, many of whom could increase their earnings through the use of a good instrument How much better it would be for the deaf if the hearing aid industry and the Ministry of Health could coöperate in fitting and service, leaving the Medical Research Council and the Post Office to provide a background of fundamental research

Amplivox Ltd,
London W 1

A EDWIN STEVENS
Governing Director

SICKLE-CELL ANÆMIA IN GREECE

SIR,—Professor Choremis and his colleagues, in their article of May 26, bring evidence for the existence of the sickle cell trait amongst the inhabitants of Petromagoula The fact that the individuals showing sicklæmia were also anæmic does not, however, justify a diagnosis of sickle cell anæmia—i e, of an anæmia caused by sickle cell hæmolysis Anæmia, a high serum bilirubin, and an enlarged spleen are findings not unexpected near "a swamp which was dried out by an English company a few years ago," a location which "comprised one of the most malaria stricken areas of Greece" Jaundice, abdominal pain ("crises"), joint pain, pyrexia, and an enlarged spleen—all are common to both malarial and sickle cell anæmia If the parasites are not discovered the only means of differentiation is the response to antimalarial treatment

Ultimate positive proof for the existence of a sickle cell anæmia involves an exchange transfusion demonstrating the abnormally short lifespan of the patient's red cells This is, of course, impracticable in the field In the few cases of sickle cell anæmia which I was able to find in Uganda—where the rarity of the disease contrasts strangely with the high incidence of the trait—it was noteworthy that the red cells showed an increased resistance to hypotonic salt solutions (only partial hæmolysis in 0 28% sodium chloride [1]) This lowered red cell fragility differentiated sickle cell anæmia from malarial and other hæmolytic anæmias where the fragility is usually raised

Department of Pathology
St. Bartholomew's Hospital London E C 1

H LEHMANN

---

[1] Burns E Gunn W *Brit med. J* 1944 ii 178

[2] Alexander M B Elser Y *Ibid* p 425

[1] Lehmann H Milne A H *E Afr med. J* 1949 26 247

Letters to the Editor

PNEUMOCONIOSIS IN COALMINERS

SIR,—We welcome your leading article last week, which gives a timely reminder to the world of medicine of the importance of this disease and of some of the *proposals that are being made for its control*

You appear, however, to contrast those who wish to prevent pneumoconiosis by dust suppression with those who wish to see periodic examinations used for its control, and you imply that we fall only into the latter group This implication is mistaken , there is no antithesis between the two methods of approach The final proof of the adequacy of dust suppression must be biological, and, we think, a system of periodic examinations is the best way of achieving it Without such examinations the excellent work now being done to suppress dust must lack the test of its efficiency which the engineers seek [1] Without medical evidence it will be impossible to establish safe levels of dustiness in the pits

Your article suggests to us that there are still some misunderstandings about the nature of coalworkers' pneumoconiosis We maintain that radiological signs of coalworkers' pneumoconiosis appear before the condition can in any way be described as a disease, and that even advanced *simple* pneumoconiosis is seldom a cause of serious disability Therefore, if men were advised to work in less dusty conditions before they have developed sufficient simple pneumoconiosis to become liable to massive fibrosis (not *after* they have developed this degree of simple pneumoconiosis, as you state), then they should be saved from the most serious disabling effects of the disease Massive fibrosis may advance independently of further dust exposure and does cause severe disability These facts enable radiological examination to be used for evaluating the adequacy of dust suppression, and at the same time to control a scheme of prophylactic medicine by warning miners of the necessity to reduce their dust exposure when they have reached a certain stage of simple pneumoconiosis It should be stressed that these facts contrast with the evidence available about silicosis A workman may leave a silicotic risk with a normal radiograph and develop severe silicosis later,[2] thus rendering prophylactic medicine by the use of radiology far less effective

In spite of what Meiklejohn says, we believe that our scheme is perfectly practicable It is confined to radiological examination because we know of no evidence to suggest that clinical examinations can assist in determining the prognosis in simple pneumoconiosis, whereas we have good evidence about the prognostic value of radiology We have considerable experience suggesting that the statement about "mass psychosomatic disorder" is a gross exaggeration All medical examinations run a small risk of producing some neuroses, but if periodic radiological examinations are well administered the risks will be negligible Indeed, there is evidence from other industries that they improve morale and aid recruitment A pilot scheme of examining miners at 20 representative pits which we have proposed would show how the men would react to examinations and whether an extension to the whole industry would really be as difficult as Meiklejohn's timid estimates suggest

You ask what test could be applied to doctors to prove their ability to diagnose early simple pneumoconiosis in radiographs in the absence of pathological confirmation A simple and valid test would be to see whether the doctors could distinguish the radiographs of men who had had dust exposure from those of men who had not A doctor who diagnoses pneumoconiosis from the film of a man without any history of exposure to dust and fails to diagnose it where his more experienced colleagues can do so confidently and correctly, should surely be regarded as insufficiently expert to undertake this work This type of study should gradually convince the doubting "chest physicians," whom you quote, that there are radiographic signs truly characteristic of dust exposure

While we agree with you that the Pneumoconiosis Medical Panels have the confidence of the men, the evidence which you quote for this confidence, given by Mr Harold Neal in the House of Commons, might equally be taken as evidence of economic pressure in South Wales [3] We agree that a widening of the work of the Pneumoconiosis Panels would be a possible way of providing periodic examinations, but we would rather see preventive medicine separated from compensation

You quote Meiklejohn's suggestion that the employers should provide certificates of fitness for the working places You do not say on what basis this certificate is to be granted On the basis of an arbitrary level of dustiness without any medical justification ? Surely it should be based on the demonstration by periodic examinations that the men working in these places are not developing any evidence of pulmonary abnormality

Space does not allow for detailed comment on some other points for instance, the accuracy of early radiological diagnosis of silicosis has never been determined and there is reason to believe that it would be similar to that of pneumoconiosis , again, the value of pre-employment radiographs is very limited unless followed by periodic examinations later

At present, the National Coal Board are spending large sums of money on dust suppression Your fear that emphasis on periodic medical examination will lead to such effort being "ignored" is surely rather absurd, and we claim that such examinations would lead to a more efficient direction of the engineering work

Your article suggests that to prevent pneumoconiosis *the engineers should get on with the job of dust suppression unassisted by medical study* We consider it unfortunate that you should advocate a policy contrary to the established practice—the full cooperation of doctor and engineer We want to see them working hand in hand to ensure the eradication of this serious disease from British coalmines

Medical Research Council
Pneumoconiosis Research Unit
Llandough Hospital
Penarth Glam

A L COCHRANE
C M FLETCHER
J C GILSON
P HUGH JONES

INTRAVENOUS FLUID THERAPY IN CHILDREN

SIR,—It would be unfortunate if Dr Mann's statement last week that cutting down is a "bad procedure" were accepted at its face value Experience has shown that in really malignant infantile gastro-enteritis cases it is the best life saving measure , these are not comparable to the prevalent mild types responding to a single drip, many of which would recover equally well without parenteral fluid

The use of warmth, oxygen (in a tent), and oral Hartmann's solution (without glucose) can convert an ill, even a dehydrated and shocked, patient into a recovering one in a matter of hours , continuance of vomiting and profuse diarrhœa after admission, however, are indications for intravenous fluid therapy I have used the subcutaneous and intramuscular routes (with and without hyaluronidase), the peritoneal cavity, the longitudinal sinus and scalp veins in turn and at the same periods, and have come to the conclusion that the limb around the stellate ganglion (this naturally was associated with a Horner's syndrome), and I stated that equally gross dilatation of the same vessels occurred after injection around the 2nd and 3rd dorsal ganglia by the posterior route which did not result in a Horner's syndrome, therefore D1 must have been unaffected by the anæsthetic This proved conclusively that the nerve roots to D1 do not carry the majority—if indeed any at all—of the preganglionic vasomotor fibres for the vessels of the head and neck, for there was dilatation of the vessels of the conjunctiva, but there was no constriction of the pupil nor any narrowing of the palpebral fissure

---

[1] Hudson A Warner C C Proceedings of the South Western Society of Mining Engineers March 17 1951 (in the press)

[2] McQuitty M Cuddihy B MacIntish C A Adams G T *Canad med Ass J* 1950 63 69

[3] Hugh Jones P Fletcher C M Med Res Coun Lond memorandum no 25 1951 H M Stationery Office

You further state that I did not give my criteria for diagnosis or assessment of results I had dealt with the criteria for diagnosis in earlier papers,[1] and time did not permit of their repetition I did, however, give a method of exact selection by previous procaine block, and a detailed assessment of the results in 110 cases of Meniere's disease, tinnitus, and nerve deafness All my cases had been subjected to medical treatment without any material benefit, therefore I feel that sympathectomy (which by the way is neither ' complicated" nor " hazardous ") is fully justified by the results

London W 1 E R GARNETT PASSE

Parliament

Hospital Finances

IN the House of Lords on May 30 the Marquess of READING asked the Government whether they would appoint such a committee as they might think appropriate to inquire into, and report on, the operation of the system under which the finances of hospitals coming within the scope of the National Health Service Act, 1946, were at present administered, and moved for papers

He said it was not part of his argument to suggest that there should be any reduction of the services rendered by hospitals to the public, nor to suggest that the public making use of the services should be invited or compelled to make any greater financial contribution than at present He was asking for no more than that the Government should institute an inquiry into the operation of the present system, with the inference that if, as a result of that inquiry, it was found to be unsuitable, and a more suitable system could be found, the recommendation would be in favour of such a system as the committee proposed It was at least possible that, by revision of the financial system, very substantial retrenchment could be effected One of the difficulties was that there were no uniform costing standards, but, said Lord Reading, he understood that an investigation on this was now being carried out Some interchange between the Ministry and those responsible for the day-today administration of hospitals might adequately inform one group of the difficulties confronting the others. The system by which the savings of a careful hospital in a group might be filched and handed to a careless hospital was objectionable in practice and principle It discouraged and frustrated those who were making a determined effort to save public money to use it in a proper priority of needs Lord Reading thought that the weakness of the present system was that it was centralised, rigid, and wasteful He hoped that the Government would not procrastinate, but that they would make sure that the committee of inquiry was composed of people well qualified to carry out an onerous but essentially worth while task, thereby opening up the possibility of effecting a real saving of what was at present a most costly branch of the public service

Lord AMULREE said he felt that it was very proper and sensible to impose some kind of ceiling to expenditure on the National Health Service Care must however, be taken to see that the economies were real and genuine, it would be quite easy to make a number of false economies Money could be saved by shutting down hospital wards or by cutting staffs, but that would produce only a secondary service instead of a first-rate one The country as a whole would not be party to such a policy It would be much better that this matter should be inquired into by an independent committee rather than by a department of the Ministry or the Treasury, because they were busy with other matters and had not the time to consider any of these questions with the quietness and calmness which they required The problem was not at all simple, because it was very difficult to find any convenient yardstick which would cover all the various types of hospital in the country Quite obviously, a teaching hospital in London would require more money proportionately to its patients than would some small cottage hospital in the country He was pleased to see that the Ministry had requested the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund for London to make an inquiry into hospital costing But he rather doubted whether that inquiry would provide the final answer to the question, because he did not think it would take into consideration the differences in the running of the different types of hospital

It should be possible to arrive at the cost of inpatient treatment and outpatient treatment in the various types of hospital, and to pay each hospital a capitation fee Such a system would ensure that hospitals would try to achieve a reasonably quick turnover of beds, thus reducing the waiting-lists Block grants were a good way of financing hospitals because they were subject to a five-year revision. The system by which certain consultants on the staffs of hospitals were paid merit awards could affect the running of the hospital If some doctor was granted a merit award that sum became an additional burden on the maintenance charges for the period that he remained with the hospital The money required to make up that sum was taken from the hospital. It was very largely a paper transaction from the Treasury point of view, but from the hospital point of view it might be a serious cut

Lord SHEPHERD, for the Government, said that, except for one or two modifications, the system of estimating the costs of the hospital services was the same today as it had been from the start of the scheme There were few instances in the country, public or otherwise, where better arrangements were in force for governing finances If estimating was much more strictly dealt with today than it was a year ago that was not because of any change of policy on the part of the Government or the Minister, but because of a change of international circumstances which made it necessary to rearm The Minister looked upon the hospital service as a developing institution and likely to call upon Parliament for greatly increased grants in the next few years unless rearmament rendered such development out of the question Inevitably, normal developments would cost a great deal of money because of increased prices All the management committees and regional boards were equally anxious that their hospitals should be developed, and for that purpose they would require money from the Government The most effective way in which applications could be made was by enabling them to put through estimates upon the basis of whether they could make out their case to the Minister Merely to get rid of these estimates and bring in block grants would not reduce the claims of the hospital services The working of a priority system would be impossible were it merely a case of a block grant being applied for It could be properly carried out only when full estimates were placed before the authorities who had to give the decision. The unspent balances which might exist at the end of a year were not cash If a hospital authority had not exhausted its authority to spend and a balance remained, it merely lapsed This question of spending balances towards the end of a year had to be determined not by principle but according to the circumstances of the time A case had not been made out for the appointment of a committee of inquiry Hospital accounts were investigated by the Public Accounts Committee and the Estimates Committee The latter was giving special attention this year to the hospital service, and evidence would be given before it by officers of the Ministry, representatives of two regional boards, three management committees, the Royal College of Surgeons and the Royal

---

[1] Passe E R G Seymour J S *Brit med J* 1948 ii 812 Passe E R G Paper read at International Congress of Otorhinolaryngology London 1949 (in the press)

STEVENS-JOHNSON SYNDROME

SIR,—The article by Dr Ashby and Dr Lazar in your issue of May 19 prompts me to record three cases successfully treated with 'Aureomycin'

CASE 1—A married woman, aged 29 years, was seen on May 5, 1950 Pruritus vulvæ had been present for three days and sore throat for two days Ulceration of lips and mouth had started twenty four hours previously, and was rapidly worsening The previous day she had been given penicillin 300,000 units

When seen, the patient had a temperature of 99°F, and severe ulceration of lips, buccal mucosa, tongue, and pharynx, with a membrane on the surface of the ulcers The mouth could hardly be opened, and she had severe dysphagia The palms and soles were of a blotchy red colour and were itching, and she had two erythematous patches on the dorsum of the feet She complained of pruritus in the rectum and vagina, but as her period was on, these areas were not examined The cervical lymph glands were markedly enlarged and tender, but no other lymph glands were enlarged and the spleen was not palpable The lungs were clear The heart rate was 110 per min, and a loud pericardial rub was present The eyes were normal

Stevens Johnson syndrome was diagnosed and aureomycin started immediately—0 5 g followed by 0 25 g six hourly through the night The following morning she was transferred to a R A F hospital where aureomycin therapy was continued Improvement was rapid and dramatic Within forty eight hours of starting treatment she was non toxic, and sloughs were separating in the mouth, and five days after admission she had made a complete recovery Altogether 6 g of aureomycin was administered

CASE 2—A man, aged 69 years, seen on Sept 23, 1950, had for the past eighteen months suffered from neurasthenia Four months previously he had noticed a "lump on the left eye which spread to the right eye," and later raised red areas on the hands and sores on the lips This condition cleared in three weeks without treatment On Sept 3 he had developed severe conjunctivitis, and the rash reappeared on the hands, Two weeks later the lips became ulcerated, and he had pruritus in the rectum

When seen as an outpatient he had numerous ulcers on pharynx, buccal mucosa, tongue, and lips a yellow slough covered the buccal ulcers, and the lips bled readily On the dorsum of the hands and wrists were several dusky red indurated areas, some with tiny yellow vesicles There was no glandular enlargement, and no detectable abnormality of heart, lungs, abdomen, or central nervous system There was marked blepharitis and conjunctivitis He was admitted to hospital, where he was found to have a temperature of 99–100°F, heart rate 100 per min., blood pressure 160/95 mm Hg, and total leucocytes 7200 per c mm

He was given aureomycin 0 25 g six hourly, and in forty eight hours the lesions in the mouth were regressing and eyes improving rapidly At the end of a week all lesions had cleared except the skin lesions on hands Aureomycin was continued for three weeks, to try and prevent exacerbation, altogether 21 g was administered When he was discharged on Oct 18, all lesions had cleared He was seen as an out patient on March 3, 1951, with recurrence of ulcers in the mouth These were still present a fortnight later, but cleared without treatment in a further week

CASE 3—A married women, aged 60, had had sore bleeding lips since an attack of quinzy three years before, this had been treated by sulphathiazole and penicillin and later an autogenous vaccine (*Staphylococcus aureus*) One month before admission a rash had appeared on the body which had spread rapidly

When seen on Oct 8, 1949, she had ulcerated, bleeding lips and large, red, raw weeping areas over the greater part of the anterior aspect of both legs and thighs, the forearms, the lower abdominal wall, and about one third of the back Near the edges of the raw areas were numerous, almost confluent, vesicles up to 1 cm in diameter on a dusky red base, many of these were breaking down There were no abnormal signs in the heart, lungs, or central nervous system She was severely toxic and was admitted immediately Her leucocyte count was 18,800 per c mm with 8% eosinophils Temperature 97 6°F

She was given aureomycin 0 25 g six hourly Within twenty four hours the vesicles were drying, and her general condition had dramatically improved The raw areas began to become epithelialised within three days Treatment with aureomycin was continued until Nov 17, when further supplies of the drug were unobtainable Yellow capsules containing sodium bicarbonate were substituted, and within two days fresh vesicles appeared and her general condition deteriorated When aureomycin was started again on Dec 1, her condition again improved rapidly, and she was discharged on Feb 22 1950, with all lesions healed except for small fissures on the lips Altogether 113 g of aureomycin had been administered Since discharge she has been seen regularly as an outpatient The ulceration of the lips remains unchanged Occasionally a red indurated area has appeared on the legs or arms, but these have cleared with Lassar's paste Her general condition remains excellent

Case 1 was the most acute, and responded most rapidly, and the presence of pericarditis is noteworthy Case 3 was not so obviously benefited; but the patient's rapid relapse when the drug was discontinued, although a visually identical placebo was being given, and her improvement on re starting the drug, makes its value seem highly probable

Deductions from such a small number of cases must be tentative, but aureomycin should be tried in all cases of this most distressing disease

Wing Commander H E Bellringer kindly provided me with notes about case 1 in the R A F hospital

London W 1

IDRIS JONES

THE BODY'S IRON

SIR,—Your leading article of April 14 gives a fine review of much of the recent work There is, however, one error to which I should like to call attention You quote me as saying "he puts the figures at 1 mg Fe daily for men, and at 15 mg daily for women of menstrual age" My remarks on this point actually were as follows

> "The daily loss of iron in fæces, sweat, etc, for normal adult men and women is probably between 0 5 and 1 mg To this figure, in adult women prior to the menopause, must be added an average of 1 mg per day to cover menstrual blood loss The amount of iron which must be assimilated by adult women, therefore, if they are to remain in iron balance, varies from about 1 0 to 2 0 mg per day If it is assumed that 10 per cent of the iron in food is absorbed, then women require a diet which contains 10 to 20 mg of iron per day"

The figure of "15 mg daily for women of menstrual age" for excretion of iron is much too high It would be almost impossible to assimilate this much iron from any reasonable diet

Washington University
Saint Louis Mo U S A

CARL V MOORE.

SURGICAL TREATMENT OF MÉNIÈRE'S DISEASE

SIR,—In your annotation of April 7, which refers to the symposium on this subject given before the Royal Society of Medicine by Mr Seymour, Mr Tappin, and myself, it is obvious that owing to the complexity of this subject not everything that was said by us was clearly comprehended

You say that interruption of the sympathetic outflow below D1 would, according to Smithwick, not denervate the main vascular supply to the head and neck A few months ago Smithwick was definitely not of this opinion, in fact he was of the opinion that it may be necessary to remove not only D2 and D3 but also D4 and possibly D5 I was pleased to read Professor Mitchell's letter (April 21), also disputing this assertion of D1 being responsible for most of the sympathetic vascular control to the head and neck Clinically, I am able to confirm the work of Hyndman, Wolkin, and Soetz that the majority of the preganglionic vasomotor sympathetic fibres for the head and neck are found in the 2nd thoracic nerve roots

In my paper, referred to above, I gave the following experimental evidence

> Slides were shown demonstrating gross dilatation of the vessels of the membrana tympani after injection of procaine

around the stellate ganglion (this naturally was associated with a Horner's syndrome), and I stated that equally gross dilatation of the same vessels occurred after injection around the 2nd and 3rd dorsal ganglia by the posterior route which did not result in a Horner's syndrome, therefore D1 must have been unaffected by the anæsthetic. This proved conclusively that the nerve roots to D1 do not carry the majority—if indeed any at all—of the preganglionic vasomotor fibres for the vessels of the head and neck, for there was dilatation of the vessels of the conjunctiva, but there was no constriction of the pupil nor any narrowing of the palpebral fissure.

You further state that I did not give my criteria for diagnosis or assessment of results. I had dealt with the criteria for diagnosis in earlier papers,[1] and time did not permit of their repetition. I did, however, give a method of exact selection by previous procaine block, and a detailed assessment of the results in 110 cases of Menière's disease, tinnitus, and nerve deafness. All my cases had been subjected to medical treatment without any material benefit, therefore I feel that sympathectomy (which by the way is neither "complicated" nor "hazardous") is fully justified by the results.

London W 1 E R GARNETT PASSE

Parliament

Hospital Finances

IN the House of Lords on May 30 the Marquess of READING asked the Government whether they would appoint such a committee as they might think appropriate to inquire into, and report on, the operation of the system under which the finances of hospitals coming within the scope of the National Health Service Act, 1946, were at present administered, and moved for papers.

He said it was not part of his argument to suggest that there should be any reduction of the services rendered by hospitals to the public, nor to suggest that the public making use of the services should be invited or compelled to make any greater financial contribution than at present. He was asking for no more than that the Government should institute an inquiry into the operation of the present system, with the inference that if, as a result of that inquiry, it was found to be unsuitable, and a more suitable system could be found, the recommendation would be in favour of such a system as the committee proposed. It was at least possible that, by revision of the financial system, very substantial retrenchment could be effected. One of the difficulties was that there were no uniform costing standards, but, said Lord Reading, he understood that an investigation on this was now being carried out. Some interchange between the Ministry and those responsible for the day-today administration of hospitals might adequately inform one group of the difficulties confronting the others. The system by which the savings of a careful hospital in a group might be filched and handed to a careless hospital was objectionable in practice and principle. It discouraged and frustrated those who were making a determined effort to save public money to use it in a proper priority of needs. Lord Reading thought that the weakness of the present system was that it was centralised, rigid, and wasteful. He hoped that the Government would not procrastinate, but that they would make sure that the committee of inquiry was composed of people well qualified to carry out an onerous but essentially worth while task, thereby opening up the possibility of effecting a real saving of what was at present a most costly branch of the public service.

Lord AMULREE said he felt that it was very proper and sensible to impose some kind of ceiling to expenditure on the National Health Service. Care must however, be taken to see that the economies were real and genuine; it would be quite easy to make a number of false economies. Money could be saved by shutting down hospital wards or by cutting staffs, but that would produce only a secondary service instead of a first-rate one. The country as a whole would not be party to such a policy. It would be much better that this matter should be inquired into by an independent committee rather than by a department of the Ministry or the Treasury, because they were busy with other matters and had not the time to consider any of these questions with the quietness and calmness which they required. The problem was not at all simple, because it was very difficult to find any convenient yardstick which would cover all the various types of hospital in the country. Quite obviously, a teaching hospital in London would require more money proportionately to its patients than would some small cottage hospital in the country. He was pleased to see that the Ministry had requested the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund for London to make an inquiry into hospital costing. But he rather doubted whether that inquiry would provide the final answer to the question, because he did not think it would take into consideration the differences in the running of the different types of hospital.

It should be possible to arrive at the cost of inpatient treatment and outpatient treatment in the various types of hospital, and to pay each hospital a capitation fee. Such a system would ensure that hospitals would try to achieve a reasonably quick turnover of beds thus reducing the waiting-lists. Block grants were a good way of financing hospitals because they were subject to a five-year revision. The system by which certain consultants on the staffs of hospitals were paid merit awards could affect the running of the hospital. If some doctor was granted a merit award that sum became an additional burden on the maintenance charges for the period that he remained with the hospital. The money required to make up that sum was taken from the hospital. It was very largely a paper transaction from the Treasury point of view, but from the hospital point of view it might be a serious cut.

Lord SHEPHERD, for the Government, said that, except for one or two modifications, the system of estimating the costs of the hospital services was the same today as it had been from the start of the scheme. There were few instances in the country, public or otherwise, where better arrangements were in force for governing finances. If estimating was much more strictly dealt with today than it was a year ago that was not because of any change of policy on the part of the Government or the Minister, but because of a change of international circumstances which made it necessary to rearm. The Minister looked upon the hospital service as a developing institution and likely to call upon Parliament for greatly increased grants in the next few years unless rearmament rendered such development out of the question. Inevitably, normal developments would cost a great deal of money because of increased prices. All the management committees and regional boards were equally anxious that their hospitals should be developed, and for that purpose they would require money from the Government. The most effective way in which applications could be made was by enabling them to put through estimates upon the basis of whether they could make out their case to the Minister. Merely to get rid of these estimates and bring in block grants would not reduce the claims of the hospital services. The working of a priority system would be impossible were it merely a case of a block grant being applied for. It could be properly carried out only when full estimates were placed before the authorities who had to give the decision. The unspent balances which might exist at the end of a year were not cash. If a hospital authority had not exhausted its authority to spend and a balance remained, it merely lapsed. This question of spending balances towards the end of a year had to be determined not by principle but according to the circumstances of the time. A case had not been made out for the appointment of a committee of inquiry. Hospital accounts were investigated by the Public Accounts Committee and the Estimates Committee. The latter was giving special attention this year to the hospital service, and evidence would be given before it by officers of the Ministry, representatives of two regional boards, three management committees, the Royal College of Surgeons and the Royal

---

[1] Passe E R G Seymour J S *Brit med J* 1948 ii 812
Passe E R G Paper read at International Congress of Otorhinolaryngology London 1949 (in the press)

College of Physicians, King Edward's Hospital Fund, Nuffield Provincial Hospitals Trust, and the British Medical Association The Central Health Services Council, whose report in 1950 had just been published, had also dealt with hospital administration Some investigation of costing standards was being made, and departmental accounts on the basis of the circumstances of individual hospitals would be prepared this year for 108 hospitals of widely differing types, controlled by four regional boards and nine management committees The results of these inquiries should be awaited, and if there was then found to be need for further inquiry the Minister would be prepared to give consideration to the claim

Lord Webb-Johnson said that no one could enter a hospital without seeing a change in the number of officials operating it not directly dealing with patients but with administration. Yet there was less work to be done on the administrative side because the administrative staff of the voluntary hospitals had to raise the money and to assess the income of patients He often wondered whether more advantage should be taken now of voluntary service An overhaul of administration and financial control was urgently needed, because this was not merely a matter of money but a matter of service Every pound wasted on administration was taken away from the patient, just as every bit of hospital accommodation taken up by management committees was lost to the treatment of patients A serious result of the high cost of hospital beds arose from the fact that the charges in private wings were based on the general hospital costs, which were so high that people who were prepared to pay for their treatment could not afford to do so It was not only to the disadvantage of the patients but also to the disadvantage of the reputation of British medicine when those distinguished colleagues who came to visit us from abroad found that patients who were willing to pay could not get into the hospitals

Lord Dowding said that one basic defect in the organisation was the large number of hospital groups which a regional board had to administer The number was entirely beyond their capacity

Lord Haden-Guest, Lord-in-Waiting, said that it gave a wrong impression if a hospital service were considered as if it were the main feature of the National Health Service, although it was an extremely important one In the bad old days there was no hospital centralisation, and sometimes very little hospital control, the grotesque over-expenditure and bad conditions in many hospitals were well known Now that matters were getting on to a more definite and formal basis they had their own special problems, but these could be solved by common sense and the application of business principles It was less than three years since the National Health Service came into existence, and there had been built up in that time a service which had already produced very remarkable results in the health conditions of the country Whereas under the panel system there were 20,000,000 people entitled to receive medical aid without actual cash payment, under the National Health Service there were 43,000,000 Health was improving to an extent which was having at present a marked effect on the national physique and expectation of life That was worth paying for The consultants who before the National Health Service came into existence were largely concentrated in the large towns were now spread over the regions There was a good deal of room for improvement in methods of administration, and he thought that some of the costs could certainly be brought down This year there had been a reduction in the total cases of tuberculosis notified The work which the National Health Service was doing was worth every penny we were paying —and a good deal more At the moment it would be a mistake to set up a special committee

The motion for papers was by leave withdrawn

QUESTION TIME

Care of the Chronic Sick

Mr G C Touche asked the Minister of Health if he was aware that the South West Metropolitan Regional Hospital Board had refused an offer from the Jewish Blind Society to take care of a number of chronically ill Jewish blind patients at the Jewish Home for the Blind, Rokefield, Westcott, at an all in figure of £5 per person a week on the ground that the board had not the money available, and if he would make special arrangements for this offer to be accepted in view of the fact that the cost to the regional board was less than the full maintenance of these patients in other hospitals —Mr Marquand replied I regret that the board cannot at present add to its existing contracts for beds in private institutions

Commander A H P Noble asked the Minister, in view of the fact that on Dec 31, 1950, there were 1324 patients on the waiting list for chronic sick beds in National Health Service hospitals in the county of London, what arrangements he was making to provide alternative accommodation to the 60 beds no longer available in St Luke's Hospital owing to transfer of certain wards to the Chelsea Hospital for Women for pathological laboratory work, and when this alternative accommodation would be available —Mr Marquand replied Alternative arrangements are being considered but I cannot make any further statement at present

Tuberculosis Treatment in Swiss Sanatoria

Brigadier Frank Medlicott asked the Minister if, in view of the fact that 10,000 people suffering from tuberculosis were awaiting admission to hospital in Great Britain, he could arrange with the hospital authorities in Switzerland a considerable increase beyond the 130 beds so far promised for patients from the United Kingdom —Mr Marquand replied I regret that this is not practicable

Waiting for Hearing-aids

In answer to a question Mr Marquand stated that on April 30 the waiting list for hearing aids stood at 112,36[illegible].

Training for Uneducable Children

Mrs E M. Braddock asked the Minister what was the number of uneducable children who were not receiving any form of education, and what provision was being made to give them the specialised tuition they required —Mr Marquand replied On Jan 1, 1950, 13,680 mental defectives under the age of sixteen were in the care of local health authorities Of these 3600 were receiving some form of training That number has probably since increased by about 30% as the services are being progressively developed In addition, there are 6424 mental defectives under the age of sixteen in institutional care where, of course, they are receiving training

Complaint of Medical Negligence

Lord John Hope asked the Secretary of State for Scotland whether he would order an inquiry into the complaint by Miss Elizabeth Jessop of negligence against the medical authorities, particulars of which had already been sent to him —Mr H McNeil replied that the local executive council's medical services committee had decided that Miss Jessop's complaint could not be further considered under the relative regulations, and he had no power to overturn such a decision

Lord John Hope Is not the right hon gentleman aware—I am sure he is, because I told him the whole story—that this lady after a bad motor smash, had only her skull X rayed? If they had X rayed her neck she would have been spared many months of pain and ill health It was only when that had been discovered that she made this complaint, and does he not think that on prima facie grounds this case ought to be looked into?—Mr McNeil I have looked into it and I agree that the lady in question suffered greatly I am also aware that a whole range of experts on the subject missed this particular piece of diagnosis But I cannot set aside the regulations, nor do I think the hon gentleman would ask me to do so on reflection

Lord John Hope Has the right hon gentleman no power at all over these people? What happens about a case of suppression? Has he no ultimate jurisdiction to order an inquiry into it?—Mr McNeil Certain remedies are available to the patient, but the question of suppression is quite a different matter from the action I am being asked to take here, which is to overturn a decision

Radiologists in Malaya

Air Commodore A V Harvey asked the Colonial Secretary how many vacancies there were in Malaya for radiologists, and what steps he was taking to recruit them —Mr I F Cook replied that there were two which had been advertised in the medical press and brought to the attention of any doctor with radiological interests and experience who inquired about s in the Colonial Service Air Commodore HARVEY then he had heard there were seven pieces of equipment at h and not even a part-time radiologist —Mr COOK eed to look into the matter

Special Diets Advisory Committee

n answer to a question Mr MAURICE WEBB, the Minister Food, stated that on all matters concerning extra rations l supplies of controlled foods for invalids and persons on cial diets he was advised by the Food Rationing (Special ets) Advisory Committee of the Medical Research Council e members of the committee were Dr H P Himsworth, C.P (chairman), Prof L S P Davidson, F.R C.P, Sir ancis Fraser, F.R C P, Lord Horder, F.R C.P, Dr R D wrence, F R C.P, Prof R A McCance, F.R C.P, F.R S, Norman Smith, F.R C P, Sir James Spence, F.R C.P, and of M. L Rosenheim F R C.P (secretary)

Obituary

ROBERT WILLIAM BASIL HALL

K.C.B, O B E, M R C S

Surgeon Vice-Admiral Sir Basil Hall, whose death we have already announced, was medical director-general of the Royal Navy and honorary physician to the King from 1934 to 1937

Hall came of a naval family and background He was born in 1876, the son of Robert Hall, R N, and he was educated at Portsmouth Grammar School In 1900 he qualified at Guy's Hospital and lost no time in joining the medical branch of the Navy Here his reputation for ability and conscientiousness quickly grew, and in 1913, while serving in H M S *Active*, he received the thanks of the Scottish Office for his work during an outbreak of influenza at St Kilda

During the first world war he served in the cruiser *Lowestoft*, which took part in the Dogger Bank action Hall had always shown special interest in the physiological problems arising in under-water craft, and in 1917 he was appointed senior medical officer of the submarine service His experience with this branch is lucidly set out in his *Handbook for Medical Officers of the Submarine Service* which was published in 1920 The same year he became an assistant to the medical director-general of the Navy Two years later he was awarded the Gilbert Blane medal in recognition of his zeal and professional ability, and in 1924 he was appointed O B E From 1926 to 1929 he was deputy D M D G, and in 1930 he was appointed C B and given charge of the R N hospital at Plymouth, where he remained till he was appointed director general in 1934 In 1936 he was promoted K C.B

After he retired from the Navy in 1937 he acted for two years as director of medical services to the International Council for Non-Intervention in Spain During the late war he proved an able chairman of the National Service medical board at Guildford

He married Miss Gertrude Goldsmith in 1906 She died in 1948, and in 1950 he married Dorothy, widow of Rear-Admiral (S) Cyril Capner Sir Basil died at Haslemere on May 16

MORTIMER PHILIP REDDINGTON

M B N Z F R C S M R C O G

Mr Mortimer Reddington, who died in London on May 25, at the age of 51, was born in New Zealand, and he graduated M B at Otago in 1922

In 1926 he came to this country and in resident posts at the Jessop Hospital in Sheffield and at the Royal Waterloo Hospital and the Grosvenor Hospital in London, he gained varied and practical experience in gynæcology and obstetrics In 1933 he took the F R C S and three years later the M R C O G Senior appointments in his specialty quickly followed, he was appointed to the staffs of the Woolwich Memorial Hospital, Royal Hospital, Richmond, and Joyce Green Hospital, and six years ago he also became consultant gynæcological surgeon to Queen Mary's Hospital, Sidcup From 1932 to 1940 he served as a surgeon lieutenant commander in the R N V R and he was for a time a consultant gynæcologist to the Admiralty His published works included papers on hysterectomy and postpartum hæmorrhage

C E writes "Reddington could not bear fools or slow-moving people gladly, for drive and brilliant activity were the dominant forces in his make-up But 'Rastus,' as his friends called him, was beloved by those that knew him well, and respected by those who appreciate high standards in surgical procedure Apart from professional life he had many interests, in his earlier years he played rugger for Middlesex Hospital, and latterly he took an active interest in royal tennis, often playing at Lord's and Hampton Court he was also a member of the M C C and St George's Hill Golf Club Not many of his friends realised his love for poetry, he composed many poems and a play in blank verse For the past year he had fought a losing battle with ill health, but he died unexpectedly after a period of convalescence"

Mr Reddington leaves a widow and three sons, two of whom are medical students and one an officer in the Regular Army

JOHN GRAHAM MARTIN

M D Lpool

By the death of Dr Graham Martin, at the age of 76, Liverpool has lost one of its best known and most trusted practitioners, and the country a great patriot

Graham Martin qualified in 1896, and, after holding appointments as resident medical officer, commenced what was to prove to be his constant devotion to national service by volunteering as a civilian surgeon for service in the South African war Whilst there he was, for a short time, a prisoner-of-war in the hands of the Boers He received the South African medal with four clasps No doubt inspired by this experience, he joined the Volunteers immediately on his return to Liverpool and was appointed surgeon lieutenant to the 2nd V B, the King's Liverpool Regiment When the Territorial Army superseded the Volunteers this battalion was renamed the 6th Battalion the King's Liverpool Regiment—the Liverpool Rifles—a battalion of the highest standing and repute in the city On the outbreak of the first world war he went to France with the rank of major

Those who served with him at that time remember with special gratitude his work during the first German gas attack on Ypres His was the only regimental aid post actually in Ypres and was situated in the old casemates He gave assistance to soldiers and civilians alike, and undoubtedly saved many lives Whilst, doubtless, he would have wished to continue service with his regiment his abilities were recognised and he was called upon to become first acting D A.D.M.S 55th Division and then D.A D M.S 5th Division until, in February, 1917, he was appointed to command the 58th C C.S After the war, when the Territorial Army was re formed he was appointed to command the 2nd (West Lancs) Field Ambulance, but in a very few months he became A.D M S of the 55th (West Lancs) Division In this appointment he did a tremendous amount of hard work re forming the R A M C units of the division His period of tenure of the appointment was extended more than once so that he held it for a total of eight years, finally retiring in December, 1928 He had been awarded the T D, and in 1927 he was appointed K H P The esteem and affection in which he was held by his brother officers was reflected in his appointment in 1930 as honorary colonel of the R A M C units of the 55th (West Lancs) Division

The details of his voluntary military service give measurable evidence of the devotion and worth of his work in that sphere, but there is no similar means of recording all that he achieved as a family doctor He was indeed the trusted and beloved adviser of very many His gift for friendship, his keen sense of humour, and his warmth of heart endeared him to all who came in contact with him His patients and their relatives have good cause to recall with gratitude his close attention to all the details of medical care His qualities were recognised by his colleagues who elected him to the council of the Liverpool Medical Institution for two periods, to the vice presidency in 1929, and to life membership in 1946

He died on May 18, and leaves a widow and only son, Captain H N G Graham Martin A A G

Diary of the Week

JUNE 10 TO 16

Monday, 11th

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
2.30 P.M. (1, Wimpole Street, W.1.) *Festival programme* Ophthalmology

Tuesday, 12th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Prof. J. M. Yoffey: The Lymphatic System—a film (Arris and Gale lecture.)
ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10.30 A.M. *Festival programme* Plastic Surgery
WEST END HOSPITAL FOR NERVOUS DISEASES, 10, Marylebone Lane, W.1
2.30 P.M. Dr. Douglas Gordon: Radiological Techniques
WEST LONDON HOSPITAL MEDICAL SCHOOL
8.30 P.M. (11, Chandos Street, W.1.) Dr. Leonard Colebrook, F.R.S.: Outstanding Problems of Burns and Scalds (Alex Simpson Smith lecture.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5 P.M. Dr. D. I. Williams: Sex Hormones in Dermatology
INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5 P.M. Prof. Torston Sjögren (Stockholm): Hereditary Neurological Diseases Associated with Certain Eye Diseases

Wednesday, 13th

UNIVERSITY OF LONDON
5.30 P.M. (University College, Gower Street, W.C.1.) Dr. G. G. Simpson: Origin and Early Evolution of the Primates
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. R. W. Riddell: Medical Mycology—Trichophyton Infections
INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S.E.5
3 P.M. Professor Sjögren: Heredity of Pick's Disease and other Presenile Conditions

Thursday, 14th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. W. E. Lloyd: Pulmonary Tuberculosis in Young Adults (Mitchell lecture)
ROYAL COLLEGE OF SURGEONS
3 P.M. Mr. Harvey Jackson: Surgery of Orbital Tumours
5 P.M. Dr. Henry Cave, F.A.C.S.: Emergency Surgery of the Abdomen
ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
2 P.M. *Festival programme* The Central Nervous System
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, S.W.1
4.30 P.M. Sir Paul Mallinson: Psychiatry lecture demonstration
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. S. C. Gold: Systemic Lupus Erythematosus
CHADWICK LECTURE
4 P.M. (Chelsea Physic Garden, Swan Walk, S.W.3.) Prof. T. A. Bennet Clark, PH.D., F.R.S.: Capacity of Vegetation to Support Human Population
UNIVERSITY OF DURHAM
5.15 P.M. (Royal Victoria Infirmary, Newcastle upon Tyne.) Prof. Warren H. Cole (Chicago): Carcinoma of the Stomach
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. John Macaskill: Retinal Changes in Hypertension

Friday, 15th

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
4.30 P.M. *Festival programme* Anæsthetics
GUY'S HOSPITAL MEDICAL SCHOOL, S.E.1
5 P.M. Prof. E. K. Rideal, D.SC., F.R.S.: Matter in the Boundary State (Fison lecture.)
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. S. Thomson: Clinical demonstration
UNIVERSITY OF EDINBURGH
5 P.M. (Surgery Lecture Theatre, University New Buildings.) Professor Warren Cole: Electrolyte Imbalance in Surgery

Saturday, 16th

BIOCHEMICAL SOCIETY
1.45 P.M. (Department of Physiology, Medical School, Hospitals Centre, Birmingham, 15.) Short papers

---

CORRIGENDA: *Sequelæ of Radical Gastric Resections.*—In this article by Mr. Brain and Professor Stammers (May 26, p. 1137) the last two words in the caption of fig. 1 should be "after inflation."

Prevention and Treatment of Travel Sickness.—In table III of Dr. Harper's article of May 26 (p. 1141) the sixth column should be headed "treatment unsuccessful," and the last column "treatment successful."

General Medical Council.—Our account last week (p. 1223) of the council's meeting should have included the name of Sir Henry Wade as a member, for Scotland, of the Medical Disciplinary Committee. This committee (see p. 1218) has altogether 19 members, including the president; and it is *not* responsible for striking dentists off the Register.

Appointments

ARNOLD, E. L., M.A., M.B. Camb., D.O.M.S.: S.H.M.O., Manchester Royal Eye Hospital.
BICKMORE, D. M. H., L.M.S.S.A.: M.O., H.M. Prison, Gloucester.
* JACKSON, MARY, M.B. Sheff.: resident aural registrar, Hospital for Sick Children, Great Ormond Street, London.
LEES, V. T., M.B. Manc., D.O.M.S.: S.H.M.O., Manchester Royal Eye Hospital.
TAYLOR, R. B., M.R.C.S., D.P.M.: asst. psychiatrist, Whittingham Hospital, Manchester.
TRESIDDER, GERALD, F.R.C.S.: asst. surgeon, genito-urinary department, London Hospital.
WILSON, MARJORIE S., M.B. N.Z., D.I.H.: senior asst. M.O. for maternity and child welfare, City of Leicester.

University College Hospital

FLETCHER, W. D., M.B. Leeds, D.PHYS.MED.: S.H.M.O., department of physical medicine.
KININMONTH, D. A., M.B. Lpool, D.PHYS.MED.: S.H.M.O., department of physical medicine.
MCALLEN, MONICA, M.D. Lond., M.R.C.P.: S.H.M.O., chest department.
MCROBERT, SIR GEORGE, C.I.E., M.D. Aberd., F.R.C.P.: consultant physician, Hospital for Tropical Diseases.

Western Regional Hospital Board

BARR, G. M., M.B. Glasg., M.R.C.O.G.: consultant obstetrician and gynæcologist, Stobhill Hospital, Glasgow.
DONALDSON, ROSE, I. L., M.D. Edin.: asst. tuberculosis physician, County of Dumfries and Galloway.
KEIR, R. M. S., M.B. Aberd., D.A.: consultant anæsthetist, Dumfries and Galloway Royal Infirmary.
MCHARG, J. F., M.B. Edin., M.R.C.P., D.P.M.: deputy physician superintendent, Glasgow Royal Mental Hospital.
MUNRO, W. L., M.B. Glasg., B.SC., D.M.R.(D.): consultant radiologist, Ayrshire.
SCOTT, AGNES L., M.B. Glasg., M.R.C.P.E., D.P.H.: consultant pathologist, Dumfries and Galloway hospital group.

Appointed Factory Doctors

BETHUNE, A. D., M.B. Edin.: Newcastleton district, Roxburghshire.
CRAWFORD, R. P., L.R.C.P.E.: Taynuilt district, Argyllshire.
EVANS, W. B., M.D. Camb.: Milford Haven district, Pembrokeshire.
HICKS, C. A. N., M.R.C.S.: Huntingdon district, Huntingdonshire.
MACKENZIE, G. N., M.B. Glasg.: New Galloway district, Kirkcudbrightshire.
MELECK, SIMON, M.B.E., M.B. Lond.: Truro district, Cornwall.
ROBINSON, M. G., M.R.C.S.: Newent district, Gloucestershire.
ROBSON, I. J. W., M.B. Durh.: Newburn district, Northumberland.
RUDD, P. F., M.B. Birm.: Winslow district, Oxfordshire.
TIMINGS, L. J., M.R.C.S.: Witney district, Oxfordshire.

Colonial Service

BANKS, L. W., M.B. Edin.: senior M.O., Nigeria.
SHAW, F. O. J., M.R.C.S.: M.O., Kenya.
SWEETHAM, J. P., B.A., M.B. Dubl.: M.O., Nigeria.

North East Metropolitan Regional Hospital Board

BURBURY, W. M., M.A., M.B. Lond., D.P.M.: part-time consultant psychiatrist, Chelmsford child guidance clinic.
BUSH, F., M.A., M.B. Edin., D.M.R.E.: part-time consultant radiologist, St. George in the East Hospital.
ELKELES, A., M.D. Edin., D.M.R.E.: part-time consultant radiologist, Metropolitan Hospital.
HEATHFIELD, K. W. G., M.D. Lond., M.R.C.P.: part-time consultant neurologist, Bethnal Green and Mile End Hospitals.
NEVILLE, N. A., B.M. Oxfd, M.R.C.P.: full-time consultant physician in diseases of the chest, Hertford group of hospitals and Bishop's Stortford, Hertford, and Waltham Abbey chest clinics.
WARD, B. C. H., M.R.C.S., D.M.R.: part-time consultant radiologist, Queen Elizabeth Hospital for Children.

* Amended notice.

Births, Marriages, and Deaths

BIRTHS

BOWERS.—On May 31, at Folkestone, the wife of Dr. V. H. Bowers—a daughter.
CHAMBERLAIN.—On May 27, in Leeds, the wife of Mr. Digby Chamberlain, F.R.C.S.—a son.
LANGDON DOWN.—On May 29, in London, the wife of Dr. Norman Langdon Down—twin daughters, the elder of whom survived only three days.
STRINGER.—On June 1, in London, the wife of Mr. Paul Stringer, F.R.C.S.—a daughter.

MARRIAGES

GARRATT—KILN.—On May 26, at Forest Row, Sussex, Cecil Douglas Garratt, M.R.C.P., to Ann Kiln, M.B.

DEATHS

DICKSON.—On May 29, at Aspley Guise, Beds, Arthur Norman Dickson, M.C., M.B. Camb., colonel I.M.S. retd, aged 70.
HUNTER.—On May 17, at Newcastle upon Tyne, Kenneth Downie Hunter, M.B. Durh.
IRVING.—On May 28, at Totland Bay, I.O.W., William Irving, M.D. Camb., M.R.C.O.G., formerly of Christchurch, New Zealand, aged 81.
NORTON.—On May 31, at Bury St. Edmunds, Edgar Lionel Robert Norton, M.D. Lond., formerly of Winnipeg.
YOUNG.—On May 31, at Twyford, Berks, Frederic Charles Young, M.B. Camb.

THE NUCLEIC-ACID CONTENT OF THE CELL

J. N. DAVIDSON
D.Sc., M.D. Edin., F.R.F.P.S.
GARDINER PROFESSOR OF PHYSIOLOGICAL CHEMISTRY

I. LESLIE
B.Sc.
I.C.I. RESEARCH FELLOW

DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF GLASGOW

J. C. WHITE
M.B. Birm.
LECTURER IN HÆMATOLOGY, POSTGRADUATE MEDICAL SCHOOL OF LONDON

THE nucleic acids are essential constituents of living matter. Two forms of the acid are known to be present in all nucleated cells, and one or other form (in rare instances both) in viruses and bacteriophages. They are invariably found in combination with the various proteins of the cell.

In normal animal and plant cells deoxyribonucleic acid (D.N.A.) is located entirely within the nucleus, whereas ribonucleic acid (R.N.A.) is concentrated more particularly in the cytoplasm and in the nucleoli. R.N.A. is particularly abundant in the cells of growing tissues or of tissues showing high metabolic activity—e.g., in the production of protein secretions.

Some idea of the metabolic activity of the nucleic acids may be obtained by measuring their rate of renewal in the cell by techniques involving isotopes of phosphorus or of nitrogen. In a tissue such as the normal liver, in which the cells are not dividing rapidly although they are metabolically active, the turnover of D.N.A., as measured with P^{32} or N^{15}, is very low in comparison with that of R.N.A. (Davidson 1947, Furst et al. 1950). On the other hand, when such a tissue regenerates after injury, as rat liver after partial hepatectomy, the turnover of D.N.A. is very greatly increased and approaches that of R.N.A. This state of affairs is found in embryonic tissues and in such rapidly growing tissues as bone marrow and the abnormally proliferating leukæmic and malignant tissues (Hevesy 1948).

Ribonucleic Acid and Protein Synthesis

Owing largely to the work of the Caspersson (1947, 1950) school, a connection between nucleic acid metabolism and protein synthesis is widely postulated, both in the course of tissue growth by mitotic division of cells and in the elaboration of special proteins during differentiation and secretion. The exact way in which the nucleic acids take part in such processes is still unknown, but several mechanisms have been suggested (for discussion see Brachet 1947 and Davidson 1950).

Value of Quantitative Studies

The study of cellular nucleic acids and proteins is of value in both the practical and the theoretical approach to quantitative cellular pathology. In the familiar procedures for fixing and staining cells in tissue sections, smears, &c., the cellular constituents chiefly involved are the nucleic acids and proteins. The absolute amounts of these constituents per cell can be determined either by cytochemical techniques applied to the individual cell or by microchemical techniques applied to aggregates of cells. With mixed or growing tissues and cell populations the values obtained by microchemical techniques may require expression as averages, unless special methods are used. Such data may lead to an understanding of cellular activity.

Methods of Quantitative Study

The pioneer application of optical methods to the quantitative study of single cells is due to Caspersson and his colleagues, who have concentrated largely on the ultraviolet and near visible spectral regions, and have made abundant use of the fact that nucleic acids show an intense and specific absorption of ultraviolet light at 2600 Å (Caspersson 1950). The reflecting microscope (Barer 1949) has been used for a similar purpose (Barer et al. 1950). By these methods large numbers of single cells in cytochemical preparations can be analysed, and the distribution of certain constituents which possess clear cut properties of light absorption in various parts of the visible, ultraviolet, or infra red spectrum may be expressed quantitatively. A limitation is the difficulty of controlling completely all the physical characteristics of the systems under investigation (Commoner 1949, 1950, Pollister and Swift 1950).

The alternative method is to determine microchemically the amounts of nucleic acids in tissue samples in which the cells can be counted. From the number of cells it is possible to calculate the average content per cell or nucleus.

Constant Value of Cellular D.N.A.

The work of Boivin et al. (1948), Vendrely and Vendrely (1948, 1949), and Mirsky and Ris (1949) on the analysis of nuclei isolated from various vertebrate genera and species suggests a very constant value for the amount of D.N.A. per nucleus for the different tissues of any one species, though considerable variation may occur between species. Each of the haploid spermatozoa contains about half the amount of D.N.A. present in a somatic nucleus. This fact has obvious implications in genetics, and is evidence that the genes are deoxyribonucleoprotein units.

An important practical implication is that by determining the amount of D.N.A. in a sample of tissue, one can calculate the number of cells present and consequently the amount, per cell, of any other substance of which the total amount in the sample is known (Davidson and Leslie 1950a and b). It is, however, of vital importance to know the possible variations in the amount of D.N.A., per nucleus, of any given tissue in different physiological and pathological conditions.

Present Work

Our investigations have been largely concerned with human bone marrow and blood leucocytes in health and disease and with spermatozoa, because suspensions of these tissues can be made in which the cells are sufficiently evenly distributed to allow them to be counted as a basis for determination of the average amount of D.N.A. and R.N.A. per cell.

METHODS

Bone marrow.—Small samples of 0·2–0·3 ml. of mixed marrow and blood were aspirated from the sternum of healthy volunteers and from patients with various blood disorders. The sample, of known weight, was evenly suspended in heparinised 0·85% sodium chloride solution, and a small aliquot was removed for dilution and enumeration of nucleated cells in the Neubauer hæmocytometer chamber. The remainder was used for chemical micro determination of deoxyribonucleic acid phosphorus (D.N.A.P.) and of ribonucleic acid phosphorus (R.N.A.P.). As in previous work on marrow tissue (Davidson et al. 1948), the acids were separated by the Schmidt and Thannhauser (1945) method, and phosphorus determined by Davidson and Waymouth's (1943) modification of the Berenblum and Chain (1938) method.

Blood Leucocytes.—Samples were handled similarly, but often the leucocytes were separated from the erythrocytes and plasma with the aid of bovine fibrinogen (Minor and Burnett 1948).

Reticulocytes.—Blood samples rich in reticulocytes were examined from two cases of hæmolytic anæmia. All the ribonucleoprotein containing reticular material was retained in the stromal precipitate separated at pH 5·6

Diary of the Week

JUNE 10 TO 16

Monday, 11th

Royal Society of Medicine and British Medical Association
2 30 P M (1 Wimpole Street, W 1) *Festival programme* Ophthalmology

Tuesday, 12th

Royal College of Surgeons Lincoln's Inn Fields, W C 2
5 P M Prof J M Yoffey The Lymphatic System—a film (Arris and Gale lecture)

Royal Society of Medicine and British Medical Association
10 30 A M *Festival programme* Plastic Surgery

West End Hospital for Nervous Diseases, 40, Marylebone Lane W 1
2 30 P M Dr Douglas Gordon Radiological Techniques

West London Hospital Medical School
8 30 P M (11 Chandos Street, W 1) Dr Leonard Colebrook F R.S Outstanding Problems of Burns and Scalds (Alex Simpson Smith lecture)

Institute of Dermatology, St John's Hospital Lisle Street W C 2
5 P M Dr D I Williams Sex Hormones in Dermatology

Institute of Neurology, National Hospital, Queen Square, W C 1
5 P M Prof Torsten Sjögren (Stockholm) Hereditary Neurological Diseases Associated with Certain Eye Diseases

Wednesday, 13th

University of London
5 30 P.M (University College Gower Street W C 1) Dr G G Simpson Origin and Early Evolution of the Primates

Institute of Dermatology
5 P M Dr R W Riddell Medical Mycology—Trichophyton Infections

Institute of Psychiatry, Maudsley Hospital Denmark Hill, S E 5
3 P M Professor Sjögren Heredity of Pick's Disease and other Presenile Conditions

Thursday, 14th

Royal College of Physicians, Pall Mall East, S W 1
5 P M. Dr W E Lloyd Pulmonary Tuberculosis in Young Adults (Mitchell lecture)

Royal College of Surgeons
3 P M Mr Harvey Jackson Surgery of Orbital Tumours
5 P M Dr Henry Cave, F A C.S Emergency Surgery of the Abdomen

Royal Society of Medicine and British Medical Association
2 P M *Festival programme* The Central Nervous System

St George's Hospital Medical School, Hyde Park Corner, S W 1
4 30 P M. Sir Paul Mallinson Psychiatry lecture demonstration

Institute of Dermatology
5 P M Dr S C Gold Systemic Lupus Erythematosus

Chadwick Lecture
4 P.M. (Chelsea Physic Garden, Swan Walk S W 3) Prof T A Bennet Clark PH D F R S Capacity of Vegetation to Support Human Population

University of Durham
5 15 P.M (Royal Victoria Infirmary Newcastle upon Tyne) Prof. Warren H Cole (Chicago) Carcinoma of the Stomach

Honyman Gillespie Lecture
5 P.M (University New Buildings Teviot Place, Edinburgh Dr John Macaskill Retinal Changes in Hypertension

Friday, 15th

Royal Society of Medicine and British Medical Association
4 30 P M *Festival programme* Anæsthetics

Guy's Hospital Medical School, S E 1
5 P M Prof E K Rideal D.SC, F R.S Matter in the Boundary State (Fison lecture)

Institute of Dermatology
5 30 P M Dr S Thomson Clinical demonstration

University of Edinburgh
5 P M (Surgery Lecture Theatre University New Buildings) Professor Warren Cole Electrolyte Imbalance in Surgery

Saturday, 16th

Biochemical Society
1 45 P M (Department of Physiology Medical School Hospitals Centre Birmingham, 15) Short papers

---

Corrigenda *Sequelæ of Radical Gastric Resections*—In this article by Mr Brain and Professor Stammers (May 26, p 1137) the last two words in the caption of fig 1 should be "after inflation"

Prevention and Treatment of Travel Sickness—In table III of Dr Harper's article of May 26 (p 1141) the sixth column should be headed "treatment unsuccessful," and the last column "treatment successful"

General Medical Council—Our account last week (p 1223) of the council's meeting should have included the name of Sir Henry Wade as a member, for Scotland, of the Medical Disciplinary Committee This committee (see p 1218) has altogether 19 members, including the president, and it is *not* responsible for striking dentists off the Register

Appointments

Arnold, L L M A M B Camb, D O M S S H M O, Manchester Royal Eye Hospital

Bickmore, D M H, L M S.S A M.O, H M. Prison, Gloucester

* Jackson Mary M B Sheff resident aural registrar, Hospital for Sick Children Great Ormond Street, London.

Lees V T, M B Manc, D O.M S S H M O, Manchester Royal Eye Hospital

Taylor R B, M R C.S, D P M asst psychiatrist, Whittingham Hospital Manchester

Tresidder, Gerald F R C.S asst surgeon genito-urinary department, London Hospital

Wilson Marjorie S M B N Z D I H. senior asst. M O. for maternity and child welfare City of Leicester

University College Hospital

Fletcher W D, M B Leeds, D PHYS.MED S H M O, department of physical medicine

Kininmonth, D A M B Lpool D PHYS.MED S.H.M.O department of physical medicine

McAllen Monica M D Lond, M R C P S H M O chest department

McRobert, Sir George C I E, M D Aberd, F R C.P consultant physician Hospital for Tropical Diseases

Western Regional Hospital Board

Barr, G M M B Glasg M R C O G consultant obstetrician and gynaecologist Stobhill Hospital Glasgow

Donaldson Rose, I L M D Edin asst tuberculosis physician, County of Dumfries and Galloway

Keir, R M S, M B Aberd D A consultant anæsthetist, Dumfries and Galloway Royal Infirmary

McHarg, J F M B Edin, M R C P, D P M deputy physician superintendent, Glasgow Royal Mental Hospital

Munro W L, M B Glasg B.SC, D M R (D) consultant radiologist, Ayrshire

Scott, Agnes L, M B Glasg, M R C P E, D P.H consultant pathologist, Dumfries and Galloway hospital group

Appointed Factory Doctors

Bethune, A D M.B Edin Newcastleton district, Roxburghshire

Crawford, R P, L.R.C P E Taynuilt district, Argyllshire.

Evans W B, M D Camb Milford Haven district, Pembrokeshire

Hicks, C A N M.R C S Huntingdon district Huntingdonshire

MacKenzie, G N, M B Glasg New Galloway district Kirkcudbrightshire

Melleck, Simon, M B E, M B Lond Truro district Cornwall.

Robinson M G, M.R C.S Newent district, Gloucestershire

Robson T J W, M.B Durh Newburn district Northumberland

Rudd, P F M B Birm Winslow district Oxfordshire

Timings L J, M R C.S Witney district, Oxfordshire

Colonial Service

Banks L W, M B Edin senior M O, Nigeria

Shaw F O J M R C.S M O Kenya

Sweetham, J T B A, M B Dubl M O, Nigeria

North East Metropolitan Regional Hospital Board

Burbury, W M. M A, M B Lond, D P M part time consultant psychiatrist, Chelmsford child guidance clinic

Bush F, M A M.B Edin, D M R E part time consultant radiologist, St. George in the East Hospital

Elkeles A M D Edin D M R.E part time consultant radiologist, Metropolitan Hospital

Heathfield K W G M D Lond M R C P part time consultant neurologist, Bethnal Green and Mile End Hospitals.

Neville, N A B M Oxfd, M R C P full time consultant physician in diseases of the chest Hertford group of hospitals and Bishop's Stortford, Hertford, and Waltham Abbey chest clinics

Ward B C H, M R.C.S D M R part time consultant radiologist Queen Elizabeth Hospital for Children

* Amended notice

Births, Marriages, and Deaths

BIRTHS

Bowers—On May 31 at Folkestone the wife of Dr V H Bowers—a daughter

Chamberlain—On May 27 in Leeds the wife of Mr Digby Chamberlain F R C.S—a son

Langdon Down—On May 29 in London the wife of Dr Norman Langdon Down—twin daughters the elder of whom survived only three days

Stringer.—On June 1 in London the wife of Mr Paul Stringer F R C.S—a daughter

MARRIAGES

Garratt—Kiln—On May 26, at Forest Row Sussex Cecil Douglas Garratt, M R C P, to Ann Kiln M B

DEATHS

Dickson—On May 29 at Aspley Guise Beds, Arthur Norman Dickson M C M B Camb colonel I M S retd aged 70

Hunter—On May 17 at Newcastle upon Tyne, Kenneth Downie Hunter M B Durh

Irving—On May 28 at Totland Bay I o W William Irving, M D Camb M R C O G, formerly of Christchurch New Zealand aged 81

Norton—On May 31, at Bury St Edmunds Edgar Lionel Robert Norton M D Lond formerly of Winnipeg

Young—On May 31 at Twyford, Berks Frederic Charles Young M B Camb but worse on coughing. It was keeping her awake at night.

There was nothing relevant in her history. She was a diabetic. She had previously been investigated elsewhere, and a barium meal, a cholecystogram, and a barium enema had all been negative.

On examination a small area of localised tenderness was found about 3 in. to the left of, and 1 in. above, the umbilicus. On palpation there seemed to be a small nodule at the site of the tenderness.

Because the tenderness was so localised it was decided to try the effect of local anæsthesia. On Sept. 3, Proctocaine 10 ml. was injected into the tender and painful area. The tenderness and pain immediately disappeared. For the next five nights, for the first time for five months, the patient was able to sleep at night, and had no pain. Then the pain returned, and again the same site was tender. Again a small nodule seemed to be palpable.

On Sept. 12, 1950, under general anæsthesia, a transverse incision was made over the tender area and was deepened through the subcutaneous fat. The rectus sheath and the external oblique aponeurosis were cleared. A small protrusion of fat, about 0·5 × 1 cm. was seen emerging through the semilunar line. Closely related to the fat lobule was a small vessel. By careful dissection it was possible to demonstrate clearly that the fat lobule was a fatty hernia through a small defect in the linea semilunaris and that the vessel also emerged through this small defect. Deeply the fatty hernia was dragging up a small pouch of peritoneum. The peritoneum was separated from the deep aspect of the aponeurosis of the transverse abdominis muscle and from the edges of the defect. The fatty lobule was excised. The defect in the linea semilunaris was closed with mattress sutures, and the wound closed.

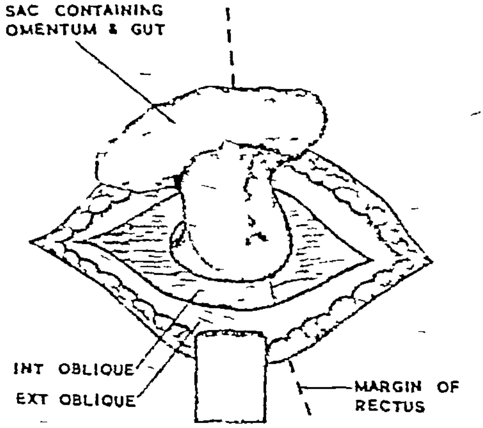


Fig 2—Hernial sac emerging from linea semilunaris at operation on case 3

From the time of operation the patient was free from pain, and when last seen in Feburary, 1951, she was a much happier woman.

ANATOMY

The literature shows some difference of opinion as to what constitutes Spigel's line.

Watson (1938) states that the linea semilunaris is formed by the aponeurosis of the internal oblique muscle at its point of division to enclose the rectus muscle. He describes it as extending from the ninth costal cartilage to the pubic spine, and identifies it with the lateral border of the rectus abdominis muscle. River (1942) on the other hand states that it is the line of transition between the muscle bundles and aponeurosis of the transversus abdominis muscle. Its convexity is outward, and it lies decreasingly distant from the midline as it is followed from the umbilicus. River says it does not coincide with the line of transition in the internal oblique muscle, which, unless extreme muscular aplasia exists, follows the rectus muscle closely.

It is certain, however, that the relationship of the lines of transition of the transversus and internal oblique muscles varies in different patients. Where the two lines coincide, with the result that the aponeuroses fuse lateral to the rectus muscle, it seems likely that herniation through any defect in this layer of aponeurosis would be easier.

ÆTIOLOGY

In case 4 the small fatty hernia was clearly associated with a vascular bundle, and had escaped through a vascular foramen. This view of the causation of these hernias was put forward by Cooper, Makrocki, Reigner, and others (cited by Watson 1938). Barthelemey and Molière are quoted by Watson as stating that the cause of these hernias was the arrangement of the layers of aponeurosis in relation to the rectus muscle. In some cases the fascia is loosely attached to the muscle, and may give rise to a diverticulum or pocket opening downward or inward into which a hernia may be pushed during a sudden strain when the body is bent forward (Watson 1938). River (1942) describes numerous irregular slit like defects up to 3 or 4 mm. long where the aponeurosis of the transversus abdominis muscle passes forward and fuses with that of the internal oblique muscle.

SYMPTOMS AND SIGNS

A patient with a Spigelian hernia may present complaining of pain or of a lump, or of both pain and a lump. It is the patient complaining only of pain, with no visible or even palpable lump, who causes the greatest difficulty in diagnosis, as in case 4.

A Spigelian hernia in its earliest form is simply a protrusion of retroperitoneal fat through the semilunar line—a condition similar to fatty hernia of the linea alba. The small fatty lump may be palpable, or the hernia may be interstitial, penetrating the aponeurosis of the transversus abdominis muscle only, and spreading out in the abdominal wall beneath the internal oblique muscle. In an early stage the patient complains of pain localised in the abdominal wall and aggravated by coughing or straining. There may also be some vague symptoms of dyspepsia, probably related to the pull exerted by the fatty hernia on the parietal peritoneum. In this early stage the only physical sign may be a localised area of tenderness, which can be banished by the injection of a local anæsthetic. If the fatty lump is large enough, or the patient not obese, a small mass may be palpable.

As the condition progresses, so the symptoms and signs become more prominent, and are similar to those of external hernias elsewhere in the body.

TREATMENT

Surgical repair is required for these hernias because of pain and the very real danger of strangulation. Cases with symptoms of intestinal obstruction following incarceration with impending strangulation have been described by River (1942), Bryant (1947), Mason and Ruge (1948), and Holloway (1922). The hernial sac should be removed if there is one, and the defect in the abdominal wall is best repaired by the Mayo overlap method with mattress sutures.

REFERENCES

Bryant, A. L. (1947) *Amer. J. Surg.* 73, 396.
Holloway, F. (1922) *Ann. Surg.* 75, 677.
Mason, M. L., Ruge, D. (1948) *Quart. Bull. Nthwest. Univ. (med.)* 22, 71.
Paul, M., Hill, W. C. O. (1943) *Brit. J. Surg.* 30, 385.
Reid, D. R. K. (1949) *Ibid*, 36, 433.
River, L. P. (1942) *Ann. Surg.* 116, 405.
Watson, D., Scotter, B. (1951) *Brit. med. J.* i, 74.
Watson, L. F. (1938) Hernia. 2nd ed. St. Louis.

One advantage of knowing the D N A content of the nucleus is that a determination of D N A as well as other chemical constituents in a sample of tissue enables us to calculate the amount of such constituents in each cell In this way the amount of lipid phosphorus, protein, nitrogen, and R N A P in the kidney and prostate cells have been determined This procedure opens up a new approach in the study of cellular pathology, since it is now possible to express the composition of a tissue in terms of the average composition per cell, and to compare the results of chemical estimations with those of microscopy The results of such a comparison are particularly interesting in marrow from cases of megaloblastic anæmia, in which the D N A content of the nucleus is significantly raised, and a greatly increased R N A content of the cell explains the very pronounced basophilia of the cytoplasm of the younger megaloblasts

Our thanks are due to many colleagues for their interest in this work, and for facilities to study patients, and to Miss Margaret Meikle for valuable technical assistance One of us (J N D) was in receipt of an expenses grant from the Medical Research Council

REFERENCES

Barer R (1949) *Lancet*, i 533
— Holiday, E R Jope E M (1950) *Biochim biophys Acta*, 6, 123
Berenblum, I, Chain, E (1938) *Biochem J* 32 295
Boivin, A, Vendrely, R, Vendrely, C (1948) *C R. Acad Sci, Paris*, 226 1061
Brachet J (1947) *Symp Soc exp Biol* no 1 p 207
Caspersson T (1947) *Ibid* p 127
— (1950) Cell Growth and Cell Function New York and London
Commoner B (1949) *Science* 110, 31
— (1950) *Ibid* 111 71
Davidson J N (1947) *Cold Spr Harb Symp quant Biol* 12, 50
— (1950) The Biochemistry of the Nucleic Acids London
— Leslie I (1950a) *Nature Lond* 165 49
— — (1950b) *Cancer Res* 10 587
— — Sherlock S White J C (1951) in preparation
— — White J C (1948) *J Path Bact* 60, 1
— — — (1950) *Biochem J* 47 xvi
— Waymouth C (1943) *Ibid*, 37, 271
Furst S S Roll P N, Brown G B (1950) *J biol Chem* 183 251
Hevesy, G (1948) in Lawrence, J H, Hamilton J G, Advances in Biological and Medical Physics New York, vol I p 409
Howard A, Pelc S R. (1950) *Brit J Radiol.* 23, 634
Mandel P, Metais P, Cuny S (1950) *C.R Acad Sci Paris* 231 1172
Minor A H Burnett L (1948) *Blood* 3 799
Mirsky, A E Pollister, A W (1946) *J gen Physiol* 30, 117
— Ris H (1949) *Nature Lond* 163 666
Pollister A W Swift H H (1950) *Science*, 111 68
Schmidt, G Thannhauser S J (1945) *J biol Chem.* 161, 83
Schrader F, Leuchtenberger C (1949) *Proc nat Acad Sci* 35, 464
Swift H H (1950a) *Ibid* 36 643
— (1950b) *Physiol Zool* 23, 169
Vendrely R Vendrely, C (1948) *Experientia* 4 434
— — (1949) *Ibid*, 5, 327
White J C (1947) *J Path Bact* 59 223
— (1950) *Biochem J* 46 xxiv

SPIGELIAN HERNIA

HERNIA THROUGH THE LINEA SEMILUNARIS

REPORT OF FOUR CASES

SIR CECIL WAKELEY
K B E, C B, M Ch, D Sc, F.R C S
SENIOR SURGEON AND TEACHER OF CLINICAL SURGERY, KING'S COLLEGE HOSPITAL, LONDON, CONSULTING SURGEON TO THE ROYAL NAVY

PETER CHILDS
M.A, D M, M.Ch Oxfd, F R C S
SURGEON, SOUTH DEVON AND EAST CORNWALL HOSPITAL, PLYMOUTH

A SPIGELIAN hernia is one of the less common forms of hernia It is a herniation through the semilunar, or Spigel's line (fig 1) River (1942) found that only 116 cases of true spontaneous lateral ventral hernia through Spigel's line had been reported up to 1942 In this country cases have been reported by Paul and Hill (1943), Reid (1949), and Watson and Scotter (1951) We report here four more cases

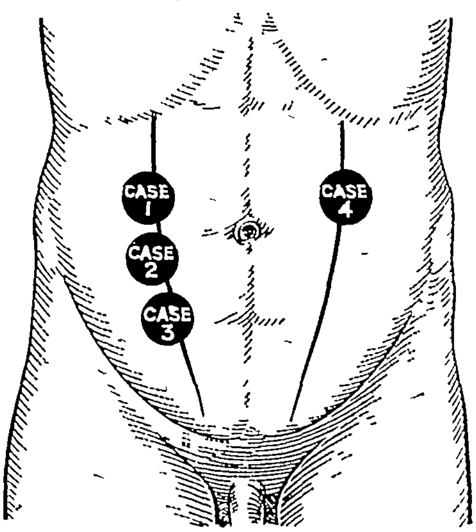


Fig 1—Sites of Spigelian hernias in cases 1–4.

CASE RECORDS

Case 1 —A naval stoker, aged 50, was admitted to hospital on May 5, 1916, complaining of a diffuse lump on the right side of his umbilicus The lump was about the size of a cricket ball It was painful, dull on percussion, and non translucent. So far as the patient knew, it had been present for two years and was getting larger There was no history of trauma The patient had had one or two attacks of vomiting

On July 6, 1916, under general anæsthesia, the lump was explored through a transverse incision A hernial sac containing a large mass of omentum and part of the transverse colon was exposed The sac of peritoneum emerged from a rounded hole in the right linea semilunaris just above the level of the umbilicus The omentum was resected and the transverse colon returned to the abdomen. The sac was excised and the hernial defect closed with three mattress sutures

Recovery was uneventful When the patient was seen again in January, 1919, there was no sign of recurrence

Case 2 —A fat married woman aged 55, was admitted to hospital on March 10, 1922, complaining of a swelling situated to the right of her umbilicus The lump had appeared some eighteen months previously, after the birth of her sixth child The swelling was diffuse and about the size of a billiard ball It was dull on percussion and painful on pressure

On March 11, 1922, under local anæsthesia a transverse incision was made over the swelling, and a hernial sac exposed emerging through the linea semilunaris The sac was incised and found to contain some omentum and the cæcum The omentum was excised and the cæcum returned to the abdomen. The hernial sac was transfixed, ligatured, and excised, and the defect in the abdominal wall was closed with two mattress sutures

Recovery was uneventful

Case 3 —A married woman, aged 62, was admitted to hospital on April 3, 1930, complaining of a lump on the right side of her abdomen just below and lateral to the umbilicus (fig 1) The lump was about the size of a hen's egg and disappeared when the patient lay down

On April 4, 1930, under general anæsthesia, a transverse incision was made over the lump and a hernial sac exposed (fig 2) The sac was found to contain omentum and the cæcum The omentum was excised, and the cæcum returned to the abdominal cavity The hernial ring was closed with mattress sutures

Recovery was uneventful

Case 4 —A married woman aged 53, was first seen in August, 1950, with four months' history of pain on the left side of her abdomen The pain was becoming more pronounced The patient described the sensation as being as though "there's something there that shouldn't be and it's sticking into me all the time The pain was constant,

TABLE III—MORTALITY IN CASES WHERE BLEEDING RECURS OR STARTS AFTER ADMISSION TO HOSPITAL OR THERE ARE OTHER FACTORS INCREASING THE MORTALITY, AND THE SIGNIFICANCE OF THE TYPE OF BLEEDING

Type of bleeding		Whole series		Perforation and/or severe pain and/or bleeding starting in hospital			
				Incidence		Fatal cases	
		No	%	No	%	No	%
Hæmatemesis	recurring or starting in hospital	68	22	18	40	11	61
Melæna	recurring or starting in hospital	26	8	12	27	3	25
Total		94	30	30	67	14	47
No hæmorrhage after admission		221	70	15	33	1	7
Total		315	100	45	100	15	33

Nearly all the operations had been done a considerable time before.

Table II shows the patients listed under only one symptom, even though they had others, and the symptoms take precedence in the order shown from top to bottom—e g, a patient with pain and cachexia is listed only under pain

The age incidence is not shown but is of the usual significance

The first four factors listed in table I increased the mortality, and must be taken to mean that the patient had a severe, penetrating, and usually chronic ulcer This accords with the findings of other workers (Allen and Benedict 1933, Baker 1947, Finsterer 1947, Gordon-Taylor 1946, Avery Jones 1947)

In the present series the factors increasing the mortality may be reduced to severe pain and/or hæmorrhage starting in hospital (table II), in the presence of one or both of these factors the mortality from hæmatemesis after admission to hospital was about 60% (tables III and IV) In hospital the incidence of these factors in the presence of melæna is comparatively higher than in hæmatemesis, yet the mortality is considerably lower (table III), but the patients with melæna were on the average somewhat younger than those with hæmatemesis The group of 68 patients who had hæmatemesis in hospital, with a mortality of 31% (table IV), is divisible, by other easily recognisable signs (hæmorrhage starting in hospital and/or severe pain), into 16 with a mortality of 63% and 52 with a mortality of 21% (table IV)

14% had previously undergone operation for peptic ulcer, and the gross mortality among them was the same as that of the entire series Little interest seems to have been shown in this aspect Welch and Yunich (1940) had no deaths among their patients with bleeding peptic ulcer who had previously undergone gastro enterostomy

TABLE IV—MORTALITY FROM HÆMATEMESIS IN HOSPITAL COMBINED WITH OTHER SYMPTOMS

Hæmatemesis in hospital	No	Fatal cases	
		No	%
Entire series	68	21	31
Severe pain in hospital and/or bleeding starting in hospital	16	10	63
Other cases of hæmatemesis	52	11	21
Only one hæmatemesis	39	9	23
More than one hæmatemesis	29	12	41
History of manifest hæmorrhage *	28	8	29
No manifest hæmorrhage in the past	39	12	31

* Data lacking in the case of one death

The incidence of previous attacks of bleeding is very high, as Rischel (1936) and Hesser (1942) also found in their series Among the "relapsers" the mortality is lower, if anything, than among the patients bleeding for the first time Of 27 deaths 17 took place in connection with the first episode of hæmorrhage A similar finding has been reported by Christiansen (1935), Allen and Benedict (1933), Blackford and Allen (1942), Welch (1949), and Baker (1947), but not by Sullens et al. (1949)

It is clear from table V that the prognosis is the same, whether manifest bleeding has taken place once or three times or more, if only the present bleeding is in the form of hæmatemesis Every time a hæmorrhage takes place, the patient has the same chance—i e, that appropriate to his age group It will be seen from the table that the difference in the mortality among patients admitted to hospital during the first attack (17 out of 164) and those who have had one or several attacks before (10 out of 150), is due almost exclusively to a difference in mortality from hæmatemesis and from melæna alone

Conclusion

The mortality is increased in the presence of the following symptoms perforation, severe pain in hospital, hæmorrhage starting in hospital, stenosis, and cachexia No such increase is caused by previous operations for peptic ulcer (gastro enterostomy) or previous manifest bleeding

The combination of hæmatemesis in hospital with severe pain in hospital or with hæmorrhage starting in hospital entailed a mortality of 60%

TABLE V—MORTALITY RATE IN RELATION TO PREVIOUS ATTACKS OF HÆMORRHAGE

No of previous attacks of hæmorrhage	Mode or manifestation of hæmorrhage at present admission					
	Hæmatemesis before and/or after admission		Melæna only		Entire series	
	No of admis	Deaths *	No of admis	Deaths	No of admis.	Deaths
None	113	15 (*13%*)	51	2 (*4%*)	164	17 (*10%*)
Only one	43	5 (*12%*)	24	1 (*4%*)	67	6 (*9%*)
Two or more	39	4 (*10%*)	45	0	84	4 (*5%*)
Three or more	22	2 (*9%*)	30	0	52	2 (*4%*)
One or more	82	9 (*11%*)	68	1 (*2%*)	150	10 (*7%*)

* Data not available in one excluded case

This analysis illustrates how impossible it is to compare most mortality statistics, especially gross mortalities (Avery Jones 1947, Pedersen 1941, 1949)

CRITERIA OF OPERATION

Not all the results obtained by the present analysis are applicable directly to the criteria of operation The present analysis was based on the entire series, including patients who did not die from exsanguination and non-operable patients The criteria of operation, on the other hand, can be based only on operable patients with hæmorrhage after admission and, according to my previous investigations (Pedersen 1941, 1949), only on operable patients with hæmatemesis in hospital This reduces the material which can be used in assessing the criteria of operation from 68 with hæmatemesis in hospital of whom 21 died (table IV) to 50 of whom 9 died (For my estimation of the operability among the deceased and the survivors see *Pedersen 1949*)

As might be expected, the significance of the factors studied is restricted by their occurrence in relatively few of the deceased patients who had been operable Therefore, the entire analysis will not be repeated on the basis of the relevant material, but table VI illustrates the result of a study of a few factors in this material

CHOICE OF CONSERVATIVE OR SURGICAL TREATMENT IN BLEEDING PEPTIC ULCER*

JØRGEN PEDERSEN
M D Copenhagen
SENIOR ASSISTANT PHYSICIAN, MEDICAL DEPARTMENT B, FREDERIKSBERG HOSPITAL, COPENHAGEN

THE mortality attending gastric surgery has much decreased of late, and in a few hospitals the treatment of acute bleeding ulcer has therefore been modified, consisting now of surgical as well as conservative measures The great majority of cases are still treated conservatively in the acute phase, surgery is reserved for the relatively few in which the prognosis with medical treatment is regarded as poor

The introduction of this surgical treatment has led to renewed interest in the prognosis of bleeding peptic ulcer In a small group of patients who are elderly or have persisted or repeated bleeding the mortality is normally high (about 30%) Such patients are therefore potential subjects for surgery, but the final selection for operation is made according to more definite criteria

The time of operation is a key problem, for the operation mortality depends on how often or how long the patient has been in a state of shock It is important to detect at an early stage of the bleeding those cases which require operation, and to operate at once, and it is equally important not to operate in the acute phase on patients who will recover with conservative treatment

The surgical treatment can be divided into two types surgery after trial, and immediate surgery "Surgery after trial" means that conservative treatment (blood transfusion) has been tried to stop the bleeding, and that no operation is done unless conservative treatment has been unsuccessful "Immediate surgery" means that the patient undergoes operation as soon as possible after admission to hospital with massive hæmorrhage, here the amount of bleeding is the decisive factor Surgery after trial is advocated by Avery Jones (1947) and Dunphy and Hoerr (1948), and immediate surgery by Finsterer (1947), Tanner (1949a), and Stewart et al (1948)

TABLE I—PROGNOSTIC SIGNIFICANCE OF VARIOUS SYMPTOMS AND SIGNS

Symptoms and signs	Whole series (315 cases)		Fatal cases (28)		
	No	Incidence %	No	Incidence %	Mortality %
Perforation	2	1	1	4	50
Bleeding starting in hospital,	18	6	7	25	39
Severe pain in hospital	30	10	9	32	30
Stenosis and / or cachexia	27	9	6	21	22
Previous operation for peptic ulcer	44	14	4	14	9
Previous manifest hæmorrhage*	150	48	10	36	7

* Data lacking in 1 fatal case

I have previously proposed (Pedersen 1949) the following criteria for operation in cases of acute bleeding peptic ulcer (1) patients aged 50 or more, with a definite peptic ulcer, should be submitted to operation—in the absence of serious contra indications—if hæmatemesis occurs in hospital after admission, and (2) operation should be done as soon as possible after the first hæmatemesis in hospital

This proposal was the result of an analysis of the mortality of bleeding peptic ulcer treated conservatively in Copenhagen The series included 31 fatal cases, and 90–100% of the patients who, in my opinion, might have been saved by appropriate surgery did not die until one or several brisk hæmatemeses had occurred in hospital. Fatal cases showing melæna alone are rare (Pedersen 1941, 1949) and generally inoperable

In the present investigation I studied the prognostic significance of factors which had not been studied in my previous analysis (Pedersen 1949) to see whether the criteria for operation then suggested needed any alteration.

MATERIAL

The material consisted of the same series as before—i e, patients in medical department B (Prof E Meulengracht) of Bispebjerg Hospital, Copenhagen, from May 1, 1938, to May 1, 1948 It includes all the patients aged 40 or more who had manifest bleeding of at least 1 litre either as hæmatemesis or as melæna and showed signs of peptic ulcer either on radiography or at necropsy The group comprises 317 admissions for hæmorrhage in a total of 288 patients During the period under discussion 31 patients died in connection with bleeding peptic ulcer (found by the perusal of about 2500 necropsy records) and no less than 30 of these 31 patients were in the group selected for analysis, 1 was aged less than 40 and thus is not included in the series

TABLE II—ANALYSIS OF FACTORS (LISTED IN TABLE I) WHICH INCREASED THE MORTALITY

Symptoms and signs	Total no of cases	Fatal cases	
		No	%
Perforation	2	1	50
Severe pain in hospital (no perforation)	30	9	30
Bleeding starting in hospital (no perforation, no pain)	13	5	38
Stenosis and/or cachexia (admitted to hospital because of bleeding, no perforation no pain)	15	1	[illegible]
Total	60	16	27

TREATMENT

The treatment was conservative, according to Meulengracht's (1947) principle of early and liberal feeding, administration of ample fluid, and blood transfusion Transfusions were given more often during the latter part of the period than at the outset Only 1 patient was operated on

ANALYSIS

The analysis comprises only 315 hæmorrhages (28 fatal), 2 patients died, from severe meningitis and from severe heart disease, without the hæmorrhage being manifest in life and so are excluded The following factors were studied (1) perforations, (2) hæmorrhage starting in hospital, (3) severe pain in hospital, (4) stenosis and/or cachexia, (5) operation for peptic ulcer, and (6) manifest hæmorrhage in the past (tables I–V)

In table I, if a patient has pyloric stenosis as well as pain he is included in both groups The two perforations listed were chronic, and there was no acute diffuse peritonitis "Bleeding starting in hospital" includes bleeding during ulcer management, "interval bleeding," and bleeding starting in another department (7 patients were transferred from a surgical department, and 1 from a psychiatric department) Patients who have had multiple operations are listed only once With partial gastrectomy taking precedence over gastroenterostomy, the latter over suture, and suture over other minor interventions, of the 44 patients listed 5 had had partial gastrectomy, 29 gastro enterostomy 7 simple suture, and 3 some other operation

---

* Supported by a grant from Kong Christian den Tiendes Fond

TABLE III—MORTALITY IN CASES WHERE BLEEDING RECURS OR STARTS AFTER ADMISSION TO HOSPITAL OR THERE ARE OTHER FACTORS INCREASING THE MORTALITY, AND THE SIGNIFICANCE OF THE TYPE OF BLEEDING

Type of bleeding		Whole series		Perforation and/or severe pain and/or bleeding starting in hospital			
				Incidence		Fatal cases	
		No	%	No	%	No	%
Hæmatemesis	recurring or starting in hospital	68	22	18	40	11	61
Melæna		26	8	12	27	3	25
Total		94	30	30	67	14	47
No hæmorrhage after admission		221	70	15	33	1	7
Total		315	100	45	100	15	33

Nearly all the operations had been done a considerable time before

Table II shows the patients listed under only one symptom, even though they had others, and the symptoms take precedence in the order shown from top to bottom—e g, a patient with pain and cachexia is listed only under pain

The age incidence is not shown but is of the usual significance

The first four factors listed in table I increased the mortality, and must be taken to mean that the patient had a severe, penetrating, and usually chronic ulcer This accords with the findings of other workers (Allen and Benedict 1933, Baker 1947, Finsterer 1947, Gordon-Taylor 1946, Avery Jones 1947)

In the present series the factors increasing the mortality may be reduced to severe pain and/or hæmorrhage starting in hospital (table II), in the presence of one or both of these factors the mortality from hæmatemesis after admission to hospital was about 60% (tables III and IV) In hospital the incidence of these factors in the presence of melæna is comparatively higher than in hæmatemesis, yet the mortality is considerably lower (table III), but the patients with melæna were on the average somewhat younger than those with hæmatemesis The group of 68 patients who had hæmatemesis in hospital, with a mortality of 31% (table IV), is divisible, by other easily recognisable signs (hæmorrhage starting in hospital and/or severe pain), into 16 with a mortality of 63% and 52 with a mortality of 21% (table IV)

14% had previously undergone operation for peptic ulcer and the gross mortality among them was the same as that of the entire series Little interest seems to have been shown in this aspect Welch and Yunich (1940) had no deaths among their patients with bleeding peptic ulcer who had previously undergone gastro-enterostomy

TABLE IV—MORTALITY FROM HÆMATEMESIS IN HOSPITAL COMBINED WITH OTHER SYMPTOMS

Hæmatemesis in hospital	No	Fatal cases	
		No	%
Entire series ..	68	21	31
Severe pain in hospital and/or bleeding starting in hospital	16	10	63
Other cases of hæmatemesis	52	11	21
Only one hæmatemesis	39	9	23
More than one hæmatemesis	29	12	41
History of manifest hæmorrhage *	28	8	29
No manifest hæmorrhage in the past	39	12	31

* Data lacking in the case of one death

The incidence of previous attacks of bleeding is very high, as Rischel (1936) and Hesser (1942) also found in their series Among the "relapsers" the mortality is lower, if anything, than among the patients bleeding for the first time Of 27 deaths 17 took place in connection with the first episode of hæmorrhage A similar finding has been reported by Christiansen (1935), Allen and Benedict (1933), Blackford and Allen (1942), Welch (1949), and Baker (1947), but not by Sullens et al (1949)

It is clear from table V that the prognosis is the same, whether manifest bleeding has taken place once or three times or more, if only the present bleeding is in the form of hæmatemesis Every time a hæmorrhage takes place, the patient has the same chance—i e, that appropriate to his age group It will be seen from the table that the difference in the mortality among patients admitted to hospital during the first attack (17 out of 164) and those who have had one or several attacks before (10 out of 150), is due almost exclusively to a difference in mortality from hæmatemesis and from melæna alone

Conclusion

The mortality is increased in the presence of the following symptoms perforation, severe pain in hospital, hæmorrhage starting in hospital, stenosis, and cachexia No such increase is caused by previous operations for peptic ulcer (gastro enterostomy) or previous manifest bleeding

The combination of hæmatemesis in hospital with severe pain in hospital or with hæmorrhage starting in hospital entailed a mortality of 60%

TABLE V—MORTALITY RATE IN RELATION TO PREVIOUS ATTACKS OF HÆMORRHAGE

No of previous attacks of hæmorrhage	Mode or manifestation of hæmorrhage at present admission					
	Hæmatemesis before and/or after admission		Melæna only		Entire series	
	No of admis	Deaths *	No of admis.	Deaths	No of admis.	Deaths
None	113	15 (*13%*)	51	2 (*4%*)	164	17 (*10%*)
Only one	43	5 (*12%*)	24	1 (*4%*)	67	6 (*9%*)
Two or more	39	4 (*10%*)	45	0	84	4 (*5%*)
Three or more	22	2 (*9%*)	30	0	52	2 (*4%*)
One or more	82	9 (*11%*)	68	1 (*2%*)	150	10 (*7%*)

* Data not available in one excluded case

This analysis illustrates how impossible it is to compare most mortality statistics, especially gross mortalities (Avery Jones 1947, Pedersen 1941, 1949)

CRITERIA OF OPERATION

Not all the results obtained by the present analysis are applicable directly to the criteria of operation The present analysis was based on the entire series, including patients who did not die from exsanguination and non operable patients The criteria of operation, on the other hand, can be based only on operable patients with hæmorrhage after admission and, according to my previous investigations (Pedersen 1941, 1949), only on operable patients with hæmatemesis in hospital This reduces the material which can be used in assessing the criteria of operation from 68 with hæmatemesis in hospital of whom 21 died (table IV) to 50 of whom 9 died. (For my estimation of the operability among the deceased and the survivors see Pedersen 1949)

As might be expected, the significance of the factors studied is restricted by their occurrence in relatively few of the deceased patients who had been operable Therefore, the entire analysis will not be repeated on the basis of the relevant material, but table VI illustrates the result of a study of a few factors in this material

CHOICE OF CONSERVATIVE OR SURGICAL TREATMENT IN BLEEDING PEPTIC ULCER*

JØRGEN PEDERSEN
M.D Copenhagen
SENIOR ASSISTANT PHYSICIAN, MEDICAL DEPARTMENT E,
FREDERIKSBERG HOSPITAL, COPENHAGEN

THE mortality attending gastric surgery has much decreased of late, and in a few hospitals the treatment of acute bleeding ulcer has therefore been modified, consisting now of surgical as well as conservative measures The great majority of cases are still treated conservatively in the acute phase, surgery is reserved for the relatively few in which the prognosis with medical treatment is regarded as poor

The introduction of this surgical treatment has led to renewed interest in the prognosis of bleeding peptic ulcer In a small group of patients who are elderly or have persisted or repeated bleeding the mortality is normally high (about 30%) Such patients are therefore potential subjects for surgery, but the final selection for operation s made according to more definite criteria

The time of operation is a key problem, for the operation mortality depends on how often or how long the patient has been in a state of shock It is important to detect at an early stage of the bleeding those cases which require operation, and to operate at once, and t is equally important not to operate in the acute phase on patients who will recover with conservative treatment

The surgical treatment can be divided into two types surgery after trial, and immediate surgery "Surgery after trial" means that conservative treatment (blood-transfusion) has been tried to stop the bleeding, and that no operation is done unless conservative treatment has been unsuccessful "Immediate surgery" means that the patient undergoes operation as soon as possible after admission to hospital with massive hæmorrhage, here the amount of bleeding is the decisive factor Surgery after trial is advocated by Avery Jones (1947) and Dunphy and Hoerr (1948), and immediate surgery by Finsterer (1947), Tanner (1949a), and Stewart et al (1948)

TABLE I—PROGNOSTIC SIGNIFICANCE OF VARIOUS SYMPTOMS AND SIGNS

Symptoms and signs	Whole series (315 cases)		Fatal cases (28)		
	No	Incidence %	No	Incidence %	Mortality %
Perforation	2	1	1	4	50
Bleeding starting in hospital,	18	6	7	25	39
Severe pain in hospital	30	10	9	32	30
Stenosis and / or cachexia	27	9	6	21	22
Previous operation for peptic ulcer	44	14	4	14	9
Previous manifest hæmorrhage*	1[illegible]0	48	10	36	7

* Data lacking in 1 fatal case

I have previously proposed (Pedersen 1949) the following criteria for operation in cases of acute bleeding peptic ulcer (1) patients aged 50 or more, with a definite peptic ulcer, should be submitted to operation—in the absence of serious contra indications—if hæmatemesis occurs in hospital after admission, and (2) operation should be done as soon as possible after the first hæmatemesis in hospital

This proposal was the result of an analysis of the mortality of bleeding peptic ulcer treated conservatively in Copenhagen The series included 31 fatal cases, and 90–100% of the patients who, in my opinion, might have been saved by appropriate surgery did not die until one or several brisk hæmatemeses had occurred in hospital. Fatal cases showing melæna alone are rare (Pedersen 1941, 1949) and generally inoperable

In the present investigation I studied the prognostic significance of factors which had not been studied in my previous analysis (Pedersen 1949) to see whether the criteria for operation then suggested needed any alteration

MATERIAL

The material consisted of the same series as before—i e, patients in medical department B (Prof E Meulengracht) of Bispebjerg Hospital, Copenhagen, from May 1, 1938, to May 1, 1948 It includes all the patients aged 40 or more who had manifest bleeding of at least 1 litre either as hæmatemesis or as melæna and showed signs of peptic ulcer either on radiography or at necropsy The group comprises 317 admissions for hæmorrhage in a total of 288 patients During the period under discussion 31 patients died in connection with bleeding peptic ulcer (found by the perusal of about 2500 necropsy records) and no less than 30 of these 31 patients were in the group selected for analysis, 1 was aged less than 40 and thus is not included in the series

TABLE II—ANALYSIS OF FACTORS (LISTED IN TABLE I) WHICH INCREASED THE MORTALITY

Symptoms and signs	Total no of cases	Fatal cases	
		No	%
Perforation	2	1	50
Severe pain in hospital (no perforation)	30	9	30
Bleeding starting in hospital (no perforation no pain)	13	5	38
Stenosis and/or cachexia (admitted to hospital because of bleeding no perforation no pain)	15	1	[illegible]
Total	60	16	[illegible]7

TREATMENT

The treatment was conservative, according to Meulengracht's (1947) principle of early and liberal feeding, administration of ample fluid, and blood transfusion Transfusions were given more often during the latter part of the period than at the outset Only 1 patient was operated on

ANALYSIS

The analysis comprises only 315 hæmorrhages (28 fatal), 2 patients died, from severe meningitis and from severe heart disease, without the hæmorrhage being manifest in life and so are excluded The following factors were studied (1) perforations, (2) hæmorrhage starting in hospital, (3) severe pain in hospital, (4) stenosis and/or cachexia, (5) operation for peptic ulcer, and (6) manifest hæmorrhage in the past (tables I–V)

In table I, if a patient has pyloric stenosis as well as pain he is included in both groups The two perforations listed were chronic, and there was no acute diffuse peritonitis "Bleeding starting in hospital" includes bleeding during ulcer management, "interval bleeding," and bleeding starting in another department (7 patients were transferred from a surgical department, and 1 from a psychiatric department) *Patients who have had* multiple operations are listed only once With *partial gastrectomy taking precedence* over gastro enterostomy, the latter over suture, and suture over other minor interventions, of the 44 patients listed 5 had had partial gastrectomy, 29 gastro enterostomy 7 simple suture, and 3 some other operation coma, or gastro intestinal hæmorrhage, do not show a similar biochemical disturbance.

---

* Supported by a grant from Kong Christian den Tiendes Fond

Many factors complicate head injury, which of themselves may alter the ionic balance of body fluids. Of these only mild water deprivation and chest infection were found with significant frequency among the patients under consideration. However, the chloride ion "retention" of pneumonia (Atchley and Benedict 1930) combines low urinary concentration of the ion with low plasma concentration, and water deprivation has the opposite effect of producing high concentrations in both plasma and urine (McCance and Young 1944). The coexistence of high plasma and low urinary concentrations appears therefore to be the result of neither of these factors acting singly, and in only one patient did they operate simultaneously. Furthermore, other patients in the series suffered mild water deprivation and later developed chest infections following their head injuries without ever displaying such a biochemical disturbance. It is therefore thought unlikely that the disturbance is primarily the result of these complicating factors.

It is unlikely that acid-base balance disturbances have affected our patients, though in one or two instances the plasma bicarbonate ion concentration reached the lower limits of normal. The reaction of all urine specimens was acid, and had there been a tendency to acidosis it might have been expected that the kidney would have excreted chloride ions to compensate, in the usual way. Furthermore, there was no reciprocal correlation between day-to day variations of plasma chloride and bicarbonate ion concentrations as might have been expected had the increase in the former been compensatory for reduction of the latter.

The hypothesis that the initial fault lies in the inability of the kidney to excrete the chloride ion is supported by Fullerton et al. (1932) who remark:

> 'the kidney normally excretes chloride in abundance when the plasma chloride is over 520 mgm.%. The fact that the urine of our patient contained only minimal traces of chloride, while the plasma chlorides were over 600 mgm.%, is ample evidence of the inability of the kidney to excrete this substance."

The detailed data of Luetscher and Blackman (1943) show convincingly that because of the inability of the kidney to excrete the chloride ion, even hypotonic intravenous saline leads to a hyperchloræmia. In only two of their four necropsies were they able to find local renal lesions in the tubules which could in any way account for this lack of chloride ion excretion.

Two isolated observations appear to indicate that the inability to excrete chloride is due to complete tubular reabsorption of the ion. McCance and Widdowson (1939) noted that one of their patients with high plasma chloride and sodium concentrations was excreting inulin freely, so that "it may be assumed that the sodium chloride was passing through the glomerular membranes into the tubules" and then being absorbed again. Luetscher and Blackman (1943) performed a mannitol clearance test in one patient while the electrolyte disturbance was subsiding. This showed a reduction of glomerular filtration to 30% of normal and indicated that 97% of the chloride in this glomerular filtrate was reabsorbed.

Borst has attempted an explanation of these phenomena:

> but very rarely does one find an increase of sodium and chloride ions in the blood accompanied by an almost complete absence of these minerals in the urine. Those cases in which it did occur had possibly one accompanying condition in common: an insufficient filling of the blood vessels or at least of the arterial system since it appeared in cases of severe hæmorrhage, dehydration, nephrotic œdema, post operative shock and in some cases of heart failure.

Among our patients, such a hypothesis is difficult to maintain. In cases 2 and 3, early and adequate transfusion was given, and in only one of the remaining four patients was there a severe degree of dehydration.

In view of the diverse diseases in which this metabolic disorder has been found, and the apparent lack of any common primary cause, the question must arise as to whether such changes do not constitute an unusual response by the individual patient. This aspect of disease has recently been discussed fully by Selye (1950). Hyperchloræmia occurs during the counter shock and resistance phases of the General Adaptation Syndrome. The charts of Selye show, however, that the urinary chloride concentration rises simultaneously. Since in our patients the urinary chloride concentration fell, it is difficult to assign them to any phase of the General Adaptation Syndrome; nor would such an assignation yield information about the intimate mechanism involved. It may be noted, however, that the biochemical changes recorded in this paper are similar to those following injections of deoxycortone acetate in man.

In patients with head injury, the further problem arises as to whether intracranial damage specifically initiates this disturbance, or whether the latter is the product of non specific changes developing during the illness. That kidney mechanisms may be affected by stimulation of the brain has been claimed by Cort (Livingstone et al. 1948) who has reproduced the renal shunt mechanism of Trueta et al. (1947) in cats by stimulating various parts of the brain including the posterior hypothalamus, the sensorimotor cortex, and area 13 on the orbital surface of the frontal lobe. Lewy and Gassman (1935) have produced hyperchloræmia and hypochloruria in cats by unilateral stimulation and subsequent destruction of the paraoptic nucleus of the hypothalamus. Sweet et al. (1948) reported hyperchloræmia in four patients after operation on the frontal lobe, and McLardy (1950) refers to "uræmia" after prefrontal leucotomy. In our patients, the frontal and hypothalamic areas were examined with care. All had contusion of the under surface of the frontal lobes, one had contusions in the hypothalamus, and two had blood clot around the pituitary region. In addition, however, there were often severe contusions elsewhere in the brain, particularly in the temporal lobes. Though at first sight the frontal lobe lesions might seem to support the previous work and suggest a direct relationship with the renal disturbance, their presence should be interpreted with care, for in head injuries the under surface of the frontal lobes is often damaged yet there is no evidence that these metabolic disturbances are common. Nevertheless, the possibility that cerebral damage may lead specifically to metabolic disorders merits further study.

DIAGNOSIS AND TREATMENT

The ward test of Fantus (1936) for urinary chloride concentration is frequently used in clinical practice, and the absence of that ion from the urine is usually taken, following Marriott (1947), to be an indication for treatment with saline fluids. Should this be done in patients with hyperchloræmia and hypochloruria there is a risk of aggravating the condition and producing œdema, particularly of the lung bases. The difficulty may be overcome by estimating both plasma and urinary chlorides. On the present evidence it would seem unwise, if a patient has hyperchloræmia, to give sodium chloride until either the plasma chloride level falls to normal or chloride ion appears in the urine in amounts greater than 1 g. per litre.

Summary

Six cases of severe head injury are described in which there was hyperchloræmia without excretion of the chloride ion in the urine.

It is suggested that the essential mechanism is inability of the kidney to excrete chloride ion. Possible ætiological factors are discussed.

BIOCHEMICAL FINDINGS IN BLOOD AND URINE

Case	Days after accident	Plasma		Serum		Serum		Plasma		Plasma protein	Blood urea	Urine		
		Cl	Cl	Na+	Na+	K+	K+	HCO_3	HCO_3			pH	Cl	Urea
		mg / 100 ml	m eq / litre	mg / 100 ml	m eq / litre	mg / 100 ml	m eq / litre	mg / 100 ml	m eq / litre	g / 100 ml	mg / 100 ml	—	g / litre	g / 100 ml.
1	2	575	98	312	136	14 5	4	39	17	6 2	66	6 5	5 0 2 0	
	3	605	103					51	23		54	6 5	0 8 0 8	3 85
	4 5	652 650	111 111					42	19	6 1 6 2	40 80	6 5	1 8 0 4	3 11 51
	6 7	650 580	111 99	320	139	13 4	3	42	10	5 8	92 48		0 1 0 7	4·05
2	1 2	555 720	95 123	356	155	17 3	4	42	19	8 2 6 7	34 86		1 3 0 0	3 1
3	2 4	610 690	104 118					41 44	18 20	6 1 5 9	104 84		Nil Nil	
	5 6	680 670	116 114	336	146	18	5			6 1	90 148	5 5	Nil Nil Nil	3 1
4	10	672	115	354	154			37	17	7 8	380	6 0 5 5	Nil Nil	3 8 3 3
	11	626	107	310	135	14 7	4			7 0	310	5 5	0 1 Nil	
	12	590	101					28	12		400			
5	4 5	604 627	103 107	336	146	19 5	5			6 2	124 173	5 5 6 5	Nil Nil	
	6	615	105	360	156			42	19		210	5 5 5 5	Nil Nil	
	7 8	590 615	101 105	320	139	14 5	4	32	14	6 1	230 240	5 5 5 0	0 3 0 3	2 85 2 14
6	8 9	790	135					28	12	6 5	320 310	5 5	Nil Nil	1 55

amounted at the most to 3 g per day in the milk feeds Even without urinary, fæcal, or perspiratory excretion, this could not raise the extracellular chloride ion concentration by 50 mg per 100 ml in 24 hours unless dispersed in a volume as little as 6 litres There is no evidence that the extracellular fluid was reduced to anything like this volume The other possibilities are that chloride ions were liberated from the tissues into the extracellular spaces, or that water was absorbed by the tissues from the extracellular spaces This latter hypothesis would, however, involve a concentration of all electrolytes and plasma proteins, of which we have no evidence

Case 2 shows the effect of giving intravenous transfusions of sodium chloride containing fluids to a patient in whom this inability to excrete chloride ion develops Approximately 19 g of sodium chloride were given in this way and the plasma chloride ion concentration rose to very high levels, yet the urinary chloride concentration fell to 0 6 g NaCl per litre

Of the remaining patients, cases 3 and 6 displayed the typical urinary findings with plasma chloride levels exaggerated by transfusions of salt containing fluids Case 4 showed severe water deprivation, and although rehydration restored the plasma protein and sodium ion and chloride ion levels to normal, the urine remained chloride free throughout Case 5 demonstrated the typical urinary findings without the plasma sodium and chloride concentrations being consistently above normal

It will be noted that in three of the five patients in whom the estimation was made, the serum sodium ion concentration was raised in addition to plasma chloride Unfortunately, in none of the patients was the urinary sodium ion concentration estimated

A reasonable hypothesis to account for the facts presented seems to be

1 An unknown mechanism causes reduced excretion of chloride ion by the kidneys
2 In the presence of this, sodium chloride intake by mouth and especially by vein, or mild water deprivation, or both may raise the plasma chloride level above normal without causing the excretion of chloride in the urine

Urea —The urinary urea concentrations in five of the six patients were high, indicating that the raised blood ureas which were present resulted from extrarenal rather than renal causes This conclusion is supported by the absence at necropsy of significant histological damage to the kidneys Such factors as fever, hypotension, chest infection, and inadequate nutrition, which themselves tend to raise the blood urea concentrations, varied with each patient and from day to day, so that it has proved impossible to attribute the high blood urea concentrations to any particular cause

Potassium —In two patients in whom serial determinations were made, the serum potassium ion concentration fell during the course of illness, but in two others the level was normal after the chloride ion disturbance had developed On this evidence, therefore, there would not appear to be a close relation between the serum potassium concentration and the chloride ion changes

POSSIBLE ÆTIOLOGICAL FACTORS

Simultaneous hyperchloræmia and hypochloruria is well established in pædiatric practice and has been previously described in adults in whom it is found in four groups of diseases

1 Disturbances in acid base balance (Fullerton et al 1932, McCance and Lawrence 1935, Allott 1939, McCance and Widdowson 1939)
2 Gastro intestinal hæmorrhage (Allott 1939, Borst 1938)
✓3 Cerebral damage (Allott 1939)
4 Sulphathiazole poisoning (Luetscher and Blackman 1943)

There appears to be no common factor among these groups Analysis of the case histories reveals a marked paucity of renal lesions at necropsy and a very high mortality rate Including our own cases, there are twenty deaths in the twenty nine reported

All authors emphasise the unusualness of the picture they describe, both in disease as a whole, and in the particular disease from which their examples were taken Thus most patients with equally severe degrees of diabetic

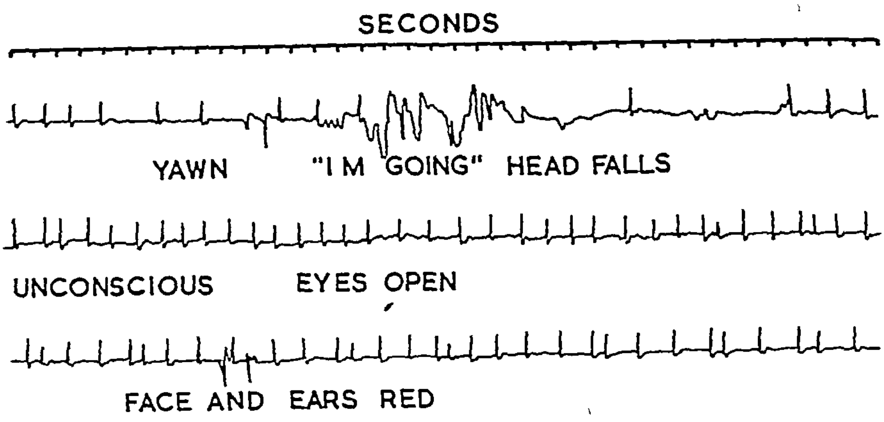


Fig 1—Lead II electrocardiogram at start of faint.

faint and a third at its start The forearm blood flow was measured each minute by the venous-occlusion plethysmographic method, using the principle of Brodie and Russell (1905) The method was similar in detail to that of Barcroft and Edholm (1945), and a pressure of 35 mm Hg was used throughout in the collecting cuff so as to interfere as little as possible with the arterial inflow during the faint

It was impractical to have the subject standing up, so he sat on a high stool with his legs and thighs as nearly vertical as possible He was supported from behind while fainting The room temperature was 19 5°C

RESULTS

The stimulus of seeing venepuncture done on another person was less effective on the second occasion than it had been on the first While preparations were being made, as obviously as possible, the student's forearm blood flow (fig 2) rose from a resting value of about 2 ml. to 7 5 ml. per 100 ml per minute, his arterial pressure rose from 110/78 to 130/88 mm Hg, and his heart rate increased No further increases occurred when the blood was withdrawn. These are normal reponses to an emotional stimulus insufficient to cause fainting

As the subject did not faint, a needle was now inserted into his arm, but no blood was withdrawn There was again an increase in forearm blood flow, but no faint It was therefore decided to increase the stimulus by asking him to drink the few ml of blood he had seen withdrawn from the other person's arm This stimulus was immediately effective, and a negligible amount of blood was swallowed

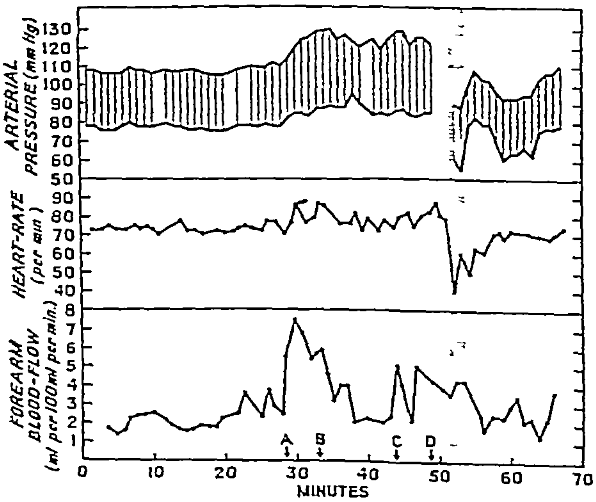


Fig 2—Circulatory changes during emotional faint A watches preparations B watches venepuncture C needle into arm D drinks 5 ml of blood The stippling represents loss of consciousness.

The subject became pale, yawned, and said " I'm going " He lost consciousness, and would have fallen from the stool had he not been supported The heart rate slowed, only 37 beats being recorded in the first minute, and there were consecutive periods of 11 sec and 7 sec during which no QRS complex was detected (fig 1) The electrical record naturally shows a good deal of background swing when the subject slumped forward, but careful inspection shows that it is most unlikely that a QRS complex is lost in this The forearm blood-flow was maintained throughout the period of the faint at 4–5 ml. per 100 ml. per minute, well above the resting level. The first arterial pressure reading during the loss of consciousness was 90/60 mm Hg, but this was about 40 sec after the asystolic periods mentioned above.

As soon as the essential observations had been made, the subject's legs were raised to the horizontal position Consciousness was probably lost for $1^1/_2$–2 minutes During its return one observer noticed some flushing of the ears and face, which is a rather unusual finding The action of the heart was irregular, with coupled beats for several minutes, but this is not unusual (Lewis 1932) During recovery there was an episode of nausea and retching accompanied by renewed slowing and irregularity of the heart beats for about 30 sec This is not shown in fig 1

DISCUSSION

Apart from the insertion of the needle into his arm, the stimuli applied to the subject were all emotional. The needle was sharp and caused little pain If the time relation of the faint to the drinking of blood is taken into account, it seems probable that this faint was mainly of emotional origin

The changes observed in the circulation are similar to those in posthæmorrhagic fainting (Barcroft et al. 1944, Barcroft and Edholm 1945) The combination of increased forearm blood flow and reduced arterial pressure is clear evidence of vasodilatation of the peripheral vessels in the forearm In association with pallor of the skin, this almost certainly means that the vessels to the muscles were dilated Dilatation of the vessels to the muscles in posthæmorrhagic fainting has been shown by Barcroft et al. to depend on sympathetic vasodilator fibres Presumably the same is true of emotional fainting Lewis (1932) has shown by the use of atropine that the slowing of the heart in similar faints is of vagal origin

SUMMARY

Circulatory changes in an emotional faint are described these were similar to those in posthæmorrhagic fainting

My thanks are due to Prof A St G Huggett, in whose department these observations were made, Dr D McK Kerslake and Mr J Hancock, who assisted with the observations, and Mr A. T for fainting

REFERENCES

Barcroft H Edholm O G (1945) *J Physiol* 104 161
— — McMichael J Sharpey-Schafer E. P (1944) *Lancet* i, 489.
Brodie T G Russell, A. E (1905) *J Physiol* 32 xlvii.
Lewis T (1932) *Brit med J* i 873

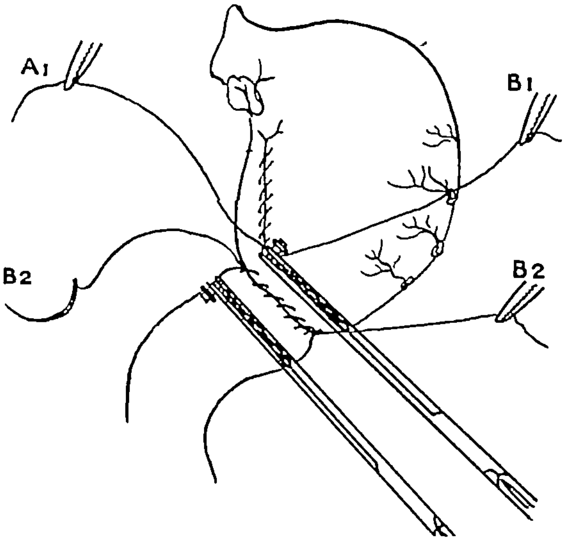


Fig 6—Suture of gastric stump to duodenal stump : A1, B1, and B2 as in fig 5

The gastric stump is now ready for anastomosis, the stoma being held securely in the grip of the small clamp, and the terminal tooth transfixing both walls of the stomach, thus preventing any slipping out at the tips of the clamp The conjoining clamps, and the technique described considerably simplify the preparation of a measured gastric stoma and a new lesser curve, an important step in modern subtotal gastrectomy which both facilitates anastomosis and improves function These light and slender clamps replace the heavier and larger instruments more commonly used in gastrectomy

The clamps also assist in the anastomosis (particularly in the Billroth I operation) by making the gastric and duodenal stumps easily controllable while the posterior seromuscular suture is being placed (fig 6) Similarly, it is an additional advantage (in the Polya operation), although perhaps a small one, to have the selected segment of the jejunum controlled by one of the small clamps (fig 7) The antimesenteric margin of the jejunum can be neatly placed in the grip of one of the clamps by the method described by Pannet (1945) In this way the jejunal opening can be measured to the gastric opening , aligning for the postseromuscular suturing is facilitated , and the clamp tends to seal serosa and mucosa together, thus minimising pouting of the mucosa and oozing By circumcising the seromuscular coats of the gastric stump just below the clamp (Maingot 1941) the vessels in the edge can be identified and ligatured, thus producing a bloodless anastomosis which is completed in the usual way As regards closing the duodenal stump, the rail clamp is useful The same technique is used which has been described for the first row closure of the lesser curve A single seromuscular suture is then placed in the middle of the stump, and the ends of this suture are clipped and held long A three point form of purse-string is placed round each corner The suture in the middle is used as the fourth point of resistance for the burying of each corner Two or three more interrupted sutures complete the closure

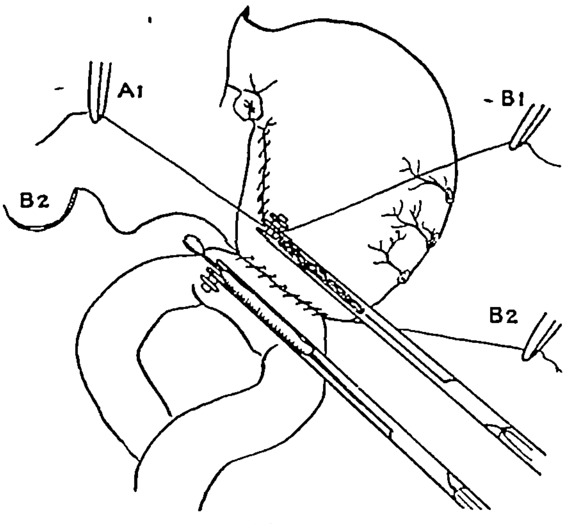


Fig 7—Control of segment of jejunum with special clamp in Polya operation : A1 B1 and B2 as in fig 5 A small needle with margin of redundant jejunum is excised before clamp on jejunum is removed

The conjoining clamps give the same help in resections at the cardia of the stomach The gastric opening is reduced to the size of the œsophageal opening, and the subsequent anastomosis is simplified by having the stomach and the œsophagus in the grip of the two small clamps The conjoining clamps make an end to-end ileotransverse colostomy after a right hemicolectomy a most satisfactory operation The technique used is similar to that described for preparation of the gastric stump, the lumen of the colon being reduced to the size of that of the small bowel

During the past three years I have used these instruments in both the Polya and the Billroth I forms of gastric resection Polya has been used for most of the duodenal ulcers, and Billroth-I for all gastric ulcers The clamps have proved of considerable value in simplifying both forms of gastrectomy, and it is hoped that the instruments may contribute in a small way to the eventual standardisation of technique in partial gastrectomy

I wish to thank Mr H R Thomson for much helpful criticism and advice The clamps are made by T H. Spicer & Son, 45, Marylebone High Street, London, W1

REFERENCES

Maingot, R (1941) Technique of Gastric Operations London
Pannet C A (1945) *Brit J Surg* 32, 418
Stevenson D L (1943) *Brit med J* i 13

AN EMOTIONAL FAINT

A D M GREENFIELD
M B , M Sc Lond
DUNVILLE PROFESSOR OF PHYSIOLOGY, QUEEN'S UNIVERSITY, BELFAST , FORMERLY SENIOR LECTURER IN EXPERIMENTAL PHYSIOLOGY, ST MARY'S HOSPITAL MEDICAL SCHOOL, LONDON

In 1945 a student, aged 19, fainted and fell while watching blood being withdrawn from another person's arm vein He had previously been healthy and has remained so An attempt was made to cause him to faint again in the same way while under close observation, so that the responses of an emotional faint could be compared with those of posthæmorrhagic fainting described by Barcroft et al (1944) and Barcroft and Edholm (1945) The faint that resulted may *not have* been so purely of emotional origin as the first , but we have very little information about such faints, and there has since been no opportunity of making similar observations on another person So the findings are presented here

METHODS

A lead II electrocardiogram was recorded continuously with an ink writing instrument The Q R S complexes could be identified with certainty, but the record (fig 1) was not good enough for the mechanism of cardiac irregularities to be analysed The arterial pressure was measured at intervals of a minute by auscultation Unfortunately two readings were missed just before the emboli showed it to be of recent but ante mortem origin. The right femoral vein contained a large ante-mortem thrombus which histologically was identical with the embolus

The stomach and intestines were normal, but no appendix was seen, instead there was a small dimple on the cæcum at the point where the appendix usually arises When the cæcum was opened, the appendix was seen to be completely inverted and protruding into the lumen. It measured 5 × 2 cm and was red and inflamed, with gangrene appearing imminent at the tip (fig 1) The remainder of the alimentary tract was completely normal, there being no other lesion from which the hæmorrhage might have arisen Microscopically, the appendix showed considerable disorganisation of the various tissues The epithelial cells were hyperplastic, with papilliferous formations, and there were accumulations of mucin in some areas, surrounded by epithelial formations suggestive of a mucocele (fig 2) The epithelial nuclei were hyperchromatic and showed frequent mitoses There was also subacute inflammation, with much dilatation of the blood vessels

The only other abnormal conditions found were acute passive congestion of the liver, with some fatty change, and mild nephrosclerosis (not excessive for the patient's age)

It was concluded that the cause of this patient's gastro intestinal complaints and of her heavy melæna was complete inversion of the appendix leading to early gangrene of its tip The cause of the inversion was in all probability a mucocele The immediate cause of death was the multiple pulmonary infarctions secondary to thrombosis of the femoral vein

COMMENTS

Neither the clinical picture nor the laboratory and radiological reports suggested the correct diagnosis in this case The profuse bleeding into the bowel in a woman of this age naturally pointed to a carcinoma somewhere along the gastro intestinal tract That an inverted appendix with early gangrene of the tip could cause this hæmorrhage and yet not give rise to some symptoms or signs of trouble implicating the appendix is particularly surprising The complaints had persisted for over three months before death from pulmonary emboli It is impossible to state whether or not the appendix had been completely inverted for the whole of that time, but one might be justified in assuming that at least partial inversion persisted throughout her illness

We are indebted for the early clinical history to Dr H. J Nicholson and Dr W Latimer, who attended the patient before her admission to hospital The photographs of the appendix were taken by Mr George Pendlenton, F I.M L.T

REFERENCES

Fraser K (1943) *Brit J Surg* 31 23
Skarby H G (1941) *Acta radiol Stockh* 22 471

THE ÆTIOLOGY OF DUPUYTREN'S CONTRACTURE

E G Herzog
M B Lond
ORTHOPÆDIC REGISTRAR ROTHERHAM HOSPITAL, YORKS

In the two years 1948 and 1949 I saw 20 patients with Dupuytren's contracture at this hospital, 13 attended for the first time, 4 had been on the waiting list from previous years, and in 3 the contracture was an incidental finding For a hospital of 150 beds this seemed a rather large number, and it suggested that Dupuytren's contracture was common in the Rotherham area

Several of the patients raised the question of compensation and would have liked us to say that years of hard work had brought their trouble on It was therefore decided to look into this problem

A review of the literature gives a very confusing picture Astley Cooper (1842) seems to have been first to describe, in 1822, what we today know as Dupuytren's contracture He stated that it was produced by a chronic inflammation of the aponeurosis and thecæ from " excessive action of the hand in the use of hammer, oar, plough, &c " Dupuytren (1832, 1833) established the exact pathology by dissection He, too, thought that trauma was the cause, or, as he put it, it occurred in " people who were obliged to make efforts with the palm of the hand or frequently to handle hard bodies " His first case seems to have been in his own coachman, and the holding of reins for hours on end seemed to him a most reasonable explanation However, already Dupuytren mentions predisposition, and he noticed a similar condition in the foot It is here not quite clear whether he was aware of the thickening of the plantar fascia or whether he was describing what is now known as clawing of the toes

Windsor (1834) stated that his tutor, Henry Cline, jun, had lectured on Nov 8, 1808, on the subject of " permanent contractures of the fingers " and had stated that the " aponeurosis palmaris became contracted and that *cutting of it was efficacious* "

Since then a very large literature on this subject has grown up, and Skoog (1948) lists over 400 references Trauma, single or long continued, has been put forward as a cause time and again by workers in all countries, but as often as this theory has been advanced it has been refuted Among the causes given are gout, rheumatism (Hedges 1896), diabetes, ulnar nerve lesions (Hoffa 1921), tuberculosis, arteriosclerosis, hyperparathyroidism, and neurosis (Reeves 1881) It seems obvious from this list that many earlier writers confused conditions such as hysterical contractures, scarring of skin and tendon, nerve paralyses, and stiff joints with a true contracture of the palmar fascia, but we are here only concerned with the question of the influence of hard work on the development of the contracture

RELATION TO WORK

There are three possible relationships (1) Dupuytren's contracture is always caused by hard work, (2) it is never caused by hard work, or (3) hard work is a contributory cause

There can be no doubt that Dupuytren's contracture sometimes occurs in people who have sustained no injury and have never worked hard in their life Holdsworth (1950) states that he has operated on at least three women in private practice Bunnell (1944) describes a case in a boy of 14 Corlette (1944) says that he himself has Dupuytren's contracture and has not done heavy manual work He emphasises the strong evidence that the condition is hereditary, its occasional occurrence in the plantar as well as in the palmar fascia of affected persons, and its tendency to be bilateral The familial element is brought out well in a family reported by Krogius (1921), in which there were 16 cases in four generations

If Dupuytren's contracture were never caused by excessive strain on the palmar fascia, the incidence in manual and non manual workers should be equal, provided that allowance is made for age and that a sufficiently large number of persons are examined to eliminate the error of chance distribution The same investigator should see both groups and should exclude carefully cases of scarring due to burns or to septic wounds and the stiffness following injury or arthritis I believe that it is of no value to investigate the occupation of patients seen at a hospital Langston and Badre (1948) said that of 88 cases they had collected, 64% were in labourers and 36% in doctors, clerks, and salesmen Kanavel et al. (1929), who found only 30 cases in more than 80 000 admissions, state that there were twice as many non manual as manual workers An objection here is

COMPLETE INVERSION OF THE APPENDIX

T H Boon
M D Durh , M R C P
ASSISTANT PHYSICIAN,
ROYAL VICTORIA INFIRMARY,
NEWCASTLE UPON TYNE

J C Sibley
M D Queen's Univ , Ontario
DEMONSTRATOR IN
PATHOLOGY IN THE
UNIVERSITY OF DURHAM

Complete inversion of the appendix as a result of a previous mucocele seems to be fairly rare The clinical features of the case described here are particularly interesting because during life there were no signs or symptoms indicating that the appendix was at fault The massive melæna which was a prominent early symptom was especially misleading

Fraser (1943) reviewed the published cases of all types of intussusception of the appendix and added 7 of his own, making a total of 82 Of these, only 8 were proven to be complete inversion of the appendix into the cæcum and uncomplicated *by intussusception of* the cæcum or of the ileum Further, in only 6 of the 82 cases was there an intussusception of a mucocele of the appendix It therefore follows that the present case represents a relatively rare condition, for not only had there been a previous mucocele of the appendix but also the appendix had become completely inverted, the ileum and cæcum being normal

In a discussion of the clinical features Fraser emphasised that characteristically there is a very severe colic with periods of complete remission between the colics The interval between the onset of symptoms and the establishment of the diagnosis varied from a few hours to a few months Rigidity and other physical signs pointing to a disorder of the appendix were absent in most cases A barium enema helped in a few cases to establish the diagnosis when a shadow like that of a papilloma could be seen projecting into the lumen of the cæcum Skarby (1941) reported 1 case diagnosed radiologically A second radiological examination after the symptoms had abated showed that the intussusception had undergone spontaneous remission

From his analysis of these cases Fraser concluded that the cause of the intussusception in 6 cases was a mucocele of the appendix, other possible causes being an attempt to extrude a concretion, a papilloma, or a foreign body from the appendix *If the foreign body* or the tumour was in the distal part of the appendix, the intussusception would be of the distal part into the proximal Once developed it may progress to a complete inversion of the appendix or give rise to a compound intussusception, or both

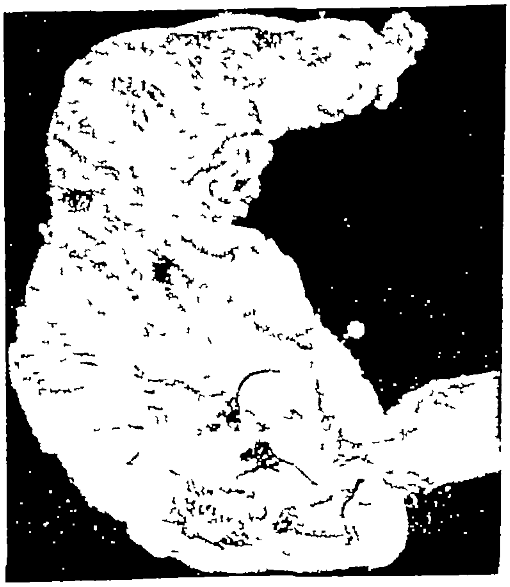


Fig 1—Completely inverted appendix in opened cæcum

CASE RECORD

On the morning of July 24, 1949, a housewife, aged 69, complained of severe diarrhœa, nausea, and passing of blood per rectum Her previous medical history was not relevant Her pulse rate was slightly higher than normal, but there was no evidence of shock There was no abdominal rigidity or localised tenderness, but general moderate tenderness was elicited along the line of the entire colon Gastro-enteritis was diagnosed, sulphaguanidine and kaolin were prescribed, and within a week the patient was well Eight weeks later another attack of diarrhœa came on and two pints of altered blood was passed per rectum After this episode the patient stayed in bed because of weakness, anorexia, and spasmodic abdominal pain, although normal bowel movements were established within a day or two On one occasion her physician felt a doubtful mass just below the hepatic flexure She was seen by one of us (T H. B) three weeks later and, because of persisting symptoms, the anæmia, and loss of weight, carcinoma of the alimentary tract was suspected, and the patient was admitted to hospital

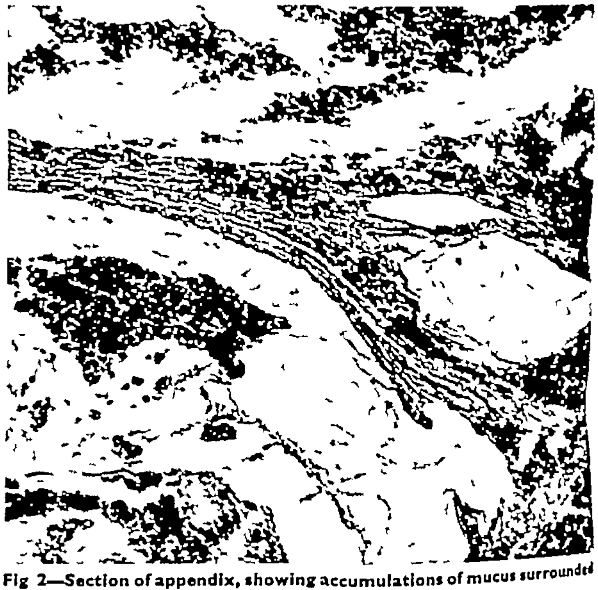


Fig 2—Section of appendix, showing accumulations of mucus surrounded by epithelial formations, suggesting mucocele.

In hospital her general condition remained poor for sixteen days, but she made no specific complaint, and repeated abdominal examinations revealed no mass or tenderness. Her temperature was normal, apart from one rise to 100°F for a few hours Her pulse rate remained at 90–100 Laboratory investigations showed hæmoglobin 58% (8 g), red cells 4,180,000 per c mm , and colour index 0 7 Occult blood was present in three out of four specimens of fæces Gastric analysis revealed free hydrochloric acid No radiological abnormality was detected after a barium meal or a barium enema The diagnosis of carcinoma of the alimentary tract was maintained, and gastroscopy was attempted Difficulty was encountered in passing the instrument, and the examination was discontinued The patient returned to bed in a satisfactory state, but half an hour later she collapsed Her condition steadily deteriorated, and she died fifteen hours later

Necropsy Findings—The body was well nourished, and there were no significant external findings Both lungs were heavy wet, and œdematous, the right weighing 510 g and the left 420 g The lower lobes were atelectatic, and section revealed multiple infarcts Almost all the branches of the pulmonary arteries on both sides contained ante mortem thrombi A little red brown fluid was present in both pleural cavities Microscopy of the lungs confirmed the macroscopical *finding of recent* pulmonary *infarction and generalised* pulmonary œdema A section through one of the pulmonary emboli showed it to be of recent but ante-mortem origin. The right femoral vein contained a large *ante-mortem* thrombus which histologically was identical with the embolus

The stomach and intestines were normal, but no appendix was seen, instead there was a small dimple on the cæcum at the point where the appendix usually arises When the cæcum was opened the appendix was seen to be completely inverted and protruding into the lumen. It measured 5 × 2 cm. and was red and inflamed with gangrene appearing imminent at the tip (fig 1) The remainder of the alimentary tract was completely normal, there being no other lesion from which the hæmorrhage might have arisen. Microscopically the appendix showed considerable disorganisation of the various tissues The epithelial cells were hyperplastic with papilliferous formations, and there were accumulations of mucin in some areas, surrounded by epithelial formations suggestive of a mucocele (fig 2) The epithelial nuclei were hyperchromatic and showed frequent mitoses There was also subacute inflammation, with much dilatation of the blood vessels

The only other abnormal conditions found were acute passive congestion of the liver with some fatty change, and mild nephrosclerosis (not excessive for the patient's age)

It was concluded that the cause of this patient's gastro intestinal complaints and of her heavy melæna was complete inversion of the appendix leading to early gangrene of its tip The cause of the inversion was in all probability a mucocele The immediate cause of death was the multiple pulmonary infarctions secondary to thrombosis of the femoral vein

COMMENTS

Neither the clinical picture nor the laboratory and radiological reports suggested the correct diagnosis in this case The profuse bleeding into the bowel in a woman of this age naturally pointed to a carcinoma somewhere along the gastro intestinal tract That an inverted appendix with early gangrene of the tip could cause this hæmorrhage and yet not give rise to some symptoms or signs of trouble implicating the appendix is particularly surprising The complaints had persisted for over three months before death from pulmonary emboli. It is impossible to state whether or not the appendix had been completely inverted for the whole of that time, but one might be justified in assuming that at least partial inversion persisted throughout her illness

We are indebted for the early clinical history to Dr H. J Nicholson and Dr W Latimer who attended the patient before her admission to hospital The photographs of the appendix were taken by Mr George Pendlenton, F.I.M.L.T

REFERENCES

Fraser K (1943) *Brit J Surg* 31 23
Sharby H G (1941) *Acta radiol Stockh* 22 471

THE ÆTIOLOGY OF DUPUYTREN'S CONTRACTURE

E G Herzog
M B Lond
ORTHOPÆDIC REGISTRAR ROTHERHAM HOSPITAL, YORKS

In the two years 1948 and 1949 I saw 20 patients with Dupuytren's contracture at this hospital, 13 attended for the first time, 4 had been on the waiting list from previous years, and in 3 the contracture was an incidental finding For a hospital of 150 beds this seemed a rather large number, and it suggested that Dupuytren's contracture was common in the Rotherham area

Several of the patients raised the question of compensation and would have liked us to say that years of hard work had brought their trouble on It was therefore decided to look into this problem

A review of the literature gives a very confusing picture Astley Cooper (1842) seems to have been first to describe, in 1822, what we today know as Dupuytren's contracture He stated that it was produced by a chronic inflammation of the aponeurosis and thecæ from "excessive action of the hand in the use of hammer, oar, plough, &c" Dupuytren (1832, 1833) established the exact pathology by dissection He, too, thought that trauma was the cause, or, as he put it, it occurred in "people who were obliged to make efforts with the palm of the hand or frequently to handle hard bodies" His first case seems to have been in his own coachman, and the holding of reins for hours on end seemed to him a most reasonable explanation However, already Dupuytren mentions predisposition, and he noticed a similar condition in the foot It is here not quite clear whether he was aware of the thickening of the plantar fascia or whether he was describing what is now known as clawing of the toes

Windsor (1834) stated that his tutor, Henry Cline, jun, had lectured on Nov 8, 1808, on the subject of "permanent contractures of the fingers" and had stated that the "aponeurosis palmaris became contracted and that cutting of it was efficacious"

Since then a very large literature on this subject has grown up, and Skoog (1948) lists over 400 references Trauma, single or long continued, has been put forward as a cause time and again by workers in all countries, but as often as this theory has been advanced it has been refuted. Among the causes given are gout, rheumatism (Hedges 1896), diabetes, ulnar nerve lesions (Hoffa 1921), tuberculosis, arteriosclerosis, hyperparathyroidism, and neurosis (Reeves 1881) It seems obvious from this list that many earlier writers confused conditions such as hysterical contractures, scarring of skin and tendon, nerve paralyses, and stiff joints with a true contracture of the palmar fascia, but we are here only concerned with the question of the influence of hard work on the development of the contracture

RELATION TO WORK

There are three possible relationships (1) Dupuytren's contracture is always caused by hard work, (2) it is never caused by hard work, or (3) hard work is a contributory cause

There can be no doubt that Dupuytren's contracture sometimes occurs in people who have sustained no injury and have never worked hard in their life Holdsworth (1950) states that he has operated on at least three women in private practice Bunnell (1944) describes a case in a boy of 14 Corlette (1944) says that he himself has Dupuytren's contracture and has not done heavy manual work He emphasises the strong evidence that the condition is hereditary, its occasional occurrence in the plantar as well as in the palmar fascia of affected persons, and its tendency to be bilateral The familial element is brought out well in a family reported by Krogius (1921), in which there were 16 cases in four generations

If Dupuytren's contracture were never caused by excessive strain on the palmar fascia, the incidence in manual and non manual workers should be equal, provided that allowance is made for age and that a sufficiently large number of persons are examined to eliminate the error of chance distribution The same investigator should see both groups and should exclude carefully cases of scarring due to burns or to septic wounds and the stiffness following injury or arthritis I believe that it is of no value to investigate the occupation of patients seen at a hospital Langston and Badre (1948) said that, of 88 cases they had collected, 64% were in labourers and 36% in doctors, clerks, and salesmen Kanavel et al. (1929), who found only 30 cases in more than 80 000 admissions, state that there were twice as many non manual as manual workers An objection here is

COMPLETE INVERSION OF THE APPENDIX

T H Boon
M D Durh , M R C P
ASSISTANT PHYSICIAN, ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE

J C Sibley
M D Queen's Univ , Ontario
DEMONSTRATOR IN PATHOLOGY IN THE UNIVERSITY OF DURHAM

Complete inversion of the appendix as a result of a previous mucocele seems to be fairly rare The clinical features of the case described here are particularly interesting because during life there were no signs or symptoms indicating that the appendix was at fault The massive melæna which was a prominent early symptom was especially misleading

Fraser (1943) reviewed the published cases of all types of intussusception of the appendix and added 7 of his own, making a total of 82 Of these, only 8 were proven to be complete inversion of the appendix into the cæcum and uncomplicated by intussusception of the cæcum or of the ileum Further, in only 6 of the 82 cases was there an intussusception of a mucocele of the appendix It therefore follows that the present case represents a relatively rare condition, for not only had there been a previous mucocele of the appendix but also the appendix had become completely inverted, the ileum and cæcum being normal

In a discussion of the clinical features Fraser emphasised that characteristically there is a very severe colic with periods of complete remission between the colics The interval between the onset of symptoms and the establishment of the diagnosis varied from a few hours to a few months Rigidity and other physical signs pointing to a disorder of the appendix were absent in most cases A barium enema helped in a few cases to establish the diagnosis when a shadow like that of a papilloma could be seen projecting into the lumen of the cæcum Skarby (1941) reported 1 case diagnosed radiologically A second radiological examination after the symptoms had abated showed that the intussusception had undergone spontaneous remission

From his analysis of these cases Fraser concluded that the cause of the intussusception in 6 cases was a mucocele of the appendix, other possible causes being an attempt to extrude a concretion, a papilloma, or a foreign body from the appendix If the foreign body or the tumour was in the distal part of the appendix, the intussusception would be of the distal part into the proximal Once developed it may progress to a complete inversion of the appendix or give rise to a compound intussusception, or both

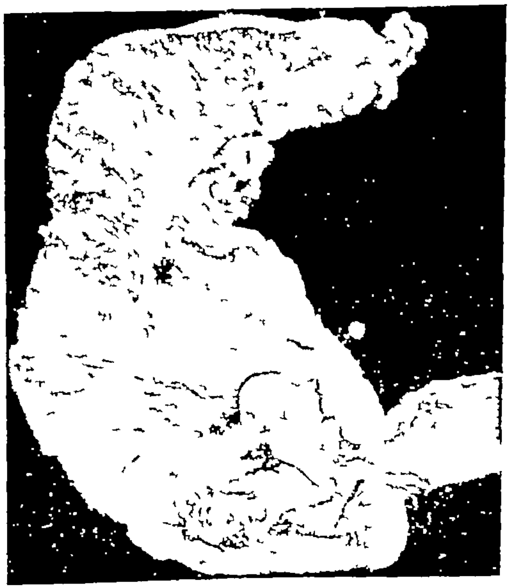


Fig 1—Completely inverted appendix in opened cæcum

CASE RECORD

On the morning of July 24, 1949, a housewife, aged 69, complained of severe diarrhœa, nausea, and passing of blood per rectum Her previous medical history was not relevant Her pulse rate was slightly higher than normal, but there was no evidence of shock There was no abdominal rigidity or localised tenderness, but general moderate tenderness was elicited along the line of the entire colon. Gastroenteritis was diagnosed, sulphaguanidine and kaolin were prescribed, and within a week the patient was well Eight weeks later another attack of diarrhœa came on and two pints of altered blood was passed per rectum. After this episode the patient stayed in bed because of weakness, anorexia, and spasmodic abdominal pain, although normal bowel movements were established within a day or two. On one occasion her physician felt a doubtful mass just below the hepatic flexure She was seen by one of us (T H B.) three weeks later and, because of persisting symptoms, the anæmia, and loss of weight, carcinoma of the alimentary tract was suspected, and the patient was admitted to hospital.

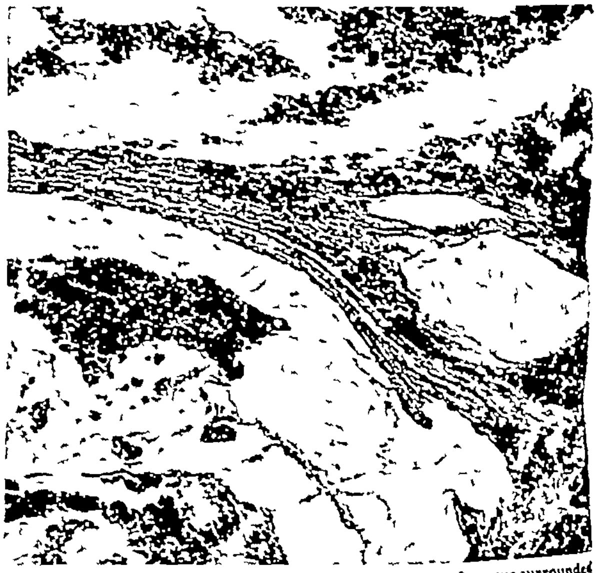


Fig 2—Section of appendix, showing accumulations of mucus surrounded by epithelial formations suggesting mucocele.

In hospital her general condition remained poor for sixteen days, but she made no specific complaint, and repeated abdominal examinations revealed no mass or tenderness Her temperature was normal apart from one rise to 100°F for a few hours Her pulse rate remained at 90-100 Laboratory investigations showed hæmoglobin 58% (8 g), red cells 4,180,000 per c mm , and colour index 0·7 Occult blood was present in three out of four specimens of fæces Gastric analysis revealed free hydrochloric acid No radiological abnormality was detected after a barium meal or a barium enema The diagnosis of carcinoma of the alimentary tract was maintained, and gastroscopy was attempted Difficulty was encountered in passing the instrument, and the examination was discontinued The patient returned to bed in a satisfactory state, but half an hour later she collapsed Her condition steadily deteriorated, and she died fifteen hours later

Necropsy Findings—The body was well nourished, and there were no significant external findings Both lungs were heavy wet, and œdematous the right weighing 510 g and the left 420 g The lower lobes were atelectatic, and section revealed multiple infarcts Almost all the branches of the pulmonary arteries on both sides contained ante mortem thrombi A little red brown fluid was present in both pleural cavities Microscopy of the lungs confirmed the macroscopical finding of recent pulmonary infarction and generalised pulmonary œdema A section through one of the pulmonary

THE LANCET

LONDON SATURDAY, JUNE 16, 1951

"A Very Good Pennyworth"?

"THE building of such hospitals, and maintaining f them, will be a great charge to the public especially fter such a War as we are lately got out of" So hey said in 1714 by way of objection to the ambitious cheme of the Quaker JOHN BELLERS for hospitals in ondon He was ready for his critics "If medicines an be improved, by which the great miseries, that ttend men by diseases, can be to any degree lessened, he purchase will be a very good pennyworth to the ich, as well as a great charge to the poor" Now, wo and a half centuries later, there has been another var The hospital programme for which BELLERS leaded is a fait accompli, but still the question ooms ahead, is it not going to prove too great a harge? Professor VINES, whose letter we print on nother page, comes forward to echo BELLERS in the elief that hospitals are "a very good pennyworth," nd to plead for some attempt to assess the balance n terms of benefit to the community, lest the Chanellor be tempted to stint the pennies Do not our egislators realise, he asks, that the services rendered o some 40,000,000 patients in the year have a nonetary value?

There is much to be said for Professor VINES's oint of view, but if we are going to argue thus we nust do so with our eyes open BELLERS apart, it is new thing to think and speak about hospitals in these terms Public health is one thing, the provision of hospitals something rather different Since the days of CHADWICK the pioneers of public health have not hesitated to indicate the economic value of the measures that they have proposed and carried through, but to speak thus of hospital provision is to enter a new and different field Only here and there have hospitals ever been provided with the conscious motive of economic worth to the community Indeed there is danger in thinking at all in such terms The point has been discussed with vigour by Dr EDWARD CHURCHILL Tracing the history of the non logical (or humanitarian) concept of hospital provision, he writes

> It is of more than passing interest to learn that in England, where the postwar need for industrial production is urgent and skilled labor is in short supply, a logical concept of hospital function in industry has appeared in a few centers such as Birmingham So far neither management nor labor has grasped the utilitarian potential of the hospital"[1]

Dr CHURCHILL, alive to the danger of these trends, adds 'Developments towards scientific precision in the care of an increasing number of patients offer the temptation to regard the hospital solely as a utility"

Reflection suggests that hospitals have in fact a double function It sould seem that, in approaching the still unsolved problem of the limit to be placed on hospital expenditure in the Welfare State, we must apply two distinct criteria One criterion will be the need of the patient for relief from suffering and pain, and escape from the "spectrum of fear" which Dr CHURCHILL describes as ranging "from the negativism of ignorance to a pressing insistence that things beyond all reason be provided and accomplished" The second criterion will be the need of the community for a wise ordering of its resources so that hospitals shall not be stinted when more spent on them would yield a dividend in terms of national income as measured by the economists and statisticians It is idle to pretend that as a profession or as a country we are ready with the answers All we can hope to do for a while yet is to narrow the issues and try to think more clearly about them We can try to get the history clearer—for the hospital history of this last all important half century has scarcely been recorded, save in the most superficial terms We have heard of new buildings and flag days, of the contributory schemes and white papers, but of the uses to which the hospitals have been put, medically speaking, who can speak with any accuracy at all? We can try, too, to get our statistics into order, so that we can know, not only how many patients have been treated by particular hospitals, but whether they benefited or not, when we can do this it may be possible to make a start on Dr VINES's project for a national balance sheet in terms of man hours lost The new Hospital Administrative Staff College established by King Edward's Hospital Fund (which is mentioned on a later page) intends, it is said, not to limit itself to the training of administrators, but to address itself to the task of creating a milieu in which such matters as these can be discussed and clarified and the inquiry now being undertaken under the auspices of the Nuffield Trust into the function and design of hospitals is also likely to provide valuable data

If these efforts succeed, we may yet see a radical transformation of our whole approach to the problem of hospital costs

---

[1] The Hospital in Contemporary Life Cambridge Mass 1949

Familial Leukæmia

IN the transmissible leukæmia of mice at least one of the factors influencing the success or failure of transmission is the animal's genetic constitution Much information has been gathered about the importance of heredity in mouse leukæmia ENGELBRETH HOLM[1] remarked on the lack of firm agreement about the exact mode of inheritance, but observed that inherited susceptibility was a very specific affair, so that one particular strain of leukæmia could be easily transmitted to one family of mice but not to others In order to ensure successful transmission workers use highly inbred, and therefore genetically uniform, susceptible strains, and in addition the animals are previously given a large dose of X rays that temporarily puts out of action their own blood-forming tissues Results obtained with such artificial conditions might be expected to have little relation to human disease, for the genetic uniformity of the susceptible mouse families is never paralleled in man Nevertheless there is some evidence that heredity may influence the incidence of leukæmia in man since it has occurred

---

[1] Engelbreth Holm J Spontaneous and Experimental Leukæmia in Animals Edinburgh 1942

Reviews of Books

ndividual Differences in Colour Vision

R W PICKFORD, M A, PH D, D.LITT, *senior lecturer on* psychology, Glasgow University London Routledge & Kegan Paul 1951 Pp 386 30*s*

ONCE when a doctor ordered a change of medicine for a hospital patient, a nurse was heard to say indignantly "Purgatives are *our* business" The author of this book s a wise man who realises that sensory neurology belongs neither to psychologists nor to physiologists, but o both Starting as an experimental psychologist who found existing tests for colour-vision unsatisfactory and who accepted the Young-Helmholtz theory of colour-vision, Dr Pickford was driven, as the result of his findings, to reconsider this theory and the many others put forward

He used chiefly a pair of rotating discs, made up of Hering's coloured papers, and a specially designed anomaloscope for coloured filters Other subsidiary methods confirmed his results He could find no evidence of the third kind of colour-blindness due to absence or weakness of the blue receptors, and to be expected on the basis of the Young-Helmholtz theory Moreover, he found that yellow vision could vary independently of red, green, and blue sensitivities, and could be normal n the red-green blind Further, brightness-level was associated in some degree with hue sensitivity, but not always in a positive way, and to a large extent it was ndependent This strongly suggested the hypothesis of a special brightness receptor Dr Pickford tested over 1100 people, and he found neither sensitive normals nor variations nor abnormalities which could not be accounted for by the existence of four primaries, red-green and blue yellow, and a receptor for brightness He therefore believes that all observed facts of colour-vision are adequately explained by the theory of Hering with its modification by Houston, provided white is accounted for, perhaps as in Granit's theory Other interesting conclusions relate to the sex-linked red green colour vision defects, and a number of pedigrees are given Further points brought out are the absence of sex linkage in the blue yellow defects, and the relationship of colour defects to race

This book is a well arranged and clearly written account of careful work Though definite in his views, Dr Pickford is reasonable about the beliefs of those who think differently, and whether his readers agree with him or not, they cannot fail to be stimulated

Functional Anatomy of the Limbs and Back

W H HOLLINSHEAD, PH D, head of the section on anatomy, Mayo Clinic, Rochester, professor of anatomy, Mayo Foundation, University of Minnesota London W B Saunders 1951 Pp 341 30*s*

Professor Hollinshead is to be congratulated on his attempt to present a readable account of anatomy for "students of physical therapy and others interested in the locomotor apparatus" The book has been written primarily for students with only a slight knowledge of biology, and it undoubtedly meets the need of those studying physiotherapy or occupational therapy, for it bridges the gap between the small books and the larger tomes

The book provides a broad outline of the locomotor system and it has preliminary sections on histology and the general characteristics of the organs, brief surveys of the head and neck, thorax, and abdomen are included In the description of the limbs emphasis is laid on surface anatomy—an aspect especially important to those who have not the opportunity to dissect the body The text is supplemented by over a hundred diagrams On the whole these are simple and clear and those of muscles usually indicate their actions Perhaps, on occasions, the diagrams are over simplified for instance, in some of those devised to show muscle actions, reference points such as the general attachments of the muscles are omitted A few diagrams would have been improved by enlargement

Objection might possibly be made to the nomenclature Most commonly the anglicised form of the B N A terminology is used in preference to the Birmingham revision, and this may give rise to confusion in those countries, such as Great Britain, where the B R is generally accepted Occasionally, B R words are used in place of those of the B N A This criticism could be made of other American works, but in these the alternative nomenclature is usually given in parenthesis Again, too much space seems to have been devoted to certain groups of muscles where precise information is relatively unimportant—for instance, the deep muscles of the back and of the suboccipital triangle, the muscles of facial expression, the small muscles of the foot, and the serratus posterior superior and inferior Space saved by omitting or condensing these descriptions could usefully be employed to amplify the anatomy of the central nervous system, and to include a section on posture and locomotion. Nevertheless this is an excellent book which can safely be recommended to those for whom it is intended

Selected Studies on Arteriosclerosis

R ALTSCHUL, M U DR, professor of histology, University of Saskatchewan Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1950 Pp 18 40*s*

THOUGH this work deals almost entirely with the histology of experimental arteriosclerosis the clear descriptions and excellent photomicrographs will interest the clinician as well as the pathologist Professor Altschul's experiments on cholesterol arteriosclerosis were carried out with 14 different techniques, he describes the changes produced in the vessels, and also gives a detailed account of cholesterolosis of organs and tissues He concludes, however, that forty years' work on experimental cholesterol arteriosclerosis has thrown little or no light on the problem of arteriosclerosis in man But Altschul's investigations show that the histological approach is not sterile, though the biochemist may ultimately solve the problem he can do so only in association with the morphologist

Tumors of the Head and Neck

G E WARD, M D, D SC, F A C S, J W HENDRICK M D, M S Baltimore Williams & Wilkins Co London Baillière, Tindall, & Cox 1950 Pp 832 114*s*

THIS book places proper emphasis on early diagnosis and on the value of biopsy The authors recognise the need for the clinician treating malignant disease to have a sound knowledge of pathology, and this aspect is dealt with in each section Throughout this work they compare surgical and radiological treatment, and proclaim their choice as a result of years of experience in each The necessity for adequate follow-up is not overlooked but rather than the recommended 5 year period some workers would prefer reviews at lengthening intervals for the rest of the patient's life

In the section on cancer of the tongue and floor of the mouth, the work of Butlin is highly praised, and his advice to remove all small pre malignant lesions is quoted at length The authors state "if this advice of Butlin had been followed down through the years and all small pre malignant lesions removed, many lives would have been saved the horrible death from lingual cancer" For most cases of cancer of the tongue and floor of the mouth the authors recommend preoperative irradiation followed by hemiglossectomy and block dissection of the neck They suggest that all mixed tumours of the salivary glands should be completely excised, but they point out that in some series the recurrence rate has been as high as 40 %, and they attribute this to inadequate removal. There is some force in the argument that if such a tumour is small and not increasing in size, it may be left alone and the patient kept under observation, but since practically all salivary-gland tumours are radio resistant treatment is wholly surgical The authors are justifiably anxious to extend the surgical treatment of carcinoma of the tonsil They point out that the outlook for the patient with cancer of the hypopharynx and base of the tongue is not good but there is cause for hope that with surgery the outlook for these patients will be much brighter Regarding cancer of the larynx, they express the opinion that greater standardisation of techniques is necessary for accurate comparison of the value of surgical and irradiation therapy, particularly in the early cases

This work is stimulating and useful it contains much valuable information The illustrations are profuse and clear and the whole book is beautifully produced it was held to be "as unscientific as it was unfashionable", but recent advances have changed the picture Last year, with the Medical Research Council, the foundation received 1 kg of 'Cortisone' from Merck & Co, of New Jersey, for clinical trial in this country, and the two bodies have set up a joint committee to allocate the drug In continuation of this side of its work the foundation also made last year a grant to the University of Cambridge to survey the incidence of rheumatism in East Anglia, to the University of Birmingham for research by Prof M Stacey, D SC, F.R S, on the organic chemistry of tendons, cartilage, and tissues, and to Birkbeck College, where Mr D H R Barton, D SC, is attempting to synthesise cortisone from ergosterol. In all, from an income of £550,000 the foundation has distributed over £336,000 It seems to have been money well spent

SIR WILLIAM GOODENOUGH

Sir William Goodenough, who died on May 23, had many interests in addition to his profession of banking His activities in medicine grew over a period of many years, starting in Oxford where he was treasurer of the Radcliffe Infirmary This interest soon spread from the purely financial affairs of hospitals to the whole field of hospital administration. He was quick to see the need for coördinating the service provided by voluntary and local authority hospitals With the late Alderman William Hyde he was responsible from the beginning for the organisation and administration of virtually all of the Nuffield benefactions As time passed these benefactions covered a very wide field in medicine Goodenough was chairman up to the time of his death of the Nuffield Provincial Hospitals Trust, whose basic object is the coördination on a regional basis of the hospital and ancillary services It is not, perhaps, generally known that the trust's groundwork in the regional field was largely accepted as a basis for the hospital organisation under the National Health Service Goodenough was governing trustee of the Nuffield Medical Fund for the University of Oxford, which established a series of clinical chairs at the Radcliffe Infirmary in an attempt to raise the status of clinical medicine in Oxford to the very high level attained by the preclinical departments Many other trusts owed their inception to the inspiration of Lord Nuffield, Will Goodenough, and William Hyde The last and greatest benefaction was the Nuffield Foundation, which, although not confined to medicine, has already done much to further medical education and research. Goodenough was the original chairman of the foundation, and its work was very near to his heart

Goodenough's interest in medical education was recognised when he was appointed chairman of the Inter Departmental Committee on Medical Schools, soon to be known as the Goodenough Committee The report of this committee was issued in 1944 and has largely been accepted as the official blue print for the development of the medical schools of Great Britain In two years the committee covered an immense amount of ground, both literal and metaphorical, under difficult war time conditions

Will Goodenough's boyish enthusiasm endeared him to all who knew him It was a great experience to sit on a committee of which he was chairman He often jokingly pretended that he knew nothing of medical matters, but it was unwise to accept this He had a wonderful capacity for getting on with the business of a meeting without obvious haste He would encourage the hesitant, check the garrulous, and destroy the cantankerous with a charm that left no rancour, but only respect and affection Withal he was often in private diffident and humble to an extent which those who did not know him well found difficult to believe His services to medicine were very great, and his understanding will be sorely missed

INTRAVENOUS ADMINISTRATION OF ALCOHOL

NOWADAYS ethyl alcohol has little place in routine medical treatment, though whisky, brandy, or champagne are still prescribed sometimes as a pleasant adjuvant in threatened circulatory failure From medieval times alcoholic fumes were used for anæsthesia, and its intravenous administration was described as early as 1668 [1], but, because of the complications, this technique did not become popular

In modern times the complications of intravenous administration have been found to include agglutination or hæmolysis of the erythrocytes, shock, decreased urinary output, and sclerosis of the blood vessels, but these effects do not appear unless the blood alcohol concentration exceeds 30%, and over 2000 infusions of 5–10% of 95% alcohol in saline or glucose were given without ill effect [2] The physiological action of alcohol administered parenterally is manifold, it has sedative, hypnotic, analgesic, euphoric, vasodilator, and energy functions It causes mental sedation with dulling of the memory accompanied by loss of anxiety and a sense of well being, it also increases the respiration rate and pulse-rate, and so the body temperature may fall slightly Thinking remains fairly normal, and the patient does not feel doped It lessens the sensitivity to pain by affecting first the cerebrum and lastly respiration, in contrast to morphine which depresses the cerebrum and respiratory centres simultaneously According to Mellanby,[3] a normal person receiving alcohol by mouth can metabolise 10 ml. in an hour About 98% of the alcohol is completely oxidised as a nutrient for immediate use, and this rate is constant regardless of the concentration in the blood Thus parenteral administration of a solution of 5% alcohol in 200 ml glucose within one hour should be safe, and at this rate up to 100–150 g alcohol can be administered per 24 hours in 2–3 litres of glucose or saline [2 4]

Attempts have been made to employ intravenous alcohol during induction of anæsthesia,[5] but it has been used mainly for the postoperative period. Karp and Sokol,[4] who administered it to 2000 surgical patients in a 5–10% solution, found that opiates and other sedatives could be entirely eliminated They suggested that the first 200 ml. should be infused within 20–30 minutes, and a further 800 ml. within 3–6 hours In the postoperative period alcohol intravenously may have some value, not only as a sedative and analgesic that does not provoke nausea, but also possibly by preventing pulmonary complications and atelectasis through its influence on the respiratory centres It seems also to improve the motility of the gastro intestinal tract and to increase the tone of the bladder At the same time it improves the immediate postoperative nutritional state by supplying about 550–900 calories in 1 litre of glucose saline Karp and Sokol,[4] like Mueller [2] emphasised its merits in undernourished geriatric patients and Behan has used it as a postoperative sedative since 1925 [6] During the postoperative period some patients, especially the elderly, who have been ill for a long time may become acutely depleted of the B vitamins,[7] which should thus be incorporated in the drip There is one further possible indication for this therapy Brown [8] and later Gillespie [9] described its application in status asthmaticus, and both underlined the prompt effect

---

1 Macht, D J *J Amer med Ass* 1916 66 856
2 Mueller S *Surg Clin N Amer* 1939 19 401
3 *Spec. Rep Ser Med Res Coun Lond* 1919 no 31
4 Karp M. Sokol J K *J Amer med. Ass* 1951 146 21
5 Moore D C Karp M. *Surg Gynec Obstet* 1945 80 523
6 Behan R J *Amer J Surg* 1945 69 227
7 Leitner Z A *Brit med J* 1948 i 917
8 Brown E A *Ann Allergy* 1947 5 193
9 Gillespie J D *Rocky Mtn med J* 1949 46 547

of all the available information, including the recommendations of the Spens Report already accepted by both sides In other words, let both sides get together and look at the merits of the case, knowing that there is common desire to apply new monies where the shoe pinches most "

The Ministers' reply did not exclude this wider discussion, but the final paragraph of their letter makes it clear that whatever the findings of any such wider investigation the resultant settlement could be no different

> "The Ministers feel that they ought to make it clear, however, that they could approve proposals which would involve additional Exchequer money only if they covered the points mentioned in the letter of the 23rd May, and that the maximum amount of additional funds which can be made available under present circumstances is £2 million a year "

Faced with this categorical reiteration, the committee felt they had no alternative but to call a special conference of local medical committees, to seek instructions for future action For its part the committee feels that the right course would now be for the Minister of Health "to refer to arbitration the determination of the proper size of the central pool, having regard to the recommendations of the Spens Report and to present day money values " Once the proper size of the central pool had been determined by arbitration the committee would be willing to help "to apply a form of distribution which is in accordance with the recommendations of the Spens Committee and which will enable the best possible medical service to be available to the public "

The gist of this report was made available at the Annual Representative Meeting of the B M A on Thursday

PSEUDOCYESIS—A PSYCHOSOMATIC DISORDER?

THE somewhat cursory account of pseudocyesis that is to be found in most standard textbooks of gynæcology always contains some mention of the patient's mental state, and a report by Fried and his colleagues[1] may throw more light on possible endocrine mechanisms effecting the interaction between psychic and somatic components of the disorder

Bivin and Klinger[2] collected the records of 444 cases in 1937, and apparently only 21 have been reported since then Probably many cases are missed, for in the series now described by Fried et al the case incidence was 1 in 250 of the admissions to a maternity clinic In their series of 27 cases the patients' ages ranged from 18 to 36 All were married, and only 1 had a living child, 11 had never been pregnant The total number of pseudocyesis episodes observed was 36, some patients had had as many as 4 Usually menstrual function was disturbed, 19 patients had hypomenorrhœa, and 7 had amenorrhœa 24 had abdominal swelling Breast changes were common, consisting of enlargement, tenderness, venous engorgement, secretion of cloudy or milky fluid, and darkening of the areola 22 of the women reported fœtal movements In 19 the cervix was found to be softened, of these, 11 had some uterine enlargement but never beyond the size of a six week gestation Increases in weight were usually greater than in normal pregnancy Other symptoms of pregnancy were sometimes present, such as nausea, increased frequency of micturition, and faintness Fried and his associates acknowledge that pseudocyesis may tax the diagnostic acumen of the ablest doctor of their 27 patients 9 had been diagnosed as pregnant by several experienced physicians Wrong diagnosis may give rise to psychological and medicolegal complications In this series the main psychogenic factor was thought to be the intense wish for a child, often motivated by a precarious marital situation, and complicated by superstitions and by early experiences and teaching which had produced fears of pregnancy, but no very convincing evidence for this conclusion is given

By hormonal assays, vaginal smears, and endometrial biopsies it was decided that these women had persistent luteinisation of the ovaries This was believed to be due to ovarian stimulation by the pituitary lactogenic (luteotropic) hormone, and Fried thinks that the psychic factors acted on the endocrine system by pathways from the cortex through the hypothalamus to the anterior pituitary, causing release of the luteotropin and suppression of the follicle stimulating hormone For therapy the patient was first informed of the diagnosis, and this was followed by a psychiatric interview and in some cases psychotherapy, and finally endocrine therapy Curettage was done in some cases Fried argues that just telling the patient the truth is not enough, at best it will only produce a symptomatic cure, with ultimate recurrence, and it may cause suicidal depression The aim of psychotherapy was to get the patient to understand the reasons for her condition Patients who gained only limited insight required adjuvant therapy such as testosterone propionate, to evoke menstrual bleeding, or curettage to demonstrate conclusively that the uterus was empty

THE NUFFIELD FOUNDATION

THE Nuffield Foundation is the responsible and discerning administrator of large funds It has always considered that this trust includes the duty of tendering each year a full account of how it has spent its money and of why it has backed particular ventures, and its sixth report[1] is at once a record of the work of the foundation for 1950–51 and an affirmation of policy

The foundation is now well embarked on its second five year plan It has two avowed aims for this quinquennium The first—to support fundamental biological and social studies—has found ready response. The foundation last year allotted £46,000 to biological projects, including grants to the University of Cambridge for the completion and development, under Prof. F G Young, D SC, F R S, of a mass spectrograph, and for equipment for a team of research workers led by Mr A L Hodgkin, F R S, who are studying the interior of living cells Another grant has been made to University College Hospital Medical School, where Prof C Rimington, PH D, is establishing a unit to investigate the chemistry and biochemistry of blood and the blood pigments in health and disease The grant to the department of Prof J Z Young, F R S, at University College, included provision for bringing electronics to bear on biological problems One result, the flying spot microscope, has already been described in our columns[2] A further £111,000 was allotted to sociological research, and from this sum grants were made for community studies to the University of Birmingham for a midland market town, to the University of Leeds for a local industrial village, and to the University of Liverpool for a dock working community But the foundation's second aim—to encourage specialists to tackle the practical application of abstract knowledge—is apparently proving less attractive An investigation into African education is planned for next year, but it is proving difficult to find contemporary problems on which, without the stimulus of war, scientists are willing to work for the sake of a solution rather than for the sake of new knowledge

The only specific disease with which the foundation is concerned is chronic rheumatism When in 1947 the foundation first began to finance research in this disease,

---

[1] Fried P H Rakoff A E Schopbach R R Kaplan A J *J Amer med Ass* 1951 145 1329

[2] Bivin G D Klinger M P Pseudocyesis Bloomington Indiana 1937

[1] Report of the Nuffield Foundation 1950–51 12 Mecklenburgh Square London W C 1

[2] *Lancet* March 31 1951 p 729

INTERNATIONAL CONGRESS OF ORTHOPÆDICS

THE Fifth Congress of the International Society of Orthopædic Surgery and Traumatology was opened in Stockholm on May 21 by Prof. Sten Friberg, in the presence of the King of Sweden. The congress was an outstanding social, as well as scientific, success. Hundreds of members from many countries attended with their wives; the exhilarating sunshine of the Swedish spring, the beauty of the city and its waterways, and the lavish entertainments provided by their hosts, culminating with a memorable banquet on the last day of the meeting, left them with the happiest memories of the occasion.

Professor Friberg, reviewing the evolution of orthopædic surgery, suggested that too much emphasis had been laid in the past on purely mechanical aspects; in future it would be necessary to incorporate the great biochemical and biological advances of recent years. This note was struck by many contributors to subsequent discussions.

LOW BACK PAIN AND SCIATICA

Dr. JOSEPH BARR (U.S.A.) reminded his audience that these pains were cerebral and not located, as all patients and too many doctors believed, in the low back and sciatic region themselves. Psychosomatic aspects deserved greater attention, for the unit of treatment was the patient and not his back; it was as important to know what sort of patient had a disease as what sort of disease the patient had. The great technical success of disc surgery (for which, incidentally, Dr. Barr might justifiably have taken most of the credit) must not obscure the fact that at least one third of all patients recovered spontaneously from their first attack, often completely and for ever. And while it was true that 80% of operated cases did well it would be wise to begin to pay some attention to the failures and complications of operation. He still thought myelography advisable, despite the trend away from it, because of the risk of overlooking nerve root tumours or of removing the wrong disc; there was little harm in using a safe water soluble medium which was removed at the same sitting. The surgeon should not delay a necessary operation, for otherwise irreversible root fibrosis and degeneration might develop. He must select cases carefully, always treat the considerable mental component of the disease, and avoid surgery in cases of rapidly progressive degeneration of many discs, which did badly after operation. Operative mortality should be less than 1%, due usually to pulmonary embolism. There was sepsis in some 4% of cases, but superficial sepsis was far less important than the grumbling obscure infection of an intervertebral space which came on with slight symptoms some weeks after operation. Operation inevitably traumatised the elastic spinous ligaments, replacing them with scar, the nerve roots, and sometimes the facets. Structure and function were always somewhat impaired; the dilemma was between minimal exposure and removing enough of the normal architecture to see the lesion properly. Excessive fibrosis, an internal keloid, was particularly likely after facetectomy and might necessitate spinal fusion. Operation could be relied on to relieve sciatica in 9 cases out of 10, but at least every other patient with initial severe low back pain still had trouble with his back after simple laminectomy, and so a combined operation with fusion was preferable. Careful comparison of results showed that the combined procedure offered a moderate but definite advantage over the simpler operation.

Mr. ROBERT YOUNG spoke of the results of operation in nearly 1000 personal cases.[1]

Dr. L. POUYANNE (France) reminded the meeting that, because the operation was so recent, the follow up could only be recent; the 20–30 years results were unknown. As the surgeon's experience increased his number of negative explorations decreased, and so did the width of his exposure. It was the 4th lumbar disc that was notorious for recurrences. He fused the vertebræ in only 10–15% of cases and found the indications for fusion still very indefinite; different surgeons often had very different clientèles, and in many cases tables of results could not be meaningfully compared.

Dr. RALPH GHORMLEY (U.S.A.) discussed 2000 cases in which low back pain, with or without sciatica, was a major symptom, which were seen at the Mayo Clinic in a single year. These showed clearly that there were very many causes of such pain other than disc prolapse, even if the number of cases in some of the individual categories might be few. In his series disc lesions accounted for only 22% of cases.

In the discussion the rôle of the intervertebral facets aroused opposing views; some denied altogether that they were ever responsible for symptoms, while others—notably Dr. EDOUARD SAMSON (Canada), M. DELCHEF (Belgium), and M. MARINO ZUCO (Italy)—regarded facet arthritis, often based on anomalies of articular tropism in the lumbar region, as of great intrinsic importance. Swedish workers favoured myelography in diagnosis of disc prolapse. Dr. FOLKE KNUTSSON remarked that a rapidly absorbed water soluble medium, such as 20% 'Abrodil,' need not be removed, though, owing to its irritative properties, preliminary spinal anæsthesia was necessary. Dr. K. LINDBLOM described a striking technical advance which he has introduced—discography, in which the opaque medium is injected directly into the nucleus under radiographic screening, using a transdural approach. The value of this method was confirmed by Dr. P. ERLACHER (Austria). When the offending disc was injected the characteristic pain was evoked; discograms (perhaps we should say nucleograms) were sometimes positive when myelography was negative, and, for those who operated in the lateral position, they indicated the most likely side to approach in cases with bilateral symptoms.

A number of valuable contributions from Swedish investigators dealt with the basic problems of the structure and the normal and pathological physiology of the intervertebral disc. Dr. B. SYLVEN showed some beautiful electron microscope studies demonstrating the three dimensional lattice-gel system of the healthy nucleus pulposus. The fibrils exhibited the typical periodicity of collagen, and were closely bound chemically to the interfibrillar polysaccharide which was responsible for the great water binding power of the nucleus. Disc degeneration with age might consist of a physiological disappearance of this mucoid material, which seemed to be chondroitin rather than hyaluronic acid, with consequent dehydration and fibrillary overgrowth. Dr. PAULSON and Dr. SNELLMAN described physical methods of measuring rates of diffusion within the nuclear mesenchyme.

Mr. JOHN CHARNLEY (Great Britain) described some experiments demonstrating the enormous pressures which could develop within the disc owing to its hydrophylic properties—a hydrophilia of colloid imbibition and not an osmosis—and suggested that acute episodes of turgidity might account for recurrent lumbago or actual herniation. Many other speakers discussed methods and results in lumbosacral fusion, and Dr. L. HULT (Sweden) aroused much interest with his operation of retroperitoneal fenestration of lumbar discs, done as a relatively blind decompression procedure after careful nucleographic study of the last three discs. But it was left to Mr. BRYAN MCFARLAND to voice characteristically, in a delightful

---

[1] Burns, B. H., Young, R. H. *Lancet*, Feb. 3, 1951, p. 245.

REMUNERATION OF MEDICAL ADMINISTRATORS

ON a later page we print the Industrial Court's award on the claim of administrative medical officers in the hospital service This award acknowledges the responsibility that these doctors carry, by placing their remuneration more or less on a par with that of consultants Other medical administrators—and notably full time public health workers, who even after the recent increases[1] still count themselves at a financial disadvantage—may be tempted to envy their colleagues in the hospital service, but this latest amendment will provide a strong point in favour of public health workers when next their remuneration comes under review

TUBERCULOSIS IN NEIGHBOURING HOUSEHOLDS

SOMETIMES the essential findings of work involving a great amount of detailed study can be stated in one sentence. This is true of an investigation[2] which has shown unequivocally that in the period 1921–48 notifications of tuberculosis from adjacent houses in a typical county borough (Northampton) were more common than would be expected on a random basis, and, further, that these second notifications tended to occur more often within twelve years than would be expected This result has been obtained only by close study of all notifications in the period and by new statistical techniques House to house infection is the most likely explanation of the result, but it is perhaps unfortunate that Dr Josefine Webb and Dr Alice Stewart, the authors of this study, do not consider other possible causes more fully True, they exclude the possibility of bias from relations living next door to each other, but there are surely other possibilities For example, could the result not have been produced by a tendency for neighbours to present themselves for examination when a case of consumption has been found next door? There is a large, though diminishing, pool of undiagnosed cases, and any one group that is examined more often than others may be expected to have a relatively high notification-rate

It seems, however, that spread of infection accounts for at least some of the excess The increasing number of workers who attach little importance to superinfection would attribute the preponderance to primary infection of neighbours and their children There is, indeed, some evidence for this view, for the inclusion of the small number of meningeal and miliary cases with the pulmonary cases increases the percentage excess of notifications in next door houses from 16 to 20 Since pulmonary notifications are about 15 times as numerous as miliary plus meningeal, it appears that a large part of the excess may be due to the tragic sequelæ of primary infection Because of this, and the fact that the excess of notifications for other types of tuberculosis was apparently small, it would have been interesting to know something of the state of the milk supply to the town if for a large part of the time much tuberculous milk was being consumed "other tuberculosis" and, to some extent, meningeal tuberculosis could not be expected to occur especially often as a result of proximity to human sources of infection Since so much information is given to show that the notifications and deaths for the town follow the usual pattern with regard to housing, economic circumstances, and occupation, this omission is surprising

This investigation does not seem to indicate a need to alter current practice in the examination of contacts, for, while second notifications from the same house were more than three times as common as would be expected, notifications from adjacent houses were only one third more common, and thus the number of cases found would scarcely justify the effort It would seem reasonable, however, to examine neighbours when they have been in close contact, or when the source of a primary lesion in a child cannot be found Obviously special care is necessary in some of the new housing estates where a high proportion of families have been re housed because of a case of infectious tuberculosis in the household

BAGS UNDER THE EYES

"DISCUSS bags under the eyes" would be an interesting, if unpopular, question for the final examination This common and unsightly condition is often secondary to renal or cardiac disease or hypothyroidism, and treatment of these disorders may cause the bags to diminish or disappear But there remain the bags which "just growed" What of these? Some light—albeit dim—has been thrown on this question by four anonymous authorities[1] It seems that various types of food or inhalant allergy are occasionally responsible for bags under the eyes Drug allergies and allergy to cosmetics may also be involved Then again, local stasis or œdema in the loose vascular tissue of the lower eyelid may reflect even slight changes in muscle tone, elasticity of the skin, or other factors relating to the patient's general condition Anæmia, malnutrition, and late pregnancy are other conditions which may give rise to bags under the eyes. It is gratifying to learn that bags are "not necessarily an indication of debauchery and dissipation" The size of the bags may vary at different periods of the year or times of day, relative cardiac insufficiency, not enough to be diagnosed clinically, may produce "evening bags" Bags under the eyes may be familial One of these American authorities states frankly that "no one knows the exact cause of this condition"

BIRTHDAY HONOURS

THE promotions and appointments to the orders of chivalry announced this year on the King's Birthday include five new medical knights and—a greater rarity—a medical dame Dr G S Todd, who is promoted from C V O to a knighthood in the Royal Victorian Order, has been, since 1934, superintendent of the King Edward VII Sanatorium, at Midhurst, in which the Royal Family have always taken much more than nominal interest Prof Hilda Lloyd, F R C O G, who becomes a dame of the British Empire, is the first woman to have presided over one of the Royal Colleges, and she has created a valuable precedent with dignity and tact

The new knights bachelor include Mr P S Messent, director of surgical studies at the University of Adelaide The remaining accolades will fall on professional shoulders nearer home Prof C A Lovatt Evans, F R S, has not only held three chairs of physiology and served University College as an outstanding medical dean, but has presided over Government committees and taken part in the counsels of the Royal Society and of the Medical Research Council He spent the late war on Salisbury Plain as principal scientific officer at the Experimental Station, Porton Mr E F Finch, a vice president of the Royal College of Surgeons and lately professor of surgery in the University of Sheffield, has long shown special concern for the organisation of a cancer service to provide timely diagnosis and treatment Dr J W McNee is physician to the King in Scotland and holds the regius chair of medicine in Glasgow, but beyond the borders of Scotland many will remember him as a surgeon rear admiral in the late war The profession may be rightly proud of the long list of other medical honours, reproduced on another page, for it testifies to work well done in all parts of the world.

---

[1] See *Lancet* 1950 ii 918 *Ibid* Jan 6 1951 p 58 *Ibid* May 26 1951 p 1176

[2] Webb J Stewart A *Brit J soc Med* 1951 5 13

[1] *J Amer Med Ass* 1951, 145, 858

d receive any additional food, during the second six months of the homes, Vogelnest, would ipplied with unlimited amounts lditional bread, so that all the lren could satisfy their appetites ıe full. Extra jam would also rovided to spread on the bread, concentrated orange juice to e as a drink Supplementary d had already been shown to note excellent growth at another ıanage (Widdowson 1948) Dur- the second six months the lren at Bienenhaus would con- e to be weighed and measured before but would receive no itional food. In this way it hoped to get a direct com son of the growth rate of dren with and without the itional bread

'he children were weighed naked r emptying their bladders, and measurements were always made at the same time lay, at least four hours after the last meal

ls the first six months went by it became apparent t the children were gaining weight at very different es at the two homes A group of boys and girls of these s should gain an average of about 1 4 kg in six months Brien et al. 1941) At Vogelnest the average gain was ıost exactly 1 4 kg , at Bienenhaus the mean gain was s than 0 5 kg

)uring the second six months the position was reversed spite of the extra food provided for the children at gelnest, their average growth rate was less than it d been during the first six months when no additional d was supplied (fig 1) At Bienenhaus, on the other nd the weight curve immediately began to rise steeply, hough these children were getting only their German ıons as before. There was clearly some other factor work which was more than counteracting the beneficial ect of the additional food we supplied

At the beginning of 1948 Bienenhaus was in the arge of Fräulein Schwarz, while Vogelnest was esided over by Fräulein Grün Just at the time when e additional food was first provided at Vogelnest it so ppened that Fräulein Grün left the orphanage to take charge of a children's convalescent home at the seaside Fräulein Schwarz was thereupon transferred from Bienenhaus to Vogelnest, and a third woman, Fräulein Weiss, came to take charge at Bienenhaus Fraulein Grün and Fräulein Weiss were very similar in temperament, bright, happy persons, genuinely fond of the children and the children of them Fräulein Schwarz was quite different She was older, rather stern and forbidding, and she ruled the home with a rod of iron Children and staff lived in constant fear of her reprimands and criticisms, which sometimes seemed quite unreasonable For instance, one day a child was scolded for wearing gloves and getting them wet, the next day the same child was in disgrace for not wearing gloves Fraulein Schwarz often chose the times when the children were at their meals to administer public rebukes and would single out individual children for special ridicule The children had to sit in silence while this was going on, with their bowls of soup in front of them By the time she had finished the soup would be cold, all the children would be in a state of considerable agitation, and several of them might be in tears

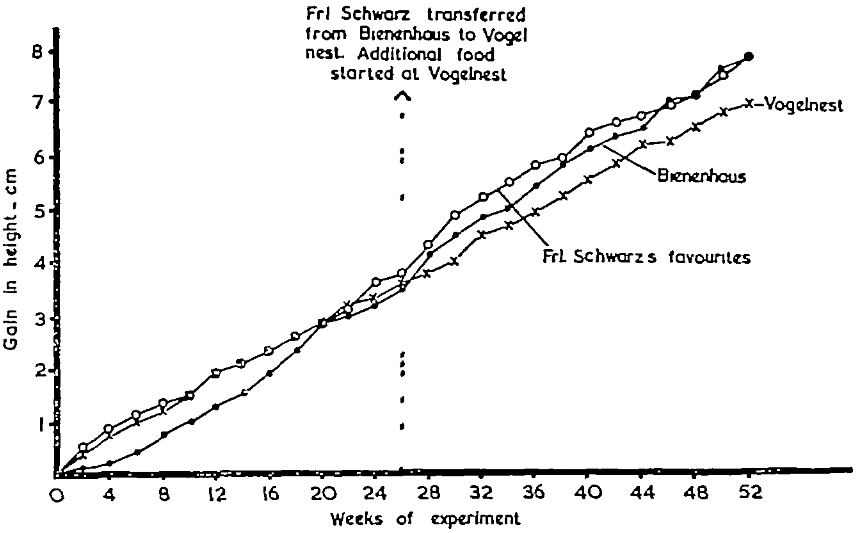


Fig 2—Average growth in height.

Fräulein Schwarz had her favourites, however, and when she was transferred from one home to the other she persuaded the authorities to allow her to take these eight children with her These children could do no wrong and they were always assured of praise rather than blame Their average growth curve has been plotted separately from the others in fig 1 During the first six months, while they were at Bienenhaus, these children gained more weight than the others in the same home, and from the day they went to Vogelnest and got the additional food they started to put on weight very rapidly, so that in the next six months they gained more than twice the standard amount

Growth in height did not seem to be subject to emotional influences to such an extent as weight (fig 2), but the same trends can be seen

Records were kept of the amounts of food eaten by the children at various stages of the experiment The calories pro

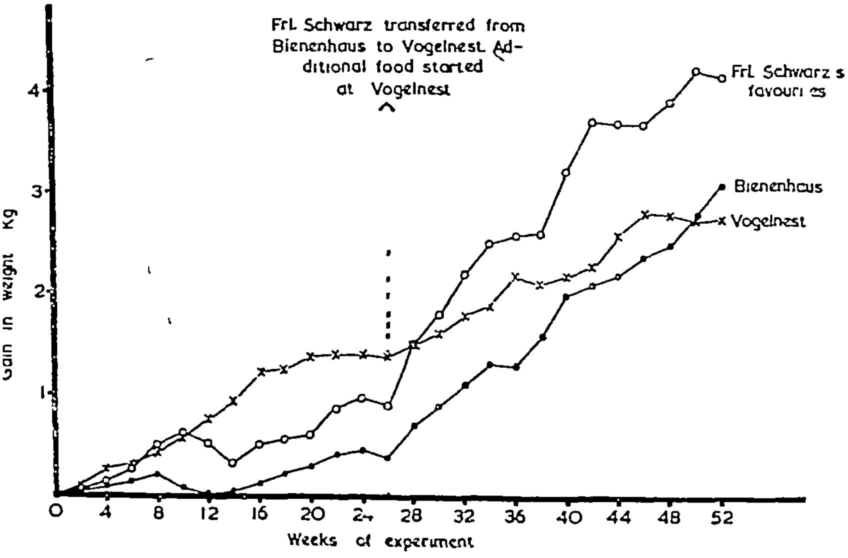


Fig 1—Average growth in weight

mixture of French and English, a general feeling against "trop d'interventions sanglantes" in these cases A disc prolapse was only an acute episode in a chronic spinal disorder, and both conditions could and should be managed conservatively in the great majority of cases

AVITAMINOSIS AND OSTEOPATHY

Dr R **Zanoli** (Italy) gave an exhaustive review of the influence of vitamins on the structure and function of bones and joints, and contributions were added by several other Italian workers Dr **Annovazzi** discussed his experiments in modifying Selye's formalin arthritis in guineapigs by deprivation of ascorbic acid Dr E **Kodicek** (Great Britain) had also studied the effects of ascorbic acid deficiency on joints and the healing of fractures and soft tissue wounds in the guineapig, chronic deprivation produced a condition in the knees closely resembling rheumatoid arthritis in man

CONGENITAL DISLOCATION OF THE HIP

Here again there was disparity in views on treatment Among the more conservative Dr E **Severin** (Sweden) maintained with some convincing arthrographic studies that closed reduction should be the standard method of treatment In most cases there was soft tissue interposition between femoral head and acetabulum immediately after reduction, but this interposition usually disappeared spontaneously and did not in itself call for operation Dr A **Trèves** (France) also favoured conservatism, with early functional splintage allowing free movements except adduction, to mould the head and acetabulum and undo any excessive anteversion of the femoral neck Dr E **Platou** (Norway), on the other hand, stated that at least half the cases were left with marked anteversion, and advocated more general performance of rotation osteotomy In this he was supported to some extent by British visitors—Mr J H **Seddon** and Mr **David Trevor**—who had found a need for rotation osteotomy or acetabuloplasty in selected cases which were not doing well.

SOME OTHER TOPICS

Dr P K **Duraiswami** summarised the experimental work done by him at Liverpool on the causation of skeletal abnormalities by injecting insulin into chick embryos—work which has already been reported,[2] and which may be of the greatest significance for orthopædic surgery in the future Prof J **Trueta**, noting that osteomyelitis in which the shaft was primarily involved was often accompanied by overgrowth of long bones, had surmised that this might be due to obstruction of the medullary circulation with a re routing of blood to metaphyseal and epiphyseal vessels, so stimulating epiphyseal growth This was confirmed by experimental ligation of nutrient arteries to the shaft, and the way was now open for the first time to stimulate growth in short limbs by blocking marrow circulation with a bone graft until the inequality in leg length was made up But the results would take much time to assess

Various workers, including Dr **Svante Orell** (Sweden), discussed the effect of chemotherapy on the management of surgical tuberculosis Earlier and more radical operation was now possible, without the risk of spread of the disease Joint disease might heal without loss of movement in primarily synovial disease treated by total synovectomy, or even when a localised osseous focus had been removed Radical operation on the vertebral focus in Pott's disease was now a practical possibility The great value of streptomycin and *para* aminosalicylic acid was confirmed, more cautiously, by Dr **Chakir Chakar** (Turkey) who said that these agents could not be relied on to clear up the disease without orthopædic and operative treatment

Dr **Jean Judet** (France), discussing the treatment of old congenital hip dislocations by a resection reconstruction which replaced the femoral head by the well known acrylic prosthesis invented by himself and Dr R **Judet**, gave his audience the opportunity of voicing its appreciation of this new and promising method of hip arthroplasty

The conference is held every three years, and the 1954 meeting will be in Switzerland

---

Special Articles

MENTAL CONTENTMENT AND PHYSICAL GROWTH

E M Widdowson
D Sc , Ph D Lond

From the Medical Research Council Department of Experimental Medicine, Cambridge

The observations of Beaumont (1833) on his long suffering subject, Alexis St Martin, a Canadian trapper who had had a gunshot wound which resulted in a gastric fistula, showed for the first time "the effect of violent passion on the digestive apparatus" Later, Pavlov (1910), Alvarez and his associates (see Alvarez 1929), and many others have made notable contributions to our knowledge of the effect of the emotions on the processes of digestion There seems to be no scientific doubt that the secretion of the digestive juices may be induced by pleasurable emotions and inhibited by unpleasant ones It has also been shown that painful emotions will hinder the movements of the digestive tract and that food may remain in the stomach many hours longer than normal if a person becomes frightened or angry after he has eaten a meal

Macy and her co workers (Macy 1942) have made an interesting observation on the same topic, but from another angle They were carrying out long term metabolic studies on women during pregnancy and lactation The mother of one of their subjects died during the investigation, and during the week of emotional disturbance the woman showed a large negative calcium balance in contrast to her positive balance at other times, although she went on eating her usual amount of food Similar observations have also been made on children (Stearns 1951)

Most people would undoubtedly agree in principle with the recommendation of Harington (1608)

> "Use three physicians still, first Doctor Quiet,
> Next Doctor Merryman, and Doctor Dyet"

Nevertheless the importance of getting these three wise men to collaborate in nutritional experiments is often neglected or not appreciated, and the following observations show what may happen when due account is not taken of their advice

Near the industrial town in Germany where our unit had its headquarters in 1948 there were two small municipal orphanages We may call them for the present purpose "Bienenhaus" and "Vogelnest" Each housed about fifty boys and girls between 4 and 14 years of age, the average age was 8 years 8 months in both homes These children had nothing but their official rations to eat, and, although these were considerably better than they had been in 1946 and 1947, they were still barely adequate for the children's requirements The children were below normal as regards height and weight, those at Bienenhaus being a little worse than those at Vogelnest We decided to follow the heights and weights of all these children by weighing and measuring them every fortnight for a year, during the first half of which neither home

---

[2] Duraiswami P K. *Brit. med J* 1950 ii 381

The prime essential is a continuity of personal supervision for months and years The patients need this, and it pays economically

Already in the South East Metropolitan Region a plan for well placed diabetic clinics has been easily put in action by the cooperation of interested doctors and the keenness of the senior administrative medical officer This Region (see figure) contains many densely populated areas stretching from SE London along the Thames, includes towns and also sparsely populated districts in Kent and Sussex, and sweeps round the coast as far as Brighton It was recognised that the teaching hospitals in this area, Guy's and King's, each needs a diabetic clinic for efficiency and teaching purposes, and these were fortunately already established King's College Hospital has an enormously overweighted department and so has been recognised as the main consultative centre in the region for difficult cases, for training doctors and nurses for diabetic work, and for planned research A few other centres—e g, at Greenwich, Brighton, and Hastings—were already busily established by interested doctors, but many parts of the counties had no centres, so diabetics had to travel 30–50 miles to seek the solution of their problems Practically all these gaps have been filled by the appointment of interested physicians, chosen by the consent of their local colleagues, in various hospital management committee groups

Some of these centres are in their infancy or will never be large But they do provide facilities within reasonable distance for the continuity of inpatient, and (more important) outpatient, guidance by an interested doctor and staff, known and friendly

Two other aspects of treatment are under consideration in regional planning The *tuberculous diabetic* receiving treatment in various sanatoria too often lacks the adequate control of diet and insulin essential for the best results Plans are being made to concentrate such patients in a sanatorium where both aspects of their treatment can be well looked after Secondly, the difficult and not so rare problem of the care of *pregnant diabetics* is felt to merit their concentration in one or two specially experienced centres

It is hoped that, encouraged by the Ministry, all regions will make special arrangements necessary for the best health of diabetics

HOSPITAL ADMINISTRATIVE STAFF COLLEGE

SPEAKING last week at the Hospital Administrative Staff College set up by King Edward's Hospital Fund for London, Mr H A Marquand, Minister of Health, congratulated the Fund on its initiative, and promised the fullest support for its work Hospital management committees, said Mr Marquand, would be encouraged to release administrative officers to attend the college's full course, and arrangements would be made for these officers to remain on full pay He went on to say that in concentrating on short refresher courses for existing administrators, and on long courses for younger students who might be expected to become the administrators of the future, King Edward's Hospital Fund had rightly selected the most important and urgent tasks in this field He understood that there was no lack of applications for the refresher courses, though in this respect London was more backward than the Provinces, and he hoped that boards and management committees in the four Metropolitan regions would take full advantage of the opportunities offered

The college is being operated by the Fund, at a cost of about £20,000 a year, as one of its new functions in connection with the National Health Service The courses—those for younger men will last two years—will be run on the lines of university training, but there will be no examinations or diplomas The college has two houses (at 2 and 14, Palace Court, London, W 8) which contain lecture, administrative, common, and dining rooms, and a library, each house has living accommodation for 12 residents The first course, held in April this year, was attended by 11 senior administrators The second course is now in progress The two-year course will comprise nine months spent in residence at the college, and fifteen months spent on practical work in various hospitals and headquarters of the National Health Service

REGISTRAR ESTABLISHMENTS IN SCOTLAND

THE Department of Health for Scotland has now determined provisionally the establishment of senior registrar and registrar posts within which each regional board may make appointments (R.H B [S][51]7) The Department found that at the beginning of 1950 senior registrars totalled 191 and registrars 269[1] As the following table shows, the total establishment for senior registrars is to be 160 and for registrars 199

Specialty	Region					
	Northern	North eastern	Eastern	South eastern	Western	Total
Senior Registrars						
General medicine Chest medicine	1	4	4	11	19	39
Medical pædiatrics	—	1	1	2	2	6
Dermatology	—	1	1	1	2	5
General surgery	1	4	3	9	13	30
Orthopædics	1	1	1	2	4	9
Otolaryngology	—	1	—	3	4	8
Obstetrics and gynæcology	1	1	1	4	7	14
Psychiatry	1	3	1	3	7	15
Anæsthetics	1	1	1	3	5	11
Radiology and radio therapy	—	2	2	4	4	12
Ophthalmology	—	1	1	3	6	11
Total	6	20	16	45	73	160
Registrars						
General medicine Chest medicine	2*	5	6	17	23	53
Medical pædiatrics	—	1	1	3	2	7
Dermatology	—	1	1	1	3	6
General surgery	2*	5	5	12	15	39
Orthopædics	—	1	2	3	5	11
Otolaryngology	—	1	1	3	5	10
Obstetrics and gynæcology	—	2	2	5	10	19
Psychiatry	1*	3	2	4	8	18
Anæsthetics	—	2	1	4	7	14
Radiology and radio therapy	—	2	—	3	5	10
Ophthalmology	—	1	1	4	6	12
Total	5*	24	22	59	89	199

* To be employed in 2nd year only

The establishments, says the circular, are calculated on the following basis

1 The establishments are calculated as training establishments and not by reference to the need to staff hospitals

2 The numbers of those completing training as senior registrars are related as closely as can be estimated to the demand for trained specialists In estimating the demand the Department have taken account of the prospects in the hospital service in Scotland and in the faculties of medicine in the Scottish universities, and also in those fields outside Scotland to which specialists trained in Scotland have customarily proceeded

3 The normal period of training for registrars is assumed to be two years The establishment for senior registrars is calculated on the assumption that the normal training period will be four years instead of three as hitherto assumed The Department intend to discuss with the universities and the profession whether this change should be made, but

---

[1] See *Lancet* 1950 i 1165

vided by the German rations were a little higher at both homes during the second six months than the first, probably as a result of the currency reform, and this no doubt partly explains the increased growth rate at Bienenhaus But during the second six months the children at Vogelnest were undoubtedly eating more than those at Bienenhaus, and nearly 20% more than they themselves had eaten during the first six months, and yet they failed to put on so much weight

This kind of experiment is difficult to "repeat" or "confirm," but there is no doubt that even the most perfectly planned nutritional investigation may be ruined by psychological factors over which the investigator may have no control Those about to embark on feeding experiments would do well to remember "Better is a dinner of herbs where love is than a stalled ox and hatred therewith" (*Proverbs*, xv, 17)

SUMMARY

Work in two orphanages has shown that psychological stresses due to harsh and unsympathetic handling may seriously curtail growth rates

REFERENCES

Alvarez W C (1929) *J Amer med Ass* 92 1231
Beaumont W (1833) Experiments and Observations on the Gastric Juice and the Physiology of Digestion Plattsburgh U S.A
Harington J (1608) The Englishman s Doctor or the School of Salerne London Reprinted in The School of Salernum Regimen sanitatis Salernitanum Edited by F R Packard and F H Garrison New York 1920
Macy I G (1942) Nutrition and Chemical Growth in Childhood Vol I Evaluation Springfield Ill, U S.A
O Brien R Girshick M A, Hunt E P (1941) *Misc Publ U.S Dept Agric* no 366
Pavlov I P (1910) The Work of the Digestive Glands 2nd ed, translated by W H Thompson London
Stearns G (1951) Private communication
Widdowson E M (1948) *Brit med J* ii 104

REGIONAL CENTRES FOR TREATMENT OF DIABETES

R D LAWRENCE
M A, M.D Aberd, F R C P
PHYSICIAN IN CHARGE, DIABETIC DEPARTMENT, KING'S COLLEGE HOSPITAL, LONDON

DIABETES is as common a disease as active tuberculosis, but, perhaps because it is not infectious, far less care has been given to its organised treatment At a conservative estimate 3 per 1000 of the population have their health seriously affected by diabetes, and as many more have minor and latent forms It is a disease for which there is no cure at present, and which must be lived with daily and treated largely by the patients themselves As part of their treatment they need *initial training* in the details of their diabetic life, and in diet (with or without insulin), followed by regular supervision, involving special tests and experience Lacking such supervision they will not get the changes of treatment, dosage, and so on, which often make the difference between a healthy working life and semi invalidism These requirements can really only be properly met in special centres created for this purpose

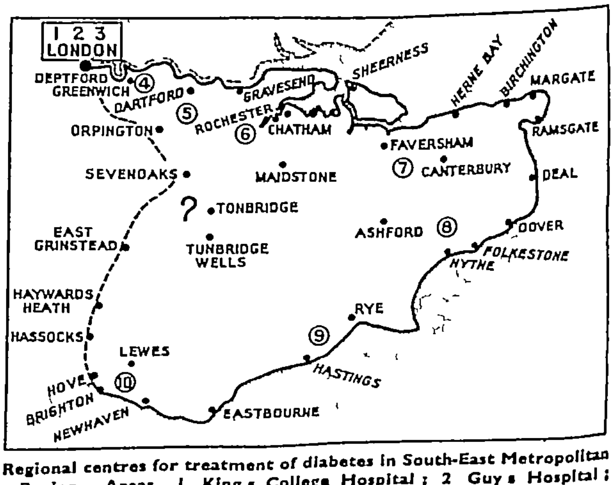
Most busy practitioners, with only about 6–12 diabetics in their care, welcome such centres for most of their patients Most general consultants (and their house physicians!) likewise feel that they are ill equipped to deal with diabetics in general wards or afterwards as outpatients Diabetics themselves crowd to any centre where their problems can be helped or solved The Diabetic Association, an organisation of lay diabetics, has been pressing for organised centres for years, and hopes and expects much from the new health service with its possibilities of adequate regional organisation The Ministry recognises the need and is encouraging its planning

To establish centres would be easy and not costly Indeed, it would be economical both in bed requirements and working health For example, all too often the odd diabetic or two in a general hospital is kept for two or three months in an attempt to "stabilise" his condition, and finally referred in despair to a special centre where the "impossible stabilisation" is easily achieved in some ten days Indeed, in one outpatient consultation the life of many "problem" diabetics may be made secure and normal by experienced advice

Numerically, the problem is clear At a minimum there are 250 diabetics in 100,000 population, or 1250 in 500,000, which makes a good sized unit for a city And 1 bed is needed for every 50 diabetics (20 beds for a clinic of 1000) to deal with initial treatment and training and for the treatment of relapses and of complications—medical and surgical—which make diabetes at least temporarily more severe and difficult to handle coma and insulin coma, infections, imbalance, gangrene, operations, &c It is obvious that diabetics suffer from all types of added disease, and the doctor in charge must not be a narrow diabetician but a physician widely versed in general medicine

The ideal for adequate treatment of most diabetics is a special centre within reasonable access—preferably not more than 20 miles from the patient's home, though this may be impossible in sparsely inhabited rural areas The same interested doctor should treat them as inpatients and subsequently as outpatients

In a small centre with some 300 diabetics, the doctor needs one sister trained in diets and insulin and able to teach, a nurse to help her, and a cooperative house physician The same team should see the outpatients at their regular visits, at least three or four times a year In outpatient departments ready facilities for testing urine and blood sugar are necessary One experienced doctor with this organised help can deal efficiently with 20–30 patients, the probable number of weekly attendances, in one session, so most of his time will be occupied with other work As the numbers grow (and they grow quickly), more sessions, perhaps another nurse and nurse dietitian, and perhaps a part time registrar, are needed When the clinic grows to 1000 or more, usually necessary for a population of 500,000 and making perhaps the best sized unit, more staff and certain ancillaries are required for full efficiency more medical, nursing, and dietetic help, a part time almoner and a part time chemical technician, and a chiropodist to prevent months of illness from foot sepsis and gangrene The cooperation of the county medical officers and health visitors has been found most useful at several clinics



Regional centres for treatment of diabetes in South-East Metropolitan Region Areas 1 King s College Hospital ; 2 Guy s Hospital ; 3, Bermondsey and Southwark group ; 4 Greenwich and Deptford group ; 5 Dartford group 6, St. Bartholomew s Hospital and Medway and Gravesend group ; 7 Canterbury group 8 Ashford and Folkestone group ; 9 Hastings group ; 10 Brighton group ? not yet chosen

BIRTHDAY HONOURS

The list of honours published last week contains the names of the following members of the medical profession

K C V O

Geoffrey Sydney Todd, C.V.O., O.B.E., M.B Sydney, F.R.C.P
Superintendent, King Edward VII Sanatorium, Midhurst

D B E.

Prof Hilda Nora Lloyd (Mrs. Rose), M.B Birm, F.R.C.S
President, Royal College of Obstetricians and Gynæcologists, professor of obstetrics and gynæcology, University of Birmingham

Knights Bachelor

Charles Arthur Lovatt Evans, D.Sc Lond, LL.D Birm, F.R.C.P, F.R.S
Emeritus professor of physiology, University of London

Ernest Frederick Finch, M.D, M.S Lond
Formerly professor of surgery, University of Sheffield

John William McNee D.S.O M.D., D.Sc Glasg., F.R.C.P
Regius professor of medicine, University of Glasgow

Philip Santo Messent, M.S. Adelaide F.R.A.C.S
Director of surgical studies University of Adelaide

C.B (Military)

Major General John Mandeville Macfie, C.B.E M.C, M.B Glasg K.H.S, late R.A.M.C

C.M G

John Merrill Cruickshank, O.B.E., M.D McGill.
Director of medical services Fiji inspector general, South Pacific Health Service

Herbert John Seddon D.M. Oxfd F.R.C.S
Member of the Colonial Advisory Medical Committee clinical director Royal National Orthopædic Hospital, London.

John William Field, M.D Birm.
Director Institute for Medical Research, Federation of Malaya.

C V O

Alexander Greig Anderson, M.D Aberd F.R.C.P
Hon. physician His Majesty's Medical Household in Scotland

George Ritchie Mather Cordiner, M.B St And.
Radiologist, St George's Hospital, London

C B E (Military)

Air Vice Marshal William Edward Barnes, M.R.C.S R.A.F

Colonel William Alexander Duncan Drummond, O.B.E. F.R C.S. late R.A.M C

C B E (Civil)

Thomas Beaton, O.B.E, M.D Lond F.R.C.P
Superintendent St James Hospital, Portsmouth.

Edmund Cecil Bevers B.M Oxfd F.R.C.S
Lately chairman, United Oxford Hospitals consulting surgeon, Radcliffe Infirmary Oxford

Eustace Henry Taylor Cummings M.B.E., M.D Lpool
For services to the municipality of Freetown, Sierra Leone

Evan Stanley Evans M.D Lond. F.R.C.S
Chairman, Queen Elizabeth Training College for the Disabled Leatherhead.

Lee Tiang Keng M.B
Member for Health, Federation of Malaya

Joseph Stanley Mitchell, M.B PH.D Camb
Professor of radiotherapeutics, University of Cambridge

Matthew John Stewart LL.D M.B Glasg, F.R.C.P
Emeritus professor of pathology University of Leeds

Edwin Lawrance Sturdee, O.B.E., M.R.C.S
A principal medical officer Ministry of Health.

James Mathewson Webster M D Birm., M.B St And, F.R.C.S.E
Director West Midland Forensic Science Laboratory Birmingham.

O.B.E (Military)

Lieut Colonel Derek George Levis, M.B Camb, R.A.M.C.

Surgeon Commander William MacFarlane Davidson, M.B Belf R.N

Lieut Colonel Angus John MacIver, M.B Glasg, R.A.M.C

O B E (Civil)

William Blood, M.R.C.S
Chairman, Brook Green disablement advisory committee

Arthur Joseph Boase, M.R.C.S
Ophthalmologist, Uganda

Miss Elizabeth Casson M.D Brist
Founder and director Dorset House School of Occupational Therapy, Churchill Hospital, Oxford.

Gerald Samuel William de Saram, M.B Lond.
Lately judicial medical officer Colombo

James Leslie McLetchie, M.B Glasg
Senior medical officer i/c Sleeping Sickness Service, Nigeria

George Marangos
Hon. consulting surgeon, Limassol Hospital, *Cyprus*.

John Percy Truelove Musson, M B Leeds
Deputy director general of medical services, Ministry of Pensions

Miss Lena Frances Gordon Priestman, M.B Lond.
Medical officer Molai Leper Colony, Nigeria.

Henry Douglas Weatherhead, M.R.C.S
Lately director of medical services North Borneo

Harry Montefiore Wilson, M.B Camb, F.R.A.C.S.
Medical practitioner, Hawkes Bay, New Zealand.

M.B.E (Military)

Major Richard Swinton Hunt, F.R.C.S.E. R.A.M.C

M B.E (Civil)

Mrs Margaret Merry Brotherston, M.B Edin.
Organising secretary and hon treasurer, Voluntary Health Workers Association, Edinburgh.

Miss Elizabeth Catherine Gunn M.B Edin.
Former director of the School of Hygiene Wellington, New Zealand

Ninian George Trotter, M.D
For public and social welfare services in New Zealand.

John Richard Wilson, M.D
Visiting physician, Tuberculosis Hospital Welisara, and consultant to the Chest Hospital, Ragama, Ceylon.

M B E (Honorary)

Abdul Latif bin Abdul Razak, L.M.S
Medical officer, Federation of Malaya.

Medicine and the Law

Responsibility in the Operating-theatre

A few weeks ago, in the High Court,[1] a widow with three young children was awarded £2604 compensation for the death of her husband, who died when adrenaline was injected instead of a local anæsthetic for the removal of a cyst

An anæsthetist is personally responsible, not only for doing his work skilfully, but also for seeing that his drugs are correct and that his apparatus is in good working order As his work becomes more complex he must rely on some help from others in the operating-theatre, but whoever has changed the cylinders, got the apparatus ready and prepared drugs for injection the anæsthetist is responsible for ensuring that this work is properly done

Anæsthetists themselves have long been concerned about their responsibilities which have lately been discussed at two important meetings. In Dublin[2] Mr Arthur Cox a lawyer, said

> The anæsthetist is responsible for anything he himself does and anything that falls within the scope of his duty
>
> The Court would hold that it is the duty of the anæsthetist to see that the cylinder used is the right cylinder ’

---

[1] *Times* May 8 1951

[2] *Irish J med Sci.* April 1951 p. 137

even if the final decision is to retain the present three years and the establishment has to be reduced, a temporary addition will have considerable advantages in a period of transition

4 In a few branches of medicine and surgery the normal training period for senior registrars is exceptionally long No special provision for this has been made in the establishment, but it is to be understood that senior registrars in those specialties may remain for an extra year

5 The relative numbers of registrars and senior registrars are calculated so as to permit a progressive selection as training proceeds The extent to which the progress of registrars is reviewed, and the number reduced at the end of the first year, is for each board to determine after consultation with the authorities responsible for medical education The decision on this will determine whether half the registrar posts should normally be first-year and half second year, or whether the fractions should respectively be higher and lower

6 The number of senior registrar posts available to those completing training as registrars will entail fairly severe competition There may be some progressive reduction in the numbers of senior registrars in the course of their training, but, generally, the intention is that once a doctor has obtained a senior registrar post he should be regarded as capable of completing his training and having a reasonable prospect of obtaining a substantive appointment

The circular continues The establishment both at the registrar and senior registrar levels *excludes* the relatively small numbers of university posts in some branches of clinical medicine that are normally held by lecturers of equivalent status in association with clinical duties in a teaching hospital It should be observed, however, that these doctors normally proceed to a senior university post or to the hospital service, and all the higher posts in these fields have been taken into account in assessing the prospects to which the senior registrar establishment has to be related Any material increase in the number of junior university posts would, therefore, in due course increase the number of those competing for the higher posts in the universities or the hospital service, and would, therefore, have to be taken into account in reviewing the size of senior registrar establishments The numbers of those in the senior registrar posts and the junior university posts together must be reasonably related to the prospects, otherwise the future careers of some of the doctors concerned would be seriously prejudiced

In the present circumstances in which a substantial proportion of the posts in laboratory medicine, both senior and junior, are held by members of the university staffs, the Department think it is premature to determine registrar establishments in laboratory medicine The numbers should be adjusted between each regional board and the university concerned, having regard to the general principle on which the other registrar establishments have been calculated, and the agreed numbers notified to the Department

The numbers of senior registrar posts in the several specialties have been adjusted to take account of the needs for specialists in the various fields Provision has been made for sufficient posts at the registrar level in general medicine and surgery to enable those who ultimately elect for a narrower specialty to obtain the necessary fundamental training and experience

In this respect and in others there will have to be a measure of flexibility For example, registrars may elect to spend a period in research work or in hospitals abroad The board will have to decide in each case whether the doctor concerned should be retained in the establishment or treated as supernumerary during this period The essential principle is that in the aggregate the number of those in training should be balanced against the prospects

As the numbers are based on estimates of the need which can only be provisional and will have to be adjusted in the light of experience, the intention is to review the establishments annually each spring in consultation with the regional hospital board so that a beginning can be made with any necessary adjustments in the autumn when it seems likely that most of the new appointments will be made

There is no provision in the establishment for either

1 Registrars whom the board may wish to retain for an extra year primarily for staffing purposes. This is to be regarded as a temporary arrangement to meet staffing difficulties, and such registrars will be treated as supernumerary to the establishment, or

2 Senior registrars who desire to remain for a limited period after the completion of their normal training while they are seeking higher posts The intention is that it should always be open to the senior registrar to take advantage of this, but these appointments also will be supernumerary

Each regional board may now proceed to review the existing appointments and to make new appointments with effect from Oct 1, 1951, within the establishment referred to above Those registrars who do not obtain registrar or senior registrar appointments may be advised, if the board are satisfied that their services are required, that they are likely to be offered supernumerary posts for one year But before any appointments are made to these posts the Department would like to be informed of the number of posts it is proposed to fill

The existing senior registrars, the circular concludes, will fall into one of the following groups

1 Senior registrars in name only, who have in fact completed their training * and are employed on essential duties in substantive posts They should be told that until the forthcoming discussions on the present structure of hospital medical staffing are completed the board are unable to reach a final decision as to their future appointment, but that the board are willing to retain them in their present duties until further notice

2 Senior registrars proper, whose training is not yet complete or on the point of completion—i e , in their first, second, or third years Any who cannot find a place within the training establishment as now authorised should have their appointments terminated Any necessary selection should be made on the basis of merit and promise and not merely seniority or stage of training reached

3 Senior registrars who are about to complete their training If they wish, they may remain for a period not exceeding one year on the supernumerary basis mentioned above

R H B HEADQUARTERS STAFF

A DIFFERENCE lately arose between the management and staff sides of committee B of the medical council of the Whitley Councils for the Health Services The staff side's proposals for revised salary scales for the headquarters medical staff of regional hospital boards were not accepted by the management side The matter was referred to the Industrial Court, which has made the following award

Senior Administrative Medical Officers

Regions	*Salary Scales* (£)
Each of the four Metropolitan regions, Birmingham, Liverpool Manchester, and the Western region of Scotland	2500 per annum rising by annual increments of 150 to 3250 per annum
Bristol Leeds Newcastle Sheffield Wales and the South Eastern region of Scotland	2250–150–3000
East Anglia and Oxford	2000–150–2750
Eastern and North Eastern regions of Scotland	1850–125–2475
Northern region of Scotland	1750–100–2250

Deputy Senior Administrative Medical Officers

Each of the four Metropolitan regions Birmingham Liverpool Manchester, and the Western region of Scotland	1650–100–2150
Bristol Leeds Newcastle Sheffield Wales and the South Eastern region of Scotland	1600–100–2100
East Anglia and Oxford	1550–100–2050

These scales will apply to any administrative medical officer fulfilling the functions of a deputy senior administrative medical officer whether or not so designated

Regional Psychiatrists

Each of the four Metropolitan regions Birmingham Liverpool and Manchester	2000–125–2625
Bristol Leeds Newcastle Sheffield and Wales	1900–125–2525
East Anglia and Oxford	1800–125–2425

The new scales of salary set out in the award are to apply from Oct 1, 1950 and a high proportion of dwellings and farms are now connected This policy must have contributed, not only to the advancement of rural amenities and agriculture and the suppression of infectious water borne diseases, but also to the avoidance of cases of cyanosis in infants

---

* For the present the normal period should be taken as four years.

Doubtless a similar policy, based partly on chemical analyses including nitrates, has been an important factor in avoiding cases in this country as a whole According to one account,[1] nearly 200 cases of cyanosis in infancy due to well waters have been described , and the country mainly concerned has been the U S.A., with some cases in Belgium and Canada It should be made clear that analyses in the U S.A and in this country are usually expressed in terms of nitrate nitrogen (N) and not as the nitrate radical (NO_3) The suggested provisional limit of 20 p p.m refers to nitrogen However, there must still be numerous dwellings in rural districts using water with over 20 p p m of nitrate nitrogen It would appear that the incidence of cyanosis in infants taking feeds made with water containing this amount of nitrate nitrogen must be very low, and that it may not be high even when the amount approaches 50 p p m

The Counties Public Health Laboratories
66 Victoria Street London, S W 1

Roy C Hoather

OFFICE MANNERS

Sir,—Prof. Leslie Banks (June 2) appears to have missed the meaning of Brigadier Hardy-Roberts's reference (May 19) to a cup of tea Surely the brigadier was reminding us that the best way to understand fully another man's problem, and possibly to find a mutually agreeable solution, is to talk over the matter in an atmosphere of informality and comradeship This important fact is unfortunately all too often overlooked not only by doctors, but also by those in administrative posts.

London N W 11

Bernard Johnson

PROPHYLAXIS AGAINST TETANUS IN BURNS

Sir —I was interested to read Mr Clarkson's letter (March 24) commenting on the question raised by Dr Colebrook (March 10) of the risk of tetanus in burns Mr Clarkson states that he has seen only 3 cases of tetanus complicating 2000 cases of burns in the course of 10 years

It so happens that I have seen the same number of cases of this 'undoubtedly rare' complication of burns in the past 2 months. I think that those who have had experience amongst primitive communities in the tropics will agree that tetanus is a common complication of all types of injury to the surface of the body As is well known some such cases are due to the ignorant practices which are part of the tradition of the people—for example in some parts of Africa cow dung or mud poultices are applied to the female perineum and infant umbilical cord after delivery Incidentally, the aboriginals in our area, the Konds apply a fresh egg to the umbilical area of their newborn infants which is probably, as it happens the most sterile' thing at their disposal I think that the most important factor making burns complicated by tetanus more common here is the long delay which often separates sustaining of the injury and admission to hospital.

The 1st case seen here on March 30 was of a woman, aged 35 burned 3 weeks previously who had had trismus for 10 days and generalised spasms for 4 days The burns were of 3rd degree over most of both hands and she died several days after being taken home on April 12

The 2nd case was of a boy, aged 20, admitted on May 6, 4 days after sustaining a 3rd-degree burn of the left ankle during an epileptic fit On May 9 he developed generalised spasms with opisthotonos the following day , his condition rapidly deteriorated and he died on the 13th.

The 3rd case is of an epileptic woman admitted on May 17 with a grossly infected 3rd-degree burn of the right foot on the day of admission she had spasms, and the next day opisthotonos

In primitive communities, where difficulties of transport and age old practices delay admission to hospital, routine prophylaxis of all burned patients, whilst indicated for the symptom free, cannot put back the clock for the less fortunate

Udayagiri, Orissa. India.

D Stewart McLaren

CORTISONE AND INFECTION

Sir,—I have just read with interest your excellent leading article of April 28, and I am struck with your repeated statement that 'Cortisone' therapy produces hyperadrenalism I presume you are referring to the "Cushingoid" hormonal side effects which are associated with increased glucocorticoid excretion in the urine but I would suggest that the word hyperadrenalism is somewhat misleading in this respect since from an anatomical and physiological standpoint the effect of cortisone upon the adrenal cortex is quite the opposite and in this way fundamentally different from that of ACTH

Just as œstrogen therapy diminishes pituitary follicle-stimulating hormone, so cortisone therapy diminishes pituitary adrenocorticotrophic hormone, and this would seem to explain its beneficial action in those cases of the adrenogenital syndrome which are due to hypercorticism , it also explains the transient hypocorticism which may follow the abrupt termination of a course of cortisone therapy

A leading article is properly concerned only with scientific facts, but in a letter one may perhaps be permitted more latitude There is little at present that can be said *in favour of* combined therapy with cortisone and antibiotics, although some recent reports on its use with chloramphenicol in typhoid fever seem quite *encouraging* , but in this company, which pioneered in the industrial production of the first antibiotic, we remember that penicillin has only been available for ten years and cortisone for less than two Some of us, therefore, look forward, though admittedly through a glass darkly," to a mythical era when cortisone or some suitable substitute, will become the handmaid of improved antibiotics enabling them to penetrate chronic inflammatory tissue and destroy the organisms therein embedded

Merck & Co Ltd Montreal

J H Laurie
Medical Director

AMMI VISNAGA

Sir —Those working with the *Ammi visnaga* plant, an active principle of which acts on the coronary vessels, when dealing with the historical aspects cite only the popular herbal tradition in Egypt We believe that the plant s history can be traced still further back.

Maimonides [1] who left us perhaps the oldest pharmacology of the brilliant Hispano-Arabic period, mentions under the name *duqu* (daucus) the Arabic term *al-ahillah* (evidently the same as *khillah*) To contribute to the identification of this plant, he notes that the rays of its umbels were used as tooth picks

Later on the Spaniard Andrés Laguna physician to Charles V and Pope Julius III, in his commentary on the Dioscorides [2] also identifies visnaga with daucus, and gives extensive details about its therapeutic applications at that time—notably, 'to provoke menstruation and urine," uses already described in Dioscorides

Later still, the plant was classified by Lamarck as an ammi (*Ammi visnaga*) This has prompted even some modern botanists to relate visnaga with the ammi of the ancients, erroneously

Department of Pharmacology
University of Barcelona

F G-Valdecasas
S Glanzmann

---

[1] *Bull. World Hlth Org* 1950 3 165

[1] Glossaire de Matière Médicale Cairo 1940

[2] Pedacio Dioscorides Anazarbeo Acerca de la Materia Medicinal Translated by Andrés de Laguna. Valencia, 1635

with my colleague, Dr R J Reynolds, radiologist to the Kingston group, who, in his department at Charing Cross Hospital, has a 5×4 in apparatus Technically, the requirements of a good chest film are usually obtained on the 5×4 in miniature From the point of view of economy the 5×4 in film, which is single coated, costs 3*d*, whereas the 14×17 in film, normally used now for chests, costs 4*s* 7*d* I came to the conclusion that in a year's work in my own clinic the change over to small film would mean a saving of something like £1000 in film alone The cost of installing apparatus for this work is in the region of £1200, but this cost would be met easily in two years' running Another important point is the greater ease of storage

Comparing the usefulness of the 5×4 in miniature with that of the 35 mm film, I can only agree whole heartedly with Dr Clarke that we will have to readjust our outlook on the roll film The 35 mm film still has great usefulness, I am sure, in the Services for filtering large numbers of personnel, but it is not useful in hospital and clinic services I think we should admit this, and alter our planning accordingly

SINCLAIR R WILSON

Kingston upon Thames Surrey Chest Physician

SIR,—Dr Owen Clarke's proposal deserves every support Fortunately the situation is not as difficult as is suggested by his statement that "equipment for 5 × 4 in radiography is not available in this country"

There are already in existence here some prototypes of a 7 in F/1 5 lens designed to cover a 5 × 5 in plate, these could be modified for mass radiography if required Recently I was permitted to test one of these lenses for this very purpose, and it proved promising The 5 × 5 in aero camera is admirably adaptable to the same needs, and so the complete units could be made in Britain and to British designs as soon as the authorities require them Such a development, I am given to understand, is at present held up by our rearmament programme, but the economics of this decision seem unquestionable

London, W 1 BRIAN STANFORD

CONGENITAL SYPHILIS IN A FIJIAN

SIR,—Your issue of March 17 contained a most interesting letter by Dr Manson Bahr

I spent twelve years in Fiji, and one of the subjects of constant argument was whether a Fijian could contract syphilis Practically all had positive Kahn tests (blood) in those days, and it was not until 1948 that I found two young Fijian males with negative reactions A careful watch was kept for any indications of syphilis in a pure blooded Fijian, and it was in 1948 that I saw, for the first and only time, what appeared to be syphilitic chancres on the genitals of a pure blooded Fijian

The patient was a young soldier who had three sores on the penis (glans and sulcus) all of which on dark field examination showed what the laboratory reported as "spirochætes morphologically resembling *S pallida* or *S pertenue*" The lymphatic glands draining the penile region were enlarged but painless His blood Kahn was ++++ He admitted to contact with pure blooded Fijian girls all of whom had Kahn ++++ Whether he had contact with a non Fijian I cannot say

As treatment was instituted at once no other signs developed, and I could not rightly say that this was definitely syphilis But in twelve years, during which I have seen numerous cases of yaws at all stages, I have never see nor heard of yaws presenting as a penile chancre Has anyone seen such a manifestation? Like Dr Manson Bahr I wonder if too great zeal in controlling yaws might not open the door to its malignant first cousin—syphilis

Seychelles Hospital
Mahe
Seychelles Islands

JAMES TAYLOR
Senior Medical Officer Seychelles

METHÆMOGLOBINÆMIA

SIR,—The paper by Dr Ewing and Dr Mayon White in your issue of April 28 is of particular interest because previously no case of cyanosis from nitrates in drinking water had been recorded in the British Isles

Dr Ewing and Dr Mayon White state "theoretically it is possible for coliform organisms to be held back by the soil as water percolates through it, yet for nitrates in solution to pass into a well, in practice this rarely seems to happen, coliform organisms being usually demonstrable in well waters containing nitrates" I suggest that this statement may mislead

Firstly, the great majority of well waters of superlative bacterial quality (many of them used for public supplies) contain small but appreciable amounts of nitrates when the wells are situated in an outcrop formation (e g, 5 p p m of nitrate nitrogen) Under the present climatic conditions there is in some instances a slight increase in nitrate content but without deterioration in bacterial quality On the other hand, examples of well waters free from nitrates are those derived from the chalk under the London tertiary beds, but in such waters reduction has taken place so that a comparable quantity of nitrogen is found in the form of ammonia

Secondly, with regard to the relation between nitrates and coliform organisms in shallow wells at farms and cottages in rural districts, the accompanying table summarises data for 600 such wells, samples from which have been examined in my laboratory Detailed classification of the bacteriological results is omitted for conciseness, but the description of "passable" is based on a low number of coli-aerogenes organisms, with *Bact coli* absent from 100 ml in most instances. It will be seen from these figures that there is only limited correlation between nitrate content and bacteriological pollution, the lowest percentage of satisfactory bacteriological results corresponding to the range of 20–50 p p m of nitrate nitrogen. With regard to variations in an individual well, water from one of appreciable size in a gravel formation has been sampled at monthly intervals for five years, and the content of nitrate nitrogen found to vary between 16 and 32 p p m without serious bacteriological pollution in any sample Out of the total of 600 wells it will be noted that 470 showed a nitrate nitrogen content below 20 p p m, and of these 286 were also of passable bacterial purity, 130 (21 6% of the total) showed a nitrate nitrogen content above 20 p p m, and of these 64 were of passable bacterial purity

Range of nitrate content (p p m nitrogen)	Samples within stated range of nitrate content		Samples of passable bacterial purity within stated range of nitrate content	
	No	%	No	%
<10	357	59 5	216	60
10– 20	113	18 8	70	62
20– 50	103	17 2	47	46
50–100	24	4 0	14	58
> 100	3	0 5	3	—
Total	600	100	350	58

Nitrates represent organic pollution from sources sufficiently distant for oxidation to have taken place through several stages, whereas free ammonia is more commonly an indication of recent pollution However, it has been our practice for very many years to report adversely on the presence of considerable amounts of nitrate nitrogen in terms such as "indicative of derivation from a manurially contaminated soil" About half the samples referred to in the table were from wells at farms in Essex, examined for the public health department, the results tabulated being taken for convenience over the period from 1945 to 1949, although many others were taken in earlier years The percentages are similar if these samples are separated from the other wells at farms and cottages included in the total of 600 The object of the sampling programmes was to obtain improvement in the surroundings of the wells or to replace them by better sources and particularly by a piped supply when necessary Practically the whole of rural Essex is now covered by a network of public water supplies, 0, 1 The jackdaw seemed to remember that it had not taken five baits, it came out again and went along the line of boxes, *bowing its head once before the first box, twice before the second box, and once before the third box* before it opened the fourth and fifth boxes and secured the fifth bait Koehler says that this behaviour "seems to prove that the bird remembered its previous actions" But, if it had done so, surely it would have gone direct to the fourth box Moreover the jackdaw, if it did realise that it had not done its task properly, possibly felt guilty or, at any rate, expected punishment, in which circumstances it is customary for a jackdaw to bow, presenting the nape of its neck to its persecutor or acknowledged superior[3]

MEDICAL ASSOCIATION FOR THE PREVENTION OF WAR

A GENERAL meeting of this association was held at the Royal College of Surgeons on June 8 Dr Duncan Leys was in the chair, and the meeting was attended by 120 doctors In a letter Lord Boyd Orr expressed his support for the association and his willingness to act as one of its sponsors In his opinion war was the worst of the psychological diseases of human society, and its prevention might well be regarded as the most important part of preventive medicine A statement of policy was introduced by Dr Douglas McClean, who pointed out that the extent of the evil resulting from preparation for war was not always realised It hindered social development, produced a shortage of medical supplies, and resulted in widespread development of psychopathological reactions The principal object of the association was to unite doctors in efforts to prevent war, but in working for this object the association would need to undertake diverse activities, including study of the causes of war and of the psychological mechanisms by which people are conditioned to accept war as a necessity It would also be concerned to seek the coöperation of all doctors having the same aims in all countries Dr Martin Pollock reported on a visit he had paid, as a representative of the association to a meeting of French doctors devoted to the same objects he had also been in touch with a doctor who hoped to start a similar movement in Denmark. Dr Alex Comfort read extracts from letters which he had suggested sending to professional representatives in the U S.A and U S S R The bringing together of doctors from such countries to discuss methods for the preservation of peace, on a professional basis, was one of the most valuable contributions which the association could make

Dr Duncan Leys was elected chairman, Dr Douglas McClean vice-chairman, Prof Lionel Penrose secretary, Dr Richard Doll assistant secretary and Dr David Pyke treasurer

University of Oxford

On June 2 the following degrees were conferred

D M—E N Allott, J W Gerrard E H Seward J M K Marsh *R H Hardy

B M—J B Dossetor *Tristram Freeman

* In absentia

University of Sheffield

Applications are invited for the J G Graves fellowship for full time medical research The stipend will be £1300 a year Further particulars will be found in our advertisement columns

University of London

The following have been recognised as teachers of the university in the faculty of medicine

N Asherson and Maxwell Ellis otorhinolaryngology Institute of Laryngology and Otology Diana Kinloch Beck surgery Middlesex J W D Bull, radiology Ernest Landau anæsthetics St. George s Amy Fleming obstetrics and gynæcology R M. Haines pathology Institute of Obstetrics and Gynæcology

Royal College of Physicians of Ireland

On June 1 the following members were admitted to the fellowship

M. I F Drury P D J Holland A F Kennedy J P Malone S P O Toole B E R Solomons F S Stewart E W L Thompson.

The following were admitted to the membership

A D H Browne E M. Cheffins A L Jones S G McComb T C Milliken N B O Donohoe D G Simpson H B C Wallace

National Coal Board

Dr S W Fisher has been appointed consultant to the board

Royal Appointment

Surgeon Captain E S McPhail, R.N Z.N, has been appointed an honorary surgeon to the King

Ross Foundation for the Prevention of Blindness

The foundation are inviting applications for part-time research work on any subject related to ophthalmology Further particulars will be found in our advertisement columns

Society of Apothecaries of London

Dr T Jenner Hoskin will deliver the Joseph Strickland Goodall lecture at Apothecaries' Hall, Black Friars Lane, London E C 4, on Tuesday, June 26, at 5 P M He is to speak on Thyroid in Heart disease

Royal Society

On Thursday, June 14, at 4 30 P.M, at Burlington House, Piccadilly, London, W 1, Sir Cyril Hinshelwood, D SC, F.R.S, will describe Some Researches on the Physical Chemistry of Bacterial Cells

Association of Industrial Medical Officers

This association will hold their annual provincial meeting in Sheffield, from July 16 to 20 Further particulars may be had from the hon secretary, Dr J A A Mekelburg, Peek Frean & Co Ltd, Keetons Road, London, S E 16

Addison Lecture

On Thursday, July 5, Prof F G Young D SC, F.R.S, will deliver the fifth Addison lecture at Guy s Hospital Medical School, London, S E 1, at 5 P M He is to speak on Thomas Addison and the Background to 'Cortisone' Further particulars will be found in our advertisement columns

W H O Executive Board

The eighth session of the executive board of W H.O opened in Geneva on June 1 The board has decided to set up a W H O regional office for Africa, and to approve, the nomination of Dr I C Fang as director of the W.H O regional office for the Western Pacific

London Association for Hospital Services

At the annual general meeting on June 6 Dr Russell Brain, F R C.P, was re elected chairman The assets of the association now exceed £65 000, and more than £100,000 has been paid to contributors against the cost of treatment in hospital private wards or nursing homes

A New Guy's

In the next five years about £1 million is to be spent on rebuilding part of Guy s Hospital, London This is the first part of a plan for the complete rebuilding of the hospital during the next fifty years The present plan includes the addition of a new block to house 350 beds, and it is hoped that the hospital will eventually provide 800 beds, compared with the present 575 and 620 before the late war

Royal Society of Tropical Medicine and Hygiene

For the benefit of overseas fellows and other visitors to this country two special meetings of this society are to be held at 26, Portland Place, London, W 1, next month On Wednesday, July 18, Sir Harold Scott will speak on British Contributions to Tropical Medicine, and on Thursday, July 19, Prof H E Shortt, F.R S, will give a paper on the Life Cycle of the Malaria Parasite Both meetings will take place at 7 30 P M

Belt Fellowships for Medical Research

The following awards have been made

JUNIOR FELLOWSHIPS

PAMELA M HOLTON M.A Camb, D.PHIL Oxfd To investigate the chemical transmission at nerve-endings at the physiological laboratory University of Cambridge

H F JARVIE B SC M B Glasg To study the psychological manifestations of organic nervous disease at the department of neurology Radcliffe Infirmary Oxford

ELEANOR W MCCLOY B A. M B Dubl To study a lysogenic bacillus strain at the London School of Hygiene

A F PHILLIPS M A Camb, M B Edin To study the mechanism of the therapeutic action of X and gamma rays at the department of radiotherapeutics Cambridge University and the radiotherapeutic centre Addenbrooke s Hospital.

E V ROWSELL, B A Camb To study the biochemical changes associated with physiological activity in nerve tissue at the University of London Institute of Psychiatry Maudsley Hospital

W G SPECTOR, M.A. M.B Camb M R C P To study the mechanism of protein synthesis in premature and full term neonates in infancy and childhood, at the Graham research department University College Hospital Medical School London

---

[3] Fisher J Birds as Animals. London 1939 p 141

Obituary

SOPHIA GRAHAM

M B Lond , D P.M

Dr Graham who died on May 8 at the age of 49, was in many ways an exceptional woman. Born Sophia Antonovitch, she was the first Serbian woman to be trained in medicine, for the profession was still closed to women in Yugoslavia when at the age of 19 she was awarded the first scholarship at the Royal Free Hospital by the Women's Medical Mission The intention of the mission was that after qualifying she should return to her country as a pioneer of medical education for women, but after a brilliant career as a student, Toni found herself more attracted to the laboratory than to the clinic or the lecture-room She showed her character by allowing intellect precedence over patriotism Despite the handicaps of language and physical disability, she soon became an important member of the team of workers at the central pathological laboratory of the London County Council's mental hospitals department led by Golla at the Maudsley Hospital

In this group she distinguished herself not only by her quick intelligence but also by the warm personal qualities derived from the South, the Slav, and her sex She was firmly loyal but frankly critical , where she lacked discipline she acquired deftness, where understanding faltered she supplied intuition These gifts were of special value in the studies of the nervous system in which she collaborated with Golla, for their chosen field was in that borderland between physiology and psychiatry where those with more conventional constitutions soon perish from factual starvation In 1932 she took the D P M and shortly afterwards she began the studies of clinical electro-encephalography with which her name will always be linked Her unique value to the laboratory may be measured by the fact that when she married Dr John Graham in 1935, the strict rule requiring women to resign on marriage was waived on her behalf

In 1939 domestic cares began to encroach upon her scientific enthusiasm and she was obliged to retire From that time she helped her husband in his practice, a task which she carried on single-handed during the war For a year before her death she endured with characteristic fortitude the progress of an illness the origin and course of which she was, ironically, well qualified to trace The memory of her fervent spirit will live with her friends and her name will survive with her work

W G W

Births, Marriages, and Deaths

BIRTHS

Denham —On June 9 in London the wife of Mr R A Denham, F R C.S E —a daughter

Thomas —On June 4 the wife of Dr D M E Thomas, of Warwick —a daughter

Todd —On June 1 at Cuckfield the wife of Dr I C C Todd —a son

Walters —On June 6 at Lincoln the wife of Mr Geoffrey A Bagot Walters F R C S E —a son

MARRIAGES

Caldwell—MacDonald —On June 6 at Aberlour Banffshire John Stewart Caldwell M B to Margaret Joan Stacey Mac Donald

Cox—Grimson —On June 2 in London John Stanley Cox M B to Molly Grimson

Flewett—Hall —On June 2 at Esher Thomas Henry Flewett M D to June Evelyn Hall

DEATHS

Asten —On June 4 at Bournemouth Walter Asten M.D Brux L.R C P E barrister at law aged 84

Gray —On June 5 in London Leo Patrick Gray M B Glasg

Hall Davis —On May 31, at Keston Kent George Hall Davis M B Dubl aged 56

Harries Jones —On June 7 at Northampton Evan Harries Harries Jones M D Edin aged 77

Longstaff —On June 7 in South Africa Eadbert Ralph Collison Longstaff M R C.S

Startin —On June 1 at Plymouth John Startin M C M R C.S , major, R.A M C retd aged 67

Stewart —On June 1 at Grouville Jersey Francis Hugh Stewart M.A Camb M D Edin D.Sc St And. I M.S retd aged 70

Taylor.—On June 2 at Cymmer Glam James McKane Taylor M B Edin

Young —On June 8 at Rickmansworth Charles Melville Young M B Aberd aged 75

Notes and News

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY

The International Society of Clinical Pathology, which was founded in 1947, is holding its first congress from July 16 to 20 in London The opening ceremony will take place at Friends House, Euston Road, N W 1, at 3 P.M on Monday the 16th, when Sir Lionel Whitby, the president, will give an address on the Science and Art of Medicine The work of the congress has been divided into four sections The section of microbiology will discuss Non bacterial Pneumonias, Bacterial Typing, the Ætiology of Infantile Gastro-enteritis, Systemic Mycoses, Variola vaccinia, and Laboratory Control of Chemotherapy The section of morbid anatomy will hold sessions on the Collagen Diseases, Histological Effects produced in Neoplasms by Irradiation, Physical Methods in Morbid Anatomy, Perinatal Pathology, and Pathology of the Pulmonary Circulation The section of chemical pathology will hear a series of papers on recent advances in biochemistry, including their application to nutritional diseases, disorders of serum proteins, and hormonal assays The section of hæmatology is to discuss Vitamin B_{12} and other Nutritional Factors in the Pathogenesis and Treatment of the Megaloblastic Anæmias, Radioactive Isotopes, Methods of Investigation and Pathogenesis of the Hæmolytic Anæmias, Laboratory Aspects of Transfusion Technique, Effect of Endocrine Organs and Hormones on the Cellular Constituents of the Blood, and Methods of Investigating the Hæmorrhagic Disorders The sections of morbid anatomy and chemical pathology will also hold a joint session on Bone Metabolism, and the sections of chemical pathology and hæmatology a joint session on Pigment Metabolism and Hæmoglobin Members of the congress are to be entertained by the Government, the Royal College of Physicians, the Royal College of Surgeons, the British Medical Association, the Goldsmiths' Company, and the University of London. The congress banquet will take place on July 20 at Grosvenor House Further particulars may be had from the hon secretary, Dr W H McMenemey, Maida Vale Hospital for Nervous Diseases, London, W 9

BIRDS THAT "COUNT"

Ever since the time of Shakespeare's " dancing horse,"[1] Banks's Morocco, which was said to be able to count money, trained performing animals have appeared that seemed able to count There are two ways of counting Obviously an animal can distinguish between one object and two objects of the same kind The animal does not need, even if it could talk, the words " one " and " two," which are merely symbolic of the numbers seen One must keep firmly in mind the fact that a word is merely a symbol of an object The first thing that happens is that one recognises the object , only later does one need a symbol (a noise, a drawing, or a gesture) of that object for the purpose of communication with another person So, in counting, one recognises first the number, and later uses a symbol to express that number Koehler's[2] birds cannot talk , so obviously they cannot count 'one, two, three " either audibly or inaudibly but there is no known reason why they cannot tell the difference between one pea, two peas, and three peas, so long as they can see them practically simultaneously and compare the groups It is no valid objection that a bird watcher entering a hide takes with him a second person, who later leaves the hide, thus deceiving the bird into thinking that the coast is clear, for the bird cannot then compare one person with two and has presumably forgotten how many persons had originally come to the hide Koehler admits this '*Our birds did not count*, for they lack words They could not name the numbers that they are able to perceive and to act upon, but in actual fact they learn to '*think unnamed numbers* ' But by intensive training, with the aid of stereotyped punishment, Koehler taught his birds to distinguish not only between different numerical groups presented simultaneously but also (unlike the bird watching the hide) between different numerical groups presented successively On one occasion an even greater advance was apparently made A jackdaw, trained to open boxes until it had secured five baits, went back to its cage on one occasion after securing only four of the five, which were distributed in the first five boxes in the following order 1 2, 1,

---

[1] Love's Labour's Lost act I scene 2

[2] Koehler O *Bull Animal Behaviour* 1951 no 9 p 41

THE TREATMENT OF PSYCHONEUROTICS

SOME PRACTICAL CONSIDERATIONS

W. LINDESAY NEUSTATTER
M.D., B.Sc. Lond., M.R.C.P.
PHYSICIAN IN PSYCHIATRY, ROYAL NORTHERN HOSPITAL, LONDON; PHYSICIAN, ST EBBA'S HOSPITAL, EPSOM

ARE psychoneurotics best treated as outpatients or as inpatients? If the latter, in general or special hospitals? How long should they stay? What is the rôle of physical therapy, much in vogue and much quicker than psychotherapy? These are topical questions having regard to problems of medical establishments and the need to make full use of man power. They are discussed here in the light of experience in general and mental hospitals.

PHYSICAL THERAPY

Opinions about the value of physical treatment in psychiatry vary widely, from Winnicott (1947), who has inveighed fiercely against it—not because it is empirical but because it led away from psycho-analytic explanation of mental disorder—to such enthusiastic exponents as Sargant and Slater (1948), Sands (1946), and Mallinson (1948). But only electroconvulsive therapy (E.C.T.) is relevant to my cases here, and it should be noted that its advocates all emphasise the importance of its judicious use, and the judicious selection of cases. Sands (1946), in particular, has shown that it is essentially the patients with psychotic depression who benefit from it, and warns against its ill effects in hysteria.

All these workers emphasise the need for careful history-taking, and the need to deal with psychological and sociological factors as well. But unfortunately the enthusiasm aroused by finding physical methods of treatment—which, one suspects, in some cases also avoid the necessity of accepting unpalatable psychopathological theory—combined with the ease of administration of E.C.T., is apt to lead to the use of E.C.T. for any patient showing symptoms of depression, without sufficient consideration of whether it is appropriate, or without making allowance for spontaneous improvement.

Preoccupation with physical methods can also induce in trainee psychiatrists a frame of mind which is somewhat disturbing. Thus, one young psychiatrist's *first* idea for the treatment of a moderately severe anxiety state of a year's duration, which was improving, was leucotomy; another wanted an incompletely investigated patient with symptoms of depression to have E.C.T. because "it wouldn't do any harm anyway."

These are two extreme examples, but it is noteworthy how even registrars who go painstakingly into psychogenic factors seem to feel impelled, *immediately* the patient shows any signs of depression, to think in terms of E.C.T., forgetting how commonly it is only a transient mood, which will resolve spontaneously.

This paper is not written in any spirit of hostility to physical treatment as such—I have seen sufficiently good results in appropriate cases—but I feel justified in recording a small series of cases as a reminder that less drastic methods can also be efficacious. These have the advantage of depending on the patients' natural powers of recuperation and thereby enhancing them, and they are free from risk.

For though physical methods are usually safe, nevertheless there is an element of risk; and though this risk may justifiably be taken if the case is severe, the milder the disorder the less warrant is there for taking even a small risk of a serious complication such as the fracture of the neck of a humerus. The physical complications of these treatments are so widely described in psychiatric literature that I do not propose to deal with them here. But I wish to say something about the undesirable psychological sequence.

Treatment being Distasteful to the Patient

That treatment is distasteful is clearly not in itself an absolute contra-indication. But when, as in the case of leptazol, an element little short of terror was introduced, its use was clearly not justified, unless there were very strong grounds for expecting it to succeed where other methods would not.

With E.C.T. this element of suffering is not present. Nevertheless there are patients who fear E.C.T. and refuse to continue with it. Very likely the neurotic element referred to by Sands (1946) is present. Sargant and Slater (1948) emphasise the undesirability of subjecting unwilling patients to this treatment. They emphasise that the response to each shock should be studied, and that there should not be a predetermined number of shocks irrespective of their effects.

A woman, aged 35, came to me after leaving hospital saying she could no longer tolerate another treatment; she was having her nineteenth E.C.T. with no effect. No one seemed to have gone into the history sufficiently to discover that this woman was living alone in a small house with a mother aged 81 and that her life was one of intense boredom. After some talks with me, although her environment could not be changed she improved considerably; but unfortunately she relapsed again in a few weeks' time. My superficial psychotherapy was therefore very little more efficacious than the E.C.T.; but, if treatment is to be ineffective it would seem preferable for failure to follow a few talks than to follow nineteen convulsions.

Failure to bring Psychological and Sociological Factors to Light

Sands (1946) refers to the fact that in unsuccessful E.C.T. further probing may reveal psychogenesis, and that the E.C.T. may be diagnostic. I should prefer it the other way round, for there always seems to be a danger that the ease with which E.C.T. can be given may breed a press-button outlook.

Actual Harmful Psychological Sequelæ

Hadfield (1950) has reported a case where the alarm engendered by E.C.T. caused subsequent hysterical symptoms. The following example also shows this, though the "psychic trauma" was of a negative kind, being due to a failure to uncover a source of the anxiety.

A woman, aged 45, developed a pain in the leg. She consulted an orthopædic surgeon, who found nothing wrong and passed her on to a psychiatrist. As she was depressed she was given four electroconvulsive treatments as an outpatient. She was then transferred, as an inpatient with hysterical paralysis of a leg, to another hospital, where I asked her how she had become depressed. Almost immediately she explained that she had been very worried about the pain in her leg, which she thought was due to a growth pressing on a nerve to her leg. Neither the orthopædic surgeon nor the psychiatrist had apparently given her any explanation of the pain. She was vigorously reassured that no organic cause had been found, given a couple of days' rest in hospital, and discharged because the paralysis had disappeared.

CASES TREATED IN A GENERAL HOSPITAL

The series of cases presented here consists of twelve women, aged 21–42, with nothing of note in their family or past history except a tendency to nervousness. One was the hysteric mentioned above; one is described below; and there were ten others admitted to Harold Wood Hospital in the course of a year. They all had diffuse anxiety symptoms of a somatic form, and/or there was undue worrying but no specific phobias. All were depressed, three very much so (two had had suicidal thoughts); two were compensation cases with a hysterical

International Council of Ophthalmology

At a meeting of the council in Paris on May 5, the following appointments were confirmed president, Sir Stewart Duke Elder, vice president, Conrad Berens secretary, Edward Hartmann (2 Avenue Ingres, Paris, XVIe), treasurer, Marc Amsler The 17th international congress of ophthalmology is to be held in New York in the autumn of 1954 under the presidency of Bernard Samuels

Society for Relief of Widows and Orphans of Medical Men

At the annual general meeting of this society on June 6, Sir Ernest Rock Carling, the treasurer, presented the accounts for 1950 At present 39 widows receive grants, and the total amount distributed last year was £5028 The membership of the society is 240 Further particulars may be had from the secretary, 11, Chandos Street, London, W 1

Conference on School Punishments

Over 200 teachers, doctors, psychologists, and parents met at the House of Commons on June 6 under the chairmanship of Mr Cyril Bibby, M SC, to discuss Education without Fear The consensus of opinion at the meeting was that coercion in schools, including specifically the use of corporal punishment, militated against good discipline, which could best be obtained by adult example, a common purpose, and mutual understanding between teacher and taught A resolution was passed calling upon the Minister of Education to expedite publication of the report on the inquiry into punishment and reward which, in 1947, he asked the Foundation for Educational Research to undertake

International Research Centre for Chemical Microbiology

The International Research Centre for Chemical Microbiology will be formally opened in Rome on June 25 The centre, directed by Prof E B Chain, F R S, is attached to the Istituto Superiore di Sanità, the chief institution for medical research and drug control of the Italian government The centre, which is recognised by W H O, will provide research and training facilities in antibiotics It is expected to meet the need of countries which lack facilities for basic research on antibiotics, particularly on problems of production An international symposium will be held on June 25–30 in connection with the inauguration of the centre, speakers from the United Kingdom will include Sir Norman Hinshelwood, F R S, Mr D D Woods, and Dr A A Miles

Award for Bravery

The King has appointed Dr P S London a member of the Order of the British Empire

In the course of transporting a 35 ton Comet tank through Birmingham it became necessary to unload the tank from the transporter in order that both vehicles could ascend a sharp incline in the centre of the city When the tank was being remounted on to the trailer it heeled over and fell to the ground, trapping a man between the tank tracks and a parapet wall Dr London was in charge of the mobile surgical unit which was summoned, and on his arrival he immediately went to the trapped man and commenced anti shock treatment In order to release the man hawsers were fixed to the tank which was then slowly raised from the wall on which it was resting To prevent further injury to the man Dr London jumped into the cavity between the wall and the still moving tank so that he could support him. Dr London was fully aware of the danger that the tank might fall back on him during the lifting operations, but without regard for his own safety he remained with the injured man until the latter had been released and removed to hospital

Commission on Narcotic Drugs

The United Nations commission on narcotic drugs met in New York from April 10 to May 21 The commission, comprising delegates from Canada, China, Egypt, France, India, Iran, Mexico, Netherlands, Peru, Poland, Turkey, U S S R, United Kingdom, U S A, and Yugoslavia, discussed the formation of an International Opium Monopoly, to limit opium production Unfortunately the delegates were unable to agree on the functions of the proposed monopoly, so it accepted an amended form of a proposal made by France to apply the provisions of the 1931 convention to opium This proposal provides for (1) an estimate system, (2) statistical returns, (3) limitation of production and import of opium within the estimates, (4) establishment of national opium monopolies, (5) international control which would permit the imposing of embargoes and local inquiries, and (6) control of the non medical use of opium

State University of New York

Dr Perrin H Long has resigned the chair of preventi medicine at Johns Hopkins University to become executi officer of the department and professor of medicine in th newly created college of medicine at the State University o New York He will take up this post in the autumn

Petrochemicals Ltd have now published the second o their technical service leaflets It is entitled the Handli and Storage of Ethylene Oxide Copies may be had from the sales department, 170, Piccadilly, London, W 1

Appointments

BERGIN, J H F, M B Camb, D M R D radiologist, Swindon, Cirencester, and Pewsey area

CURRAN, A P, M B, B SC Glasg, D I H deputy M O H and deputy schools M O, Luton

HALLIDAY, H G M B Glasg, appointed factory doctor, Oldham west district, Lancs

JONES, A G, B A, M R C O G consultant obstetrician and gynæcologist, Merthyr and Aberdare H M C

LAST, S L, M D Berlin, L R C P E, D P M psychiatrist, general and mental hospitals, Aylesbury and district H M C

LEWIS, R D, B A, M B Dubl, D A consultant anæsthetist, Central Middlesex Hospital, London

McCLUSKIE, J A W, M B Glasg, F R F P S consultant physician in charge of wards, Glasgow Western Infirmary

MELLOR, J G, M B Manc chest physician, Plymouth clinical area

SAMMAN, P D, M A, M D Camb, M R C P consultant dermatologist, Chelsea group of hospitals

SYRED, D R, M R C S, D M R D radiologist Northampton and Kettering area

Diary of the Week

JUNE 17 TO 23

Monday, 18th

UNIVERSITY OF LONDON
5 30 P M (Westminster Medical School, Horseferry Road, S W 1) Dr Edmond J Farris (Philadelphia) Male Fertility

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M (1, Wimpole Street, W 1) *Festival programme* Poliomyelitis
2 15 P M Endocrinology

Tuesday, 19th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C 2
3 15 P M Dr H D Ross Synovial Reactivities (Arnott demonstration)

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M *Festival programme* Decline of Infant Mortality
5 P M Burns

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane W 1
2 30 P M Mr G O Knight Spinal Compression

INSTITUTE OF DERMATOLOGY St John's Hospital, Lisle Street, W C 2
5 P M Dr L Forman Cutaneous Manifestations of Visceral Malignancy

Wednesday, 20th

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M *Festival programme* Peptic Ulcer
2 15 P M Experimental Endocrinology

INSTITUTE OF DERMATOLOGY
5 P M Dr R W Riddell Medical Mycology—Systemic Infections

SOCIETY FOR THE STUDY OF FERTILITY
9 15 A M (Girton College, Cambridge) Opening of two day conference

Thursday, 21st

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M *Festival programme* Nutrition and the B Vitamins
2 P M Neurosurgery

ST GEORGE'S HOSPITAL MEDICAL SCHOOL Hyde Park Corner S W 1
1 30 P M Dr Denis Williams Neurology lecture demonstration

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE 26 Portland Place W 1
7 30 P M Sir Philip Manson Bahr *Filariasis in Fiji* (film) Dr H C De Souza Araujo Two New Cultures of *Mycobacterium lepræ hominis* Pathogenic for *Macacus rhesus*

Friday, 22nd

ROYAL COLLEGE OF SURGEONS
3 15 P M Dr Ross Synovial Reactivities (Arnott demonstration)

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M *Festival programme* Problems of Cardiovascular Disease in an Ageing Population
2 15 P M Orthopædics

INSTITUTE OF DERMATOLOGY
5 30 P M Dr F R Bettley Clinical demonstration

THE TREATMENT OF PSYCHONEUROTICS

SOME PRACTICAL CONSIDERATIONS

W LINDESAY NEUSTATTER
M D, B Sc Lond, M R C P
PHYSICIAN IN PSYCHIATRY, ROYAL NORTHERN HOSPITAL, LONDON, PHYSICIAN, ST EBBA S HOSPITAL, EPSOM

ARE psychoneurotics best treated as outpatients or as inpatients ? If the latter, in general or special hospitals ? How long should they stay ? What is the rôle of physical therapy, much in vogue and much quicker than psychotherapy ? These are topical questions having regard to problems of medical establishments and the need to make full use of man power They are discussed here in the light of experience in general and mental hospitals

PHYSICAL THERAPY

Opinions about the value of physical treatment in psychiatry vary widely, from Winnicott (1947), who has inveighed fiercely against it—not because it is empirical but because it led away from psycho analytic explanation of mental disorder—to such enthusiastic exponents as Sargant and Slater (1948), Sands (1946), and Mallinson (1948) But only electroconvulsive therapy (E C T) is relevant to my cases here, and it should be noted that its advocates all emphasise the importance of its judicious use, and the judicious selection of cases Sands (1946), in particular, has shown that it is essentially the patients with psychotic depression who benefit from it, and warns against its ill effects in hysteria

All these workers emphasise the need for careful history taking, and the need to deal with psychological and sociological factors as well But unfortunately the enthusiasm aroused by finding physical methods of treatment—which, one suspects, in some cases also avoid the necessity of accepting unpalatable psychopathological theory—combined with the ease of administration of E C T, is apt to lead to the use of E C T for any patient showing symptoms of depression, without sufficient consideration of whether it is appropriate, or without making allowance for spontaneous improvement

Preoccupation with physical methods can also induce in trainee psychiatrists a frame of mind which is somewhat disturbing Thus, one young psychiatrist's *first* idea for the treatment of a moderately severe anxiety state of a year's duration, which was improving, was leucotomy, another wanted an incompletely investigated patient with symptoms of depression to have E C T because " it wouldn't do any harm anyway "

These are two extreme examples, but it is noteworthy how even registrars who go painstakingly into psychogenic factors seem to feel impelled, *immediately* the patient shows any signs of depression, to think in terms of E C T, forgetting how commonly it is only a transient mood, which will resolve spontaneously

This paper is not written in any spirit of hostility to physical treatment as such—I have seen sufficiently good results in appropriate cases—but I feel justified in recording a small series of cases as a reminder that less drastic methods can also be efficacious. These have the advantage of depending on the patients' natural powers of recuperation and thereby enhancing them, and they are free from risk

For though physical methods are usually safe, nevertheless there is an element of risk, and though this risk may justifiably be taken if the case is severe the milder the disorder the less warrant is there for taking even a small risk of a serious complication such as the fracture of the neck of a humerus The physical complications of these treatments are so widely described in psychiatric literature that I do not propose to deal with them here But I wish to say something about the undesirable psychological sequence

Treatment being Distasteful to the Patient

That treatment is distasteful is clearly not in itself an absolute contra indication But when, as in the case of leptazol, an element little short of terror was introduced, its use was clearly not justified, unless there were very strong grounds for expecting it to succeed where other methods would not

With E C T this element of suffering is not present Nevertheless there are patients who fear E C T and refuse to continue with it Very likely the neurotic element referred to by Sands (1946) is present Sargant and Slater (1948) emphasise the undesirability of subjecting unwilling patients to this treatment They emphasise that the response to each shock should be studied, and that there should not be a predetermined number of shocks irrespective of their effects

A woman, aged 35, came to me after leaving hospital saying she could no longer tolerate another treatment, she was having her nineteenth E C T with no effect No one seemed to have gone into the history sufficiently to discover that this woman was living alone in a small house with a mother aged 81, and that her life was one of intense boredom After some talks with me, although her environment could not be changed, she improved considerably but unfortunately she relapsed again in a few weeks' time My superficial psychotherapy was therefore very little more efficacious than the E C T, but, if treatment is to be ineffective it would seem preferable for failure to follow a few talks than to follow nineteen convulsions

Failure to bring Psychological and Sociological Factors to Light

Sands (1946) refers to the fact that in unsuccessful E C T further probing may reveal psychogenesis, and that the E C T may be diagnostic. I should prefer it the other way round, for there always seems to be a danger that the ease with which E C T can be given may breed a press button outlook

Actual Harmful Psychological Sequelæ

Hadfield (1950) has reported a case where the alarm engendered by E C T caused subsequent hysterical symptoms The following example also shows this, though the " psychic trauma " was of a negative kind, being due to a failure to uncover a source of the anxiety

A woman, aged 45 developed a pain in the leg She consulted an orthopædic surgeon, who found nothing wrong and passed her on to a psychiatrist As she was depressed she was given four electroconvulsive treatments as an outpatient She was then transferred, as an inpatient with hysterical paralysis of a leg, to another hospital, where I asked her how she had become depressed Almost immediately she explained that she had been very worried about the pain in her leg, which she thought was due to a growth pressing on a nerve to her leg Neither the orthopædic surgeon nor the psychiatrist had apparently given her any explanation of the pain She was vigorously reassured that no organic cause had been found, given a couple of days' rest in hospital, and discharged because the paralysis had disappeared

CASES TREATED IN A GENERAL HOSPITAL

The series of cases presented here consists of twelve women, aged 21–42, with nothing of note in their family or past history except a tendency to nervousness One was the hysteric mentioned above, one is described below, and there were ten others admitted to Harold Wood Hospital in the course of a year They all had diffuse anxiety symptoms of a somatic form, and/or there was undue worrying but no specific phobias All were depressed, three very much so (two had had suicidal thoughts), two were compensation cases with a hysterical overlay, none were obsessional, and none psychotic All appeared overwrought and overtired, and were either sleeping badly or insufficiently, and it was because of these last features that I admitted them to hospital

I should add that all the depressions appeared reactive, and, though some constitutional element was probably present as well, none were primarily endogenous in the sense that they were psychotic or appeared to have come on spontaneously The following are two examples

Mrs A, aged 35, had had a bad childhood owing to a broken home While her husband was abroad in the war, she had been greatly troubled by the responsibility of children and financial worries and even now, after the return of her husband, with whom she got on well, she was worried about these things She went to bed at 9 30 P M but was always up between 5 and 6 A M She had had no holiday for years, and was becoming progressively more tired She was lonely in the daytime, had begun to avoid meeting people, had become unsocial and generally nervy, and, when I saw her, was noticeably overtired overwrought, and depressed

Mrs E, aged 40, had no house of her own but was hoping to get one In other ways her domestic life was happy She had to sleep in the same room as her baby, and lacked sleep badly Consequently she had become depressed very easily, tearful, and had thought of committing suicide She also appeared thoroughly overwrought when I examined her

In two other cases the precipitating cause of the depression had been an accident, concerning which litigation was pending These patients had become so anxious and depressed that I thought it necessary to take them into hospital, partly for quietness and sedation, partly to abreact them

TREATMENT

The patients were treated in Harold Wood Hospital, an ex E M S hutted building, light and airy, with pleasant grounds, on the green belt of Essex The usual régime * was to keep the patients in bed for about a week, and then to start getting them up, and to discharge them at the end of two or three weeks A point was made of ensuring sleep during the first week, even if large doses of hypnotics were needed Sometimes the patients were given sedatives in the daytime as well, but nothing approaching "continuous narcosis" was used When they got up they were allowed in the wards, or in the not very extensive grounds, and given occupational therapy, but no other recreation was possible Nor were the patients allowed to leave the hospital premises, as is nowadays generally permitted in mental hospitals Consequently they tended to become somewhat bored and were not averse to going home From the outset it was also made clear that they would not be kept in longer than two or three weeks, and this rule was strictly kept

Psychotherapy was of a simple order I was only visiting once a fortnight at the time, so, except for one or two interviews with me and two abreactions under thiopentone, psychotherapy largely amounted to a sympathetic hearing by a house physician But in view of the importance of the general atmosphere of a ward in producing relaxation, it is relevant that Harold Wood Hospital is a very "happy ship", and that this friendly spirit permeated into the wards, as was shown by the spontaneous testimony of three of the patients, one of whom said she had never known a hospital could be so nice—praise indeed from a neurotic

RESULTS

If the disappearance of all major symptoms is taken as the criterion of recovery, 2 patients recovered (the patient with hysteria referred to above and the one with depression described below) If better sleep, a more rested appearance, and the patients' reports of lessened anxiety and depression are taken as constituting improvement, three improved greatly—two of them in spite of the fact that the external situation remained unaltered, and one clearly owing to learning that at last she had got a better house—six improved moderately, including both the compensation cases, and one who discharged herself, was unchanged

I tried to follow up the cases a year later, but only five patients replied, one of these was the one who had not improved, and the four others had maintained their moderate improvement, including the compensation case

The results are open to the usual criticism of follow-ups and criteria of improvement which are largely subjective, but they are probably as accurate as most clinical assessments and numerically the results are significant It can be urged that those patients were clearly a highly selective group and suited to this treatment, but all I am trying to show is that the methods described can be efficacious

My cases were not ones where E C T or leucotomy was indicated, but that they are the type which do get treated by E C T is shown by the fact that one patient had had it, and another had had it prescribed by a colleague of mine who was taken ill and could not give it In my view this second patient primarily needed rest, so I put her to bed for fourteen days, and when my colleague returned he found it unnecessary to give E C T

OPTIMUM STAY IN PSYCHIATRIC HOSPITALS

The length of stay in hospital is an important question both clinically and economically

It will be noted that I discharged my patients within three weeks, as a result of very careful selection The optimum length of stay for psychoneurotics can be a serious problem in psychiatric hospitals, which cannot always select their cases And any shortage of staff may interfere with a rapid discharge rate, and possibly be a factor in the large proportion of patients leaving early against advice, though probably the personality of the patients is the main factor

I analysed a series of cases treated last year at a progressive mental hospital Of 50 men and 50 women selected at random, whose stay averaged nine weeks, 14 recovered and 41 improved On the other hand, 9 men and 10 women (1 obsessional, 2 anxiety states, 8 hysterics, and 8 psychopaths) left within fourteen days, condition unchanged As a lengthy history is taken by the doctor and lengthy inquiries are made by the psychiatric social workers during the first week, this entailed a considerable waste of time in 20% of cases, and is an argument for judicious selection It confirms one aspect of Blacker's (1946) observations on the danger of inpatient facilities being abused "it is an easy way of disposing of awkward cases"

At the other extreme are unduly long stays Of the same 100 patients 7 were in hospital longer than six months, including 2 psychopaths who stayed for fifty two weeks and forty four weeks

The following figures of cases diagnostically comparable to mine, kindly furnished by a neurosis hospital, show that of 58 women with anxiety states or reactive depressions 22 stayed less than a month (16 improved), 20 stayed three months (18 improved), 14 stayed six months (12 improved), and 2 stayed longer than six months (both improved) In spite of the good results, these are long periods off work, and one wonders how far they could be reduced This is a thorny point, which troubled the military authorities during the late war

---

* A thoroughly old fashioned one which I had found useful in Army hospitals I am referring to base hospital treatment not battle casualties

In a mental hospital a valuable part of the rehabilitation of recovering psychotics is to get them to mix, to encourage normal interests, and to get them back to work. To facilitate these laudable aims, many and varied recreations and interesting occupational therapy are arranged. The patients are given weekend leave, efforts are made to find them work outside the hospital, even while still resident there, and everything is done to make their surroundings as pleasant and “uninstitutional” as possible. With psychotics these provisions are beneficial, for they are anxious to get out and reassert themselves as normal. With psychoneurotics, unfortunately, they often tend to act as a counter-incentive to recovery, for the neurotic has not got to prove himself anew, and admission to hospital is an excellent escape from the difficulties of life outside. Consequently such patients may develop secondary hysterical reactions with an outcrop of symptoms, and even suicidal threats, at the suggestion of discharge.

Some patients undoubtedly have very real difficulties, and very unpleasant situations to face at home; but, just as it is harder to settle down to work after a month on the Riviera than after a wet fortnight observing the houses facing “Sea View,” so the easier life is in hospital the harder is the return to the outside world. It is of course, in hysterics and psychopaths especially that the distaste for relinquishing a congenial life of arts and crafts for the hard world outside is most noticeable, as exemplified by a chronic psychopathic patient of mine whom I urged to start picking up the threads of his old work. “I get you, Doc,” he said, “You mean I'm to get fit by work,” He paused, and added “Or, of course, I might do it through playing tennis”—a prescription that he industriously carried out by regularly playing execrable tennis, but with no therapeutic result.

What is the solution? Clearly no one is deliberately going to make hospitals uncongenial and unattractive. Nor is it desirable to reverse the present tendency of treating psychotics and psychoneurotics in one hospital, for this helps to break down the artificial distinction leading to the belief that there is something shameful about mental illness.

INDICATIONS FOR OUTPATIENT AND INPATIENT TREATMENT

The best solution where possible is not to admit psychoneurotics to hospital at all, a view in keeping with Blacker's (1946).

For therapeutic purposes psychoneurotics can be considered under three heads:

1. Those with severe intractable but specific symptoms, such as phobias and obsessions, who, though of generally good personality, are unlikely to benefit much from psychotherapy.
2. Those who have developed either anxiety or depression in association with feelings of inferiority, shyness, difficulty in mixing, &c., as a result of emotional difficulties brought about by mishandling and faulty upbringing, but *not* owing to any fundamental personality defect.
3. Those who have a variety of symptoms, and, owing to either an innate hypersensitivity or an inability to cope with their emotions, over-react to ordinary stresses and strains of life. These are the real “neurotics.”

The degree of incapacity in group 1 is usually proportional to how far the symptoms affect the patient's daily life. Thus, a patient had a phobia of drowning if he entered the sea, but in no way did it affect his daily life in town. Fear of travel clearly is a serious disability which would necessitate treatment in hospital, but otherwise these patients do not need it. Group 2 patients are likely to benefit from psychotherapy, but, unless the communal atmosphere of hospital is considered necessary, they too can perfectly adequately be treated as outpatients. Group 3, being already poorly adapted, removal from their ordinary environment is most undesirable, for many months may elapse before the precarious balance which existed is restored and they are got back to work.

Three groups of psychoneurotics do need admission to hospital: (1) Those who, like my patients described here, are essentially overwrought and overtired, and need a break and a rest, which is best given in a general hospital. (2) Those needing fuller investigation and more specialised treatment than a general hospital can afford. Unless lengthy analytic treatment is to be attempted, I suggest that six weeks is the longest stay that should be aimed at; on admission it should be made clear to the patient that only a short stay is intended, and the whole atmosphere should have a spirit of urgency about it. Unless there are exceptional circumstances, a strict working régime should start at once and be adhered to, with passes out of hospital given only for short periods. Weekend passes are contra-indicated; for, if a patient's conditions warrants being in hospital, it does not warrant his going out at the weekends immediately after admission. (3) A group who at present have to be admitted to hospital owing to lack of therapeutic facilities elsewhere, especially in outlying districts. This group should be, and to some extent is being, gradually eliminated, but it is one having a special bearing on problems of medical man-power and economic considerations.

Apart from the clinical aspect, it is economically disadvantageous to treat psychoneurotics as inpatients. A mental hospital with a turnover of 1000 psychoneurotics and psychotics last year cost about £200,000 to run—an average of £200 per patient. According to the Ministry of Health five outpatients can be treated at the cost of one inpatient—i.e., £40 per outpatient in this instance. But psychotherapy requires very little equipment or auxiliary help, and this figure is therefore probably high.

At an outpatient clinic where I hold a weekly session, I saw last year 205 adults and children, and kept two assistants employed on psychotherapy. One assistant treated 30 children and 20 adults in the year, interviews ranging from 2 to 24; the other saw 155 adult old patients, treating 70 of these from 2 to 9 sessions per patient, and giving the others supportive treatment. This example illustrates how individual the number of therapeutic sessions is, and the number of times a patient should be seen is hard to dogmatise about, because it varies so with each therapist. Until there is convincing evidence that its results are so much better than those of shorter methods, psycho-analysis cannot be proposed as a routine treatment, because it takes up so much time.

I should say that a psychotherapist would see a patient on an average 8 times for treatment. On this assumption, if he sees 4 patients per session only, he would treat one patient for the equivalent of a day, and, since there are about 250 working days a year, four therapists of S.H.M.O. grade could see 1000 patients at the cost of about £6800 a year in salaries, plus relatively small overhead expenses.

I believe new psychoneurosis hospitals are being planned, but these calculations, though omitting overheads, show that, with the money needed to run only one such hospital, a substantial, or possibly complete, coverage of psychotherapists for the country could probably be obtained, thus keeping many patients not only out of hospital but also at work. Not only would this save the benefit paid them while they are off work, but it would also prevent loss of earnings and, even more important, loss of work.

This, of course, is not so simple as it sounds; for employers object to employees being away once or twice a week. Education of the employers and the extension of facilities for evening therapeutic sessions could help to meet this situation. A difficulty is that to increase facilities creates a further demand. At present it is the commendable self restraint of the general practitioner in crowded areas that prevents the swamping of available services, which over enthusiastic salesmanship of psychiatry might well bring about. Unfortunately one's appreciation of their forbearance must take the form of referring back untreatable cases, for the attendance of many "chronics" is bad for the morale of new patients (Blacker 1946). Moreover the results of accepting unsuitable cases for psychotherapy only confirm sceptics in their belief of its inefficacy. Careful selection, even though it may court temporary unpopularity, will in the end benefit clinics and patients by causing the right type of cases to be referred.

I emphasise the need for psychotherapy because in my experience most outpatients needing other than purely supportive treatment require this. I have run clinics with very few referrals for E C T, but, lest my view be considered prejudiced, I cite a personal communication from Dr T Munro, who estimated that out of 300 new patients attending Guy's Hospital outpatients department only 6% required E C T. When there are not enough facilities for psychotherapy, I am sure there is a tendency—based on a laudable desire to do something for the patients—to use E C T in unsuitable cases, as I have discussed above.

SUMMARY AND CONCLUSIONS

Objections to E C T in certain cases is discussed in relation to a small series of cases responding to simple measures in a general hospital.

Clinically and economically, it is preferable for psychoneurotic patients to be treated as outpatients. Inpatient treatment should be used sparingly, and stay in hospital should be short.

I wish to thank Dr W J S Ewan, physician, Dr R Moore, former registrar, and the doctors and nurses of Harold Wood Hospital for all they did for my patients, the improvements recorded were essentially due to their efforts.

REFERENCES

Blacker C P (1946) Neurosis and the Mental Health Service London
Hadfield J A (1950) *Brit med J* ii, 679
Mallinson, W P (1948) *Ibid* ii 641
Sands, D E (1946) *Ibid* ii 289
Sargant W Slater L (1948) Introduction to Physical Methods of Treatment in Psychiatry Edinburgh
Winnicott, D W (1947) *Brit med J* i, 688

STREPTOKINASE AS AN ADJUNCT IN THE TREATMENT OF TUBERCULOUS MENINGITIS

JOHN LORBER
M B Camb, M R C P
LECTURER IN CHILD HEALTH, UNIVERSITY OF SHEFFIELD

THERE are many causes of failure in the treatment of tuberculous meningitis, but from the pathological aspect perhaps the most important is the development of obstruction in the cerebrospinal circulation. Any method of treatment that would prevent such blocks, or remove them might be of great value.

The incidence of these blocks, their distribution, and their detection by the use of penicillin as a tracer substance and by pneumo encephalography have been described elsewhere (Lorber 1950, 1951). Pathological studies show that they are caused by deposition of fibrin and by tuberculous granulation tissue, mostly around the brain stem in the cisterna ambiens, in the cisterns at the base of the brain and round the cord in the spinal subarachnoid space. Later the deposit organises into fibrous tissue.

Because fibrin is the cause of blocks, Cathie tried the effect of giving streptococcal fibrinolysin intrathecally as an adjunct in the treatment of tuberculous meningitis. He prepared a suitable preparation (Cathie 1949a) of streptokinase, and in a preliminary report (Cathie 1949b) compared his early results in two successive series of cases. Series A consisted of 14 children treated with streptomycin alone, of whom only 3 (21%) survived. Series B consisted of the next 21 children, treated with both streptomycin and streptokinase, of whom 11 recovered (52%), 2 relapsed after apparent recovery (their fate was not stated), and 8 died. But the scheme of intrathecal streptomycin treatment was altered when streptokinase was introduced, and a later publication (Cathie and MacFarlane 1950) disclosed that there were further changes in treatment—namely, the addition of intrathecal 'Sulphetrone' and the frequent use of ventricular catheterisation. Moreover, increased experience may have played a large part in the improvement of results. The two series therefore were not strictly comparable. The only toxic symptom mentioned was a pleocytosis in the cerebrospinal fluid (C.S.F.) similar to that caused by streptomycin.

At the time of Cathie's preliminary report, our own results in the treatment of tuberculous meningitis in children showed that there were 4 survivors in our first series of 14 children and 11 in the next series of 21. Streptokinase had not been used. The patients were kept under observation for about the same length of time as in Cathie's cases.

With these considerations in mind it was decided to conduct a controlled experiment to assess the value of streptokinase.

INVESTIGATION

The present investigation was planned to take place during 1950 and to continue only if the results at the end of one year were promising. It was decided to use intrathecal streptokinase in half the cases of tuberculous meningitis admitted under the care of the unit during 1950, and cases were chosen at random. Of 27 new patients, 2 had already been treated elsewhere for several weeks, and 1 had combined tuberculous and meningococcal meningitis on admission, these 3 were excluded from the investigation. Of the remaining 24 bacteriologically confirmed cases, it happened that 12 (group A) were treated with combined intrathecal streptomycin and streptokinase, and 12 (group B) with streptomycin alone. In all other respects the treatment was similar in the two groups. Routine intrathecal treatment was given by lumbar puncture daily for two periods of twenty one days separated by one week's rest. Further intrathecal treatment was given only if the child's condition required it. Cisternal and ventricular injections were used as required in cases with spinal blocks. Intramuscular streptomycin was given in the usual daily dose of 20 mg per lb body weight for a minimum of six months if the patient survived. Intrathecal tuberculin P P D (purified protein derivative), was given to 7 children (3 in group A and 4 in group B), but only after other forms of treatment were thought to have failed. With 1 exception, treatment was begun within twenty four hours of admission. In 1 child in group A the diagnosis was in doubt for three days and treatment was delayed accordingly. A uniform dose of 6 units of streptokinase (Burroughs Wellcome), dissolved in a solution containing streptomycin 25–75 mg, was injected intrathecally daily for as long as was considered necessary. This solution was active, in vitro, at room temperature. it dissolved the fibrin clot formed in the C S F from cases of tuberculous meningitis, and the dilution was comparable to that obtained in vivo. The following remarks will apply only to the commercial preparation which has been used.

TABLE I—AGE OF PATIENTS, STAGE OF DISEASE, AND PRESENCE OR ABSENCE OF MILIARY TUBERCULOSIS IN THE TWO GROUPS

Group of patients and treatment given	Age		Stage of disease			Miliary tuberculosis	
	Under 3 years	3 years and over	Early	Intermediate	Advanced	Present	Absent
A (streptomycin and streptokinase)	4	8	2	4	6	5	7
B (streptomycin alone)	4	8	2	4	6	4	8
Total	8	16	4	8	12	9	15

In this investigation there was no selection of patients, and no case was refused admission and treatment The proportion of advanced cases was very high in both groups The ages of the children, the stage of the disease at the beginning of treatment (according to the Medical Research Council classification, 1948), and the presence or absence of miliary tuberculosis detected in life, are shown in table I The two groups were remarkably similar in all respects

In May, 1950, 14 of the 24 children were alive—7 from group A and 7 from group B The survivors were observed for six to sixteen months, far too short a time to assess the final results of treatment, but long enough to assess the specific effect of streptokinase, which is the purpose of this paper The children were investigated by the methods *mentioned elsewhere* (Lorber 1950, 1951) to detect the presence of blocks in the cerebrospinal circulation Necropsy was performed on 3 of the 5 children in group A who died, and on all 5 children in group B who died

RESULTS

None of the children had a spinal block on admission Complete spinal block developed during treatment in 4 of group A and in only 1 of group B Partial spinal block was detected in 2 children—1 from each group Of these 7 children with spinal obstruction, 5 died, and in 2 the complete block (1 in each group), and in 1 the partial block, was confirmed at necropsy These blocks were caused by tuberculous granulation tissue filling the subarachnoid spaces surrounding the spinal cord Necropsy was not carried out in the 2 other fatal cases The partial spinal block resolved completely in 1 child who recovered (observation period fifteen months), but complete block persists in another who is otherwise well and whose C S F above the level of the obstruction approached normal Both these children belonged to group A

Thus the use of streptokinase in this series was ineffective in preventing the occurrence of spinal blocks in 5 of 12 cases This proportion of spinal blocks (5 of 12) in group A was not only higher than in group B (2 of 12) but much higher than has previously been observed in cases treated by this unit (Lorber 1950)

Both groups had a high incidence of blocks at the tentorial opening and in the basal cisterns of the subarachnoid space (10 in group A and 9 in group B) This incidence may be attributed to the advanced state of the disease on admission in half the cases (table I), for such blocks are usually present in advanced cases before the start of therapy (Lorber 1951) Cathie and MacFarlane (1950) did not claim that streptokinase will dissolve established blocks, but in this series there was little evidence that it prevented further formation of blocks In 5 children in the intermediate stage of the disease obstruction was excluded by pneumo encephalography soon after the beginning of treatment of these, 3 cases were in group A and all subsequently developed tentorial obstruction In group B, 1 case later developed such a block None of the 4 children (2 in each group) who were in the early stage of the disease developed blocks

NECROPSY FINDINGS

At necropsy, the usual basal exudate was present in 2 of 3 children in group A and in 4 of 5 in group B In 1 of the cases in group A there was remarkably little exudate to be seen on the base of the brain, but the cisterna ambiens was nevertheless completely obstructed by firm exudate Of the children in group A who came to necropsy 2 were in the intermediate stage of the disease and showed no evidence of blocks at the beginning of treatment Thus there was no evidence from the pathological point of view that streptokinase was *beneficial as an adjunct in the treatment of tuberculous meningitis*

TOXIC EFFECTS

It is difficult to detect the individual toxic effects of drugs given in combination, and also when such toxic effects may closely resemble the signs and symptoms of the disease itself. Possibly for this reason no definite toxic effects were detected in 9 of the 12 children treated with streptokinase Experience in the investigation and treatment of over 100 cases of tuberculous meningitis had shown that a C.S.F cell-count of 1000 or even more per c mm may occur during intrathecal streptomycin treatment, and that this is not caused by secondary infection Such a pleocytosis did occur in 2 of the 9 patients in group A No further investigations were undertaken in these cases

In the remaining 3 children severe toxic symptoms occurred when streptomycin and streptokinase were given together, 2 of them were early cases and 1 was in the intermediate stage at the beginning of the treatment In all 3 exceptionally high cell counts were recorded during combined intrathecal treatment In 2, the count reached 3200 and 4000 white cells per c mm In addition there was sustained pyrexia of up to 104°F The children were listless, irritable, drowsy, and complained of headache All these symptoms disappeared during the usual week s rest between two courses of intrathecal treatment, the temperature returned to normal and the C S.F cell count fell abruptly The fall is well shown in the extract from the C.S F chart of case 1 (table II) This syndrome had been observed in the past with streptomycin treatment alone, though to a *lesser degree For this reason investigations* were carried out to determine whether these more severe symptoms were due to the streptokinase

TABLE II—EXTRACT FROM C.S F CHART OF CASE 1

Date		Intrathecal treatment	C.S F white-cell count	Culture
Nov	14 1950	Combined SM and SK	4000	sterile
	15		3200	
	16			
	17			
	21		162	
	24		120	
	26			
	28	Combined SM and SK	4000	
Dec	5		3600	
	21			
	27		100	
Jan	3	Single dose of SK alone	118	
	4		2400	
	9		80	

SM = streptomycin SK = streptokinase

In 2 children who showed these toxic effects during combined treatment, the effect of single intrathecal injections of streptokinase alone was observed on three occasions after intrathecal streptomycin treatment of facilities for evening therapeutic sessions could help to meet this situation A difficulty is that to increase facilities creates a further demand At present it is the commendable self restraint of the general practitioner in crowded areas that prevents the swamping of available services, which over enthusiastic salesmanship of psychiatry might well bring about Unfortunately one's appreciation of their forbearance must take the form of referring back untreatable cases, for the attendance of many "chronics" is bad for the morale of new patients (Blacker 1946) Moreover the results of accepting unsuitable cases for psychotherapy only confirm sceptics in their belief of its inefficacy Careful selection, even though it may court temporary unpopularity, will in the end benefit clinics and patients by causing the right type of cases to be referred

I emphasise the need for psychotherapy because in my experience most outpatients needing other than purely supportive treatment require this I have run clinics with very few referrals for E C T , but, lest my view be considered prejudiced, I cite a personal communication from Dr T Munro, who estimated that out of 300 new patients attending Guy's Hospital outpatients department only 6% required E C T When there are not enough facilities for psychotherapy, I am sure there is a tendency —based on a laudable desire to do something for the patients—to use E C T in unsuitable cases, as I have discussed above

SUMMARY AND CONCLUSIONS

Objections to E C T in certain cases is discussed in relation to a small series of cases responding to simple measures in a general hospital

Clinically and economically, it is preferable for psychoneurotic patients to be treated as outpatients Inpatient treatment should be used sparingly, and stay in hospital should be short

I wish to thank Dr W J S Ewan, physician, Dr R Moore, former registrar, and the doctors and nurses of Harold Wood Hospital for all they did for my patients , the improvements recorded were essentially due to their efforts

REFERENCES

Blacker C P (1946) Neurosis and the Mental Health Service London
Hadfield J A (1950) *Brit med J* ii 679
Mallinson W P (1948) *Ibid* ii 611
Sands D E (1946) *Ibid* ii 289
Sargant W Slater E (1948) Introduction to Physical Methods of Treatment in Psychiatry Edinburgh
Winnicott, D W (1947) *Brit med J* i, 688

STREPTOKINASE AS AN ADJUNCT IN THE TREATMENT OF TUBERCULOUS MENINGITIS

JOHN LORBER
M B Camb , M R C P
LECTURER IN CHILD HEALTH, UNIVERSITY OF SHEFFIELD

THERE are many causes of failure in the treatment of tuberculous meningitis, but from the pathological aspect perhaps the most important is the development of obstruction in the cerebrospinal circulation Any method of treatment that would prevent such blocks, or remove them might be of great value

The incidence of these blocks, their distribution, and their detection by the use of penicillin as a tracer substance and by pneumo encephalography have been described elsewhere (Lorber 1950, 1951) Pathological studies show that they are caused by deposition of fibrin and by tuberculous granulation tissue, mostly around the brain stem in the cisterna ambiens, in the cisterns at the base of the brain and round the cord in the spinal subarachnoid space Later the deposit organises into fibrous tissue,

Because fibrin is the cause of blocks, Cathie tried the effect of giving streptococcal fibrinolysin intrathecally as an adjunct in the treatment of tuberculous meningitis He prepared a suitable preparation (Cathie 1949a) of streptokinase, and in a preliminary report (Cathie 1949b) compared his early results in two successive series of cases Series A consisted of 14 children treated with streptomycin alone, of whom only 3 (21%) survived Series B consisted of the next 21 children, treated with both streptomycin and streptokinase, of whom 11 recovered (52%), 2 relapsed after apparent recovery (their fate was not stated), and 8 died But the scheme of intrathecal streptomycin treatment was altered when streptokinase was introduced, and a later publication (Cathie and MacFarlane 1950) disclosed that there were further changes in treatment—namely, the addition of intrathecal 'Sulphetrone' and the frequent use of ventricular catheterisation Moreover, increased experience may have played a large part in the improvement of results The two series therefore were not strictly comparable The only toxic symptom mentioned was a pleocytosis in the cerebrospinal fluid (C S F) similar to that caused by streptomycin

At the time of Cathie's preliminary report, our own results in the treatment of tuberculous meningitis in children showed that there were 4 survivors in our first series of 14 children and 11 in the next series of 21 Streptokinase had not been used The patients were kept under observation for about the same length of time as in Cathie's cases

With these considerations in mind it was decided to conduct a controlled experiment to assess the value of streptokinase

INVESTIGATION

The present investigation was planned to take place during 1950 and to continue only if the results at the end of one year were promising It was decided to use intrathecal streptokinase in half the cases of tuberculous meningitis admitted under the care of the unit during 1950, and cases were chosen at random Of 27 new patients, 2 had already been treated elsewhere for several weeks, and 1 had combined tuberculous and meningococcal meningitis on admission , these 3 were excluded from the investigation Of the remaining 24 bacteriologically confirmed cases, it happened that 12 (group A) were treated with combined intrathecal streptomycin and streptokinase, and 12 (group B) with streptomycin alone In all other respects the treatment was similar in the two groups Routine intrathecal treatment was given by lumbar puncture daily for two periods of twenty one days separated by one week's rest Further intrathecal treatment was given only if the child's condition required it Cisternal and ventricular injections were used as required in cases with spinal blocks Intramuscular streptomycin was given in the usual daily dose of 20 mg per lb body weight for a minimum of six months if the patient survived Intrathecal tuberculin I P D (purified protein derivative) was given to 7 children (3 in group A and 4 in group B), but only after other forms of treatment were thought to have failed With 1 exception, treatment was begun within twenty four hours of admission In 1 child in group A the diagnosis was in doubt for three days and treatment was delayed accordingly A uniform dose of 6 units of streptokinase (Burroughs Wellcome), dissolved in a solution containing streptomycin 25–75 mg , was injected intrathecally daily for as long as was considered necessary This solution was active, in vitro, at room temperature, it dissolved the fibrin clot formed in the C S F from cases of tuberculous meningitis, and the dilution was comparable to that obtained in vivo The following remarks will apply only to the commercial preparation which has been used

These suggest that streptokinase probably played no part in the good results obtained in the second series of Cathie and MacFarlane (1950)

SUMMARY AND CONCLUSIONS

A controlled investigation was undertaken to determine the value of intrathecal streptokinase as an adjuvant in the streptomycin treatment of tuberculous meningitis, 12 patients being treated with and 12 without streptokinase The two groups were otherwise strictly comparable

Streptokinase appeared to have no effect in reducing the number of blocks occurring during treatment, 5 children developed partial or complete spinal block during treatment in the group treated with streptokinase and streptomycin, and only 2 in the group treated with streptomycin alone, blocks at the tentorial opening or in the basal cisterns developed in 3 patients treated with streptokinase and streptomycin, and in 1 treated with streptomycin alone The necropsy findings in 3 patients treated with streptomycin and streptokinase did not differ from those in patients treated with streptomycin alone

Streptokinase may cause headache, listlessness, drowsiness, vomiting, fever, and a large increase of cells in the cerebrospinal fluid

I wish to thank Prof R S Illingworth for permission to treat and investigate his cases and for his criticism, and Dr J L. Emery for the necropsy reports

REFERENCES

Cairns H., Smith, H V, Vollum R L (1950) *J Amer med. Ass* 144, 92
Cathie L A B (1949a) *J clin Path* 2 73
— (1949b) *Lancet*, i, 441
— MacFarlane J C W (1950) *Ibid* ii 784
Flori A G (1950) *Pediatrics* 6 391
Lincoln E M (1951) *Lancet* i 236
Lorber J (1950) *Arch. Dis Childh* 25 404.
— (1951) *Ibid* 26 28
Medical Research Council (1948) *Lancet* i 582
Russell S J M. MacArthur P (1950) *Ibid* i, 59

INDUCED ASTHMA IN MAN

Herbert Herxheimer
L R C P E
RESEARCH ASSISTANT, SURGICAL UNIT UNIVERSITY COLLEGE HOSPITAL, LONDON

Bronchial asthma runs a long and varying course, irregularly punctuated by remissions and relapses The causes of this fluctuation often remain obscure. Almost any treatment seems to produce good results so long as it is new and holds the patient's confidence Hurst pointed out in 1943 that desensitisation by means of injections had no greater effect than the injection of physiological saline solution. More recently, Rackemann (1950) found that allergists in the United States achieved equally good results in asthma even when their methods differed fundamentally

It seems certain that emotional or nervous factors play a part in these fluctuations but that other factors contribute in causing them The importance of each factor varies from one patient to another, and even in the same patient from one week to another It is therefore difficult to evaluate the results of treatment Moreover, a high proportion of "psychological" successes is assured whatever treatment is adopted, so that "objective" successes are swamped by them and remain hidden Our aim must be to devise a simple experimental method which will eliminate this difficulty If it was possible to induce mild asthmatic attacks artificially in man and to abort them at will, such an attack would be convenient for investigation and for comparing the effects of various methods of treatment For this purpose we must be able to record the attack graphically from start to finish and to repeat it The method described below seems to fulfil these requirements

METHOD

The patient is connected with an ordinary Benedict-Roth spirometer fitted with a drum for making a continuous record of air movement in the circuit (fig 1) Carbon dioxide is absorbed by a soda lime container fitted outside the spirometer, and a change in the colour of the soda lime indicates when it is saturated with carbon dioxide

The spirometer is filled with atmospheric air An oxygen inlet can be adjusted so that the oxygen used by the patient is replaced at the same rate When this adjustment has been made the mean volume in the spirometer remains constant—i.e, the tracing on the drum remains level, whereas without oxygen replacement the tracing would slope upwards

A side tube from the inspiratory tube leads to a pump which compresses the air and drives it through a glass atomiser back into the inspiratory tube Several glass atomisers, each containing a different liquid, are switched in parallel so that any one of them can be brought into action by opening a clip The pressure of the atomising pump is measured by a manometer in the circuit This arrangement enables the patient's respiration and vital capacity to be recorded on the paper

When this has been done, the pump and one of the atomisers can be switched into the circuit so that the aerosol of some active substance is inhaled, and its effect can thus be observed and recorded.

Disadvantages and Advantages —The chief disadvantage of this method is that the amount of aerosol absorbed by the patient cannot be measured Not all the aerosol is inhaled—some remains in the apparatus—and even that which is inhaled is not all absorbed, since some is pushed back into the circuit during expiration. The dose of aerosol can therefore only be measured on an arbitrary scale and not in absolute values The arbitrary scale used is the duration of the patient's exposure to the aerosol. When the pressure, the atomiser, and the fluid atomised remain the same, the time of exposure is the only measurement that allows a reliable comparison to be made between different experiments A further disadvantage of the method is that it can only be used on patients who can be trained to breathe with the apparatus

There are many advantages The aerosol impinges directly on the effector organ—i e, the bronchus—and does not have to pass through the circulation before acting on it Its effect can thus be recorded as soon as it occurs. When an attack develops its course can be followed, and it may be aborted at any stage by administering aerosol from another nebuliser switched into the circuit In this way the method can be used with complete safety When there is any suspicion that an effect is psychogenic, the experiment can be repeated with another aerosol as control

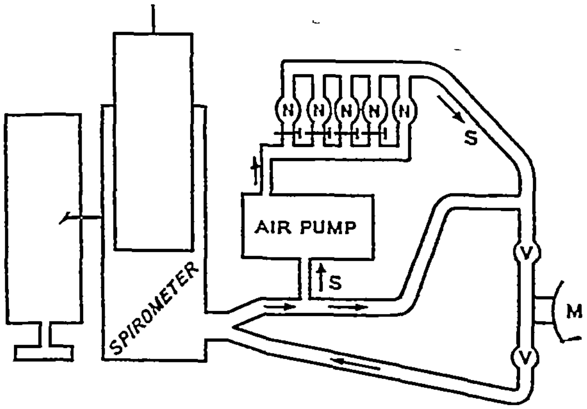
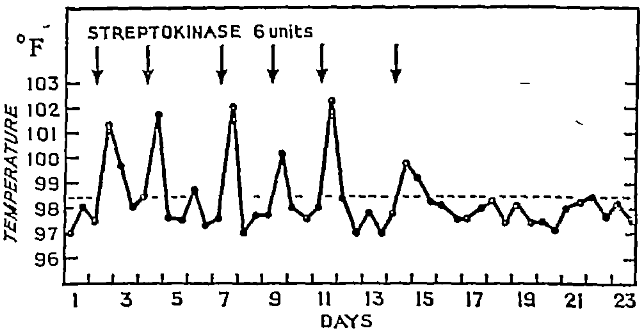


Fig 1—Apparatus for induction of asthmatic attacks S side circuit, attached to inspiratory tube of recording Benedict Roth spirometer contains a pump which takes air from inspiratory tube and drives it out through one of several nebulisers (N) which can be opened or closed by a clip. Aerosol thus produced is carried back into inspiratory tube and inhaled by patient V inspiratory and expiratory valves M mouthpiece.



Pyrexial reaction to intrathecal injections of streptokinase in child who had severe toxic symptoms five months before when receiving streptomycin and streptokinase intrathecally

had been stopped In each case enough time was allowed for the C S F cell count to settle to a steady low level (below 200 per c mm) The cell count was done again on the day of streptokinase injection, on the next day, and again after a few days (table II) In each instance there was a rapid rise in the cell count (up to 2400 per c mm), together with fever, vomiting, listlessness, and headache on the evening of the injection All these symptoms disappeared in one to two days and the C S F cell count returned to its previous level Later, the course of the illness made it necessary to start intrathecal streptomycin treatment again in both children This time streptomycin alone was given and no toxic reactions were observed clinically, there was no rise in temperature and the C S F cell count did not rise above 180 per c mm

The 3rd child showed the same toxic symptoms during combined daily intrathecal treatment These symptoms disappeared during a week's rest between courses of treatment In the fifth month of treatment she was given streptokinase intrathecally on three days a week On the days when she had streptokinase she was ill, but on the other days she was alert and playful On the evening of the day of injections she had a high fever, but she was afebrile on other days (see figure)

It seemed, therefore, that in the last 3 children the toxic symptoms were due to the streptokinase, and not to the disease or to the streptomycin

DISCUSSION

It is apparent, that in our hands, and in the doses employed, streptokinase was of no benefit An attempt was made to demonstrate the specific effect of streptokinase in preventing blocks, but no such effect was found In fact blocks developed more often in the cases given streptokinase and streptomycin than in the cases given streptomycin alone, though the difference was not statistically significant Nor was there any difference in the extent and nature of the exudate found in cases which came to necropsy Toxic symptoms were experienced by 3 children, although it was never necessary to interrupt treatment on this account

Towards the end of this investigation a further and fuller account on the use of streptokinase was published by Cathie and MacFarlane (1950) Owing to the multiplicity of factors concerned, which we have mentioned, they found the evaluation of the various therapeutic agents difficult, but considered that "streptokinase has been the most important single factor in the improvement in the second series of cases" This opinion was based on criteria different from those used in the present study There was no direct mention of the occurrence of blocks in their cases, or of their necropsy findings in the 17 patients treated with streptokinase who died No concurrent controls were included in their investigation The claim that streptokinase was of value rested on the observations that the survival rate in the group treated with streptokinase was greater, and the incidence of "increased intracranial pressure" was less Nevertheless, ventricular drainage was necessary in 26 out of 40 cases treated with streptokinase, and in 14 of the 40 (35%) "changes in the flow of the C S F" were considered to be indications for draining the ventricles These last 14 cases probably had partial or complete spinal blocks If so, their incidence of 35% would be very high

The improvement of the results of treatment was the main argument used by Cathie and MacFarlane in favour of streptokinase Their first 14 children were treated without any adjuvants or ventricular drainage and only 2 survived (3 survivors were mentioned in the previous report) The next 6 children were still treated without streptokinase, but the scheme of intrathecal treatment was changed, and the ventricle were drained when necessary Half of these children survived The next 40 children were treated with the altered streptomycin régime and ventricular drainage when considered necessary, but in addition all were treated with streptokinase, and 34 with intrathecal sulphetrone as well. For the evaluation of the results of treatment, only 30 of them can be considered because the observation period of the last 10 was only six to eleven and a half months That a longer period of observation is necessary is shown by Cathie and MacFarlane's own figures Of their first 50 patients, 29 died, and 6 of these (over 20%) died between six and seventeen months after the beginning of treatment This leaves 30 children treated with streptokinase of whom 16, or just over a half, survived. The number of cases is so small that it is not possible to come to any conclusion, but it appears that the improvement in their survival rate may have started with the introduction of the revised intrathecal régime (and ventricular drainage when necessary) before streptokinase was used

TABLE III—RESULTS OF TREATMENT OF TUBERCULOUS MENINGITIS BY VARIOUS AUTHORS

Author	Number of cases		Number of survivors		Percentage of survivors	
Cathie and MacFarlane (1950)						
Series A	20		5		25	
Series B	30		16		53	
Totals		50		21		42
Russell and MacArthur (1950)		33		15		45
Cairns Smith, Vollum (1950)		60		30		50
Lorber (1951)						
Series A	20		7		35	
Series B	47		22		47	
Totals		67		29		44
Cocchi school (Fiori 1950)						
Series 1	57		13		23	
Series 2	66		31		47	
Series 3	60		40		66	
Series 4	40		34		85	
Totals		223		118		53
Lincoln (1951)		18		12		66

All cases were observed for at least a year

As mentioned above greater experience alone, without the addition of adjuvants such as streptokinase, may considerably improve results In our own 67 cases observed for a minimum of one year, 7 of the first 20 survived, whereas of the next 47, despite a much larger proportion of advanced cases, 22 are alive In the very large series of patients treated at Cocchi's clinic at Florence, 13 of the first 57 (23%), 31 of the next 66 (47%), 40 of the next 60 (66%), and 34 of the next 40 (85%) were live after one year's observation (Fiori 1950) In table III are listed for comparison some of the best published results obtained without streptokinase eaction Conversely, in some patients the skin reaction as negative but the bronchial reaction positive

When an aerosol containing an allergen is inhaled by he method described here, there follows a typical reaction hose attributes depend on the nature and amount of he allergen inhaled Experiments of this sort have so ar been carried out with mixed pollens of various kinds, ungi, house dust, cat's fur, horsehair and horse dander, nd meat A characteristic feature of all these experinents, except those done with fungi, is that the attack ever comes on during or immediately after the inhalaion If a moderate attack develops, the first sign appears -3 minutes after the end of the inhalation The vital apacity, which till then has remained unchanged, lecreases a little, but at this stage the patient is usually naware of the attack, then the attack slowly worsens, nd presently it has to be aborted artificially Such a ypical attack is shown in figs 3 and 5 (curve A)

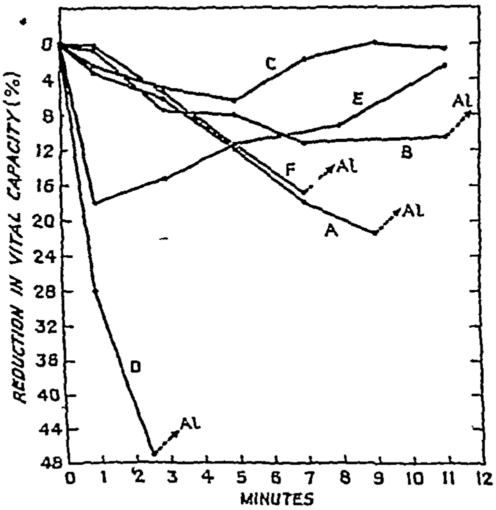


Fig 5—Influence of different types of induced attack of asthma on vital capacity A, decrease of vital capacity in moderate attack B in mild attack C, in very mild attack ; D in severe attack all induced by mixed pollen-extract aerosol In A B and C there is hardly any decrease in first minute after inhalation then vital capacity begins to fall and continues to do so until attack is aborted by isoprenaline (Al) Isoprenaline is not necessary in very mild attack (C) which subsides spontaneously In severe attack (D) vital capacity decreases during first minute and attack develops very quickly Attack caused by house-dust antigen (F) is similar to pollen-extract attack. Attack caused by inhalation of mixed mould-extract aerosol (E) is different because it is fully developed a minute after inhalation and subsides spontaneously

If an attack is very mild, the vital capacity diminishes only slightly, remains at this lower level for a while, and finally returns to its normal value (fig 5c) If too much of the allergen is administered, the vital capacity may fall sharply immediately after the inhalation, and when this happens the attack usually becomes unbearable after a few minutes (figs 4 and 5D) Not all patients develop an attack within a few minutes of the inhalation, in some it does not come on for 4–24 hours ("delayed reaction") This latent period is not related to the dose—it is just as long in mild as in violent reactions

Most attacks induced by fungal allergens are different from those described There is hardly any latent period, and the intensity of the attack is greatest at the end of the inhalation, after that it wanes and often passes off of its own accord Fig 5 illustrates these different types of attack and their effects on vital capacity

Patients vary a good deal in their subjective reaction to an attack Often the patient begins to notice a tightness in his chest only when his vital capacity has fallen 15–20% In other cases the first symptom is a peculiar itching sensation, which comes on early, after about 2 minutes, this may be felt in the neck, the chest, or the upper back, and the patient who feels it is usually familiar with the sensation because it is a feature of his natural asthmatic attacks In other patients a cough is the first sign of the attack, and after it has ended a little sputum is coughed up, but many patients never cough Mould asthma in particular seems to produce coughing It may be that these differences depend not only on the secretion but also on varying involvement of muscle spasm and mucosal œdema Methods for studying the effects of these factors separately have not yet been devised.

The method described here can thus be used to determine whether a given allergen can produce asthma in a particular patient, and if so to reveal the type of the attack The method also enables us to study the action of other asthmogenic substances, such as histamine and acetylcholine It has long been known that asthmatics are much more sensitive to aerosols of histamine and acetylcholine than are normal persons (Samter 1933, Curry 1946, Herxheimer 1949b, 1951) The attack may begin a few seconds after the inhalation The vital capacity may suddenly drop to about half or a third of its initial value These attacks differ from those of allergic asthma in their sudden onset and their greater intensity They begin with their greatest intensity and rarely get worse, after a few minutes the vital capacity begins to rise again, and the attack passes off spontaneously (fig 6)

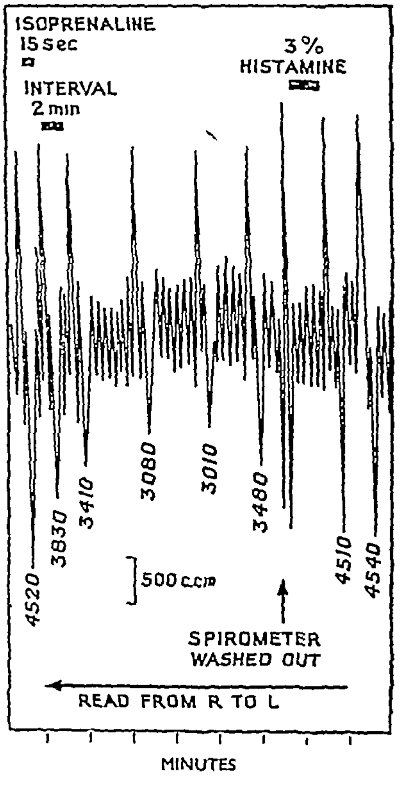


Fig 6—Histamine-induced asthmatic attack in asthmatic patient sensitive to house dust. Vital capacity before attack 4525 c.cm Patient receives 3% histamine acid phosphate aerosol through breathing circuit after 35 sec. he notices first sign of very mild constriction of chest at this moment he is disconnected from apparatus and spirometer is washed out. He rapidly becomes breathless and vital capacity a minute after end of inhalation is 3480 c.cm., falling after another minute to 3010 c.cm From now onwards attack gradually subsides and vital capacity increases within 5 min to 3830 c.cm Recovery is hastened by isoprenaline inhalation which brings vital capacity up to normal (3420 c.cm) *Typical for histamine-induced* and acetylcholine-induced attacks are their rapid development, their violence and the frequently spontaneous *recovery inspite* of their severity An allergen-induced attack of similar severity would not subside except after many hours or days.

HYPOSENSITISATION

The inhalation of aerosols can be used in the treatment as well as the diagnosis of allergic states When the tests described here were being carried out it was noted that each patient varied in his reaction to the same dose of aerosol given on different occasions When a certain dose of allergen—e g, 10 seconds' inhalation of a mixed pollen aerosol—provoked a *mild* attack, the same dose given a few days later did not cause an attack Only when the dose was raised by 20–30% was a mild attack produced

Patients who have experienced such an artificial attack of asthma and its dramatic extinction are usually much impressed and readily agree to repeat the experiment Most patients quickly learn to produce reliable records of their vital capacity—i e, their vital capacity varies little from one attempt to another The vital capacity is a useful index of bronchial obstruction, though it does not show up minimal grades of obstruction which can be overcome by voluntary muscle action When necessary, however, these fine degrees can be detected by other methods, which measure the speed of the expiratory outflow

MECHANISM OF THE ATTACK

The artificially induced asthmatic attack enables us to observe its influence on the mechanics of breathing Spirometry shows the movement of air, the movements of the thorax are recorded with Verzàr's (1946) thoracograph, and those of the diaphragm are observed radiologically on the screen These methods show that, as soon as expiration is obstructed, air is retained in the thorax This moment can be seen on the spirogram where the tracing moves upwards, since the thorax retains air, the spirometer loses an equal volume of air, and the bell falls to a lower level At the same time the chest circumference increases, and this is shown in the thoracogram On the fluorescent screen one can see that the diaphragm is lowered and reaches its lowest position at the height of the attack

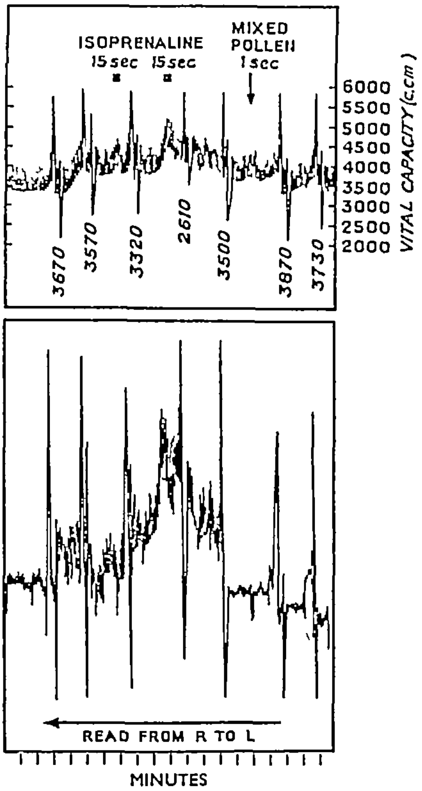


Fig 2—Synchronised spirogram and thoracogram of moderately severe induced asthmatic attack The patient is an asthmatic sensitive to grass pollen She has a basic vital capacity of 3800 c.cm (upper tracing spirogram) and, normally the ribs take little part in the breathing movements in the sitting position (lower tracing thoracogram) She inhales *mixed pollen-extract aerosol for 1 sec.* A minute later the vital capacity has decreased a little (3500 c.cm) and immediately afterwards the chest circumference increases abruptly (lower tracing) a sign that air is retained in the chest in consequence of incipient expiratory difficulty Two minutes *later the attack is well under* way the vital capacity is down to 2610 c.cm, and the chest circumference has increased further the spirogram shows an upward trend also indicating retention of air in the thorax and the ribs now move vigorously At this moment isoprenaline aerosol is given to abort the attack. *Almost immediately* the chest circumference decreases a minute later the vital capacity is 3320 c.cm a little afterwards it is 3760 c.cm almost normal The ribs return to their former relative inactivity Tracings show gradual development of attack and accompanying acute emphysema.

A spirogram and a thoracogram recorded simultaneously (fig 2) show that the transfer of air from the spirometer into the thorax occurs at the same time as the increase in chest circumference Both changes are reversed at the end of the attack, again simultaneously The mechanical effect of such an attack can easily be imitated if the expiratory tube is narrowed with a screw clip The results are similar to those found in the attack, the only difference being in the site of the obstruction (Herxheimer 1949a)

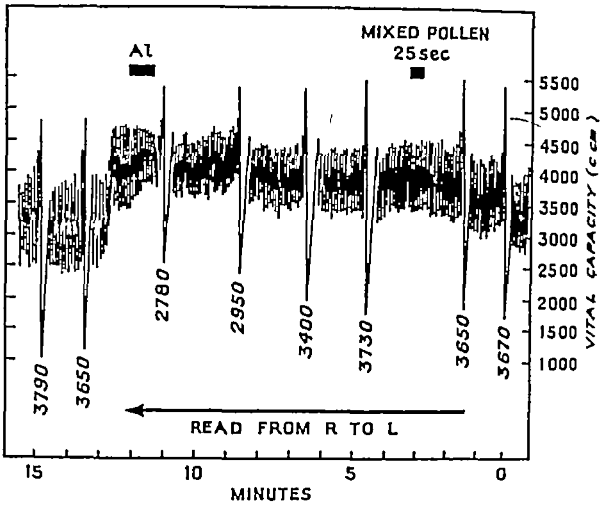


Fig 3—Spirogram of mild asthmatic attack caused by inhalation for 25 sec. of mixed pollen-extract aerosol Vital capacity before attack 3660 c.cm A minute after end of inhalation there is no sign of any attack—vital capacity 3730 c.cm.—but after 2 more minutes attack becomes evident (vital capacity 3400 c.cm) and attack steadily worsens until it reaches a degree of unpleasantness which demands its interruption (vital capacity 2780 c.cm) After a short inhalation of 2% isoprenaline aerosol vital capacity is restored to normal

THE BRONCHIAL REACTION

Until now, hypersensitivity in asthmatic patients has usually been investigated by skin tests However, in allergic hypersensitive states it is unlikely that all the organs are affected equally For this reason many authorities have doubted the value of skin tests in asthma My own experiments with house dust (Herxheimer 1951) showed that among the patients giving a positive skin reaction a high proportion did not give any bronchial

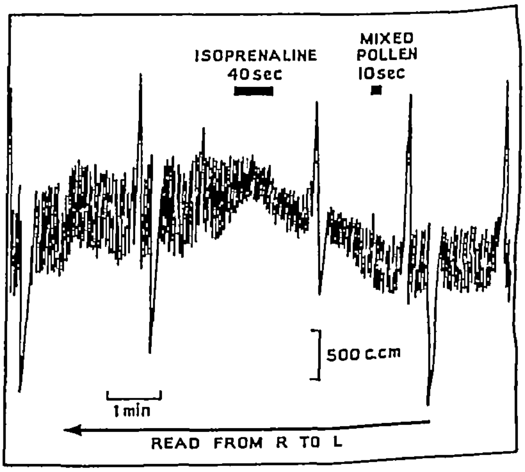


Fig 4—Spirogram of severe asthmatic attack caused by inhalation for 10 sec. of mixed pollen extract. Almost immediately after inhalation the tidal air excursions become smaller air is retained in chest (upward trend of tidal-air level) and after a minute the vital capacity *has fallen from* 3130 to 1880 c.cm Moderate dyspnœa is now present and it requires 40 seconds inhalation of 2% isoprenaline aerosol to abort the attack. Vital capacity increases to 2730 c.cm, and later to 3000 c.cm An attack of this severity must be expected to increase sensitivity of patient to mixed pollen Note stimulant influence of isoprenaline on respiration: respiratory rate increases from 15 to 18 and tidal air from about 600 to 800 c.cm

action Conversely, in some patients the skin reaction as negative but the bronchial reaction positive

When an aerosol containing an allergen is inhaled by ne method described here, there follows a typical reaction hose attributes depend on the nature and amount of ne allergen inhaled Experiments of this sort have so ar been carried out with mixed pollens of various kinds, ungi, house dust, cat's fur, horsehair and horse dander, nd meat A characteristic feature of all these experiments, except those done with fungi, is that the attack ever comes on during or immediately after the inhalation. If a moderate attack develops, the first sign appears -3 minutes after the end of the inhalation The vital apacity, which till then has remained unchanged, ecreases a little, but at this stage the patient is usually naware of the attack, then the attack slowly worsens, nd presently it has to be aborted artificially Such a ypical attack is shown in figs 3 and 5 (curve A)

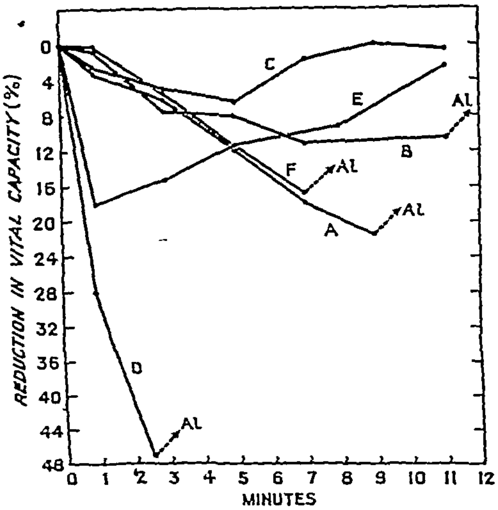


Fig. 5—Influence of different types of induced attack of asthma on vital capacity: A, decrease of vital capacity in moderate attack B in mild attack C, in very mild attack D in severe attack all induced by mixed pollen-extract aerosol In A B and C there is hardly any decrease in first minute after inhalation then vital capacity begins to fall and continues to do so until attack is aborted by isoprenaline (Al) Isoprenaline is not necessary in very mild attack (C) which subsides spontaneously In severe attack (D) vital capacity decreases during first minute and attack develops very quickly Attack caused by house-dust antigen (F) is similar to pollen-extract attack. Attack caused by inhalation of mixed mould-extract aerosol (E) is different because it is fully developed a minute after inhalation and subsides spontaneously

If an attack is very mild, the vital capacity diminishes only slightly, remains at this lower level for a while, and finally returns to its normal value (fig 5C) If too much of the allergen is administered, the vital capacity may fall sharply immediately after the inhalation, and when this happens the attack usually becomes unbearable after a few minutes (figs 4 and 5D) Not all patients develop an attack *within a few minutes* of the inhalation, in some it does not come on for 4–24 hours (" delayed reaction ") This latent period is not related to the dose—it is just as long in mild as in violent reactions

Most attacks induced by fungal allergens are different from those described There is hardly any latent period, and the intensity of the attack is greatest at the end of the inhalation, after that it wanes and often passes off of its own accord Fig 5 illustrates these different types of attack and their effects on vital capacity

Patients vary a good deal in their subjective reaction to an attack Often the patient begins to notice a tightness in his chest only when his vital capacity has fallen 15–20% In other cases the *first symptom* is a peculiar itching sensation, which comes on early, after about 2 minutes, this may be felt in the neck, the chest, or the upper back, and the patient who *feels* it is usually familiar with the sensation because it is a feature of his natural asthmatic attacks In other patients a cough is the first sign of the attack, and after it has ended a little sputum is coughed up, but many patients never cough *Mould asthma in particular seems to produce coughing* It may be that these differences depend not only on the secretion but also on varying involvement of muscle spasm and mucosal œdema Methods for studying the effects of these factors separately have not yet been devised.

The method described here can thus be used to determine whether a given allergen can produce asthma in a particular patient, and if so to reveal the type of the attack The method also enables us to study the action of other asthmogenic substances, such as histamine and acetylcholine It has long been known that asthmatics are much more sensitive to aerosols of histamine and acetylcholine than are normal persons (Samter 1933, Curry 1946, Herxheimer 1949b, 1951) The attack may begin a few seconds after the inhalation The vital capacity may suddenly drop to about half or a third of its initial value These attacks differ from those of allergic asthma in their sudden onset and their greater intensity They begin with their greatest intensity and rarely get worse, after a few minutes the vital capacity begins to rise again, and the attack passes off spontaneously (fig 6)

HYPOSENSITISATION

The inhalation of aerosols can be used in the treatment as well as the diag*nosis of allergic* states When the tests described here were being carried out it was noted that each patient varied in his reaction to the same dose of aerosol given on different occasions When a certain dose of allergen—e g, 10 seconds' inhalation of a mixed pollen aerosol—provoked a *mild* attack, the same dose given a few days later did not cause an attack Only when the dose was raised by 20–30% was a mild attack produced

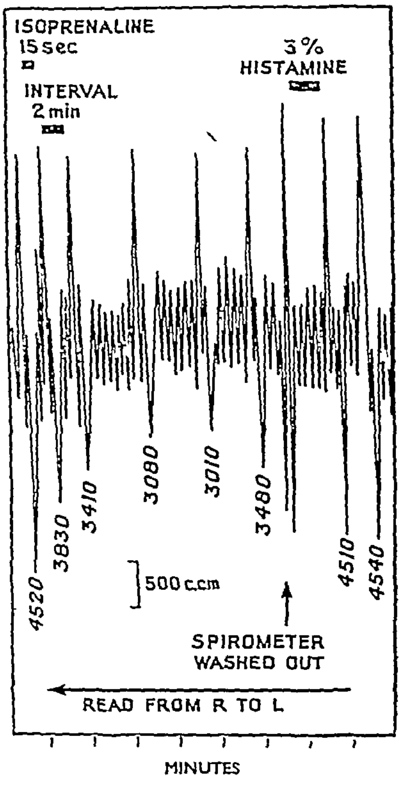


Fig 6—Histamine-induced asthmatic attack in asthmatic patient sensitive to house dust. Vital capacity before attack 4525 c.cm Patient receives 3% histamine acid-phosphate aerosol through breathing circuit after 35 sec. he notices first sign of very mild constriction of chest at this moment he is disconnected from apparatus and spirometer is washed out. He rapidly becomes breathless and vital capacity a minute after end of inhalation is 3480 c.cm falling after another minute to 3010 c.cm From now onwards attack gradually subsides and vital capacity increases within 5 min. to 3830 c.cm. Recovery is hastened by isoprenaline inhalation which brings vital capacity up to normal (3420 c.cm) Typical for histamine-induced and acetylcholine-induced attacks are their rapid development, their violence and the frequently spontaneous recovery inspite of their severity An allergen-induced attack of similar severity would not subside except after many hours or days.

By repeating this process and gradually increasing the dose of allergen inhaled, the patient developed tolerance to it By contrast, when the dose of inhaled allergen was large enough to cause a *severe* attack, the opposite happened and tolerance diminished This became apparent when the dose was considerably reduced—e g , to a third of its previous value This smaller dose now caused an even more severe attack than that caused by the original dose Only a further drastic reduction in the dose led to the desired result, a mild attack

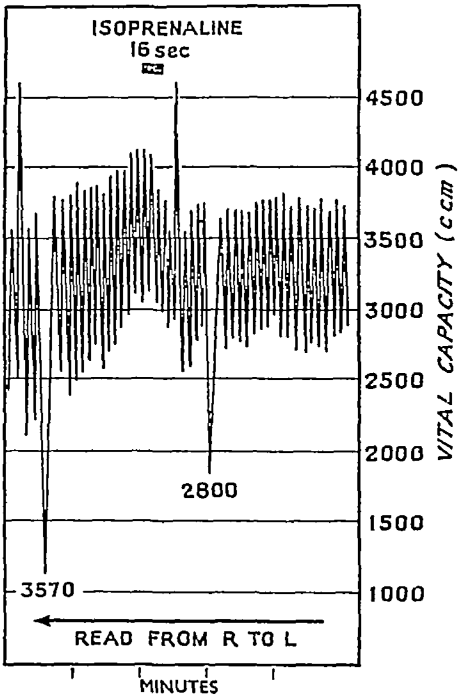


Fig 7—Rapid response of asthmatic attack to isoprenaline inhalation Pollen-induced attack in asthmatic patient sensitive to grass pollen Almost immediately after end of 16 seconds inhalation of isoprenaline tidal air increases considerably (from about 900 c.cm to about 1200 c.cm) A minute later vital capacity has increased from 2800 to 3570 c.cm Increase is entirely due to increase of reserve air some of which, during attack could not be exhaled and therefore formed part of residual air

These phenomena are evidently instances of hyposensitisation and hypersensitisation Large doses increase, and small doses diminish, the patient's sensitivity to the allergen concerned If this observation is correct, it must be possible to hyposensitise patients by using small and gradually increasing doses (this used to be called desensitisation) This has been done in some cases (Herxheimer 1951) For instance, in a patient who developed a mild attack after 8 seconds' inhalation when treatment was begun, the tolerance was so increased that three months later 100 seconds' inhalation had no effect In the first two cases of grass pollen asthma treated in this way the asthma did not appear the following summer, though oddly enough the ocular and nasal symptoms persisted in part

These observations may be of both theoretical and practical significance If it is possible to intensify or to weaken the allergic reaction of the bronchial tree in this way, the question arises whether similar processes may not occur in the daily life of asthmatics An excessive amount of allergen inhaled accidentally—e g , house dust in moving house, and grass pollen on outings in the country—would make the asthma worse and hypersensitise the patient, who now would respond severely even to doses which previously did not injure him Only after he has returned to his usual surroundings may the amount inhaled become *very* much smaller, in these circumstances the asthma improves very gradually and reverts to its usual intensity In some asthmatics it seems as if such episodes of hypersensitisation and hyposensitisation occur quite often When one tries to discover why a chronic asthmatic suddenly becomes worse one sometimes finds that shortly before the attack the patient had exposed himself to a gross overdose of "his" allergen Often such an event cannot be recognised with certainty

Factors which are not allergic also play a part Excitement from any cause, and physical exertion, can greatly increase the ventilation Under these conditions the amount of allergen inhaled may be increased to many times its usual value for purely mechanical reasons, and this alone may cause considerable "overdosage" of allergen

The practical importance of our observations lies in the fact that the treatment of allergic asthma can be put on a much firmer basis than hitherto Hyposensitisation by injection does not allow precise observation of its progress. When a patient shows a systemic reaction, this is usually regarded as a sign of overdosage When there is no reaction, it is tacitly assumed that hyposensitisation is being achieved Final success is seldom conclusively proved It can only be regarded as proved if the patient does not react on exposure to the original allergen and has had no other treatment This occurs in only a very few cases

The inhalation method has many advantages The progress of hyposensitisation can be observed directly, and the dose of allergen may be raised in such a way that the patient's reaction to it is always the same. This is of particular importance since it may be very difficult to avoid the inhalation of allergen from natural sources. It may easily happen that the dose of allergen aerosol given therapeutically is added on to an unknown dose inhaled unwittingly If the latter is large, an overdose at the controlled inhalation will be inevitable, but the severity of the attack will indicate how much the dose should be reduced at the next inhalation It is easier to carry out hyposensitisation in an allergen free environment, but in practice this is only possible when the allergen is strictly seasonal

Another difficulty which demands continuous and objective control of the process of hyposensitisation is caused by acute respiratory infections If such an intercurrent infection develops during treatment, the

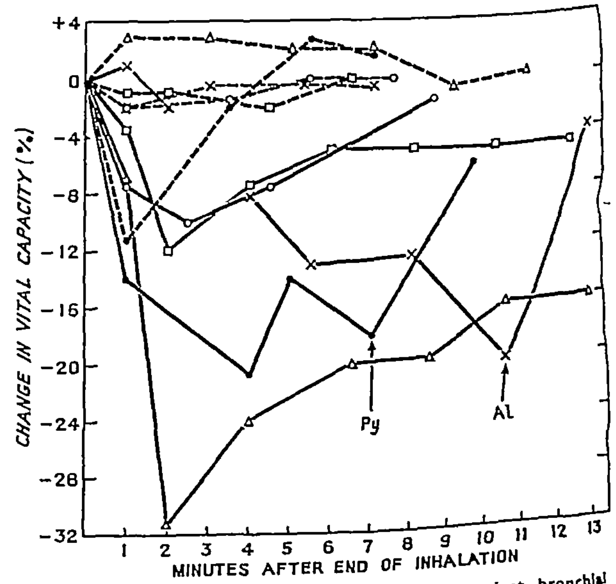


Fig 8—Protective action of anti histamine drug against bronchial asthma induced by inhalation of mixed pollen in 5 patients solid lines change in vital capacity after inhalation without protection ; interrupted lines change in vital capacity after various doses of phenergan had been given beforehand.

	Period of Inhalation (sec)	Dosage of Phenergan (mg)
△	45	37 5
×	5	25 0
○	30	37 5
□	25	37 5
●	180	50-0

Py, pyribenzamine 1 5% and Al aleudrine 1% inhaled to end the asthmatic attack (Herxheimer 1949b) patient's tolerance usually decreases A dose of allergen which did not evoke a reaction before the illness may now produce a severe reaction The common occurrence of acute respiratory infections makes it inevitable that the treatment is upset in a good many cases Apart from this, many asthmatics are sensitive to many different allergens which cannot be removed from their everyday environment They are inhaled in varying amounts and necessarily disturb any attempt at hyposensitisation, often preventing it completely This state of affairs is quickly recognised when the inhalation method is being used, with the injection method several unexplained setbacks often occur before the procedure is seen to be fruitless.

EFFECT OF DRUGS

A further field in which the inhalation method is useful is the study of drug action. The effect of anti-asthmatic drugs—e g, adrenaline, isoprenaline, and the anti-histamine drugs—can be measured objectively when they act on an induced attack Thus it can be shown that isoprenaline aerosol acts almost instantaneously (fig 7) Adrenaline and isoprenaline will suppress almost any attack if the dose is big enough, but this is not true of the anti histamine drugs These latter drugs are entirely unsuitable for the treatment of an acute attack They will, however, prevent a mild attack if given some time before the induction of the attack is attempted (Herxheimer 1949b), the dosage required varies con siderably in different patients (fig 8) Even large doses will not protect the patient from moderate and severe attacks

This method of assessing the protective action of drugs has also been used successfully by Rubitsky et al. (1949) The results are particularly useful in comparing the efficacy of one drug with that of others.

SUMMARY

A method is described for inducing asthmatic attacks by means of aerosol inhalations of allergenic extracts and other substances

The narrowing of the bronchial lumen and its effect on the mechanics of breathing in these attacks can be demonstrated graphically

The attack can be terminated at any stage by giving an inhalation of isoprenaline.

Sensitivity of the bronchial tree to asthmogenic substances can be demonstrated more reliably by this method than by skin tests

The sensitivity of the bronchial tree to allergens can be increased by giving large doses and decreased by giving small doses.

The reactions of different patients to the same allergen vary in severity, in latent period, and possibly in the degree to which muscle spasm and mucosal œdema and secretion play a part in their production

Aerosol inhalations can be used to reduce sensitivity Their main advantage over the injection method is that they allow progress to be observed objectively In many cases such hyposensitisation is impossible because the influence of exogenous allergens cannot be excluded.

The inhalation method can also be used to compare the anti asthmatic activity of drugs.

I am indebted to Dr Andrew Morland for access to some of the patients.

REFERENCES

Curry J J (1946) *J clin. Invest* 25 785 792.
Herxheimer H (1949a) *Thorax* 4 73
— (1949b) *Brit. med. J* ii 901
— (1951) *Int Arch Allergy* 2 27 40
Hurst A. (1943) *Brit. med J* i 403
Rackemann, F M. (1950) *J Amer med. Ass* 142 534
Rubitsky H J Bresnick, E. Levinson L. Risman, G Segal M. S (1949) *New Engl. J Med.* 240 45
Samter M. (1933) *Z ges. exp Med.* 89 24
Verzár F (1945) Höhenklimaforschungen des Basler Physiologischen Institutes Basle p 77

PRIMARY HYDROCELE AND ITS TREATMENT

REVIEW OF TWO HUNDRED CASES

D P Burkitt
M.D Dubl., F.R C.S.E
MEDICAL OFFICER, UGANDA

In the district of Lango, in Uganda, hydrocele is very common Its incidence over large areas exceeds 25% of the adult male population, varying geographically from 30% in the east to 1% in the west

The size of the hydrocele sacs is immense, the average content of one sac being a little over a pint In examining just over 300 cases I found bilateral hydroceles in 43% In 8% the content of fluid in one sac exceeded three pints The largest was a bilateral hydrocele with ten pints in one sac and thirty-four fluid ounces in the other

The classification of hydroceles into "vaginal" and "infantile" is fallacious, because in time most hydroceles stretch up to or near to the internal abdominal ring

Of the 3 abdominoscrotal hydroceles seen, 1 closely resembled clinically an enormously distended bladder associated with a right hydrocele. It contained six pints of fluid, of which five pints were in the intra-abdominal portion The other 2 contained about six ounces in the intra abdominal portion An abdominal hydrocele containing thirty four ounces of fluid was also treated there was no communication with a concomitant right vaginal hydrocele, though a process entered the inguinal canal and reached almost to the apex of the vaginal hydrocele

True bilocular hydroceles were rare when the hydrocele was large, for the waist tended to disappear with distension. A bilocular appearance was found with the epididymis as a belt forming the waist

About 8% of scrotal swellings were due to hæmatoceles, usually in elderly men

By virtue of their size and number hydroceles in Lango district are responsible for a great deal of disability, preventing work In addition, with the larger hydroceles, the disappearance of the penis is a complete bar to reproduction

TREATMENT

Our aim has been to combine efficiency with simplicity and economy in time, materials, and hospital accommodation Three possible lines of treatment have been advocated—simple tapping, tapping followed by the introduction of sclerosing agents, and radical operation

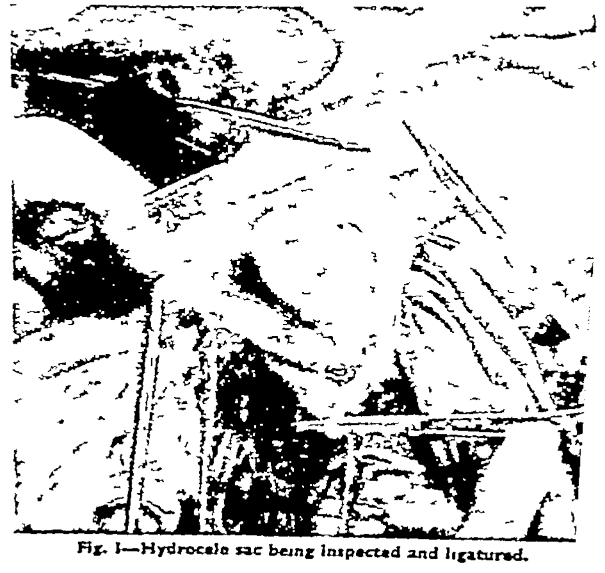


Fig. 1—Hydrocele sac being inspected and ligatured.

By repeating this process and gradually increasing the dose of allergen inhaled, the patient developed tolerance to it By contrast, when the dose of inhaled allergen was large enough to cause a *severe* attack, the opposite happened and tolerance diminished This became apparent when the dose was considerably reduced—e g , to a third of its previous value This smaller dose now caused an even more severe attack than that caused by the original dose Only a further drastic reduction in the dose led to the desired result, a mild attack

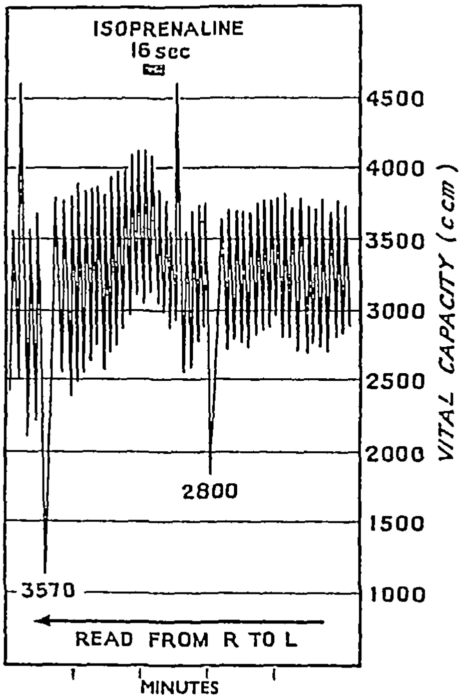


Fig 7—Rapid response of asthmatic attack to isoprenaline inhalation Pollen induced attack in asthmatic patient sensitive to grass pollen Almost immediately after end of 16 seconds inhalation of isoprenaline tidal air increases considerably (from about 900 c.cm to about 1200 c.cm) A minute later vital capacity has increased from 2800 to 3570 c.cm Increase is entirely due to increase of reserve air some of which, during attack, could not be exhaled and therefore formed part of residual air

These phenomena are evidently instances of hyposensitisation and hypersensitisation Large doses increase, and small doses diminish, the patient's sensitivity to the allergen concerned If this observation is correct, it must be possible to hyposensitise patients by using small and gradually increasing doses (this used to be called desensitisation) This has been done in some cases (Herxheimer 1951) For instance, in a patient who developed a mild attack after 8 seconds' inhalation when treatment was begun, the tolerance was so increased that three months later 100 seconds' inhalation had no effect In the first two cases of grass-pollen asthma treated in this way the asthma did not appear the following summer, though oddly enough the ocular and nasal symptoms persisted in part

These observations may be of both theoretical and practical significance *If it is possible to intensify or to weaken the allergic reaction of the bronchial tree in this way*, the question arises whether similar processes may not occur in the daily life of asthmatics An excessive amount of allergen inhaled accidentally—e g , house dust in moving house, and grass pollen on outings in the country—would make the asthma worse and hypersensitise the patient, who now would respond severely even to doses which previously did not injure him Only after he has returned to his usual surroundings may the amount inhaled become *very* much smaller, in these circumstances the asthma improves very gradually and reverts to its usual intensity In some asthmatics it seems as if such episodes of hypersensitisation and hyposensitisation occur quite often When one tries to discover why a chronic asthmatic suddenly becomes worse one sometimes finds that shortly before the attack the patient had exposed himself to a gross overdose of "his" allergen Often such an event cannot be recognised with certainty

Factors which are not allergic also play a part Excitement from any cause, and physical exertion, can greatly increase the ventilation Under these conditions the amount of allergen inhaled may be increased to many times its usual value for purely mechanical reasons, and this alone may cause considerable "overdosage" of allergen

The practical importance of our observations lies in the fact that the treatment of allergic asthma can be put on a much firmer basis than hitherto Hyposensitisation by injection does not allow precise observation of its progress. When a patient shows a systemic reaction, this is usually regarded as a sign of overdosage When there is no reaction, it is tacitly assumed that hyposensitisation is being achieved Final success is seldom conclusively proved It can only be regarded as proved if the patient does not react on exposure to the original allergen and has had no other treatment This occurs in only a very few cases

The inhalation method has many advantages The progress of hyposensitisation can be observed directly, and the dose of allergen may be raised in such a way that the patient's reaction to it is always the same. This is of particular importance since it may be very difficult to avoid the inhalation of allergen from natural sources. It may easily happen that the dose of allergen aerosol given therapeutically is added on to an unknown dose inhaled unwittingly If the latter is large, an overdose at the controlled inhalation will be inevitable, but the severity of the attack will indicate how much the dose should be reduced at the next inhalation It is easier to carry out hyposensitisation in an allergen free environment, but in practice this is only possible when the allergen is strictly seasonal

Another difficulty which demands continuous and objective control of the process of hyposensitisation is caused by acute respiratory infections If such an intercurrent infection develops during treatment, the

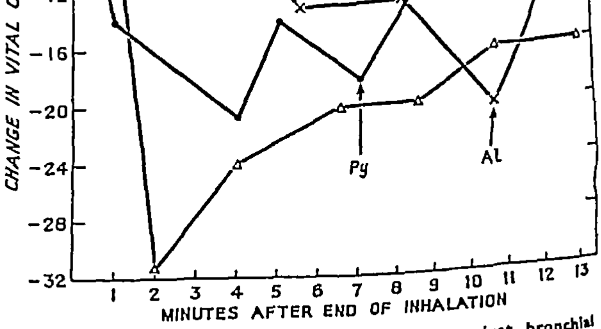


Fig 8—Protective action of anti histamine drug against bronchial asthma induced by inhalation of mixed pollen in 5 patients : solid lines, change in vital capacity after inhalation without protection ; interrupted lines, change in vital capacity after various doses of phenergan had been given beforehand

	Period of Inhalation (sec)	*Dosage of Phenergan (mg)*
△	45	37 5
×	5	25 0
○	30	37 5
□	25	37 5
●	180	50·0

Py, pyribenzamine 1 5%, and Al aleudrine 1% inhaled to end the asthmatic attack (Herxheimer 1949b) distinguishing between persistent emboli and thrombosis in situ, and regards the history of embolic incidents as all important in this respect It seems possible, however, that many of the cases described at necropsy as examples of pulmonary artery thrombosis may actually represent the result of former emboli, since an unexplained or "primary" thrombosis in such a situation is less easy to understand Carroll (1950) and Belt (1939) suggest that some cases diagnosed as Ayerza's syndrome may have a like origin The reason why these emboli persist whereas others disappear does not seem to be established. In the present case there seems little doubt that the original obstructions suffered recurrent additions to their substance, and, had the cause of the dyspnœa been understood, ligature of the veins would have been an obvious measure The point to be emphasised is that chronic heart failure does arise in this manner

REFERENCES

Belt T H (1939) *Lancet* ii 730
Carroll D (1950) *Amer J Med* 9 175
Castleman B Bland, E F (1946) *Arch Path* 42, 581
Friedberg C K. (1949) Diseases of the Heart Philadelphia

DELAYED EFFECTS OF ULTRAVIOLET BURNS IN MAN

M L THOMSON
M.B Glasg

SENIOR LECTURER, APPLIED PHYSIOLOGY DEPARTMENT,
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

IT was widely believed in the past that the sun's rays, by damaging the brain or the spinal cord, could cause pyrexia, delirium, coma, and death Aron (1911) showed that death in monkeys exposed to tropical sunlight was caused solely by a general rise in body temperature It has now been established that the biologically active ultraviolet (U V) portion of the sun's rays does not penetrate more than 1 or 2 mm into the skin, hence the possibility of direct injury to the nerve centres may be excluded It is now fashionable to regard the sun's rays as exerting no specific effect on man's ability to tolerate heat (Blum 1945) It has been shown, however, that after exposure to U V radiation there may be a reduction in sweating rate which is partly caused by occlusion of the mouths of sweat gland ducts in the necrosed surface layer of the epidermis, and probably partly by reduction of secretory pressure of sweat (Thomson 1951a and b) I report here the collapse, apparently attributable to previous U V radiation, of two men working in a heated room, and the development of sun blisters in another case

METHODS

The two men (Ha and Al) were fit young naval ratings who had previously been acclimatised by fourteen days' daily exposure to heat They worked and rested intermittently according to the same routine for four hours during all trials in the climatic chamber They were weighed nude and their rectal temperatures and pulse rates were taken at short intervals throughout each trial. Shorts and plimsolls were worn, and these were weighed separately before and after each trial The men's adjusted loss of weight was taken as a sufficiently accurate measure of their sweat-loss (sweat = loss of weight + fluids — excreta) The environmental conditions during all trials were as follows dry bulb temperature 115°F, wet-bulb temperature 85°F, air movement 200 ft per min (91°F effective temperature)

Radiation —On May 9, in the course of other trials conducted under identical conditions, one of the two men (Ha) chanced to expose his skin for four hours to uninterrupted sunshine while wearing bathing trunks On May 10 severe erythema was noted on his shoulders, chest, thighs and arms Ten days later (May 25) he and Al were both deliberately exposed to a standard mercury vapour U V lamp Two or three hours later both men developed a strong erythema Before radiation on May 28 sudamina was observed on Ha Al had papules at the sweat duct openings and itching on exposure to heat

RESULTS

Rectal temperatures and standing pulse rates (fig 1) are shown for the trials on May 25, 26, 27, and 28 for both men, and on May 10 and 24 for Ha Sweat losses (see table) on post radiation days were lower than on control days, but the difference was only significant in the case of Ha on the day of collapse (May 10) On the other hand, sweat in clothes fell appreciably after radiation as this table shows

TOTAL SWEAT LOSS AND SWEAT IN CLOTHING

Date of trial		May 10	May 24	May 25	May 26	May 27	May 28
Total sweat (g)	Ha	(1096)*	1356	1320	(1285)	1285	1310
	Al			1120	(1100)	1075	1210
Increase in weight of shorts (g)	Ha	(18)	40	62	(12)	6	58
	Al			13	(−6)	4	10

* Significant at 1 % level In parentheses one day after radiation.

The criteria of collapse in the heat were (1) a rectal temperature higher than 101 2°F, (2) a high pulse rate for the man, (3) muscular weakness, (4) evidence of postural hypotension (giddiness, faintness), (5) the men's statement that they could no longer carry on (viewed in the light of their known grit and reliability), and (6) the observers' estimate of the men's condition

On the day after the first exposure to U V radiation both men collapsed under environmental conditions which they had borne without undue discomfort on control days and are known to be readily withstood by fit acclimatised young men

In the case of Ha the first exposure to sunlight on May 9 was followed by collapse on May 10, in the case of Al the only exposure was to U V lamp on May 25 and was followed by collapse on May 26 Ha did not collapse after U V lamp treatment on May 25, and it may be presumed that the previous acute sunburn had partially protected him against the effects of the lamp (Thomson 1951b) Nevertheless this man showed a higher rectal temperature and pulse rate and lower terminal sweat loss on May 26 than on any other day except May 10, so the protection conferred by the earlier exposure does not seem to have been complete

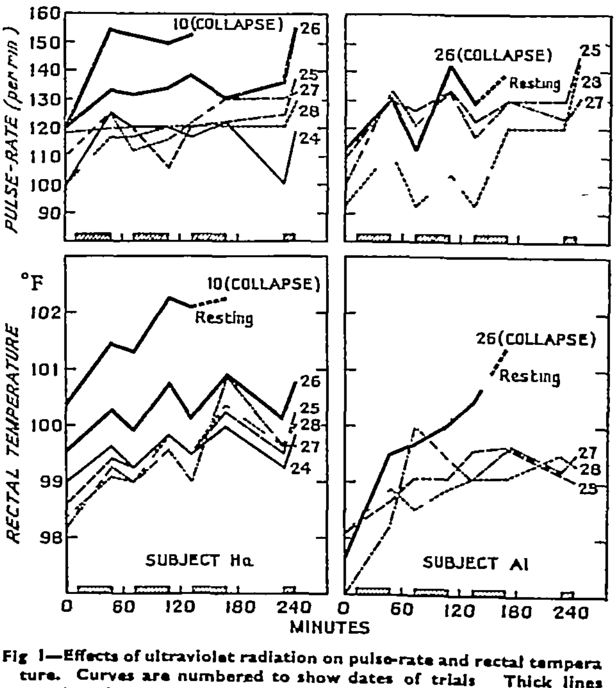


Fig 1—Effects of ultraviolet radiation on pulse-rate and rectal temperature. Curves are numbered to show dates of trials Thick lines one day after radiation. Black rectangles working-periods.

penicillin therapy should be continued until the lesion desquamates

I wish to thank the Director General, Army Medical Services, for permission to publish

REFERENCES

Baker W M (1873) *St Bart s Hosp Rep* 9 198
Barber M, Nellen M Zoob M (1946) *Lancet*, i, 125
Brunner G (1938) *Zbl Bakt* (2), 97 457
Goodwin, M A (1950) *Brit med J* i 765
Hellman F R, Herrell W E (1944) *Proc Mayo Clin* 19 340
King P F (1946) *Lancet*, ii 196
Klauder J V (1948) *Ann N Y Acad Sci* 48, 535
Kondo S (1936) *J Jap Soc vet Sci* 14, 111
Rosenbach, A J F (1884) Mikro Organismen bei den Wund Infektions Krankheiten des Menschen Wiesbaden

COR PULMONALE FROM RECURRENT PULMONARY EMBOLISM

C P Petch
M.D Camb, M R C P
CONSULTANT PHYSICIAN, ST HELIER HOSPITAL, CARSHALTON

Chronic cor pulmonale, or pulmonary heart disease, indicates hypertrophy or failure of the right side of the heart due to disease of the lungs or of the pulmonary arteries Acute cor pulmonale denotes the state of the heart immediately after the arrival of large emboli in the pulmonary artery, and usually, if this is not fatal, recovery is rapid It has long been observed, however, that recovery after non fatal embolism is not always complete, and the development of chronic cor pulmonale as a result of persistent or recurrent emboli is possible (Ljungdahl cited by Friedberg 1949) The chronic form here arises as a consequence of the acute This sequence of events has usually been reported by pathologists from necropsy findings (Belt 1939, Castleman and Bland 1946) and has received little recognition clinically, the following case might well have been diagnosed in life had the picture been familiar

CASE RECORD

A labourer, aged 46, previously free from serious disease of heart or lungs, was admitted to hospital on July 15, 1949, for repair of a right inguinal hernia The operation was uneventful, but fourteen days later the patient developed a sudden pain in the right lower chest posteriorly, with pleural friction, hæmoptysis, and pyrexia The legs were not tender or swollen Radiography of the chest showed consolidation at the right base Penicillin and sulphamezathine were given, and, a little later, a ten day course of heparin intravenously In spite of this, five weeks after the operation, on Aug 20, the patient experienced a similar sudden pain in the left side of the chest and was transferred to a medical ward At the time of transfer his pain had subsided and his main complaint was shortness of breath

On examination he had no fever, a blood pressure of 95/60 mm Hg, and bilateral basal crepitations in the lungs without signs of consolidation Electrocardiography on Sept 1 showed a well marked S wave in all leads, with steep inversion of TII and TIII (fig 1) This was regarded as compatible with acute cor pulmonale due to the episodes of pulmonary embolism already described Auricular fibrillation was observed for two days, but sinus rhythm, confirmed electrocardiographically, returned after the administration of quinidine and persisted until death

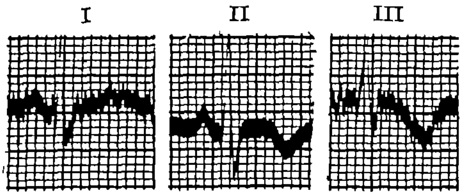


Fig 1—Electrocardiogram on Sept. 1 1949

Progress—A third attack of pain, this time in the right chest, with shortness of breath and slight staining of the sputum, developed on Sept 13, 1949, but a week later the patient was free from abnormal physical signs and well enough to go to a convalescent home During the autumn and winter he attended as an outpatient, and reported that he could work a little as a labourer, but was gradually becoming incapacitated by shortness of breath He also complained of a rather persistent, not episodic, pain in the chest Clinical examination did not reveal any adequate cause for these symptoms A radiograph of the chest was clear, and electrocardiography on Dec 12 showed restoration of an upright T wave in all leads (fig 2) In retrospect it seems that the pulmonary artery was being partly occluded The patient's condition on May 1, 1950, was so bad that he was readmitted to hospital He had had more severe attacks of chest pain, and both ankles had begun to swell

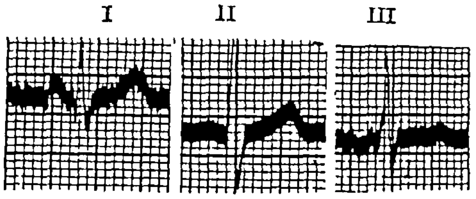


Fig 2—Electrocardiogram on Dec 12, 1949

On examination he had cyanosis, jugular venous stasis, a tender liver, and dependent œdema, he had no fever, his pulse was regular, pulse rate 80, and blood pressure 100/70 mm Hg The pulmonary second sound was loud, and protodiastolic triple rhythm was present, but signs in the lungs were minimal Electrocardiography on May 3 showed a right bundle branch block pattern, in the standard limb leads P waves were tall, and a peaked "pulmonary" P wave was present in lead II (fig 3)

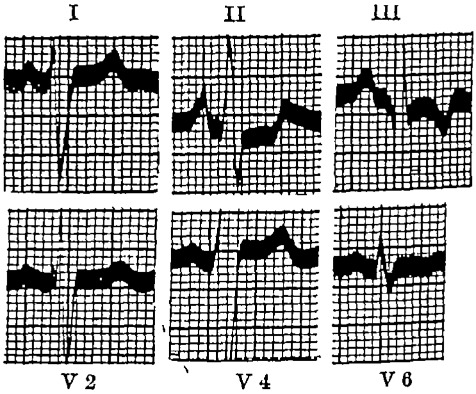


Fig 3—Electrocardiogram on May 3 1950

Course—The diagnosis of right heart-failure from chronic cor pulmonale was clear, but the manner in which it had arisen was not appreciated The patient was treated with heparin, salt restriction, and mersalyl, but during the next five days he gradually deteriorated, dying without evidence of further embolism To the last dyspnœa was his chief complaint

Necropsy Findings (Dr T Goodier)—The larger branches of the pulmonary artery on both sides were found to be filled with organised blood clot of different ages The right side of the heart was much hypertrophied and dilated, the tricuspid valve admitting five fingers No septal defect was found, the left side of the heart was normal, without valvular lesion or scar of the myocardium and the coronary arteries were patent The liver showed intense passive congestion. In the right popliteal vein were the remains of a long ante-mortem thrombus arising from the veins of the calf Fragments of this thrombus had presumably formed the emboli that had blocked the pulmonary vessels and caused death from right heart failure

COMMENT

Carroll (1950) could only find three published reports of what was unquestionably chronic obstruction of the pulmonary artery arising from embolism He added four of his own, with histories very similar to the one described here Like earlier workers he alludes to the difficulty of

penicillin therapy should be continued until the lesion desquamates

I wish to thank the Director General, Army Medical Services, for permission to publish

REFERENCES

Baker W M (1873) *St Bart s Hosp Rep* 9 198
Barber M, Nellen M Zoob M (1946) *Lancet*, i 125
Brunner G (1938) *Zbl Bakt* (2) 97 457
Goodwin, M A (1950) *Brit med J* i, 765
Hellman F R Herrell W E (1944) *Proc Mayo Clin* 19 340
King P F (1946) *Lancet* ii 196
Klauder J V (1948) *Ann N Y Acad Sci* 48 535
Kondo S (1935) *J Jap Soc vet Sci* 14 111
Rosenbach, A J F (1884) Mikro Organismen bei den Wund Infektions Krankheiten des Menschen Weisbaden

COR PULMONALE FROM RECURRENT PULMONARY EMBOLISM

C P Petch
M D Camb, M R C P
CONSULTANT PHYSICIAN, ST HELIER HOSPITAL, CARSHALTON

Chronic cor pulmonale, or pulmonary heart disease, indicates hypertrophy or failure of the right side of the heart due to disease of the lungs or of the pulmonary arteries Acute cor pulmonale denotes the state of the heart immediately after the arrival of large emboli in the pulmonary artery, and usually, if this is not fatal, recovery is rapid It has long been observed, however, that recovery after non fatal embolism is not always complete, and the development of chronic cor pulmonale as a result of persistent or recurrent emboli is possible (Ljungdahl cited by Friedberg 1949) The chronic form here arises as a consequence of the acute This sequence of events has usually been reported by pathologists from necropsy findings (Belt 1939, Castleman and Bland 1946) and has received little recognition clinically, the following case might well have been diagnosed in life had the picture been familiar

CASE RECORD

A labourer, aged 46, previously free from serious disease of heart or lungs, was admitted to hospital on July 15, 1949, for repair of a right inguinal hernia The operation was uneventful, but fourteen days later the patient developed a sudden pain in the right lower chest posteriorly, with pleural friction, hæmoptysis, and pyrexia The legs were not tender or swollen Radiography of the chest showed consolidation at the right base Penicillin and sulphamezathine were given, and, a little later, a ten day course of heparin intravenously In spite of this, five weeks after the operation, on Aug 20, the patient experienced a similar sudden pain in the left side of the chest and was transferred to a medical ward At the time of transfer his pain had subsided and his main complaint was shortness of breath

On examination he had no fever, a blood pressure of 95/60 mm Hg, and bilateral basal crepitations in the lungs without signs of consolidation Electrocardiography on Sept 1 showed a well marked s wave in all leads, with steep inversion of TII and TIII (fig 1) This was regarded as compatible with acute cor pulmonale due to the episodes of pulmonary embolism already described Auricular fibrillation was observed for two days, but sinus rhythm, confirmed electrocardiographically, returned after the administration of quinidine and persisted until death

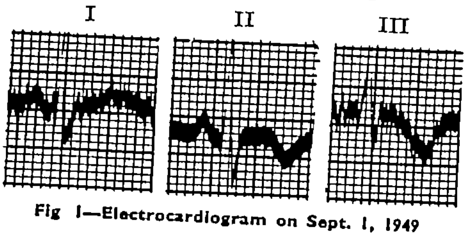


Fig 1—Electrocardiogram on Sept. 1, 1949

Progress—A third attack of pain, this time in the right chest, with shortness of breath and slight staining of the sputum, developed on Sept 13, 1949, but a week later the patient was free from abnormal physical signs and
enough to go to a convalescent home During the autu
and winter he attended as an outpatient, and reported that
could work a little as a labourer, but was gradually becom
incapacitated by shortness of breath He also complained
a rather persistent, not episodic, pain in the chest Clinic
examination did not reveal any adequate cause for the
symptoms A radiograph of the chest was clear, and electro
cardiography on Dec 12 showed restoration of an uprigh
T wave in all leads (fig 2) In retrospect it seems that th
pulmonary artery was being partly occluded The patient's condition on May 1, 1950, was so bad that he was readmitted to hospital He had had more severe attacks of chest pain, and both ankles had begun to swell

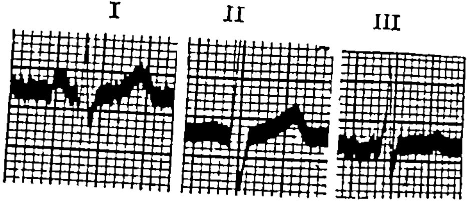


Fig 2—Electrocardiogram on Dec. 12 1949

On examination he had cyanosis, jugular venous stasis, a tender liver, and dependent œdema, he had no fever, his pulse was regular, pulse rate 80, and blood pressure 100/70 mm Hg The pulmonary second sound was loud, and protodiastolic triple rhythm was present, but signs in the lungs were minimal Electrocardiography on May 3 showed a right bundle branch block pattern, in the standard limb leads P waves were tall, and a peaked 'pulmonary' P wave was present in lead II (fig 3)

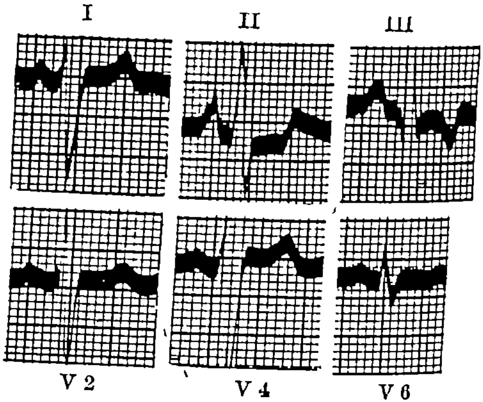


Fig 3—Electrocardiogram on May 3, 1950

Course—The diagnosis of right heart failure from chronic cor pulmonale was clear, but the manner in which it had arisen was not appreciated The patient was treated with heparin, salt restriction, and mersalyl, but during the next five days he gradually deteriorated, dying without evidence of further embolism To the last dyspnœa was his chief complaint

Necropsy Findings (Dr T Goodier)—The larger branches of the pulmonary artery on both sides were found to be filled with organised blood clot of different ages The right side of the heart was much hypertrophied and dilated, the tricuspid valve admitting five fingers No septal defect was found, the left side of the heart was normal, without valvular lesion or scar of the myocardium, and the coronary arteries were patent The liver showed intense passive congestion. In the right popliteal vein were the remains of a long ante mortem thrombus arising from the veins of the calf Fragments of this thrombus had presumably formed the emboli that had blocked the pulmonary vessels and caused death from right heart-failure

COMMENT

Carroll (1950) could only find three published reports of what was unquestionably chronic obstruction of the pulmonary artery arising from embolism He added four of his own, with histories very similar to the one described here Like earlier workers he alludes to the difficulty of distinguishing between persistent emboli and thrombosis in situ, and regards the history of embolic incidents as all important in this respect It seems possible, however, that many of the cases described at necropsy as examples of pulmonary artery thrombosis may actually represent the result of former emboli, since an unexplained or "primary" thrombosis in such a situation is less easy to understand Carroll (1950) and Belt (1939) suggest that some cases diagnosed as Ayerza's syndrome may have a like origin The reason why these emboli persist whereas others disappear does not seem to be established In the present case there seems little doubt that the original obstructions suffered recurrent additions to their substance, and, had the cause of the dyspnœa been understood, ligature of the veins would have been an obvious measure The point to be emphasised is that chronic heart failure does arise in this manner

REFERENCES

Belt T H (1939) *Lancet* ii 730
Carroll D (1950) *Amer J Med* 9 175
Castleman B, Bland, E F (1946) *Arch Path* 42, 581
Friedberg C K. (1949) Diseases of the Heart Philadelphia

DELAYED EFFECTS OF ULTRAVIOLET BURNS IN MAN

M L Thomson
M.B Glasg

SENIOR LECTURER, APPLIED PHYSIOLOGY DEPARTMENT,
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

It was widely believed in the past that the sun's rays, by damaging the brain or the spinal cord, could cause pyrexia, delirium, coma, and death Aron (1911) showed that death in monkeys exposed to tropical sunlight was caused solely by a general rise in body temperature It has now been established that the biologically active ultraviolet (U V) portion of the sun's rays does not penetrate more than 1 or 2 mm into the skin, hence the possibility of direct injury to the nerve centres may be excluded It is now fashionable to regard the sun's rays as exerting no specific effect on man's ability to tolerate heat (Blum 1945) It has been shown, however, that after exposure to U V radiation there may be a reduction in sweating rate which is partly caused by occlusion of the mouths of sweat gland ducts in the necrosed surface layer of the epidermis, and probably partly by reduction of secretory pressure of sweat (Thomson 1951a and b) I report here the collapse, apparently attributable to previous U V radiation, of two men working in a heated room, and the development of sun blisters in another case

METHODS

The two men (Ha and Al) were fit young naval ratings who had previously been acclimatised by fourteen days daily exposure to heat They worked and rested intermittently according to the same routine for four hours during all trials in the climatic chamber They were weighed nude, and their rectal temperatures and pulse rates were taken at short intervals throughout each trial Shorts and plimsolls were worn, and these were weighed separately before and after each trial The men s adjusted loss of weight was taken as a sufficiently accurate measure of their sweat-loss (sweat = loss of weight + fluids − excreta) The environmental conditions during all trials were as follows dry bulb temperature 115°F, wet-bulb temperature 85°F, air movement 200 ft per min. (91°F effective temperature)

Radiation—On May 9, in the course of other trials conducted under identical conditions, one of the two men (Ha) chanced to expose his skin for four hours to uninterrupted sunshine while wearing bathing trunks On May 10 severe erythema was noted on his shoulders, chest, thighs and arms Ten days later (May 25) he and Al were both deliberately exposed to a standard mercury vapour U V lamp Two or three hours later both men developed a strong erythema. Before desquamation on May 28 sudamina was observed on Ha. Al had papules at the sweat duct openings and itching on exposure to heat

RESULTS

Rectal temperatures and standing pulse rates (fig 1) are shown for the trials on May 25, 26, 27, and 28 for both men, and on May 10 and 24 for Ha Sweat losses (see table) on post radiation days were lower than on control days, but the difference was only significant in the case of Ha on the day of collapse (May 10) On the other hand, sweat in clothes fell appreciably after radiation as this table shows

TOTAL SWEAT LOSS AND SWEAT IN CLOTHING

Date of trial		May 10	May 24	May 25	May 26	May 27	May 28
Total sweat (g)	Ha.	*(1096)**	*1356*	1320	(1285)	1285	1310
	Al			1120	(1100)	1075	1210
Increase in weight of shorts (g)	Ha	(18)	40	62	(12)	6	58
	Al			13	(−6)	4	10

* Significant at 1 % level In parentheses one day after radiation.

The criteria of collapse in the heat were (1) a rectal temperature higher than 101 2°F, (2) a high pulse rate for the man, (3) muscular weakness, (4) evidence of postural hypotension (giddiness, faintness), (5) the men's statement that they could no longer carry on (viewed in the light of their known grit and reliability), and (6) the observers' estimate of the men's condition

On the day after the first exposure to U V radiation both men collapsed under environmental conditions which they had borne without undue discomfort on control days and are known to be readily withstood by fit acclimatised young men

In the case of Ha the first exposure to sunlight on May 9 was followed by collapse on May 10, in the case of Al the only exposure was to U V lamp on May 25 and was followed by collapse on May 26 Ha did not collapse after U V lamp treatment on May 25, and it may be presumed that the previous acute sunburn had partially protected him against the effects of the lamp (Thomson 1951b) Nevertheless this man showed a higher rectal temperature and pulse rate and lower terminal sweat loss on May 26 than on any other day except May 10, so the protection conferred by the earlier exposure does not seem to have been complete

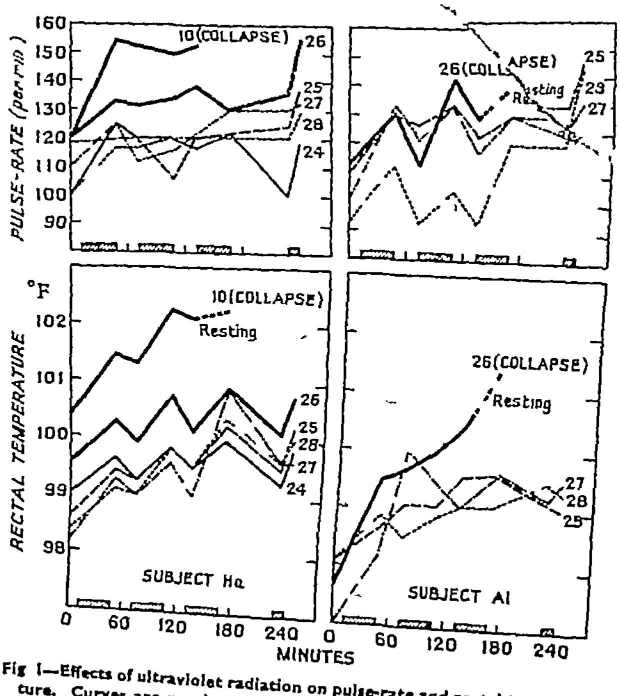


Fig 1—Effects of ultraviolet radiation on pulse-rate and rectal temperature. Curves are numbered to show dates of trials. Thick lines one day after radiation Black rectangles, working periods

e bullet passed high in this lobe Freeman and Watts
942) point out that signs are vastly greater in cases
iere both sides are affected

As regards his personality, this patient shows no change
his social relations, though there is a deterioration in
conceptual thinking He must be followed up with
re for a long time to rule out such complications as
ilepsy, as well as undesirable personality changes

I am indebted to Dr I Atkin, physician superintendent of
rk Prewett Hospital, for permission to publish this case,
d to Dr R I Roberts for his radiological report

REFERENCES

eeman W Watts, J W (1942) Psychosurgery Springfield Ill
xton H V (1947) *Med J Aust* ii 646
ttmann F (1943) *J ment Sci* 89 85
gers, L C (1948) *Med J Aust* i, 283
anson J C (1931) *J Amer med Ass* 96 1382

IN-VIVO SURVIVAL OF RABBIT'S RED CELLS RECOVERED AFTER FREEZING

H A Sloviter*
M D , Ph D Pennsylvania
*om the National Institute for Medical Research, Mill Hill,
London*

It was recently reported (Smith 1950) that blood
uted with a glycerol solution can be frozen, kept at
79°C, and subsequently thawed without producing
ore than slight hæmolysis Human red blood cells
treated can be recovered in yields of 80–90% of their
ginal number (Sloviter 1951), these recovered red
lls are normal in appearance, and their behaviour in
ro suggests that they are capable of normal function

The present study was undertaken to determine whether
bbit red blood cells recovered after freezing survive
ien they are injected into the circulating blood
eam The procedure used for this purpose was to
el, with a radioactive isotope, the cells which had been
ozen and recovered, and to determine the radioactivity
naining in the circulating red blood cells at various
nes after placing the labelled cells into the circulation

The rabbit was chosen for these experiments, for two
isons (1) the rabbit is a convenient animal for this
rpose, and (2) the red blood cells of the rabbit are
nost as permeable to glycerol as human red blood
lls (Jacobs et al 1935)

The isotope used in most of these experiments was
dioactive phosphorus (P^{32}) Labelling of the red
ood cells with P^{32} and measurement of their radio
tivity were carried out in a manner similar to that
scribed by Reeve and Veall (1949) Radioactive
romium (Cr^{51}) was also used because it remains in the
d blood cell longer and has a longer half life than
es P^{32} On these grounds, it was expected that Cr^{51}
periments would yield more conclusive results Unfor
nately, Cr^{51} was available only in low specific activity
aterial, and the results were not sufficiently precise
ells were labelled with Cr^{51} and radioactivity measured
cording to the technique described by Gray and
erling (1950)

METHOD

A 5 ml portion of rabbit blood, to which acid citrate
xtrose anticoagulant had been added, was mixed with an
ual volume of glycerol solution (30 g glycerol and 0 85 g
dium chloride per 100 ml) About one hour after mixing,
ch samples were immersed in a solid carbon dioxide alcohol
th (– 79°C) and then kept at – 79°C in sealed tubes for up
42 days After thawing, the red blood cells were recovered,
the manner previously described for human red blood
lls (Sloviter 1951) and were then suspended in an equal
lume of 0 85% sodium chloride solution To this suspension
is added approximately 30 microcuries of P^{32} (as sodium

DATA FROM P^{32} EXPERIMENT CELLS

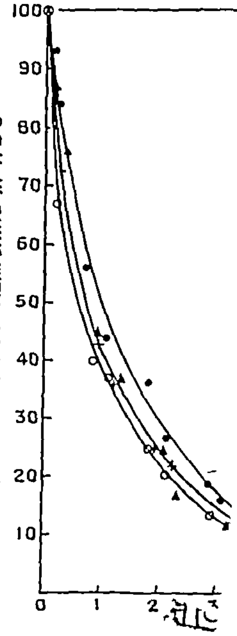
Days since injection of labelled cells	Volume of cells (ml)	Counts per min observed	Counts per min corrected for decay
0 00	0 22	1720	2230
0 25	0 19	1070	1390
0 94	0 25	830	1080
1 21	0 26	720	935
1 92	0 22	430	560
2 21	0 21	360	470
3 25	0 20	190	250
4 08	0 21	130	170
5 29	0 23	90	120
6 25	0 19	60	80
7 17	0 22	40	60

phosphate solution containing a little
and the mixture was kept at 37°C for 90 m
then separated by centrifuging, washed t
0 85% sodium chloride solution, and t
small volume of 0 85% sodium chloride
This suspension of labelled cells was
ear vein of the rabbit from which the
been obtained Small samples of bloo
radioactivity were drawn at 5 min and
8 days after injection Each sample
and plasma and the radioactivity o
A beta ray, liquid type Geiger Müller
the samples were prepared for m
by Reeve and Veall (1949) In co
drawn rabbit blood was labelled w
into the donor rabbit

The experiments with radioactive
in the same manner The cells rec
thawing of 5 ml of blood were tre
with 5–10 microcuries of Cr^{51} (as s
for 90 min The labelled cells,
were suspended in 0 85% sodium
into the rabbit Radioactivity w
window Geiger Müller counter, the
measurement as described by Gra

RESULT

The radioactivity per unit
which were withdrawn 5 min
labelled cells was designated
drawn at later times the p
remaining in the cells relativ
puted, correction being made



**Radioactivity remaining in
of P^{32} labelled cells. Blac
circles = red cell frozen 2
Triangles = red cells froz**

---

* Damon Runyon Senior Clinical Research Fellow 1950–51

THE LANCET

LONDON SATURDAY, JUNE 23, 1951

Paying Paul

AT its annual meeting last week the Representative Body of the British Medical Association heard from Dr WAND, chairman of the General Medical Services Committee, a report on the progress of negotiations for improving general practitioners' remuneration. It will be recalled that this report[1] tells of an offer by the Minister of Health and Secretary of State for Scotland of an extra £2 million to augment the practitioners' central pool, subject to conditions. These conditions include "satisfactory methods of distribution," "significantly lower effective maximum numbers of patients," and the taking by the committee of "all possible steps to eliminate extravagance in prescribing." The G M S C found itself unable to recommend acceptance of the Government's offer, and it has called a special conference of local medical committees in July to discuss future action. If the conference acts as the committee recommends, it will call on the Minister of Health to refer to arbitration the determination of the proper size of the central pool, and it will suggest that once this has been determined by arbitration the G M S C should resume discussions to find and apply the best form of distribution. As we note on a later page, the Representative Body debated at some length this report from the General Medical Services Committee. In general, representatives reacted favourably to the committee's proposals, and the discussion ended with an expression of confidence in the conference of local medical committees, and a pledge of support to the conference in its efforts to secure a full and just settlement of the practitioners' claim.

It is difficult to see how the profession could accept an arbitrary offer of £2 million, made with no contention that this is the sum required for a just settlement. The Government's argument is that this is all the money remaining when other demands on the budget of the health services have been satisfied; it offers no agreement that the size of the pool should be related to present or to future numbers of doctors in general practice. Furthermore, acceptance by the profession of the condition that everything shall first be done to eliminate extravagance in prescribing could perhaps be misread as a bid by doctors to augment their own incomes at the cost of their patients' proper needs. The *Times*[2] remarks that the profession's representatives

> "are demanding, reasonably enough, that the 'right' size of the 'pool' should be determined by arbitration. It is high time that this question, among others, should be publicly investigated by some body capable of taking an impartial view. It should not be supposed, however, that the size and the nature of the rewards appropriate to one group of doctors will ever be satisfactorily settled until some more far-ranging inquiry does what the Spens inquiries failed to do—that is, achieves a balanced view of the rewards appropriate to all the leading professions in the health service."

This is an apt comment. General practitioners' remuneration was the subject of the first of the Spens reports. The figures for doctors' incomes available to the Spens Committee were themselves already nearly ten years old, and there were no comparable figures (such as were later produced) for the earnings of consultants or specialists—or of dentists. This committee had to content itself with pointing to the need for keeping the rewards of general practice related to those of the specialist:

> "We consider that it would be disastrous to the profession and to the public if general practice were recruited only from the less able young doctors."
>
> "It is important to improve prospects in general practice in order to render this branch of medicine sufficiently attractive to prevent all the abler men endeavouring to enter specialist service."

Furthermore, a later Spens inquiry assessed the appropriate level of the general practitioner's income as one eighth more than that of a general dental practitioner.

These good intentions have not, however, been translated into facts. The volume of the general practitioner's work has risen, but his comparative income has shrunk; and now he clearly belongs to the least well off of all "the leading professions in the health service." Were this not so our present registrar problem would not have become so pressing nor so insoluble. If only the prospects for the good practitioner, undertaking satisfying and unhurried work, could stand comparison even with those for the least successful of the men reaching consultant status, the consultant field would have exerted a less magnetic attraction to the young graduate, and general practice would not need to derive its recruits—as is fast becoming the case—mainly from those who cannot gain a foothold in a specialty. The general practitioners have no quarrel with the main conception of the Spens report—that of a range of incomes attainable in different proportions by practitioners throughout the service. They would wish to retain this conception but to have it realistically translated into present day money values, with due regard to the need for more doctors in many areas, to the rising expenses of practices, and to the incomes attainable by comparable professional colleagues within the health service. It must not be forgotten that the moneys hitherto paid into the central pool have not been assessed on any agreed calculation of the proper total to satisfy the Spens recommendations, but were provided by the Minister of Health to get the scheme started.

Practitioners may reasonably decline formally to relate economy in prescribing to adjustment of their remuneration, though the far sighted are increasingly alive to the need for sensible care. There can,

---

[1] See *Lancet* June 16 1951 p 1311

[2] *Times* June 15 1951

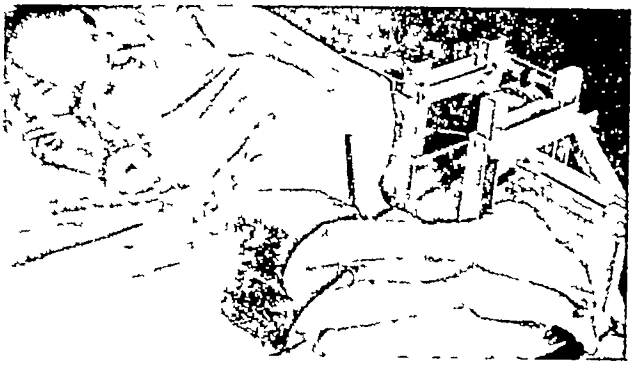


Fig 2—Position of legs before traction

skin and other tissues through which the force is applied We have found that traction of up to 150 lb applied at right-angles to a skin surface for half an hour does not damage the skin

The main features of the apparatus are apparent from fig 1 The source of power is a hydraulic jack (J) operated and released by the lever (L) Traction is exerted through a bicycle chain attached at one end to a spring balance recording up to 200 lb The bicycle chain passes over a sprocket on the jack (S) in such a way as to cause the chain to travel twice as far as the head of the jack This gives a wide range of action The counter-thrust surfaces (C) for buttocks and heels fold downwards when not in use The heels rest on a rubber pad mounted on a frame which slides distally as the legs become straightened A conveniently placed handle (H) is so fitted as to provide for the jack being returned to its lowest position before use

Figs 2 and 3 illustrate the use of the apparatus in a patient with chronic myelitis who had in recent months developed flexion contractures and pressure sores With traction of about 150 lb applied to both lower limbs together, the contracture yielded in the course of a few minutes, and correction was maintained in this way for half an hour twice daily The pull is elastic (through the spring balance) and the force applied drops as the contracture gives After treatment it is best for the patient to lie prone for an hour, as this posture tends to inhibit flexion spasms, but the best way of counter-acting flexion spasms is weight-bearing, and with suitable splints this became possible in the case illustrated

Used in this way the apparatus is very stable, and it is seldom necessary to use the fixing legs for the wheels Another application of the apparatus is seen in fig 4, where adductor spasm is being countered by traction of 100 lb maintained for half an hour at a time The counter thrust in this case is taken up by the special arms fitted for the purpose

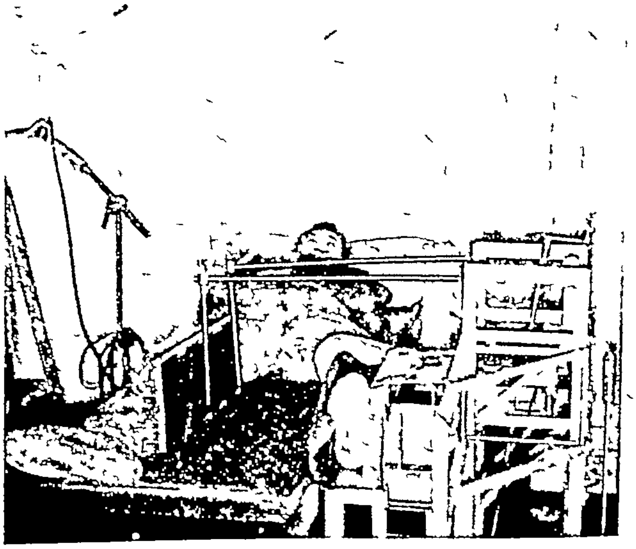


Fig 4—Apparatus applied for treatment of adductor spasm

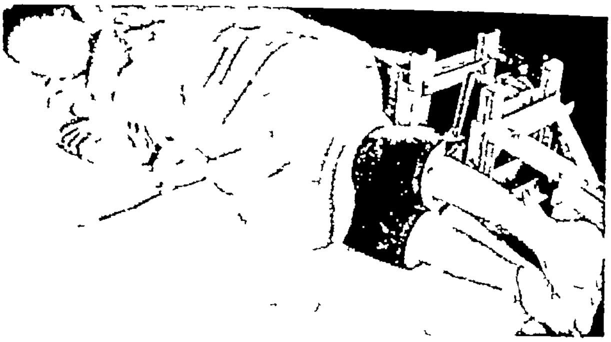


Fig 3—Position of legs after traction

The apparatus has been used with benefit in all of five cases treated, and it seems to have other possible applications which have not yet been explored

The instrument shown in figs 1 and 4 is an improved model constructed by Messrs H G East & Co, Longworth Road, Oxford

Department of Neurology,
United Oxford Hospitals

W RITCHIE RUSSELL
M D Edin, F R C P

E H J SCHUSTER
O.B E, D SC

Reviews of Books

Textbook for Health Visitors

LLYWELYN ROBERTS, M D, M R.C.P, medical officer of health, Sheffield, I G DAVIES, M D, M.R.C.P, medical officer of health, Leeds, BERYL CORNER, M D, M.R.C.P, physician, Bristol Hospital for Sick Children. London Baillière, Tindall, & Cox 1951 Pp 552, 21s

THIS book is intended primarily for the health visitor in training and after qualification It covers the revised syllabus for the examination for the health visitors' certificate of the Royal Sanitary Institute, and, as would be expected from the experience and status of the authors, does so very competently, in clear and simple language. The expanded sphere of duties placed on the health visitor by the National Health Service Act is reflected in the contents, and this "family adviser and friend" is given some guidance in geriatrics and sociology "The essentials of social care work are that it should be directed, purposeful, and specific This will distinguish it from meddlesome prying into the private lives of individuals. Like meddlesome midwifery, meddlesome social work may do great harm" This is indeed wise guidance, and we hope that the authors, in their next edition, will consider omitting the sections on anatomy and physiology to make space for further consideration of health education, the mental development of the child, the technique of interviewing, and the scope of social medicine

Hirndurchblutungsstórungen

Klinik und arteriographische Diagnose A BROBEIL, Dozent an der Universitäts Nervenklinik, Marburg Lahn Stuttgart Thieme 1950 Pp 204 D M 45

THIS monograph on the disturbances of cerebral circulation is based on Dr Brobeil's series of 16 patients suffering from thromboangiitis obliterans (Buerger's disease) with involvement of the brain In his investigations he made full use of Moniz's arteriographic method, and he shows the diagnostic application of the arteriogram in many well-reproduced examples The emphasis on the cases of Buerger's disease throws the book somewhat out of balance, and the chapters on the anatomy, physiology, and pathology of cerebral circulation are hardly more than useful, though not very critical, abstracts from textbooks Sometimes the information given is incomplete there is for instance no mention of the cerebral drainage system Cerebral vascular crises, including migraine and epilepsy, are mainly discussed from the clinical point of view, and the value of the last chapter, on arteriosclerosis of the brain, is enhanced by characteristic arteriograms at various stages of the disease The list of references contains the important publications of central European workers

however, be less ground for refusing to consider reduction in the maximum size of lists. Such a revision is clearly necessary both to ease the lot of the practitioners with the smaller lists, and to ensure that doctors shall be found where they are most needed. Spreading the hardship caused by an undersized central pool need not undermine the case for its adjustment, and readiness to take such a step would reflect both professional loyalty and professional responsibility.

Prevention of Diabetic Complications

FROM the beginning of the insulin era writers on the control of diabetes have disagreed on how complete a restoration to physiological normality should be the aim. Some, such as TOLSTOI [1] and LICHTENSTEIN,[2] advocate a "free diet" with enough insulin to prevent diabetic symptoms and acidosis, without regard to hyperglycæmia and glycosuria, whereas idealists like JOSLIN [3] and JACKSON [4] believe in using insulin and a strict diet to restore the patient's metabolism as closely as possible to normality. The "free diet" protagonists base their treatment on the assumption that the vascular, renal, and ocular complications of diabetes are part and parcel of the disease and are thus not materially affected by insulin and strict control. A good deal of published work supports this view. Thus DOLGER [5] found that every one of 200 diabetics of 25 years' standing had retinal hæmorrhages, regardless of age of onset, severity of the diabetes, or type of treatment applied. In 1938, WARREN [6] claimed that he had never seen a necropsy on a diabetic, whose disease had lasted 5 years or more, free from arteriosclerosis, regardless of age, but by 1946 he had found 4 exceptions. As lately as last year GOADBY and JACOBS [7] concluded that in their clinic routine treatment had no effect on the incidence of vascular and eye complications, although good control did reduce the incidence of neuropathy.

The burden of proving any effect of good control on these complications has rested with those maintaining exact insulin dietary balance over many years in diabetics who after 20 years' treatment are still not old enough to be at the stage of senile degeneration. Some of the earlier studies [8] included patients in whom diabetes started before insulin was available, and, however well controlled their condition may have been eventually, these patients must at first have passed through a phase of poor control. Even in the most strictly supervised cases personal and environmental factors rule out the possibility of constantly maintaining the blood sugar within the normal range. Cases can, however, be classified according to the constancy of control, and in 1949 JACKSON and his group [4] in Iowa described what they believed was the first objective evidence that the level of control is important in determining degenerative changes. In their study of 75 unselected diabetics of 10 years' standing, one worker made a numerical rating of the degree of control, while another, who was oblivious of the control ratings, examined the patients for degenerative changes. 30% had good control ratings, and these patients had no significant complications. Only the patients with poor control had the more advanced degenerative changes. JACKSON concluded that the level of control and the duration of the diabetes were important factors governing complications. This year a comprehensive study of 247 diabetics of 10–34 years' standing, seen at JOSLIN's clinic,[9] has added weight to JACKSON's results. All 247 patients in this study developed diabetes between the ages of 18 months and 30 years, and for the purpose of the survey degenerative changes were sought by numerous clinical, laboratory, and radiological investigations, including radiographs for arterial calcification and heart size, electrocardiographs, capillary-fragility tests, detailed examinations of the eyes, renal function tests, and determination of the blood-fat and blood-protein levels. Levels of control were assessed strictly, and to gain the label "excellent control" the patient had to satisfy each of the following criteria: (1) never been in coma; (2) insulin begun within a few weeks of the onset of diabetes; (3) urinary sugar tests done more than once daily since the onset, with a conscientious attempt to keep the urine sugar free before meals by varying the insulin dosage according to the tests; (4) diet weighed for at least 80% of the time since the first appearance of diabetic symptoms; and (5) physical examination and laboratory tests by a doctor at least once a year, with satisfactory blood and urine tests. One might expect that few would deserve this rating, and in fact only 7 of the 247 did so. 30 were classified as having "good control" on slightly less strict criteria, and the excellent and good groups comprised 15% of the series. 21% had fair control, and 64% poor. It was found that this classification did not cause any bias between the groups with regard to age of onset or to insulin dosage, but 63% of the patients with good or excellent control had had diabetes for more than 20 years, whereas only 38% of the patients with poor or fair control had had diabetes for such a time. This may indicate that careful control prolongs life, but there is even better reason to believe that careful control prevents severe degenerative complications. Thus no patients with excellent or good control showed advanced vascular calcification, or retinopathy, or any evidence of diabetic nephropathy, even after 20–34 years of diabetes. In the group of 103 patients with diabetes for periods of 20–34 years, 3 of the 4 cases with excellent control had no retinal lesions; and of 54 with moderate to marked retinopathy all but 5 had fair or poor control, and none excellent. DYER's group [10] in Philadelphia confirm from their series of 50 patients with diabetes for 10 or more years that retinal lesions are significantly correlated with poor control of the diabetes.

It thus seems that, in preventing degenerative complications, strict regulation of the diabetes is more important than the duration or severity of the disease. Juvenile diabetics, who as a class seem to be intellectually above average,[4 9] may by strict control be saved from tragic complications at what should be the prime of their lives.

---

[1] Tolstoi E *Amer J digest. Dis* 1943, 10 247

[2] Lichtenstein A *Acta pædiatr, Stockh.* 1945 32, 556

[3] Joslin E P, Root H F Marble A F, White P Bailey, C C Treatment of Diabetes Mellitus Philadelphia, 1946

[4] Jackson, R L, Hardin, R C Walker G L Hendricks A B Kelly H G *Proc Amer diab Ass* 1949 9 307

[5] Dolger H *J Amer med Ass* 1947 134, 1289

[6] Warren S The Pathology of Diabetes Mellitus Philadelphia 1938 p 121

[7] Goadby, H K, Jacobs J H *St Thom Hosp Rep* 1950 6, 244

[8] Eisele H F *J Amer med. Ass* 1942 120, 188

[9] Wilson J L Root H F Marble A *Amer J med Sci.* 1951 221, 418

[10] Spoont S Dyer, W W Day R Blaxer H *Ibid* p 490

Cures of Peptic Ulcer

AT Slough the waiting-room of a chemist who cures peptic ulcers is brimful of grateful patients and hopeful newcomers, and those who have encountered some of his cures will know that the gratitude is profound and the cure—apparently—complete These recovered patients eat anything, they work as hard as they please, and they are confident that this man has found the only answer to a problem still baffling the doctors Mr JOHN PARR, who is doubtless more sophisticated than the average run of the patients seeking help at Slough, tells us in a new book[1] how, after some 25 years of severe suffering he was cured of a duodenal ulcer by means of a low-fat diet, and he has since remained well for 5 years All physicians who treat large numbers of patients with peptic ulcer have many records of patients who responded to treatment, and who remained well for 5 years or longer, even in some cases for good, and they also have records of failures As Mr PARR explains at length and beautifully clearly, we do not yet understand the mechanisms producing peptic ulcers, or the conditions necessary for their cure

How much do we, in fact, know? We know that ulcers are becoming commoner, especially in men, though at one time they were commoner in women We know that gastric and duodenal ulcers behave differently (a point which Mr PARR does not make), and that acute ulcers behave differently from chronic ulcers We know, from the experiments of WOLF and WOLFF[2] on "Tom" (whose gastric mucosa was so conveniently visible), that the stomach shares with the face the vascular effects of emotion, going pale with fear and depression, red with wrath, and that the mucosa of a stomach so engorged will bleed even if stroked gently with a glass rod We are just beginning to study vascular shunt mechanisms of the stomach which may at times render the ulcer bearing area ischæmic We have evidence that acute ulcers produced experimentally in animals always heal within three weeks if the causal drug or irritant is withdrawn We have records of "ulcer families" though we cannot say whether it is a predisposition to ulcer or an ulcer temperament which is inherited, or whether the new generation is merely bred in an ulcer-provoking environment We are well aware, of course, that ulcer relapses are very often associated with anxiety, and two types of "ulcer temperament" have been described—an ambitious, tense, self driving type, anxious for success, and a quiet over conscientious worrying type, anxious to be fed and cherished and hiding his emotions under a calm exterior We have a deal of information about the secretion of acid by the stomach, and its behaviour in the ulcer-patient, and we have some evidence that hypersecretion—especially nocturnal—is often associated with duodenal, though not with gastric, ulcers We also know that chronic ulcers rarely develop during pregnancy, and that symptoms if present usually subside at this time We know that acute ulceration sometimes follows skin burns (Curling's ulcer) and that a chronic ulcer often develops at the constricting ring of a diaphragmatic hernia We know all too well that the characteristic life history of an ulcer is one of remissions—perhaps for 10 or 15 years—and exacerbations It is easy to see that the complex story is still only half unfolded, and that Mr PARR is right when he says we do not really know what causes an ulcer

In treatment the position is much the same We know that ulcers come and go without fixed rules, and that almost any diet will let an ulcer heal at some times and not at others Very strict and boring diets often fail, while a little freedom—occasionally a lot of freedom—may succeed If a patient has been dieted until he is afraid of all food except milk and eggs, and dismally tired of those, it may well be that strong suggestion will break the vicious circle "Do this (or take that) for so many days, and then go ahead and eat what you like!" may work a cure—or at any rate produce remission—where orthodox caution perpetuates the pain Again, the enthusiasm of the doctor or surgeon over a new method of treatment may carry the patient to victory, as has so often happened in the history of this disease Mr PARR tilts at such fashions in treatment—at gastro enterostomy, partial gastrectomy, vagotomy, histidine, alkalis, sedatives, and especially the Lenhartz and Sippy diets—though all of these have cures to their credit With pardonable obtuseness and loyalty he has nothing but praise for the low fat diet to which he happened to respond, or for Dr J J SPIRA who introduced him to it, and whose views on ulcer causation he gives at some length As is well known, Dr SPIRA attributes the development of ulcers to the interaction of the gastric acid with bile Mr PARR quotes him as saying that bile causes an inflammation of the mucosa, and thus allows the acid to erode the surface and cause an ulcer, and that fat "attracts the bile" into the stomach—hence, cut down fat It is a simple theory, not originated by Dr SPIRA (though Mr PARR credits him with it) As long ago as 1863 it was suggested that bile salts are toxic to the upper digestive tract, and in 1914, SMITH[3] showed that bile acids may produce ulceration in cats by direct contact with the mucous membrane Normally the layer of mucin covering the membrane probably prevents such direct contact, and the importance of this substance may well be greater than we yet realise Nevertheless the very extensive experimental studies on the relationship of bile to peptic ulceration, though often contradictory, have not suggested that bile itself plays any causative part in ulcer formation. Indeed most of the laboratory findings have been directly to the contrary in so far, for example, as removal of the bile from the stomach and duodenum in animals, either by ligation of the bile duct or by biliary drainage externally or internally, is followed by ulcer formation in between 25% and 55% of cases, furthermore such ulcers are prevented, and the animals kept in good health, if ox bile salts are fed to them by mouth No final conclusions, however, are yet possible from the many animal experiments, and unfortunately this is equally true of clinical investigations Since Dr SPIRA's book was published in 1931, low fat diets for ulcer patients do not appear to have received much support from doctors, or to have proved the universal cure for the condition which Mr PARR would like to believe The diet he was ordered was in fact so varied and generous that without necessarily subscribing to Dr SPIRA's theory many ulcer patients, and other dyspeptics, must with little doubt have often adopted it Certainly the view that hot fats are harmful to ulcer patients has little novelty, it has indeed lately received convincing support from the work of KAY,[4] who has shown that, while uncooked fat has a depressant action on gastric activity, cooked fats stimulate both acid secretion and motility, the longer the heating the more stimulant is their effect

---

[1] How I Cured My Duodenal Ulcer London Michael Joseph 1951 Pp 160 8s 6d

[2] Wolf S, Wolff H G *J Amer med Ass* 1942 120 670

[3] Smith, G M. *J med. Res* 1914, 30 147

Whatever may have been the mechanisms in Mr PARR's successful "cure," none will question that he has been freed of symptoms for 5 years; perhaps a further volume after another 5 years may carry his inquiries and experiences further still By setting out—on the whole fairly—the story of the search for the causes and cure of ulcer in a lucid and popular manner he will give some insight into their symptoms to many laymen suffering from this disability It may be questioned whether he has done a service to Dr SPIRA, who may well find the publicity unwelcome, and who would doubtless be among the first to agree that methods of treatment other than his have been and continue to be successful Such a book as Mr PARR's could have been written by many another ulcer patient, except that the vaunted remedy would be different We have not found the answer yet, nor should the public be encouraged to think we have reached the end of the search

Annotations

FLUORINE AND DENTAL CARIES

IN the U S A and Canada protracted investigations of the effect of artificial fluorination of drinking water on dental caries have so far yielded satisfactory results [5], and the enterprise of Anglesea County Council in seeking authority to add fluorine to the water supply [6] may mark the beginning of a great advance in the control of dental caries in this country A pilot survey [7] in England suggests that the optimum fluorine content for drinking water is 1 0–1 2 p p m Greater concentrations than this cause mottling of the enamel, which becomes severe at 5 p p m, at still higher concentrations toxic symptoms and bone lesions may arise Brun and his colleagues [8] believe, however, that osteosclerosis will develop only with a daily fluorine intake of at least 28 mg over many years To protect teeth fluorine must be given during the first 8 years of life, after this age and after eruption it has little or no effect [9] Opinions differ on the duration of protection Weaver [10] assesses it as the equivalent of a delay of five years in the onset of caries, while some workers in the U S A believe that the protection is permanent

In the English pilot survey three high fluorine areas (North Shields, Colchester, and Slough) were compared with three low fluorine areas (South Shields, Ipswich, and Reading), the inquiry was confined to mothers attending antenatal clinics and infant welfare centres, and to children attending day nurseries, infant welfare centres, and nursery schools In the high fluorine areas the water fluorine content ranged from 0 8 to 1 45 p p m, and in the other areas from 0 07 to 0 3 p p m No severely mottled teeth were found in the high fluorine areas, and such mottling as there was could be detected only by careful clinical examination In the high fluorine areas the incidence of caries was lower in every age group —by as much as 38% in those aged 21–25 years—with an apparent delay of 10 years in the onset of caries It was also observed that fewer teeth were missing and that caries was less severe With the children, whose ages ranged from 2 to 5 years, the reduction in the incidence of caries was already apparent at 2–3 years of age, and was as great as 59% at 2 years

It seems that the fluorination of water supplies should play a great part in the fight against dental caries Clearly, however, no one measure will ever conquer this disease

DRUG ADDICTION IN AMERICA

DRUG PEDDLING, an ugly crime by any measure, becomes peculiarly detestable when buyers are sought among children The investigation into the drug traffic which is being conducted in New York [1] by Mr Nathaniel Goldstein, the attorney general, has revealed the widespread use of drugs—marihuana, cocaine, heroin, and amphetamine—by boys and girls in the high schools of the city Some of these children acquire the habit at ages as early as 12 or 13, usually beginning by smoking marihuana cigarettes—"reefers"—which are sold to them by older children in the school Nor is it clear that these older children are necessarily the tools of adult vendors some, at least, seem to have set up in business for themselves Among the addicts whose recorded confessions were played back in the course of the inquiry, a woman of 25 told of a candy store where high school children of 14 and 15 sold drugs after school hours, and the same children could be approached during morning break, when they would peddle drugs over the playground fence A 17 year old boy, who was running a successful business as a bookie in his school, spoke of a school fellow who dealt in drugs among the children and made as much as $300–400 a day Asked how much he himself made as a bookie the informant replied "That's my business" The inquiry revealed clearly the stages in which addiction is acquired a reefer, or a "snort" of cocaine is given free at first, then a moderate charge is made, once the child becomes an addict prices rise, and to get the necessary cash the young people spend money saved to pay for education or hospital treatment, steal, housebreak, or take to prostitution It has been estimated that 1 in every 200 children in the city uses narcotic drugs, and one witness spoke of young parents who quiet their baby with a shot of heroin In 1946, of 712 people arrested for offences against the narcotic drugs laws, 3 were aged 16, and 30 were between 17 and 21 By 1950 the numbers of those arrested had risen to 2482, of whom 63 were 16 year olds and 458 between 17 and 20 The numbers of those in their 'teens who were arrested had increased sixteenfold during this period

The plight of the young addict who wishes to be cured is very unfortunate if he admits his trouble he is liable to be jailed for the offence of buying drugs A girl of 19, who asked the help of the biology teacher in her school, was nevertheless obliged to go through the courts, she was of the opinion that many young people would confess to their addiction if they could hope to be treated as patients, not as criminals There are disquieting indications that some members of the New York police force countenance drug traffic in order to collect bribes Certainly the police can hardly have failed to know how very widespread drug peddling is one addict mentioned by name over forty bars, cafeterias luncheon places, and drug and candy stores where she had bought narcotics or seen them bought One at least was opposite a police station She described the technique of the salesmen, some of whom must be approached with a request, while some come over to ask if anything is wanted or follow the customer out into the street On the broadwalk of Coney Island it seems that peddlers openly accost passers-by with offers of drugs

---

[4] Kay A W *Gastroenterologia* 1950 76 97
[5] See *Lancet* Feb 17 1951 p 399
[6] *Times* June 14 1951
[7] Forrest J R, Parfitt G J Bransby E R *Mon Bull Min Hlth P.H L S* 1951 10, 104
[8] Brun G, C Buchwald H Roholm K *Acta med scand* 1941 106 261
[9] Klein, H *Publ Hlth Rep Wash* 1948 63 18
[10] Weaver R *Proc R Soc Med* 1948 41 284 *Brit dent J* 1950 88 9

[1] *New York Times* June 13 14 15, 16

A statement by the Senate Crime Investigating Committee in Washington suggests that there, too, and in Baltimore, the trade in illicit drugs is busy, though probably not as widespread among young people as in New York The results of these inquiries have been so gravely disturbing that a national investigation is likely to be undertaken Meanwhile the police of thirty six countries, who met in Lisbon at the beginning of June, have agreed to intensify the safeguards against smuggling of narcotics by air

THE LISTER INSTITUTE

THE latest report of the Lister Institute describes the great variety of work carried out there in the past year The effect of inactivating vaccinia virus with ultraviolet light has been studied with a view to determining whether the treated virus is antigenic A preliminary dose of an antigenic preparation of killed virus might reduce the incidence of complications in those vaccinated for the first time at school age or in later life The fate of the plasma substitute dextran has been investigated It appears that, in the rabbit, in the first few weeks after intravenous injection the dextran which is not excreted is distributed throughout all the tissues, including the brain, spinal cord, and cerebrospinal fluid , the heaviest deposits are found in the liver In heavily loaded animals dextran has been detected serologically in saline extracts of the following tissues at six months after injection, in the brain, spinal cord, bone marrow, lungs, liver, kidney, skeletal and cardiac muscle, stomach, and lymph glands , at nine months after injection, in the cerebrospinal fluid, bone marrow, skeletal muscle, kidney, liver, and lymph glands , and at twelve months after injection, in the brain, cerebrospinal fluid, liver, kidney, and lymph glands

In the biochemical division the gene product responsible for the " Lewis " Le^a blood group character has been isolated and characterised The material is a mucoid very similar to the human group A substance described earlier The main components—fucose, galactose, glucosamine, chondrosamine, and eleven amino acids —appear to be common to both substances, and further studies are being made to determine the amounts of each of the components present in the group substances Preliminary experiments have been carried out on the oxidation of the Le^a substance with the periodate ion in order to compare the behaviour of this substance with that of the group A substance under similar conditions The blood group research unit has been concerned with finding " new " blood group systems, and filling gaps of knowledge in " old " ones The first problem is being approached by testing serum of persons known to have been immunised by pregnancy or transfusion , it is in such sera that antibodies defining " new " antigens have in the past usually been found. As a more active measure the unit is giving small injections of blood to more than a hundred volunteers in the hope that some of them may respond by making antibodies to antigens yet unknown or only guessed at In the filling of gaps in the knowledge of blood groups, the unit was fortunate in being sent a sample of blood which served to answer the problem of whether the three pairs of the Rh complex are separable or not The blood sample came from a person who was found to lack two of the three parts, which parts [illegible] were evidently separable Further, the missing antigens presumably reflect a small deletion in the Rh chromosome Deletion is a phenomenon familiar in species which have been well studied genetically, but no good case has previously made out for its occurrence in man

The Blood group Reference Laboratory has continued to supply blood grouping serum of all kinds to the National Blood Transfusion Service, and to other users at home and abroad Increased work has made it necessary to increase the technical and maintenance staff

THE TOXICITY OF BERYLLIUM

THE story of beryllium and the part it plays in industrial toxicology is fascinating and contradictory Few people are completely sure that beryllium is the sole cause of the illnesses ascribed to it Yet American investigators, led by the late Dr Leroy U Gardner, have built up a strong case against it, despite the findings of Fairhall and others [1] in 1943 that no specific toxic action is attributable to the beryllium ion The illnesses found amongst beryllium workers fall into two broad groups an acute pneumonitis occurring amongst workers engaged in extracting the metal and its salts from the ore, and a delayed or chronic condition variously termed " delayed chemical pneumonitis " or " pulmonary granulomatosis," usually found among fluorescent lamp makers The latter condition has many of the features of acute or subacute silicosis, but may resemble other conditions such as Boeck's sarcoidosis and miliary tuberculosis In the early stages of the investigation Gardner, with the weight of his great authority, demolished the silicosis theory, which does not seem to have been seriously considered since then , but this may well be one instance in which Gardner was wrong Both the acute and the delayed illnesses could be explained without reference to beryllium The acid radicals in beryllium fluoride and sulphate, to which the workers in the extraction processes are mainly exposed, could account for the acute pneumonitis, which somewhat resembles œdema of the lungs The powders used for coating fluorescent lamps contain much more silica than beryllium, and it seems illogical to ascribe an illness caused by the inhalation of a composite or compound dust to the smallest ingredient But as T L Shipman said in the Sixth Saranac Symposium [2]

> ' it is significant that delayed chemical pneumonitis, if it is not Boeck s sarcoid is closely similar , that it has certain characteristics in common with silicosis and that it can even resemble tuberculosis enough to make one stop and think Because of the complexity of the problem, let me speak a warning against hasty conclusions Our task demands the humility which ensures an open mind '

Throughout this conference there was a doubt, expressed and implied, whether beryllium was really the prime cause of both types of illness But one speaker was prepared " to stick out his neck," as he put it, and pronounce categorically that the cases of poisoning with which he had to deal were in fact instances of beryllium poisoning No one, however, was equally prepared to state that they were not As regards terminology, the conference came to the conclusion that it would be unwise in the present state of uncertainty to use the term " beryllium poisoning " , but that it would be better to call the acute disease " acute pneumonitis of beryllium workers " and the chronic or delayed disease " pulmonary granulomatosis of beryllium workers " was ordered was in fact so varied and generous that without necessarily subscribing to Dr SPIRA's theory many ulcer patients, and other dyspeptics, must with little doubt have often adopted it Certainly the view that hot fats are harmful to ulcer patients has little novelty, it has indeed lately received convincing support from the work of KAY,[4] who has shown that, while uncooked fat has a depressant action on gastric activity, cooked fats stimulate both acid secretion and motility, the longer the heating the more stimulant is their effect

---

[1] Hyslop F , Palmes, E D , Alford W C , Monaco A. R Fairhall L T *The Toxicity of Beryllium National Institute of Health* Bulletin no 181 Washington D C 1943

[2] Pneumoconiosis Beryllium Bauxite Fumes Compensation The Sixth Saranac Symposium Leroy U Gardner Memorial Volume Editor ARTHUR J VORWALD M D New York Paul B Hoeber 1950 Pp 659 $7 50

Whatever may have been the mechanisms in Mr PARR's successful "cure," none will question that he has been freed of symptoms for 5 years; perhaps a further volume after another 5 years may carry his inquiries and experiences further still By setting out—on the whole fairly—the story of the search for the causes and cure of ulcer in a lucid and popular manner he will give some insight into their symptoms to many laymen suffering from this disability It may be questioned whether he has done a service to Dr SPIRA, who may well find the publicity unwelcome, and who would doubtless be among the first to agree that methods of treatment other than his have been and continue to be successful Such a book as Mr PARR's could have been written by many another ulcer patient, except that the vaunted remedy would be different We have not found the answer yet, nor should the public be encouraged to think we have reached the end of the search

Annotations

FLUORINE AND DENTAL CARIES

IN the U S.A and Canada protracted investigations of the effect of artificial fluorination of drinking water on dental caries have so far yielded satisfactory results[5], and the enterprise of Anglesea County Council in seeking authority to add fluorine to the water supply[6] may mark the beginning of a great advance in the control of dental caries in this country A pilot survey[7] in England suggests that the optimum fluorine content for drinking water is 1 0–1 2 p p m Greater concentrations than this cause mottling of the enamel, which becomes severe at 5 p p m, at still higher concentrations toxic symptoms and bone lesions may arise Brun and his colleagues[8] believe, however, that osteosclerosis will develop only with a daily fluorine intake of at least 28 mg over many years To protect teeth fluorine must be given during the first 8 years of life, after this age and after eruption it has little or no effect[9] Opinions differ on the duration of protection Weaver[10] assesses it as the equivalent of a delay of five years in the onset of caries, while some workers in the U S A believe that the protection is permanent

In the English pilot survey three high fluorine areas (North Shields, Colchester, and Slough) were compared with three low fluorine areas (South Shields, Ipswich, and Reading), the inquiry was confined to mothers attending antenatal clinics and infant welfare centres, and to children attending day nurseries, infant welfare centres, and nursery schools In the high fluorine areas the water fluorine content ranged from 0 8 to 1 45 p p m, and in the other areas from 0 07 to 0 3 p p m No severely mottled teeth were found in the high fluorine areas, and such mottling as there was could be detected only by careful clinical examination In the high fluorine areas the incidence of caries was lower in every age group —by as much as 38% in those aged 21–25 years—with an apparent delay of 10 years in the onset of caries. It was also observed that fewer teeth were missing and that caries was less severe With the children, whose ages ranged from 2 to 5 years, the reduction in the incidence of caries was already apparent at 2–3 years of age, and was as great as 59% at 2 years

It seems that the fluorination of water supplies should play a great part in the fight against dental caries Clearly, however, no one measure will ever conquer this disease

DRUG ADDICTION IN AMERICA

DRUG PEDDLING, an ugly crime by any measure, becomes peculiarly detestable when buyers are sought among children The investigation into the drug traffic, which is being conducted in New York[1] by Mr Nathaniel Goldstein, the attorney general, has revealed the widespread use of drugs—marihuana, cocaine, heroin, and amphetamine—by boys and girls in the high schools of the city Some of these children acquire the habit at ages as early as 12 or 13, usually beginning by smoking marihuana cigarettes—"reefers"—which are sold to them by older children in the school Nor is it clear that these older children are necessarily the tools of adult vendors some, at least, seem to have set up in business for themselves Among the addicts whose recorded confessions were played back in the course of the inquiry, a woman of 25 told of a candy store where high school children of 14 and 15 sold drugs after school hours, and the same children could be approached during morning break, when they would peddle drugs over the playground fence A 17 year old boy, who was running a successful business as a bookie in his school, spoke of a school fellow who dealt in drugs among the children and made as much as $300–400 a day Asked how much he himself made as a bookie the informant replied "That's my business" The inquiry revealed clearly the stages in which addiction is acquired a reefer, or a "snort" of cocaine is given free at first, then a moderate charge is made, once the child becomes an addict prices rise, and to get the necessary cash the young people spend money saved to pay for education or hospital treatment, steal, housebreak, or take to prostitution It has been estimated that 1 in every 200 children in the city uses narcotic drugs, and one witness spoke of young parents who quiet their baby with a shot of heroin In 1946, of 712 people arrested for offences against the narcotic drugs laws, 3 were aged 16, and 30 were between 17 and 21 By 1950 the numbers of those arrested had risen to 2482, of whom 63 were 16 year-olds and 458 between 17 and 20 The numbers of those in their 'teens who were arrested had increased sixteenfold during this period

The plight of the young addict who wishes to be cured is very unfortunate if he admits his trouble he is liable to be jailed for the offence of buying drugs A girl of 19, who asked the help of the biology teacher in her school, was nevertheless obliged to go through the courts, she was of the opinion that many young people would confess to their addiction if they could hope to be treated as patients, not as criminals There are disquieting indications that some members of the New York police force countenance drug traffic in order to collect bribes Certainly the police can hardly have failed to know how very widespread drug peddling is one addict mentioned by name over forty bars, cafeterias, luncheon places, and drug and candy stores where she had bought narcotics or seen them bought One at least was opposite a police station She described the technique of the salesmen, some of whom must be approached with a request, while some come over to ask if anything is wanted or follow the customer out into the street On the broadwalk of Coney Island it seems that peddlers openly accost passers by with offers of drugs

---

[4] Kay A W *Gastroenterologia* 1950 76 97
[5] See *Lancet* Feb 17 1951, p 390
[6] *Times* June 14, 1951
[7] Forrest, J R, Parfitt G J Bransby E R *Mon Bull Min Hlth P H.L S* 1951 10 104
[8] Brun G C Buchwald H Roholm K *Acta med scand* 1941, 106 261
[9] Klein H *Publ Hlth Rep Wash* 1948 63, 18
[10] Weaver R *Proc R Soc Med* 1948 41 284 *Brit dent J* 1950 88 9

[1] *New York Times* June 13 14 15 16

A statement by the Senate Crime Investigating Committee in Washington suggests that there, too, and in Baltimore, the trade in illicit drugs is busy, though probably not as widespread among young people as in New York The results of these inquiries have been so gravely disturbing that a national investigation is likely to be undertaken Meanwhile the police of thirty six countries, who met in Lisbon at the beginning of June, have agreed to intensify the safeguards against smuggling of narcotics by air

THE LISTER INSTITUTE

THE latest report of the Lister Institute describes the great variety of work carried out there in the past year The effect of inactivating vaccinia virus with ultraviolet light has been studied with a view to determining whether the treated virus is antigenic A preliminary dose of an antigenic preparation of killed virus might reduce the incidence of complications in those vaccinated for the first time at school age or in later life The fate of the plasma substitute dextran has been investigated It appears that, in the rabbit, in the first few weeks after intravenous injection the dextran which is not excreted is distributed throughout all the tissues, including the brain, spinal cord, and cerebrospinal fluid , the heaviest deposits are found in the liver In heavily loaded animals dextran has been detected serologically in saline extracts of the following tissues at six months after injection, in the brain, spinal cord, bone marrow, lungs, liver, kidney, skeletal and cardiac muscle, stomach and lymph glands , at nine months after injection, in the cerebrospinal fluid, bone marrow, skeletal muscle, kidney, liver, and lymph glands , and at twelve months after injection, in the brain, cerebrospinal fluid, liver, kidney, and lymph glands

In the biochemical division the gene product responsible for the "Lewis" Le^a blood group character has been isolated and characterised The material is a mucoid very similar to the human group A substance described earlier The main components—fucose, galactose, glucosamine, chondrosamine, and eleven amino acids —appear to be common to both substances, and further studies are being made to determine the amounts of each of the components present in the group substances Preliminary experiments have been carried out on the oxidation of the Le^a substance with the periodate ion in order to compare the behaviour of this substance with that of the group A substance under similar conditions The blood group research unit has been concerned with finding "new" blood group systems, and filling gaps of knowledge in "old" ones The first problem is being approached by testing serum of persons known to have been immunised by pregnancy or transfusion , it is in such sera that antibodies defining "new" antigens have in the past usually been found As a more active measure the unit is giving small injections of blood to more than a hundred volunteers in the hope that some of them may respond by making antibodies to antigens yet unknown or only guessed at In the filling of gaps in the knowledge of blood groups, the unit was fortunate in being sent a sample of blood which served to answer the problem of whether the three pairs of the Rh complex are separable or not The blood sample came from a person who was found to lack two of the three parts, which parts are therefore evidently separable Further, the missing antigens presumably reflect a small deletion in the Rh chromosome Deletion is a phenomenon familiar in species which have been well studied genetically, but no good case has previously made out for its occurrence in man

The Blood group Reference Laboratory has continued to supply blood grouping serum of all kinds to the National Blood Transfusion Service, and to other users at home and abroad Increased work has made it necessary to increase the technical and maintenance staff

THE TOXICITY OF BERYLLIUM

THE story of beryllium and the part it plays in industrial toxicology is fascinating and contradictory Few people are completely sure that beryllium is the sole cause of the illnesses ascribed to it Yet American investigators, led by the late Dr Leroy U Gardner, have built up a strong case against it, despite the findings of Fairhall and others[1] in 1943 that no specific toxic action is attributable to the beryllium ion The illnesses found amongst beryllium workers fall into two broad groups an acute pneumonitis occurring amongst workers engaged in extracting the metal and its salts from the ore, and a delayed or chronic condition variously termed "delayed chemical pneumonitis" or "pulmonary granulomatosis," usually found among fluorescent lamp makers The latter condition has many of the features of acute or subacute silicosis, but may resemble other conditions such as Boeck's sarcoidosis and miliary tuberculosis In the early stages of the investigation Gardner, with the weight of his great authority, demolished the silicosis theory, which does not seem to have been seriously considered since then , but this may well be one instance in which Gardner was wrong Both the *acute* and the delayed illnesses could be explained without reference to beryllium The acid radicals in beryllium fluoride and sulphate, to which the workers in the extraction processes are mainly exposed, could account for the acute pneumonitis, which somewhat resembles œdema of the lungs The powders used for coating fluorescent lamps contain much more silica than beryllium, and it seems illogical to ascribe an illness caused by the inhalation of a composite or compound dust to the smallest ingredient But as T L Shipman said in the Sixth Saranac Symposium[2]

> 'it is significant that delayed chemical pneumonitis, if it is not Boeck s sarcoid is closely similar , that it has certain characteristics in common with silicosis and that it can even resemble tuberculosis enough to make one stop and think. *Because of the complexity of the problem,* let me speak a warning against hasty conclusions Our task demands the humility which ensures an open mind '

Throughout this conference there was a doubt, expressed and implied, whether beryllium was really the prime cause of both types of illness But one speaker was prepared "to stick out his neck," as he put it, and pronounce categorically that the cases of poisoning with which he had to deal were in fact instances of beryllium poisoning No one, however, was equally prepared to state that they were not As regards terminology, the conference came to the conclusion that it would be unwise in the present state of uncertainty to use the term "beryllium poisoning" , but that it would be better to call the acute disease "acute pneumonitis of beryllium workers" and the chronic or delayed disease "pulmonary granulomatosis of beryllium workers" had to have the information. The patient's consent was obtained in writing, and it was not really possible to go further than that. Dr. BROWN said that he was satisfied if the ethical committee kept the matter under review to see that there was no further undermining of the doctor-patient relationship. The motion was carried.

---

[1] Hyslop F Palmes E D , Alford W C Monaco A R Fairhall L T The Toxicity of Beryllium National Institute of Health Bulletin no 181 Washington D C 1943

[2] Pneumoconiosis Beryllium Bauxite Fumes Compensation The Sixth Saranac Symposium Leroy U Gardner Memorial Volume Editor ARTHUR J VORWALD M D New York Paul B Hoeber 1950 Pp 659 $7 50

REMUNERATION OF GENERAL PRACTITIONERS

The meeting had a lively discussion on the remuneration of general practitioners. Strong disapproval of the Government's attitude and of the delays in settling the matter was expressed, but delegates rejected a call for early resignations from the health service and agreed to support a proposal for arbitration.

Dr. S. WAND, chairman of the General Medical Services Committee, presented the report[1] to be laid before a special conference of representatives of local medical committees on July 19. Dr. Wand emphasised that the committee had offered the fullest cooperation with the Ministry to provide the best possible service to the public. General practitioners had played their part loyally and had earned the right to a just settlement. It had been pointed out to the Minister of Health and the Secretary of State for Scotland that it was clear from the Spens report that general practitioners had been underpaid for many years before the war. The general practitioner had a responsibility second to none, and his lot was worse than that of any other worker in the service. Did the Ministers' offer implement the promise of a full inquiry? They offered an inquiry with two preconceptions—first on the amount, secondly on the distribution. The offer was for a maximum of £2 million, with conditions. That amount was roughly one ninth of the practice expenses for the year ended March, 1950, since when the price of everything had gone up. Was this an offer at all? (Cries of "No.") If the practice expenses proved to have risen by over £2 million, practitioners would be worse off.

If there was an epidemic everyone but the general practitioner would be getting paid for doing more work. It was true that the Minister did suggest an improvement for the young man at the beginning—but he would have less to go for. It appeared that the large list man would have no less work, but would have less money. This might be a first step towards a levelling which would ultimately produce a full-time salaried service. "You may ask yourself if it has the effect of producing a split in the profession."

Prescribing costs were tied up with the offer. The Drug Tariff showed how prices had increased compared with 1950. Old drugs were being replaced by ones with more specific action, and it was the practitioner's duty to prescribe them. It seemed that the Ministers' proposal could only mean that a doctor, when prescribing, would have to consider whether an item in a particular prescription would affect his income; the public would feel anxious. It seemed that the Government, having plunged headlong, against the profession's advice, into a comprehensive health service, held that the general practitioner should be the one to carry the burden. In asking for arbitration on remuneration they were really asking for arbitration on betterment. Excluding any reference to additional work, there was no doubt that their claim was several times above the maximum offered.

"We have had inquiry after inquiry, delay after delay; we have been told about wage freezes and ceilings and rearmament. All the time the general practitioner has been doing his work loyally. The public knows we have had a raw deal." Yet the General Medical Services Committee was still being fair and reasonable, and it was recommending to the conference that the claim should be arbitrated on a computation of the changed value of money since 1939.

Dr. J. I. MILNE moved a resolution by Manchester that, failing a satisfactory reply from the Minister by June 30, practitioners should submit their resignations forthwith. They had been put off with one excuse after another, he remarked, and it was slowly dawning on them that they were being led by the nose. When the British Medical Guild was formed last year general practitioners felt that at last something was being done; now that feeling had given way to cynicism. Dr. F. S. CATTO (Manchester) said that their resignations would have to come some time if they were to get justice.

Dr. A. C. E. BREACH (Bromley) moved as an amendment that the principle of arbitration should be accepted, provided that the court of arbitration was independent, that its terms of reference should include as a basis the Spens recommendations, that it must take into account the remuneration of allied professions, that the findings should be binding, and that the award should be retrospective to July 5, 1948. Dr. A. V. RUSSELL (council) said that Mr. Bevan had refused arbitration because he knew the profession would win. Dr. C. P. WALLACE (Guildford) recalled that his division had suggested arbitration a year ago. The real trouble was that a grievance of three years' standing had gone unredressed.

Dr. D. P. STEVENSON, deputy secretary of the association, explained that if it was decided to ask for arbitration, the G.M.S.C. would call together committee A of the Medical Whitley Council of the National Health Service. The management side would no doubt turn down the claim for a revision of the central pool, and then the staff side would ask for arbitration. If the management side agreed, the matter could go before the Industrial Court. If not, recourse could be made to Order 1305. They would rather go to the Industrial Court.

A suggestion by Dr. L. V. GOODLIFFE (Croydon) that there should be an interim award pending an award by arbitration was greeted with cries of "No."

After further discussion the meeting rejected the call for early resignations and Dr. Breach's amendment, and expressed confidence in the conference of local medical committees, pledging support for the efforts of the conference to effect a full and just settlement.

A motion by Gateshead preferring a fixed capitation fee was referred to council. Dr. WAND said that one reason for the discrepancy of capitation fees might be found to be the inflation of lists; he also mentioned that they believed that the extent of "unsigning" was considerable. A motion from Lancaster calling for a national capitation fee was also referred to council.

Dr. WAND later made a statement on what would happen if the request for arbitration on the remuneration of general practitioners was refused. It was, said Dr. Wand, almost inconceivable that the Minister should decline to accept this reasonable statement. "Should it become clear that the Minister does decline either to examine the case on its merits or to refer it to arbitration, a new situation will arise. If such a situation should arise the committee would have seriously to consider recommending that general practitioners have no alternative but to withdraw their services from the National Health Service."

The meeting agreed with West Denbigh and Flint that in striving to secure adequate remuneration for the practitioner, due emphasis must be laid on the "alarming increase" in practice expenses.

COMMITTEE ON GENERAL PRACTICE

With a few dissentients the meeting agreed with the Chelsea and Fulham division in taking a grave view of the fact that the Minister omitted to ask the General Medical Services Committee, as the recognised negotiating body for all general practitioners, for its views on the constitution, terms of reference, and membership of the committee set up by the Central Health Services Council to study general practice It was stated that the G M S C had not yet decided whether to give evidence before this committee, and Dr Wand added that the G.M S C sought an assurance from the Minister that the new committee would not deal with terms and conditions of service; Dr D L Gullick (East Herts) thought that if the committee suggested a salaried service it might be to the advantage of general practitioners that the G.M S C had had no hand in it Dr J A Pridham, supporting the motion, pointed out that it was the Central Health Services Council that had omitted to consult the G M S C, this was another rebuff to the general practitioners

---

[1] See *Lancet* June 16 1951, p. 1311.

CONFINEMENTS IN HOSPITALS AND NURSING HOMES

The General Medical Services Committee was urged, on the proposition of Dr C R Barrington (Bromley), to secure the right of general practitioners to attend their patients who wished to be confined in hospital, and the provision of suitable accommodation for the purpose Dr Wand said he thought it likely that the Ministry would do all it could to help in this respect A resolution from Bristol, moved by Dr A G Heron, instructed council "to impress upon the Minister, as a matter of extreme urgency, the necessity of taking immediate measures to keep open efficient private maternity homes, thus adding to the efficiency and economy of the Service"

TRAINEE ASSISTANTS

Dr E E T Taylor, speaking to a motion from Northamptonshire against the present trainee assistant scheme, described the scheme as unpopular Dr H S Howie Wood (Isle of Wight) announced that the G.M.S C had set up a subcommittee to go into the whole question, and in the near future a communication would be sent to the local medical committees The motion was withdrawn

COMPLAINTS AGAINST DOCTORS

In a discussion on medical service committees and tribunals Dr H Guy Dain announced that the Ministry had agreed, as a first step, to issue to local executive councils a booklet on procedure in regard to complaints Dr J A Gorsky (Westminster and Holborn) pointed the contrast between the Medical Disciplinary Committee of the General Medical Council, under the new Medical Act, and the disciplinary procedure under the National Health Service There was the right of appeal to the Privy Council in respect of the former, in the latter the only appeal was to the Minister, who was a party Witnesses to the Medical Disciplinary Committee ran the risk of being had up for perjury, those before the tribunal did not Anyone removed from the Medical Register could be reinstated, nothing in the National Health Service Act said this could be done in regard to a practitioner removed from the list A doctor might be condemned to professional death for a lesser offence than the General Medical Council would remove his name from the Register for The meeting agreed to Dr Gorsky's motion, viewing with grave disquiet recent findings of certain medical service committees and the tribunal, demanding that the procedure should be overhauled, and reiterating the principle that there must be a right of appeal to the courts

Dr D Thomson (Dartford) deprecated any censure of a doctor by a local executive council, with its adverse publicity, "as a result of any and every trifling complaint" His motion, which was carried, further deplored that a doctor could not claim from the patient remuneration for loss of time and for the expenses of a locum tenens when the complaint was proved unjustified Dr Wand said that on the point of publicity the strongest representation had been made to the Ministry 'We feel it is thoroughly bad that trivial complaints should be made the subject of headlines in the press"

TOKEN PAYMENT FOR PRESCRIPTIONS

By a large majority the meeting rejected a proposal from Lincoln favouring a token payment for every prescription or similar service rendered by a practitioner Dr A M Maiden (Lincoln) suggested that such a payment would act as a deterrent to those who sought to exploit this so called free service No new principle was involved, because of the partial payments for teeth and spectacles It would mean a saving of national expenditure While making for economy it would not discourage any doctor from prescribing whatever he felt to be necessary for the patient's well being Old age pensioners and possibly school children and infants should be exempted, and could easily be identified The third category of exemptions—the chronic sick—presented a more difficult administrative problem, but one not incapable of solution Dr G O Barber (Mid-Essex), supporting the motion, said it was unfair for the Government now to say that if the family doctor wanted a little more money per head he must give fewer drugs Unless their pockets were touched, the public would do nothing about it Dr Barber described the "medicine bottle tasting parties" for which he had been the unwitting provider In the long winter evenings in the country there was not a great deal of night life, so anything which helped to pass the time was welcomed The technique of the medicine bottle tasting party was that the guests brought bottles of medicine and everyone had a taste "If a certain medicine is approved, the owner of the bottle is asked 'What were you complaining about to get that from the doctor?'" Dr Annis Gillie felt that a token payment would do much to restore the correct relationship of doctor and patient Dr Dain thought the token payment could easily be collected by a sixpenny stamp put on each prescription when it was presented to the chemist

Dr G Smith (Tower Hamlets) opposed the idea The token payment would act as a deterrent only to those in a low category economically Dr Wand pointed out that for many years the association had said that there should be no financial barrier between the patient and all necessary treatment The proposal was dangerously near politics Dr A Beauchamp (Birmingham) agreed. So did Dr H D Findlay (Birmingham), who pictured the politician pressing for a tax on prescriptions so as to reduce the drug bill, and at the next election saying, with crocodile tears, that it was the wicked doctors who had charged grandpa a shilling for his bottle of cough medicine and who had docked grannie's linctus, in order to raise his own capitation fee

MEMBERSHIP OF BOARDS AND COMMITTEES

A combined motion, which was carried, deplored "the tendency towards the replacing of doctors on regional hospital boards, boards of governors, and hospital management committees by laymen" It urged the Minister to reverse this tendency, to maintain adequate medical representation on all such bodies, and to take steps to overcome the difficulties existing between hospitals and general practitioners, such steps to include greater general practitioner representation at all levels in the National Health Service

ARRANGEMENTS FOR DOCTORS CALLED UP

Dr D F Hutchinson explained the scheme which the General Medical Services Committee had in mind with regard to practitioners who were called up in a national emergency He described it as being as simple and as fair as could be devised The net rate of remuneration on which the practitioner was assessed for superannuation purposes during the last quarter before he was called up would be taken as the basic rate, and his service pay would be made up to that amount throughout his service

GUY'S HOSPITAL

Reappointed Lord Cunliffe (chairman), Mrs E G M Barlas, J P, Mrs Iris Brook, **J M H. Campbell,** O B E, M C, Sir Patrick Ashley Cooper, F.R C.P, C J Conway, K C, Sir **William Kelsey Fry,** C B E, M C, M R C S, **O Gayer** LL B, Sir **Morgan,** F R C S, F J O Prescott, L B Wimble

New member R J Mellish, M P

KING'S COLLEGE HOSPITAL

Reappointed Marquess of Normanby, M B E (chairman), T H Barr, P R Colville, L M E Dent, D S O, M V Ely, Viscountess Hambleden, Hon Mrs S L Henley, Sir **Cecil Wakeley,** K B E, C B, F R C S

New member **W I Daggett,** F R C S one appointment outstanding

ST THOMAS'S HOSPITAL

Reappointed Hon A J P Howard, C V O (chairman), E F Crundwell, F H Elliott, W G R Boys, Sir Brunel Cohen, **J R Dickinson,** F R C S, Prof **T Pomfret Kilner,** O B E, F R C S, A H Montgomery, **R H. O B Robinson,** F R C S, L H Simmons

New member Sir **Max Page,** K B E, C B, D S O, F R C S

HAMMERSMITH, WEST LONDON AND ST MARK'S HOSPITALS

Reappointed **Somerville Hastings,** M P, F R.C S (chairman), **G F Grant Batchelor,** M C, F R C S, Sir **Allen Daley,** F R C P, His Honour Judge J Norman Daynes, K C, **Cuthbert Dukes,** M D, Sir **Francis Fraser,** F R C P, Geoffrey Huddle T H Jones, A E Tyler, one appointment outstanding

HOSPITAL FOR SICK CHILDREN

Reappointed T H Bischoff, M C (chairman), Sir **Allen Daley,** F R C P, **T Twistington Higgins,** O B E, F R C S, C H Hodge, J P, P K Hodgson, C M G, C V O, O B E, **Eric Lloyd,** F R C S, A E Middleton, **George Newns,** M D **Bernard Schlesinger,** F R C P

New member Prof T H Marshall, C M G

NATIONAL HOSPITAL FOR NERVOUS DISEASES

Reappointed Sir Ernest Gowers, G B E, K C B (chairman), **W Russell Brain,** F R C P, **E A Carmichael,** C B E, F R C P, Sir **Archibald Gray,** C B E, F.R C P, A C Longland Lady Milverton, P D Power

New members F C Wareham, Mrs O Deer

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL

Reappointed L E Taylor (chairman), F R Eiloart, Mrs Haydn Davies, **G H. Howells,** F R C S, W Humphrey R N Wright

New members **Maxwell Ellis,** F R C S, **J C Hogg,** F.R C S

MOORFIELDS, WESTMINSTER AND CENTRAL EYE HOSPITAL

Reappointed Lord Luke, J P (chairman) E P Carter, O B E, A Gorman, Mrs A L Hollingsworth, J P, George Parker Jervis, Earl of Rothes, G C Stanley

New members **Frank Elliott,** F R C P, Harry Hutchinson

BETHLEM AND MAUDSLEY HOSPITALS

Reappointed **C P Blacker,** G M, M C, F R C P Mrs Kathleen Wilson, Alderman T E Morris, J P Mrs N C Runge, O B E, **E F Scowen,** F R C P

New members Lady Norman, J P, Lieut Colonel G J C Welch, O B E, M C, Alderman J C Maclean

ST JOHN'S HOSPITAL FOR DISEASES OF THE SKIN

Reappointed I A M Ellison Macartney (chairman), **G B Mitchell-Heggs,** O B E, F R C P, A D A Franklin, **S Cochrane Shanks,** F R C P Long, Miss Dorothy Fox, S I Salmon

HOSPITALS FOR DISEASES OF THE CHEST

Chairman Widdrington Stafford (for the rest of the period of his office—i e, to March 31, 1952)

Reappointed **R C Brock,** F R C S Sir John Gilmour, **V C Thompson,** **J L. Livingstone,** F R C.P, H K Eaton Ostle, F R C S Mrs Sarah Candy, Mrs Marguerite Watson

New member **George Simon,** M D, three app outstanding

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL

Reappointed Louis Fleischmann, O B E (chairman), Henry Floyd, C B, C B E, W Morgans, H C Willig, M Joan Wood

New member **Reginald Nassim,** F R C P, one appoint outstanding

NATIONAL HEART HOSPITAL

Reappointed J M Oakey, M C, J P (chairman), J Cohen, **T F Cotton,** F R C P, Sir **Francis Fraser,** F.R **B T Parsons-Smith,** F R C P

New member E G Gooch, C B E, M.P

ST PETER'S AND ST PAUL'S HOSPITALS

Reappointed L E D Bevan (chairman), A Farquhar, Sir Bertram Galer, J P, **A R. C Higham,** F J Russell Kelly, L G Mitchell Innes, H Short **Winsbury-White,** F R C S, one appointment outstandi

ROYAL CANCER HOSPITAL

Reappointed Sir Edward Cripps (chairman), **Ian Aird,** F R C S, **P E Thompson Hancock,** F R C P Jacob, Prof W V Mayneord, Mrs Noel Patrick Stanley, Claude S Harvey, **E A Carmichael,** F R C

QUEEN CHARLOTTE'S AND CHELSEA HOSPIT

Reappointed Sir Frederick Minter (chairman), Arthure, F.R C S, **Aubrey Goodwin,** O B E, F Viscountess Jowitt, E Musgrove, **Charles Newman,** A M Niven, Lady Ogilvie, Alan Sainsbury G W

EASTMAN DENTAL HOSPITAL

Reappointed Sir Frank Newnes (chairman) **R A Broderick,** D S O, M C, M B, F D S, Sir **Willi Fry,** C B E, M C, M R C S, B M Lindsay Fynn, G M W R Young, F D S

New member **G J Parfitt,** M R C S, L D S

Public Health

THE LEEDS TUBERCULOSIS SCH

AN effective tuberculosis scheme depend initiative of the regional hospital boards It is to see how an energetic region is attacking the and what progress has been made since the st National Health Service, nearly three years ago

THE SURVEY

When the Leeds regional hospital board a panel of doctors was convened by the board the existing tuberculosis facilities in the r to suggest, for the consideration of the Speciali Committee, how to organise and develop the full questionary was sent to hospital manage mittees, and the information thus gained, sup by the local knowledge of members of assembled into a tabulated survey of pensaries, their housing, equipment, and numbers on their lists, and many other aspe work

On July 5, 1948, there were 42 dispensari in the region Only 1 of these, at Scar in a general hospital, 3 others were at toria and 1 other was in hospital pre not all of these had X ray equipment found that only one dispensary had modern X ray equipment, in varying degrees of obsole 37 had no X ray equipme were done in 24 not even the screening patients dispensaries had been designed as such, were said to have been adapted to their purp th of them were in converted dwell in most cases they consisted of one or two office is and an unequipped examination room Some of i were very oddly housed—one in the cloakrooms church hall, another in an old schoolhouse, another corrugated iron building, and another in a wooden hon But these standards of housing and equipment linics matched those in many other provincial s before the appointed day, and may have been stantially better than some

elatively few of the dispensaries had room for ansion—only 10 in all—and some of these were housed uildings which were in any case unsatisfactory It is eworthy that the clinics and dispensaries doing the est amount of work were not necessarily the best ised Thus at 3 out of the 5 dispensaries housed in pitals attendances (of patients and contacts) were ow 500 a year, only one session a week—or even one onth—was held, and the numbers of new cases seen re negligible The Scarborough Hospital clinic, vever, had nearly 1250 attendances and about 55 v patients yearly, and the dispensary at Bradford, in onverted dwelling house, had an annual attendance some 7200, and a new case roll of 920 The largest tendance—then some 26,500 yearly—was at the New ngate dispensary, Leeds, housed in a building put up in 366 as the Leeds Public Dispensary, which dealt mainly ith outpatients Other dispensaries with large attend ices were at Hull, Sowerby Bridge, South irby, and Pontefract, only one of these id X ray equipment, and that was out f date In two of the clinics—at Upper ill and Garforth—there was no proper ghting, and in one of them no running iater, and from one (Patrington) the iatients had to travel 25 miles for ineumothorax refills

PLANNING A POLICY

In making their proposals the panel did iot think in terms of tuberculosis alone, but had in mind a chest service of much vider scope But they had also to bear in nind, when making short term recommendations about staffing and beds, that anatorium accommodation, experienced hest physicians, and nursing staff were ll scarce They based their estimates on he 200,000 unit of population adopted r the British Medical Association[1] As long term measure they believe there hould be 200 sanatorium beds, and 50 beds in general hospitals, for each such unit of population, and taking this as their standard they found that, even supposing ll the existing beds could be fully staffed
up a steep hill need a further 1000
pedal At the e ment of pulmonary
For losis Moreover they judged that
but it did no ion of this size, 66 sessions
I stooped an weekly 12 at sanatoria,
a rose pitals, 24 at dispensaries,
patient departments, 12
My only Hom ing and social welfare
with medicine by me for X ray exam
do I find? A gen s with the thoracic
a fellow of a Royal ies Allowing 11
there, wakes in Englan doctor, such a
rabbit, and shoots it ore need
unit I am a fellow of one,
2 senior chest one you should
physicians, and 1 registrar throom

In rearranging the dispensaries the panel remembered that the diagnostic service must keep in close touch with the aftercare service, and so proposed administrative arrangements which fitted with the county, county-borough, and sanitary district boundaries Throughout they had in mind the convenience of patients and the means they had of getting to the clinics. They were anxious, wherever possible, to get rid of the unequipped visiting station, and to link up each chest centre with the outpatient department of a general hospital, and this has been achieved to a very large extent In 18 cases it has been possible either to move dispensaries into hospitals, or to arrange that they shall be moved there at an early date Already 7 new screening sets have been installed, and 2 major X ray sets and 4 more screening sets are to be delivered this year A new X ray department has been set up at Goole, in the hospital which is now to house the Goole chest clinic. Of the unequipped stations, 5 have either been closed or are to be closed as soon as new plans in the area are complete, 11 more are being retained as visiting stations for the convenience of patients, but 5 of the busiest of these are to be transferred into hospitals as soon as arrangements can be made The two maps show the former and the new distribution of clinics and the X ray facilities in the various areas A few examples will show clearly the kind of thing that has happened

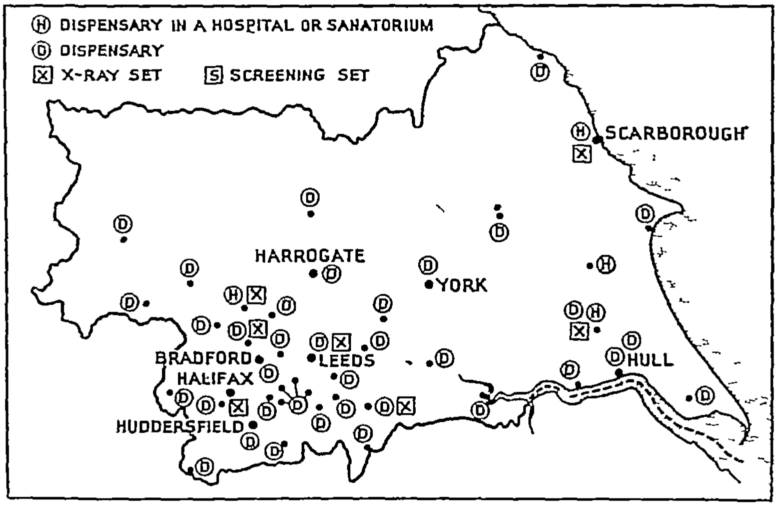


Fig 1—The Leeds Region when the tuberculosis service was taken over

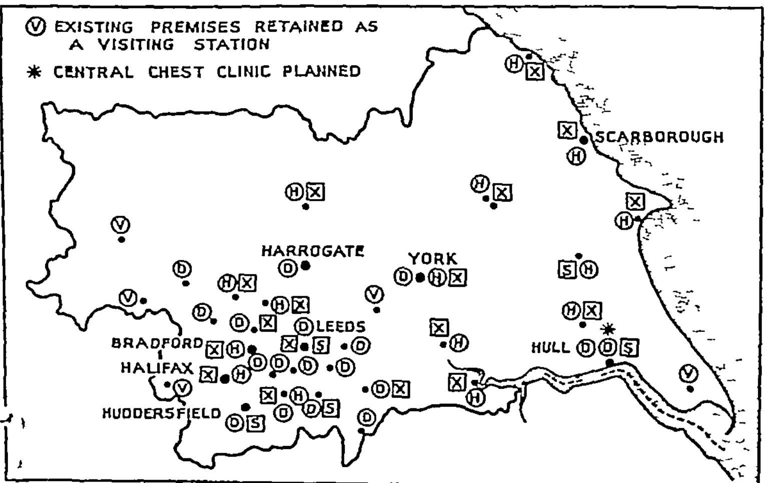

Ⓥ EXISTING PREMISES RETAINED AS A VISITING STATION
✱ CENTRAL CHEST CLINIC PLANNED
SCARBOROUGH
HARROGATE
YORK
LEEDS
BRADFORD
HALIFAX
HULL
HUDDERSFIELD

Fig 2—Increased facilities in the region after 2 years

---

[1] Tuberculosis in the National Health Service Report of the Tuberculosis and Diseases of the Chest Group Committee of the British Medical Association 1950 And see *Lancet* 1950 ii 809

A satisfactory dispensary in the outpatient department of Scarborough Hospital is being maintained. In this area there were also dispensaries at Norton, Whitby, and Bridlington—one in a general practitioner's surgery, one on the ground floor of a district health office, and one in a converted dwelling house. None of these had X-ray equipment. On the advice of the panel, the Norton dispensary is being transferred to the Malton and Norton District Hospital in the near future, and the other two have already been moved, one to the Whitby War Memorial Hospital and the other to the Lloyd Hospital, Bridlington. Patients will thus have better care without having further to go.

The Leeds clinics presented some special difficulties. As already noted, the New Briggate dispensary is the largest in the whole region, and now has some 30,000 attendances and over 2400 new cases yearly. The offices and X-ray department are on the first floor of the old-fashioned out-patient department in which it is housed. This busy clinic held clinical and X-ray sessions daily, refill and X-ray sessions in the evenings, and daily dental and ultraviolet light sessions in addition. The panel found the premises quite inadequate for the volume of work now being undertaken, and recommended that a major chest centre should be established in a general hospital in Leeds, and the outlying dispensaries at Horsforth, Garforth, Morley, and Rothwell should be closed as soon as the new centre could be opened and fully staffed. This has not been possible, and instead major alterations are now being planned to the existing clinic. The Horsforth dispensary has been closed and the patients distributed to other dispensaries in the area, the Rothwell dispensary (which is in the isolation hospital) and the Morley and Garforth clinics are being retained.

At Hull conditions were very bad, for though there were 2 dispensaries in the city neither had X-ray equipment and patients were being examined radiologically at a multiple clinic which was not the property of the board. There were also outlying dispensaries at Beverley, Patrington, and Hessle, in Driffield Sanatorium and Beverley Westwood Sanatorium (where there were X-ray facilities). The panel advised that a main chest centre for the area should be set up in one of the Hull general hospitals, with secondary clinics at Beverley Westwood and Driffield Sanatoria. Various sites in the Hull general hospitals have been suggested for the chest clinic, but none has been found really suitable, and the possibilities are still being examined. Meanwhile a new screening set has been provided in the larger of the two city clinics, one of the outlying dispensaries has been closed, one has been transferred to Beverley Westwood Hospital, and one is being retained as a visiting station. The clinic at Driffield Sanatorium is to have a new screening set installed.

The board's greatest success has been at Bradford, where a fine new chest clinic is being established in St. Luke's Hospital.

STAFFING

Short-term recommendations on staffing took account of the need for a close relation between the chest clinics and the sanatoria. The panel unanimously decided that the chest physician should be on the staff of the sanatorium and visit regularly; that the staff of the sanatorium should be regarded as a team with the medical superintendent at the head; and that the resident staff of the sanatorium should do clinical work at the chest clinics and also domiciliary work on request. They recommended that, in all, 1 senior physician, 2 assistant physicians, 5 senior registrars, 1 other registrar, 1 medical superintendent, 1 deputy medical superintendent, and 1 medical officer should be appointed immediately; and in fact, several of these appointments have been made. But increasing financial stringency, and the limitations imposed on registrar establishments, have made it necessary to modify the original recommendations.

The panel made a careful estimate of the number of beds needed by chest physicians for the treatment of short-term cases in the general hospitals of the region. These proposals were not exorbitant, amounting to only 548 for the whole region, which meant less than 50 beds in each administrative area except that of Leeds itself, where they proposed that 150 beds should be provided, in two hospitals. Hospital management committees are beginning to recognise that the need is urgent, and responding to it; and in fact the board hope to able to report, in the course of the next few w that enough beds have been found in general and inf tious diseases hospitals to reduce the waiting lists reasonable proportions.

In an attempt to make the best possible use of sanatorium beds, 3 admission bureaux have been set u those in Bradford and Hull under the direct control the senior chest physicians in the areas, and that Leeds under a sanatorium medical superintendent consultant status. These have worked well, and hav substantially reduced the waiting lists already. Thoraci surgery centres have been developed in the same thre cities: two consultant surgeons were already at wor in Leeds, and are carrying on, and two others have bee appointed at Bradford and Hull. Collaboration wit the health authorities varies: in Leeds it is very good and the medical officer of health seconds full-tim tuberculosis health visitors to the clinic.

There is of course much still to do. There are stil too many dispensaries without screening sets and oth necessary equipment, and without an adequate health visitor service. Treatment arrangements for orthopæd and other non-pulmonary tuberculosis, and for mentally ill and mentally defective patients, are still unsatisfactory. But good progress has been made in the period under review—enough to show that those regional hospital boards which are willing to use the tools to hand can hope to make a respectable job of their charge.

Notification of Leprosy

Every doctor will shortly receive a copy of regulations providing for the notification of leprosy, which came into force on June 22. In future, as soon as a doctor becomes aware that a patient has leprosy he must send to the chief medical officer of the Ministry of Health a certificate in the form set out in the schedule of the regulations. He must also notify the Ministry of any cases which he was attending on June 22. Notification direct to the Ministry is considered advisable because it enables strict secrecy to be maintained. In the past the whole family of the patient has sometimes been affected by the local disclosure of knowledge of the patient's condition. A second reason is that accurate knowledge of the location of cases of leprosy is essential if the patient is to benefit fully from recent advances. The regulations contain no statutory powers whereby a patient with leprosy can be removed to a hospital, for this might lead to concealment.

The number of patients with leprosy in this country is small, and almost without exception they have been infected abroad. Most of them are foreigners and colonial subjects, and many have been repatriated; but for some, return to their own country is impracticable. At present some non-infectious patients are being treated under private arrangements, others as outpatients at hospitals or as temporary inpatients at infectious diseases hospitals or at a small private hospital restricted to British nationals. Arrangements for treating infectious cases have sometimes presented difficulty. To help doctors to deal with these patients the Ministry of Health has now appointed as their adviser in leprosy Dr. R. G. Cochrane, secretary of the British Empire Leprosy Relief Association, 167, Victoria Street, London, S.W.1. Dr. Cochrane will advise any doctor on the diagnosis and treatment of leprosy. He will associate himself with practitioners notifying cases, and he will be available to examine close contacts. The Ministry also announces that a hospital for leprosy patients has been opened at Reigate, Surrey, by University College Hospital as an annexe to the Hospital for Tropical Diseases.

Poliomyelitis

In England and Wales poliomyelitis notifications during the week ended June 7 were as follow: paralytic 32 (16), non-paralytic 20 (12); total 52 (28). This is an increase of 21 compared with the previous week, the figures for which are in parentheses.

In England Now

A Running Commentary by Peripatetic Correspondents

"THE students appear to have been well taught," was the external examiner's last remark as he departed after the Finals. "Well-taught but ill-educated" I could not help thinking. From the vivas and clinicals it was clear that the candidates knew their work, but in the papers many of them ran close to failure simply because they could not express themselves in writing. The "old sweats" on the Examining Board assure me that this weakness is general throughout the country and I must allow for it. But why? Perhaps reading medical textbooks and articles is not much help to students who want to learn to write English. But what of their school-days? Does the clue to their mental agraphia lie there?

The Higher Certificate, or its equivalent under the new regulations, is a *sine qua non* for entrance to this medical school and many others. A man without a Higher Certificate will probably not even reach the selection committee. Nearly all medical students naturally take physics, chemistry, biology, and the like as their subjects in this examination, which means that from the age of 16 they must specialise in those subjects and eschew all other education. What a tragic paradox! We choose our entrants to a medical school from among the boys and girls with good academic records, and by so doing we ensure that we get students with a strictly limited general education. Worse still, by insisting on this standard for entry we are forcing the more able youngsters to spend the whole of their last years at school on these narrow subjects, thereby denying them their last chance of real education.

* * *

Nowadays the Council for Music in Hospitals, which supplies concerts to mental hospitals and some others, is so firmly established that we are losing sight of its early days when queer experiences were a regular feature of its work. There was that time, for instance, when just as we were about to begin a concert for some mental patients we noticed that the tenor was missing. To our cries of 'Where's George?' echo answered Where? Fortunately in the end our search revealed him. He had been put in a patient's room to change, and did not realise until he had shut the door that it was fitted with a spring lock. He opened the window the meagre 4½ inches that the blocks allowed and yelled his head off, but everybody thought he was a maniac in a violent phase and took no notice. He was a trifle hoarse when we let him out but he managed to get through his programme. Once we were visited by a foreign pianist, who played Alan Rawsthorne's "The Creel," and before starting he told his audience that it was founded on a book they all knew: '*The Whole Fisherman*.' Evidently he had read Izaak Walton in translation and was now rendering "The Compleat Angler" back into English. In our next concert the loud pedal fell off the piano at my first push. I explained the serious nature of the accident to the audience on the analogy of trying to ride up a steep hill on a hot day on a bicycle with only one pedal. At the end the audience applauded loudly, but an object came flying through the air to land at my feet. For a moment I wondered if it was a bomb or a bad egg, but it did not burst like either, nor was it a rotten tomato. I stooped and picked it up. It was—of all things—a rose.

* * *

My only Home Thought from Abroad was to catch up with medicine by reading *In England Now*. But what do I find? A gentleman writing to say that he knows a fellow of a Royal College whose son, now that April's there, wakes in England, sees, some morning unaware, a rabbit, and shoots it for the pot. Which Royal College? I am a fellow of *one* and believe that if you want a job done properly you should do it yourself. I find it easiest from the bathroom window. This means shooting across a road—illegal perhaps but at half past seven in the morning no-one notices—and as the distance is considerable a ·22 must be used. Large rabbits are almost inevitably parents, and in any case are tasteless now, but babies, although not quite so delicious as Jefferies would have us believe, are very good cooked with bacon. Unfortunately there are no pigs in that field.

I see too that a correspondent relates the calorie value of the milk of different animals to their rates of growth. In 1935, or perhaps earlier, Degkwitz of Hamburg produced a nice table showing an inverse correspondence between the number of days that baby animals took to double their birth weight and the protein content of their mother's milk. As though the picture was not confusing enough already, a second writer (June 9, p. 1277) introduces the composition of reindeer milk. This was discussed adequately in a textbook published this year, which quotes the following figures:

Animal	Contents of milk (%)		
	Fat	Sugar	Protein
Elephant	20	9	3
Reindeer	17	2	10
Woman	4	6	1
Ass	2	6	2

It then remarks: "A pædiatrician employed in the teak forests of Burma might insist on skimming elephant's milk before it was given to his patients, but his ingenuity would be more severely exercised if he was transferred to Lapland."

* * *

Our embryo group practice has its moments. I had at last satisfied and got rid of a woman who complained of inhaling mouse poison treacherously laid for her by the people upstairs and wanted a bottle of medicine to make her sneeze. Mopping my brow, I pondered on the mechanism and possible applications of this form of antidote, making up my mind that the poor old thing had finally overstepped the mark and must be "put away" if she refused to be a voluntary patient. Then I walked over to my partner's room for the word of comfort that he can always supply me on such occasions. I reached my conclusion and his door together, and was astonished to find him writing a prescription for a woman patient and "cocking a snook" at her, remarking in his most convincing manner: "There you are, my dear. This will get rid of the prussic acid, and you can do *that* to your neighbours."

It was a second or two before I realised that this was a different patient altogether.

* * *

The examination for the D.P.H. is upon us at last, and I breathe a sigh of relief. Perhaps I have been luckier than some, for my husband has spent Monday to Friday living and studying in London, and only at the weekends have we been the victims of this fell examination. That has been bad enough. With food already difficult to get, we are forbidden sausages; the ice-cream we have always enjoyed is now taboo; the weekly mite of meat is probably contaminated by some fly and must be pressure-cooked out of existence; the kitchen is badly ventilated and ill-lit; the goldfish pond breeds mosquitoes so the goldfish are doomed to a paraffiny death; if anyone else comes to stay we shall be guilty of overcrowding; and the nice healthy children I have always regarded as delightful playmates for our pre-school child—who may not go to school because the toddler is best nurtured by its mother—are apparently all carriers of mortal disease.

So whatever the outcome I am glad it will soon be over and we shall be able to revert to our normal unhealthy life.

* * *

My daughter's conversation often reflects the thoughts, expressed or not, of the adults who surround her, and her father's present preoccupations were neatly demonstrated when, at a game of doctors and patients with her dolls, she remarked: "Araminta has measles, Elizabeth has income-tax, and Rosemary has mumps."

* * *

A Consultant deals with disease; a Practitioner with illness.

Letters to the Editor

PNEUMOCONIOSIS IN COALMINERS

SIR,—In their letter of June 9, members of the Pneumoconiosis Research Unit assert that "we have good evidence about the prognostic value of radiology" This enables them to claim that "if men were advised to work in less dusty conditions before they have developed sufficient simple pneumoconiosis, then they should be saved from the most serious disabling effects of the disease"

Now for some time this team has campaigned for the use of precise terminology and the adoption of radio graphic categories based on standard films, yet they themselves still use "a small degree" and "sufficient" simple pneumoconiosis This notwithstanding, they have on occasion been quite precise Thus in 1948 Davies et al[1] recorded

> "It therefore appears that with rare exceptions, men do not undergo this risk of developing progressive massive fibrosis until the *third stage* of simple pneumoconiosis has been reached We may conclude that coalminers may be protected from developing progressive massive fibrosis by being removed from a dust hazard before they reach *category 3* of simple pneumoconiosis"

In April, 1951, however, they altered this

> "It appears that as simple pneumoconiosis progresses there is an increasing liability to develop progressive massive fibrosis and that there is a relatively rapid increase in this liability within the stage of simple pneumoconiosis covered by *category 2*"[2]

Again in 1951

> "But we do claim, on the basis of follow up studies, and correlation between radiological and pathological studies that miners with films showing abnormality as great as *category 1* have definite evidence of dust retention in the lung and may, in course of time, especially with continued dust exposure begin to *suffer* from pneumoconiosis"[3]

Is the good evidence about the prognostic value of radiology not truly represented thus?

> "The range of simple pneumoconiosis over which a significant risk of P M F arises may vary in different parts of the country, and its exact definition must await the examination of larger numbers of cases"[2]

May I, from long and bitter experience, be permitted to remark that if a workman, being a free agent, does not or cannot accept the doctor's advice or warning to change to dust free or less dusty conditions, his future condition is not mitigated?

Now as to a system of periodic medical examinations The following quotation represents the considered opinion of Fletcher[4] in January, 1948

> 'The urgent necessity for the institution of an appropriate system of periodical X ray examinations, which *alone* [my italics] can give our coalminers security from pneumoconiosis, cannot be over emphasized
>
> "The sincerity of the industry's and the Government's concern with the health of coalminers will be judged by the speed and thoroughness with which such a system is instituted in this country"

Readers might reasonably have inferred from this indictment that the unit had already agreed the blue print of "an appropriate system" But no, for in April, 1951, three years later, Cochrane et al[2] state

> "In the organisation of a scheme, such as we have outlined, there would be many administrative and technical problems whose importance cannot be forecast and whose solution could not be suggested in advance of the introduction of the scheme
>
> "Because of all these uncertainties it is our view that periodic examinations should first be introduced on a pilot basis"

Yet Fletcher[4] in 1948 was satisfied to cite suitable systems in South Africa, Ontario, and Great Britain.

In my thesis[5] I sought to suggest the unsuitability of these systems and placed the main, almost the entire, assignment for prevention of pneumoconiosis on the industry, particularly the mining engineers, and on the workmen themselves At the same time I offered them the effective help of doctors through the supervision of all recruits to the industry

Finally as to the statement, based on Canadian observations, that "a workman may leave a silicotic risk with a normal radiograph and develop severe silicosis later,"[6] let us rely on our own experience in industries and occupations in Great Britain This phenomenon in this country, so far, is even rarer than a fine summer, and I doubt if it can ever occur in future if we accept the diagnosis of category 1 simple pneumoconiosis

University of Glasgow A MEIKLEJOHN

INJUDICIOUS USE OF HÆMATINICS

SIR,—Certain commercial houses are placing upon the market preparations containing iron, together with liver or hog stomach extract and folic acid

I should like to point out the dangers in exhibiting either liver or hog stomach extract, folic acid, or vitamin B_{12} before examination of the blood has established the type of anæmia It should be widely known to practitioners that in anæmia they can do no harm and may do much good by the exhibition of iron, but that the anti anæmic factor of liver or hog's stomach, vitamin B_{12}, and folic acid should be withheld until the blood has been examined The exhibition of any of these substances before examination of the blood may so cloud the hæmatological picture that correct diagnosis becomes quite impossible The exhibition of folic acid is particularly dangerous in that in pernicious anæmia it may bring about a return of the blood picture to normal, but will do nothing to arrest —and is even thought by some to accelerate—the nervous manifestations of the disorder

In view of the fact that there is now no part of England or Wales where facilities for hæmatological examinations are not readily available through the service in clinical pathology of the N H S, there can be no excuse for omitting examination of the blood before initiating treatment with hæmatinics other than iron

Royal Hospital
Wolverhampton. S C DYKE

INTRAVENOUS FLUID THERAPY IN CHILDREN

SIR,—As Dr Todd (May 5) and Dr Gunn (June 9) observe, the "cut down" is certain to become necessary at some time in infants suffering from severe gastro enteritis That being so, the technique should surely be learnt by residents in gastro ent[illegible]spital resi[illegible] prefer ably with some other technique as we[illegible]ating infectious

Dr Mann (June 2) is to be congratulate[illegible] To [illegible] his method of continuous scalp vein "drips," Which seems to have proved satisfactory in his unit But one wonders whether a resident, having become proficient with this method on Dr Mann's unit, might not be like the colleague who first taught me the technique of direct puncture of the limb veins, and who found the occasional unavoidable cut down extremely difficult never having learnt this method Dr [illegible] been opened at that a vein, once cannulised, is [illegible]ege Hospital as an is only true of the weeks fol[illegible]cal Diseases

As to the sup[illegible] Poliomyelitis there are twe[illegible] and Wales poliomyelitis notifications direct puncture [illegible]nded June 7 were as follo[illegible] paralytic and in successi[illegible]lytic 20 (12)

---

[1] Davies I Fletcher, C M Mann K J Stewart A. Proceedings of the Ninth International Congress of Industrial Medicine 1948 p 776

[2] Cochrane, A L Fletcher C M Gilson J C Jones P H *Brit J industr Med* 1951, 8 53

[3] Explanatory Notes accompanying Pneumoconiosis Research Unit standard films

[4] Fletcher C M *Brit med J* 1948 i, 1015 1065

[5] Meikle[illegible] *Brit J industr Med* 1950 7 105

[6] Leading article *Lancet* June 9 1951 p 1215

Where continuous parenteral fluids are necessary for several days or longer, the need to change the drip each day is not without disadvantages, on the other hand, as Dr Gunn remarks, the scar from a neat and well-managed cut down can be almost negligible.

I have previously advocated [1] the wider use of direct puncture of the limb veins for continuous fluid administration, mentioning that this was a routine procedure in some units in the U S.A, and that in 1948 over half of the infusions and transfusions in the gastro enteritis unit of the Queen Elizabeth Hospital for Children, London, were being given by this method. Such drips can maintain for up to a week the full fluid requirements, including all solutions and blood, and this seems to be the best technique for a busy unit Experience teaches, however, that not all can master this technique

Is it not desirable, then that a resident who has to take care of infants with gastro-enteritis should first learn to cut down reliably, since this measure can be life saving in virulent cases with peripheral circulatory failure or marked obesity? Being thus armed, let him then graduate to methods of direct venepuncture, whether for short or longer continuous fluid administration

Charing Cross Hospital
London, W C 2

B McNicholl

THE MEDRESCO HEARING-AID

Sir,—Space did not allow us to include all our findings in our survey of users' opinions of the 'Medresco' aid, published in your issue of May 26 Your correspondent Mr A E Stevens (June 9) and other readers may, however, be interested to know that of 273 patients interviewed who had had previous experience with commercial hearing aids, 85% said that they heard better with the medresco aid

Social Survey
Central Office of Information
London W 1

P G Gray

MAMMALIAN MOMMAS' MAMMARY MIXTURES

Sir,—The calorie value of reindeer milk quoted by your peripatetic correspondent of June 9 is three times bigger than its contents justify, the value calculated from its components is 237 calories per 100 ml. But let us bring peace between your peripatetics on the question of which animal gives the richest milk by suggesting that it all depends on what you mean by 'richness',

Animal	Composition of milk (%)					Calories per 100 g
	Water	Protein	Fat	Sugar	Ash	
Mule	91·5	1·6	1·6	4·8	0·4	40·1
Ass	90·1	1·7	1·3	6·5	0·5	44·0
Mare	89·8	1·8	1·2	6·9	0·3	45·5
Woman	88·2	1·5	3·3	6·8	0·2	62·9
Cow	87·3	3·4	3·8	4·8	0·8	66·4
Camel	86·6	4·0	3·1	5·6	0·8	66·0
Llama	[illegible]	3·9	3·2	5·6	0·8	66·4
[illegible]	[illegible]	4·4	4·6	4·2	0·8	76·0
[illegible]	[illegible]	9·1	3·3	4·9	0·6	85·9
[illegible]	[illegible]	4·1	7·6	4·7	0·9	103·9
[illegible]	82·3	6·0	6·7	5·0	1·0	104·2
Sheep	81·3	5·5	6·9	5·2	1·0	105·7
Bitch	75·4	11·2	9·6	3·1	0·7	143·1
Rabbit	69·5	15·5	10·5	2·0	2·6	164·0
Elephant	67·9	3·1	19·3	8·8	0·7	213·9
Whale	48·7	7·1*	43·7	—*	0·5	421·0
Porpoise	41·1	11·2	48·5	1·3	0·6	487·0

* The 7·1% includes protein and sugar

a fellow of a k[illegible] the accompanying table, adapted from there, wakes in Eng[illegible] *Applied Chemistry* (1922, vol. iv a rabbit, and shoots [illegible] so far as protein is concerned. College [2] I am a fellow of [illegible] heritage, we should want a job done properly you should [illegible]ample, mare's I find it easiest from the bathroom [illegible] a mare's nest means shooting across a road—illeg[illegible] half [illegible] morning no-one[illegible] butter in a lordly dish'—but do porp[illegible] must be mothers?

Further information may be found in the 12th edition of *Practical Physiological Chemistry* (1947, p 204), by Hawk, Oser, and Summerson, their figures do not always agree with Thorpe's

Mental Hospitals Group Laboratory
at West Park Hospital Epsom.

W W Kay

PREVENTION OF TUBERCULOSIS IN YOUNG PEOPLE

Sir,—Regarding the interesting article (May 19) by Dr Anderson and his colleagues, and Dr Brooke's comment (May 26), I also should like to remark on the notable incidence of tuberculin conversions among the "index case negative" group These results compare a biological test with the relatively crude laboratory methods, underlining the limitations of the latter Medlar and Reid [1] showed in 1944 that among a group of 18 patients who, while in the sanatorium, had had 6 or more cultures and guineapig tests, all of which were negative, 7 had positive tests on later study when they were back at work All of these 7 had minimal lesions Pinner [2] also noted that examination of three specimens of sputum, regardless of method, detected only 83·1% of all positive cases

R N Johnston
Visiting Fellow Chest Service

Bellevue Hospital Chest Service
New York, N Y

SURGERY OF MITRAL DISEASE

Sir,—Without pretending to be a modern O W Holmes, may I suggest that the simplest, most descriptive, and most fitting name for the operation described in your leading article of April 21 is "stenotomy"

Jerusalem.

Michael Alroy

FAMILIAL LEUKÆMIA

Sir,—In your leading article last week you say "It is remarkable that none of Videbaek's 26 authentic cases were reported from this country, and we have seen no recent reports here" I would like to point out that in 1912 Campbell reported an example of familial myelogenous leukæmia at the Royal Academy of Medicine in Ireland, and that in 1944 Meikle [3] reported 'two varieties of leukæmia in one family" I myself recorded in a letter [4]—overlooked by Videbaek—two cases of monocytic leukæmia in one family—the first and only instance of familial monocytic leukæmia in the world literature

London E.17

B John

ALCOHOL AND THE MOTORIST

Sir,—Your annotation of June 9 states that in South Africa blood tests are compulsory for determining intoxication This is not quite so according to Dr A Simpson Wells,[5] the Union of South Africa has quite recently added to its legal code a law which *permits* a medical man to take a sample of blood from anyone who is suspected of being under the influence of alcohol and who has been involved in a road accident This is quite an innovation, as recently as 1949 attention was drawn [6] to the fact that chemical tests for determining intoxication have never been used in South African courts, because of the common law principle which protects the accused from giving any evidence which may incriminate him

H Pullar Strecker
Hon. Secretary

Isleworth Middlesex

Society for the Study of Addiction.

---

[1] [illegible]oll B *Lancet* 194[illegible] ii 39

---

1 Medlar E M, Reid A C *Amer Rev Tuberc.* 1944 50 490
2 Pinner M. Pulmonary Tuberculosis in the Adult. Springfield Ill. 1945 p 362
3 Meikle R W *Brit. med J* 1944 ii 463.
4 *Ibid* p 543
5 Proceedings of the First International Conference on Alcohol and Traffic. Stockholm 1950 p 162
6 *S Afr med J* 1949 23 79

Manchester Regional Blood-Transfusion Centre

This centre, whose director is Dr F Stratton, has moved to new premises at Roby Street, Manchester, 1 (Central 8181)

U S Surgeon-General

Major General George E Armstrong has been appointed surgeon general of the United States Army in succession to Major General R W Bliss, who retires after 40 years service

Diabetic Association

On Friday, July 6, at 11 30 A.M., Prof C N H Long (Yale Medical School) will deliver the Banting lecture at the Postgraduate Medical School of London He is to speak on the Endocrine Control of Carbohydrate Metabolism

Health of Oxford Students

A statute is to be promulgated on Oct 23 to provide facilities for the routine medical examination of undergraduates and to offer them an advisory health service A committee, including the regius professor of medicine, is to be set up to administer the service, which will provide clinical and X ray examinations but not treatment It is proposed to appoint a director of the service with a salary of £1500–2000

Association of Surgeons of Great Britain and Ireland

The annual meeting of the association will be held in Manchester on July 19, 20, and 21 under the presidency of Sir Geoffrey Jefferson, F R S The programme includes discussions on Head Injuries (openers, Sir Hugh Cairns and Prof Norman Dott) Infections of the Hand (Mr W Gissane, Mr R M Handfield-Jones), Carcinoma of the Colon (Mr C Naunton Morgan, Mr R L Newell), Acute Pancreatitis (Dr H T Howat, Prof John Morley), and After history of the Amputee in Peripheral Vascular Disease (Mr W A Mackey, Prof George Perkins)

Société Internationale de Chirurgie Orthopédique et de Traumatologie

At the fifth congress of this society, held at Stockholm last month, the following officers were elected

President Sir Harry Platt (Manchester) vice presidents, Prof *Étienne Sorrel (Paris), Prof José Valls (Buenos Aires), secretary* general Dr Jean Delchef (Brussels) assistant secretaries, Dr P Kempeneers (Brussels), Dr R Van Cauwenberghe (Liége), treasurer Dr M Charles Parisel (Brussels)

Professor Sorrel was elected president and Dr Marcel Dubois vice president of the sixth congress, to be held in Switzerland in September, 1954

Not too Old at Forty

In a letter to executive councils the Medical Practices Committee remarks that it has been disturbed at the tendency of executive councils not to consider the applications of doctors of middle age or older for practice vacancies, in the case of one executive council all candidates above the age of 40 years are being eliminated without further consideration The committee points out that there are many good doctors aged 60–65 who have no regular employment, and who have no prospect of obtaining any appointment under such a system, yet many of the advertised vacancies have been for practices of moderate size well within the capacity of *these older doctors* A further class of elderly applicants for modest vacancies in the more pleasant areas are those who are in busy industrial practices These doctors who, says the committee, have borne 'the heat and burden of the day," are entitled to some consideration in their efforts to find less strenuous practices The practices they vacated would, moreover, become available for younger men.

Dr R T Brain, in collaboration with the medical and pharmaceutical staff of St John s Hospital for Diseases of the Skin, has revised the hospital pharmacopœia, last issued in 1935 The new edition can be obtained from the secretary of the hospital, Lisle Street, Leicester Square, London, W C 2 (5*s*, postage 3*d*)

CORRIGENDUM *Recent Prog* *iatr* t
that the initials of Dr G W g
stated in our review (June 9)
editor

Diary of the Week

JUNE 24 TO 30

Monday, 25th

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A.M (1, Wimpole Street W 1.) *Festival programme* 'Cortisone' and A C.T H
4 P M Physiology of the Vascular System.

ROYAL EYE HOSPITAL, St George s Circus Southwark S.E.1
5 30 P M. Prof Thomas Nicol Surgical Anatomy of Orbital Exploration.

MEDICO LEGAL SOCIETY, 26 Portland Place W 1
8 15 P M Dr Theo J Curphey (Hempstead, New York) A Comparison Between the Medical Examiner's System and the Coroner's System in the United States

Tuesday, 26th

SOCIETY OF APOTHECARIES Black Friars Lane E C 4
5 P M Dr T Jenner Hoskin Thyroid in Heart-disease (Joseph Strickland Goodall lecture)

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A M. *Festival programme* *Early Diagnosis of Mental Disorders.*
4 30 P M Tropical Medicine

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W C 1
5 P.M Mr Joe Pennybacker Brain Abscess

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane W 1
2 30 P M. Dr T Rowland Hill Common Virus Infections of the Central Nervous System

Wednesday, 27th

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
4 30 P.M. *Festival programme* Epidemiology

NATIONAL HEART HOSPITAL
5 P M. (26 Portland Place W 1) Dr Pierre Duchosal Vectorcardiography (St Cyres lecture)

RENAL ASSOCIATION
4 30 P M. (41 Portland Place, W 1) Dr E M. Darmady Nephron Dissections from Cases of Acute Renal Necrosis.

Thursday, 28th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
3 45 P M. Dr F S Gorrill Red Blood Corpuscles. (Arnott demonstration.)
5 P.M. Prof. Arnold Sorsby The Newer Antibiotics (Ophthalmology lecture)

ROYAL SOCIETY OF MEDICINE AND BRITISH MEDICAL ASSOCIATION
10 A.M *Festival programme* Carcinoma of the Lung
2 15 P M Thoracic Surgery

BRITISH ASSOCIATION OF UROLOGICAL SURGEONS
10 A.M (Royal Faculty of Physicians and Surgeons 242 St. Vincent Street Glasgow) Opening of a four-day meeting

Friday, 29th

ROYAL COLLEGE OF SURGEONS
3 45 P M Dr Gorrill Blood Coagulation (Arnott demonstration.)

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES
11 Chandos Street W 1
8 P.M Dr E H Hudson Bejel

Births, Marriages, and Deaths

BIRTHS

BAIRD —On June 8 the wife of Major J P Baird, R.A.M.C —a daughter

BANGHAM —On June 14, the wife of Dr Alec Bangham—a son

CRAIG —On June 17, at Bristol Dr Jean Craig (*formerly* Simpson), wife of Dr R A Craig—a daughter

EDGCUMBE —On June 14 in London the wife of Dr J O P Edgcumbe—a son

KEELE —On June 9, in London, the wife of Dr K. D Keele—a son

MILLER.—On June 12 at Newcastle upon Tyne, the wife of Dr Henry Miller—a daughter

SAXON SNELL —On June 6 in London the wife of Dr Richard Saxon Snell—a daughter

SWERDLOW —On June 11, in Manchester, the wife of Dr Mark Swerdlow—a son

MARRIAGES

OWEN—SANGSTER —On June 11 at Claverdon, John Tudor Owen M B to Heather Sangster

REDMOND HENDERSON—REDMOND —On June 1, in London Sidney Redmond Henderson to Winifred H Redmond, M R.C.S

SUDBURY—SADLER.—On June 16 at South Croydon, John Roger Sudbury B M. to Mary Sadler

DEATHS

BACK —On June 13, in London Ivor Back M.B. Camb F R.C.S

DUKES —On April 26, at Mangonui New Zealand Edmund Sprague Dukes M B Lond aged 82

ESSEX LOPRESTI —On June 13 in Birmingham, Peter Essex Lopresti F R C S E D.A aged 35

HOPKINSON —On June 11 Emilius Hopkinson C.M.G D S O B M. Oxfd, of Balcombe, Sussex late senior commissioner of Gambia aged 82

O'NEILL.—On June 16 in London, Hugh O Hagan O Neill M.B Edin

STUART-WEBB —On June 14 at Mortlake Ralph Edwin Stuart Webb M.B. Lond.

HÆMOPHILIA IN THE FEMALE

M C G ISRAËLS
M.D , M.Sc Manc , F R C.P
LECTURER IN HÆMATOLOGY, UNIVERSITY OF MANCHESTER

H LEMPERT
M.D , M Sc Manc
ASSISTANT DIRECTOR, DEPARTMENT OF CLINICAL PATHOLOGY, MANCHESTER ROYAL INFIRMARY

ELIZABETH GILBERTSON
M.B Durh., M.R C O G
REGISTRAR, ST MARY'S HOSPITALS, MANCHESTER

HÆMOPHILIA has from the earliest times been thought of as limited to the male sex Its inheritance has been worked out, and there is one possible combination that can give rise to a female hæmophiliac , this is when a male hæmophiliac marries a female hæmophilia carrier, according to the following scheme

⊗Y	+	⊗X	⟶	⊗⊗	+	⊗X	+	⊗Y	+	XY
HÆMOPHILIC MALE		CARRIER FEMALE		HÆMOPHILIC FEMALE		CARRIER FEMALE		HÆMOPHILIC MALE		NORMAL MALE

The classical investigations of hæmophilic families had, however, failed to reveal a definite hæmophilic female

Bulloch and Fildes (1912) surveyed 600 hæmophilic families and did not find a single female among those affected

Birch (1937), in his detailed survey of 75 hæmophilic families, found one instance of the required combination a woman, who had a hæmophilic father and whose mother was the daughter of a known female carrier, had a hæmophilic son, but her own blood was normal by the criteria then applied. Birch also mentions 4 women who were daughters of hæmophilic fathers and were said to have a hæmorrhagic diathesis, but, in his opinion, none of them was a hæmophiliac

The general opinion has been that the combination is lethal and that the female hæmophiliac, if ever conceived, dies in utero

Lately, Merskey (1951) has re examined by modern methods two female members of a family that had been classed as "pseudohæmophilic" because in an early generation there seemed to have been a male to male inheritance , but, apart from this incident, which was hearsay only, the inheritance had followed the known mode of transmission of hæmophilia, and, after a first-cousin marriage, the offspring had included four female "bleeders" Merskey's examination showed that the blood of two of these women, by all present methods of testing, would be interpreted as typical of hæmophilia

There are, however, quite a number of published reports of females with a hæmorrhagic diathesis whose blood coagulation time was prolonged The case described by Bauer and Meller (1937) is an example Here a woman with a severe hæmorrhagic diathesis had a blood coagulation time of over 50 minutes , investigation of the family showed that other females were affected but no males The only other laboratory tests applied were estimations of the bleeding time, which was slightly prolonged, and the plasma fibrinogen, which was normal Because of this lack of what is now regarded as necessary investigation, a discussion of the previously reported cases must be fruitless, and we do not propose to attempt it

CAUSES OF PROLONGATION OF COAGULATION TIME

Three conditions that may greatly prolong the blood coagulation time in females as well as males are now known

(1) *Fibrinogenopenia.*—A rare condition characterised by complete or almost complete absence of fibrinogen in the plasma, and easily detected by estimating the plasma fibrinogen level

(2) *Circulating Anticoagulants*—A hæmorrhagic diathesis due to the presence of an anticoagulant in the plasma was described by Lozner et al (1940) and other examples have since been reported—for example, by Dieter et al (1949) The crucial diagnostic test is that the patient s plasma will prolong the coagulation time of normal plasma

(3) *Parahæmophilia*—A hæmorrhagic disease described by Owren (1947), due to the absence of a prothrombin accelerator factor that Owren called "factor v" and Quick (1947) refers to as "labile factor" The subject has recently been reviewed by Stefanini (1951) The special test for detecting a deficiency of labile factor is described below

The steps necessary to exclude these conditions have not been taken even in recently reported cases of hæmophilia like disease in women Thus Madison and Quick (1945) reported on two females with prolonged coagulation times , they considered neither to be a true hæmophiliac but could not assign them to any other category Hewlett and Haden (1949) had one very suggestive case—a woman whose blood coagulation time was 116 minutes and plasma would *not* correct the prolonged clotting time of a known hæmophilic blood However, two important points were missing—there was no family history, and the prothrombin consumption test was not done

A family history of hæmophilia is of great importance It will be seen from the scheme given above that at least the father should be a known hæmophiliac Mutation as a cause of hæmophilia must be assumed because cases arise de novo that cannot be certainly assigned to a long line of silent female carriers For a female hæmophiliac a double mutation would have to be assumed, and this is excessively rare

PROTHROMBIN CONSUMPTION TEST

The prothrombin consumption test is based on the observation of Brinkhous (1939) that, when hæmophilic blood clots, much prothrombin remains in the serum Quick (1947) adapted this observation to provide a test for hæmophilia , he showed that there is hardly any consumption of prothrombin when hæmophilic blood clots , even twenty-four hours after the blood has been drawn, nearly as much prothrombin is still present in the serum as was present in the original plasma , in normal blood there is hardly any detectable prothrombin in the serum twenty four hours after clotting This test is positive only in hæmophilia and in thrombocytopenic purpura when the platelet count is very low (20,000 per c mm or less)

Merskey (1950) has emphasised the importance of the prothrombin-consumption test , he has also pointed out that the presence of antihæmophilic globulin in plasma can be tested for by using its ability to correct the prolonged clotting time of known hæmophilic blood Using these tests Merskey detected with greater certainty hæmophiliacs whose blood-coagulation time was little, if at all, prolonged, and showed that the two female "bleeders ' originally thought to have 'pseudohæmophilia " have true hæmophilia.

The patient whose history and particulars we are reporting has been tested by all these methods Both her parents come from hæmophilic, but unconnected, families (see below) The various tests on her blood all gave the results expected in hæmophilia, and the other possible causes of prolonged coagulation time have been excluded

CASE RECORD

A primigravida, aged 24, first attended the antenatal clinic at St Mary's Hospitals, Manchester, on Feb 4, 1950 General examination showed no evidence of organic disease The pregnancy had reached the 12th week Arrangements were made to admit the patient to hospital for her labour because of the history of easy bruising and free bleeding The pregnancy was uneventful On Aug 26 she was delivered at term by the natural forces of a healthy girl weighing 7 lb 1 oz. The third stage of labour was completed in 15 minutes The measured blood loss was 120 ml The early puerperium was uneventful. The patient was discharged from hospital on the tenth day post partum. At this time the uterus showed slight subinvolution, but the lochial discharge was normal Immediately after her discharge, the lochia returned freely, and passed from a red discharge to frank bleeding with escape of blood-clots. Five days after discharge she was readmitted to hospital, when her hæmoglobin was found to have been reduced to 5 g per 100 ml

Treatment—She was given a transfusion of 2 pints of blood, 5 units of oxytocin intramuscularly, and morphine gr $^1/_4$ The bleeding ceased for 24 hours It then began again, so the uterus was explored digitally under general anæsthesia It proved to be empty apart from a few shreds of tissue identified histologically as blood clot with necrotic endometrium The patient bled very freely during the exploration, at the conclusion of which the uterus was tightly packed Twenty four hours later the pack was removed, and the bleeding at once started again Her hæmoglobin being now 6 g per 100 ml, the patient was again transfused, after which the uterus was repacked under general anæsthesia When the pack was once more removed, the bleeding at once recurred, although the rate was less than at the time of admission

Progress—Five days later, however, the patient began to lose blood very sharply and collapsed She required 4 pints of plasma and 3 of whole blood before she rallied, and thereafter the uterus was packed for a third time This pack was left in situ for seventy two hours When it was removed, uterine bleeding did not at once recur, but there was some oozing from vaginal abrasions immediately within the introitus The maintenance of direct pressure for about 15 minutes arrested this bleeding, and thereafter the patient's condition appeared satisfactory, the hæmoglobin being recorded as 9 2 g per 100 ml

After a further forty eight hours the uterine bleeding restarted and continued intermittently On Sept 18 there was considerable anæmia—Hb 8 8 g per 100 ml, leucocytes normal, reticulocytes 20%, platelets 290,000 per c mm (normal)—and sternal marrow showed active normoblastic erythropoiesis, no abnormal cells being present The coagulation time (Lee and White at 37°C) was 14 minutes, and the prothrombin consumption test showed the prothrombin time of the serum twenty four hours after withdrawal of the blood to be 37 sec (normal 120 sec) These findings were similar to those of hæmophilia and excluded any primary disease of the blood forming tissues Further investigation into the exact nature of the clotting defect was clearly going to take some time, so for the moment it was recommended that transfusions with fresh blood should be given, the patient was given 2 pints of fresh blood and a pint of "snap frozen" plasma

Operation—In spite of these measures free uterine bleeding continued, so it was decided to remove the uterus A total hysterectomy, with conservation of the appendages, was done by the abdominal route on Sept 23 Blood loss at operation was not great, but a persistent ooze from the edges of the abdominal wound and from the raw surfaces in the pelvic cellular tissue was troublesome It was impossible to control this by ligature or diathermy, in view of the absence of any recognisable bleeding points Reliance was placed on tight sutures The abdominal wound was closed with interrupted silk stitches, all buried, since it was felt that the wound would heal slowly, and it was considered undesirable to leave stitch apertures in the skin The excised uterus showed delayed involution, its size being equivalent to that of a three month pregnancy It contained a large blood clot Its epithelial lining was almost entirely superseded by granulation tissue

Convalescence was stormy During the first six days there were signs of peritoneal irritation, and at the end of this period fresh blood escaped from the lower end of the abdominal wound, where a considerable hæmatoma had formed A scanty vaginal hæmorrhage occurred at the same time An irregular pyrexia developed, the lower portion of the wound broke down, and a large blood-clot extended deeply behind the pubis The wound exudate produced a growth of *Proteus vulgaris*, a coagulase positive staphylococcus, a coliform organism, and a diphtheroid These were all penicillin resistant and rapidly became resistant to streptomycin. Sensitivity to 'Chloromycetin' was demonstrated, however, and on exhibition of this drug the pyrexia settled A large mass of blood clot and sloughing tissue separated about four weeks after operation, and thereafter the wound healed slowly It was completely closed ten weeks after operation During the first four weeks of her convalescence the patient was repeatedly transfused, in all she received 10 pints of fresh whole blood and 2 pints of packed cells Between admission and discharge she had been given 25 pints of whole blood and 6 pints of packed cells Details of the blood counts are given in table I. She was discharged on Dec 13, 1950 Since discharge she has remained well She was seen on Jan 10, 1951, when her red cells were 4,960,000 per c mm and Hb 15 1 g per 100 ml.

TABLE I—BLOOD COUNTS IN FEMALE HÆMOPHILIAC

Date	Hæmoglobin (g per 100 ml)	Red cells (million per c mm)	White cells (per c mm)	Reticulocytes (per 100 red cells)
1950				
Sept 18	8 8	2 91	9000	20 0
„ 22	9 9	3 63	8600	
„ 25	6 8	1 79	20,000	
„ 30	9 9	3 17	24,000	15 0
Oct 5	9 7	3 28	15 900	5 4
„ 7	4 3	1 78	22,300	23 8
„ 14	4 7	1 63	12 800	28 8
„ 18	3 9	1 25	4500	20 8
„ 31	9 1	3 12	6000	14 0
Nov 6	10 8	3 83	8400	4 4
„ 17	11 2	3 82	7000	2 2
„ 24	10 4	3 50	6000	
Dec 6	11 8	4 45	7500	
1951				
Jan 10	15 1	4 96	10 400	
March 20	14 5	4 73	9000	

PREVIOUS PERSONAL AND FAMILY HISTORY

The patient had been known to bruise easily from childhood and her schooling had been severely restricted, but apart from occasional epistaxes, there had been no notable hæmorrhages, swelling of some joints had occurred from time to time In March, 1946, she was in Withington Hospital with severe anæmia due to bleeding from vaginal lacerations, the clotting time, by Wright's method, was 20 min—greatly prolonged—even after blood transfusion, she responded well, but 9 pints of blood were needed in all

The details of the family history, so far as they can be found, are given below and in fig 1

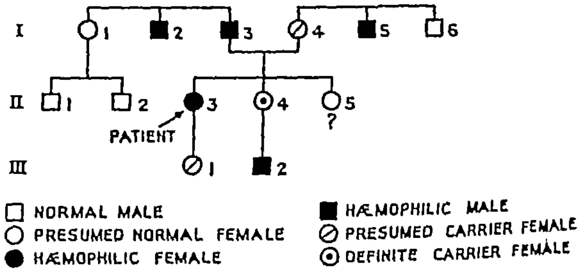


Fig 1—Family tree of female hæmophiliac.

I,3 *Patient's father*—A known hæmophiliac, with a lifelong history of easy bruising, recurrent hæmarthroses, and hæmaturia He was admitted thrice to Withington Hospital, and his records were available In September, 1940, he had hæmaturia that cleared in five days In April, 1944, he had severe bleeding from an ulcer of the tongue and round a loose molar tooth; his coagulation time (Wright's method) was 10 minutes, bleeding time and plasma fibrinogen level were normal; transfusions were needed for treatment, while in hospital he developed a hæmarthrosis of the left knee In June, 1945, he was admitted unconscious and died, necropsy showed a large subdural hæmatoma

I,2 *Father's brother*—Also a known hæmophiliac, but no details are available

I,1 *Father's sister*—Had two sons (II,1 and 2) who were unaffected

I,4 *Patient's mother*—Must be presumed to be a carrier

I,5 *Mother's brother*—A known hæmophiliac He had always bruised easily and had had hæmarthroses, the similarity between the males on the two sides had been a matter for family comment He died in hospital in 1940 from hæmorrhage following an accident. His records were no longer extant, and no laboratory results were available, the facts, however, were confirmed by the family doctor

I,6 *Mother's second brother*, unaffected

II,3 *Patient*

II,4 *Patient's sister*—Blood is normal, but is known to be a carrier since she has had a hæmophilic son (see III,2)

II,5 *Patient's second sister*—Died at the age of 9 months from burns, no evidence concerning her blood

III,1 *Patient's daughter*—If the patient is hæmophilic, will be a carrier

III,2 *Patient's nephew*—Born on Jan. 2, 1949, has bruised easily from birth. When seen on Oct. 24, 1950, he had large painless ecchymoses over the left iliac crest and left buttock. His blood coagulation time (Lee and White at 37°C) was over 30 minutes, and there was hardly any detectable consumption of prothrombin after 24 hours, he therefore had severe hæmophilia

LABORATORY INVESTIGATIONS

The aim of these investigations was to see how far the properties of the patient's blood corresponded to what is known about hæmophilic blood, and to test the possibility that she might have one of the other conditions mentioned above that prolong blood coagulation In addition some tests were done on the patient's relations

Since techniques still vary greatly in different centres, we have given full details of our own Except the blood-counts (shown in table I) one of us (H L) was responsible for all the tests The importance of using chemically clean glassware of a standard material and size cannot be overemphasised

Platelet-counts

When reticulocytes are present in larger numbers than normal, there is some difficulty in counting platelets by Lempert's (1935) method This is easily overcome by leaving out the brilliant cresyl blue, as suggested by Taylor (1940) Thus solution A contains sodium citrate 1 g, 2% mercuric chloride solution 0 2 ml., and distilled water 100 ml. Solution B remains unchanged at 20% urea

Table I shows that the patient's platelet counts have always been within normal limits—i e, 190,000–330,000 per c.mm

Whole blood Clotting time (C T)

The method used is a modification of the one devised by Lee and White (1913)

Technique—Sterile 10 ml syringes and no 2 needles were rinsed out thoroughly with sterile physiological saline solution. For children, and occasionally for adults, a no 15 needle was necessary so that only a minimum of trauma occurred when blood was withdrawn from an antecubital vein. As soon as the blood entered the syringe a stopwatch was started With practice 10 ml. of blood could be withdrawn easily in 25–40 sec The needle was removed from the syringe, and 4 5 ml of blood quickly added to 0·5 ml of sodium oxalate (1 34% solution) in a bijou bottle An assistant mixed the blood and oxalate, inverting the bottle immediately twenty times The specimen provided plasma for estimating the plasma-clotting time and plasma prothrombin time (see below) Of the remaining blood in the syringe 1 ml. was added to each of three small test-tubes which had previously been placed in a rack in a water bath at 37 5°C These test-tubes were 8·0–8 5 mm in internal diameter and 70 mm long ('Monax' glass)

When the stopwatch showed that 2 minutes had elapsed since the blood had first entered the syringe, one of the tubes was lifted out of the bath and its outside was dried with a cloth A clean dry finger was then placed over the open end, and the tube was inverted once only and replaced in the bath. This same tube was then inverted once every $^1/_2$ minute until the contents remained firm at the bottom with complete loss of fluidity. In 30 normal persons this took place in $3^1/_2$–$5^1/_2$ minutes from starting the stopwatch. The second tube was now inverted in a similar manner once every $^1/_2$ minute until its contents too had clotted Normally this took place in $5^1/_2$–$7^1/_2$ minutes Finally the third tube was inverted at $^1/_2$ minute intervals and clotting normally took place in $7^1/_2$–10 minutes.

When the clotting time in any of the tubes was seen to be more than 10 minutes the tube was thereafter inverted once every minute If the blood had not clotted in 30 minutes the test was discontinued and reported as "clotting time over 30 minutes"

Most hæmophiliacs have a first-tube clotting time of more than 30 minutes. Some hæmophiliacs however, have clotting times raised only a few minutes above the normal range mentioned above These patients may have as many hæmorrhagic episodes as the hæmophiliacs with greatly increased clotting times.

The method described has shown increased clotting times in hæmophilia, severe thrombocytopenic purpura, and severe hypoprothrombinæmia The method will probably also detect severe deficiency of labile factor (factor "v"), fibrinogenopenia, and the rare cases in which there is an excess of a circulating natural anticoagulant

TABLE II—LABORATORY FINDINGS IN FEMALE HÆMOPHILIAC

Date		Hb g per 100 ml	Red cells (millions per c mm)	Platelets (per c.mm)	Whole blood clotting time (min.)			Plasma clotting time (min)	Plasma prothrombin time (sec)	Serum prothrombin time		Plasma fibrinogen (g per 100 ml)
					1	2	3			After 4 hour	After 24 hour	
1950												
Sept	22	9 9	3 63	290 000	14	18	23	9	13	19	37	420
	26	6 8	1 79							20	38	
Oct	31	9 1	3 12	256 000	25	30 +	30 +	12	$13^3/_4$	14	15	350
Nov	17	11 3	3 82		30 +	30 +	30 +	15 +	$12^1/_2$	11	12	
	24	10 4	3 50	245 000	30 +	30 +	30 +	15 +	$13^1/_4$	13	14	450
1951												
Jan	10	15 1	4 96	222 000	30 +	30 +	30 +	15 +	$13^1/_4$	$11^1/_2$	12	370
Feb	14				30 +	30 +	30 +	15 +	$13^1/_4$	12	$12^1/_2$	394
March	20	14 5	4 73	215 000	18	30 +	30 +	11	$13^3/_4$	$13^1/_2$	13	520
June	21	13 3	4 62	263 000	30 +	30 +	30 +	15 +	13	$12^1/_2$	$12^1/_2$	340

Table II shows that, during the period when the patient was receiving multiple transfusions, the C T in the first tube was 14 minutes. A month later, after she had not needed a transfusion for twelve days, the first tube clotted in 25 minutes. A slight clotting was noted at 22 minutes Since that time the patient has made a remarkable recovery, but the C T in the first tube has been consistently prolonged month after month

Plasma Clotting time (P C T)

Oxalated blood when centrifuged produces a plasma containing the clotting factors except calcium The platelet factor varies with the speed and time of centrifuging However, if the blood is centrifuged at 3000–3500 r p m for 10 minutes, the plasma seems to contain platelet factor proportional to the platelet count Normally the recalcification of oxalated plasma produces a mass of fibrin in a few minutes As with the whole blood clotting time, the P C T is prolonged when there is gross deficiency of one or more of the clotting factors Both tests are non specific, but, when abnormal results are obtained, further investigation of individual clotting factors is indicated

Technique—Oxalated blood was prepared as before The specimen was kept for not more than two hours in the refrigerator at about 4°C After being mixed it was centrifuged for 10 minutes at 3000–3500 r p.m The plasma was then carefully pipetted off to about $^1/_2$ in. of the cell layers 0 1 ml of plasma was placed in an 8 mm test-tube in a water bath at 37 5°C, and 0 1 ml. of physiological saline (0 9% NaCl) was added. Into the mixture 0 1 ml of calcium chloride solution (0 18% $CaCl_2$) was quickly added and a stopwatch was started immediately The contents of the tube were next mixed gently, and the tube was tilted almost horizontally so that the fluid wetted the glass almost to the open end. The tube was then replaced in the bath. At $^1/_2$ minute intervals the tube was tilted once but after $1^1/_2$ minutes it was tilted at $^1/_4$ minute intervals until a sudden loss of fluidity occurred with the appearance of fibrin. With blood from thirty normal persons this took place in $1^3/_4$–$3^1/_2$ minutes If fibrin had not appeared after five minutes the tube was tilted at $^1/_2$ minute intervals Often, with these prolonged P C T plasmas, only a small pellicle of fibrin appeared at the end point

With most hæmophilic subjects the P C T was over 15 minutes, and the test was discontinued if fibrin had not appeared by that time

Table II shows that the P C T of the patient has always been greatly above normal and usually more than 15 minutes

Plasma prothrombin Time

Quick's one stage method was used The thromboplastin reagent was a saline extract of human brain The calcium reagent was a 0 18% calcium chloride solution which, although of lower concentration than prescribed by Quick, gave reliable results

Technique—Oxalated plasma was prepared as before 0 1 ml of plasma was placed in an 8 mm. test-tube in a water bath at 37 5°C, and 0 1 ml of thromboplastin reagent was added After gentle mixing for a few seconds the tube was replaced in the bath and 0 1 ml of calcium chloride solution was added A stopwatch was started immediately The tube was next dipped in and out of the bath, the contents being made to wet almost the whole length of the glass The watch was stopped when, on tilting the tube, the contents gelated and impeded the previously easy flow

Twenty normal persons had prothrombin times of 12–14$^{1}/_{2}$ sec The mean average was 13 sec , and this was designated " 100% prothrombin activity " A saline dilution curve was prepared, and this showed 30$^{1}/_{2}$ sec to be equivalent to 20% prothrombin activity

Table II shows that the patient's prothrombin times were 12$^{1}/_{2}$–13$^{3}/_{4}$ seconds, which is equivalent to prothrombin activity of 90–100%

Plasma Labile Factor

When normal oxalated plasma is stored, a labile factor disappears and the prothrombin time increases (Quick 1943) Owren (1947) described a case in which there was a deficiency of this labile factor and he called the condition " parahæmophilia " Although a normal prothrombin-time, as estimated by Quick's method, rules out a gross deficiency of labile factor, this factor was assessed in our patient

Technique—Oxalated plasma from a normal person with a prothrombin time of 13 sec was stored at 4°C for nineteen days The prothrombin time was then found to be 30 sec

0 09 ml of stored normal plasma was then mixed with 0 01 ml of fresh normal plasma The prothrombin time returned to 13$^{1}/_{2}$ sec

0 09 ml of stored normal plasma was mixed with 0 01 ml of fresh patient's plasma The prothrombin time returned to 12$^{1}/_{2}$ sec

This experiment shows that the patient's plasma was not deficient in labile factor

Fibrinogen

Table II shows that the fibrinogen content of the patient's plasma has always been within normal limits

Serum-prothrombin Time

Quick (1947) postulated an inactive precursor of thromboplastin in the plasma (thromboplastinogen) which could be activated by a factor derived from platelets Experiments showed that in hæmophilia the platelets were normal but there was a lack of thromboplastinogen and therefore lack of available thromboplastin to take part in thrombin production Thus only small amounts of prothrombin were converted to thrombin, and this was again reflected in the slow production of fibrin and hence the prolonged clotting time of hæmophilic blood

Quick described an ingenious experiment in which prothrombin free fibrinogen solution was mixed with thromboplastin reagent and to it was added serum The time for fibrin to appear was said to be a measure of the prothrombin remaining in the serum This serum prothrombin time was very much longer than the plasma prothrombin time with norma lblood, even after afew hours In hæmophilic blood the serum prothrombin time was practically the same as the plasma prothrombin time even after twenty four hours Several modifications of this test have since appeared (Quick and Favre Gilly 1949, Soulier 1950, Merskey 1950)

Stefanini and Crosby (1950) have pointed out that the serum prothrombin time is a measure of several factors unchanged prothrombin, thrombin produced during clotting, plasma labile factor, and serum accelerator globulin In spite of this criticism the estimation of serum prothrombin time, or the prothrombin consumption test as it was originally called, is a valuable aid in the diagnosis of hæmophilia

Technique—10 ml of venous blood, obtained as for clotting time estimation, was put into two tubes (70 × 10 mm.), previously rinsed with physiological saline solution. The tubes were left unstoppered at room temperature (16–18°C) for four hours After the first hour normal blood had lost its fluidity In hæmophilic blood the red cells could still be seen sedimenting and the supernatant fluid was often not completely clotted even after four hours The clots were carefully loosened with a fine glass rod, and the tubes were centrifuged for 5 minutes at 3000 r p m The separated fluid was pipetted into a tube previously rinsed out with saline solution With normal blood the fluid (serum) removed after four hours never formed a secondary clot With hæmophilic blood or blood from severe thrombocytopenic purpuras a secondary clot always formed in the fluid separated after four hours

The serum prothrombin time was now estimated (see below) The tube of serum was then corked and left in the refrigerator at 4°C for another twenty hours A second serum prothrombin time was estimated as follows 0 1 ml of fibrinogen solution and 0 1 ml of thromboplastin reagent were placed in an 8 mm. test-tube in a water bath at 37 5°C 0 1 ml of serum was added and a stopwatch started The end point was the appearance of fibrin as described in the estimation of plasma prothrombin time

The fibrinogen for the test was prepared from oxalated human plasma The prothrombin was removed with barium sulphate and the fibrinogen salted out by just over half saturation with sodium chloride The fibrinogen was separated by centrifuging and washed with cold distilled water It was then redissolved in 0 3% sodium chloride and stored in corked tubes at 4°C A fresh batch had to be made every two or three weeks owing to deterioration after this time The best concentration for the test was 100–200 mg of fibrinogen per 100 ml

In fifteen normal persons the serum prothrombin time after four hours was 42–105 sec , after twenty four hours it was 85–120 sec or more

Table II shows the serum prothrombin times of the patient During the period when she was receiving multiple blood transfusions the serum prothrombin time after four hours was 19 or 20 sec , after twenty four hours it was 37 or 38 sec Since her recovery the serum prothrombin time after four hours has been 11–14 sec , and after twenty four hours 12–15 sec

These results are identical with those obtained with the majority of a large series of male hæmophiliacs

Addition of Hæmophilic Plasma to Patient's Plasma

Various amounts of plasma from a hæmophiliac with a P C T of 9 minutes were added to the patient's plasma when her P C T was 12 minutes Fig 2 (*a*) shows that the alteration of the P C T was practically directly proportional to the amount of plasma added This suggests that both patients were hæmophilic and that the

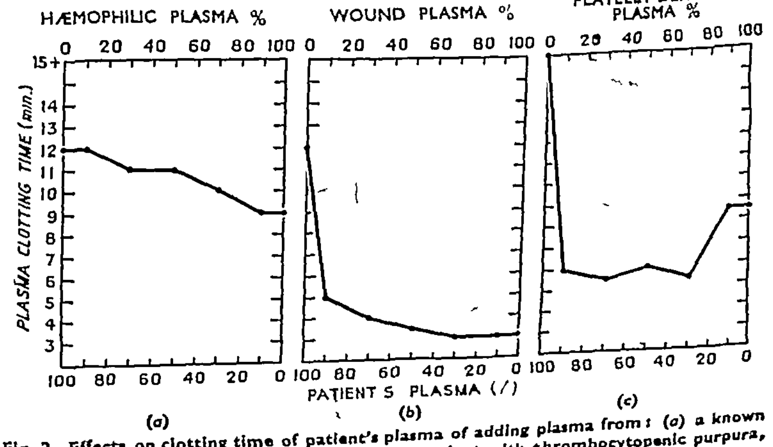


Fig 2—Effects on clotting time of patient's plasma of adding plasma from : (*a*) a known hæmophiliac (*b*) a normal person ; and (*c*) a patient with thrombocytopenic purpura, containing very few platelets.

TABLE III—HÆMATOLOGICAL FINDINGS IN FEMALE HÆMOPHILIAC AND RELATIONS

Source of blood	Whole-blood clotting time (min)			Plasma clotting time (min)	Plasma prothrombin time (sec)	Serum prothrombin time (sec.)	
	1	2	3			After 4 hr	After 24 hr
Patient	30+	30+	30+	15+	13¼	12	12½
Mother	5	7	8½	2½	13¾	40	115
Sister	4	6½	8½	3	13½	52	120+
Nephew	30+	30+	30+	15+	13½	12	13½

deficiency of plasma factor was perhaps a little more marked in our patient

Addition of Normal Plasma to Patient's Plasma

Various amounts of plasma from a normal person with a P C T of 3 minutes were added to the patient's plasma when her P C T was 12 minutes Fig 2 (*b*) shows that, when only 10% of normal plasma was added to the patient's plasma, the P C T was reduced to 5 minutes When more than 30% of normal plasma was added, the P C T was in the normal range

These results are typical of hæmophilia If the patient had had a circulating anticoagulant, the addition of a small amount of her plasma to the normal plasma would have raised the P C T considerably

Addition of Platelet deficient Plasma to Patient's Plasma

The P C T of a patient with thrombocytopenic purpura was found to be 4½ minutes Centrifuging the plasma for a further thirty minutes at 4000 r p m increased the P C T to 8½ minutes Various amounts of this plasma were added to our patient's plasma with her P C T at over 15 minutes Fig 2 (*c*) shows that, when 10% of the relatively platelet free plasma was added to our patient's plasma, the P C T was reduced to 6 minutes On the other hand, when 30% of our patient's plasma was added to the relatively platelet free plasma, the P C T was reduced from 8½ minutes to 5½ minutes

This experiment agrees with Quick's views that thrombocytopenic plasma contains adequate amounts of thromboplastinogen but lacks platelet factor, whereas hæmophilic plasma contains adequate amounts of platelet factor but lacks thromboplastinogen

Tests on Near Relations

These are shown in table III The mother and the sister show no abnormal findings The sister's son has typical hæmophilia clinically, and laboratory investigations confirm this

DISCUSSION

The evidence that this female patient has true hæmophilia has been set out in detail. The family history is highly suggestive, it is a great pity that the records of her affected maternal uncle had been destroyed, but the hearsay evidence that he had hæmophilia is very good. The evidence from blood clotting studies is complete, and the various tests applied have given results characteristic of hæmophilia in every instance We know that the coagulation time of the patient s blood is greatly prolonged and has been so for at least four years, that the serum prothrombin time is pathologically short, that her plasma will *not* correct the defective coagulation of known hæmophilic blood and conversely, that the defective coagulation of *her* blood *is* corrected by normal plasma We have excluded fibrinogenopenia by showing that the plasma fibrinogen level is normal, circulating anticoagulants have been excluded by showing that the patient s blood will not prolong the coagulation time of normal blood, and the demonstration that plasma prothrombin accelerator factor (factor V, labile factor) is normally present excluded parahæmophilia

In a male patient such findings would be interpreted without question as showing hæmophilia The findings only need discussion because, except for Merskey's (1951) *two re examined cases, no properly investigated case of* female hæmophilia has been published That a hæmophilia like disease can occur in the female sex has been shown by Brinkhous (1950) Graham et al. (1949) had described a remarkable family of setter dogs afflicted by a hæmorrhagic condition that resembled human hæmophilia in all respects, including its mode of inheritance Brinkhous (1950) mated an affected male dog to a known carrier bitch—i.e , a bitch that had been previously mated to a normal male and had produced an affected male pup This mating did produce affected bitches, but he was unable to breed from these affected bitches because uterine hæmorrhage killed the fœtuses

It is remarkable that our patient should have conceived and carried to term a normal child, and that menstruation should have been normal. It is less surprising that she escaped serious bleeding at the time of delivery, in view of the generally accepted belief that the control of the hæmorrhage from the placental site is by retraction of the muscle fibres in the uterine wall. In conditions other than hæmophilia associated with prolonged coagulation time of the blood such absence of bleeding has been noted, as in the regularly menstruating patient (Hewlett and Haden 1949) who had had five normal pregnancies and had a sixth normal pregnancy and labour at a time when her coagulation time was known to be prolonged

The mechanism by which the later bleeding was induced in our patient is a matter for speculation, but its time of onset is consistent with the effects of a minor infection of the placental site developing when the involution of the uterus had reduced the efficiency of the muscular control of bleeding There had been no systemic signs of such infection, but there was histological evidence of its existence

The value of the surgical treatment of this patient is doubtful. It did not completely arrest the bleeding, and possibly, in view of the stormy convalescence, the patient was exposed to even more risk than was present at the time of operation In retrospect, however, we believe that the operation was justified, since the rate of blood loss from the uterine cavity was so very great that it would have been difficult to keep pace with it by blood transfusion The regret felt at removing the uterus in any young woman is tempered in this case by the fact that we should have felt it necessary to advise this patient to have no further family As regards the surgical technique adopted it is felt that two points influenced the eventual result favourably—the insistence on the use of interrupted non absorbable sutures for the rectus sheath, without which it is almost certain that the wound would not have healed, and the avoidance of skin piercing sutures, through the apertures of which further bleeding would have taken place

SUMMARY

A case of true hæmophilia in a woman is described

All the tests of the blood coagulation mechanism applied gave results typical of hæmophilia

Fibrinogenopenia, parahæmophilia, and the presence of circulating anticoagulants were excluded

The patient had given birth to a healthy female child without, at first, excessive hæmorrhage During the puerperium severe hæmorrhage came on, and hysterectomy was successfully done

The family history of the patient fits in with the current theory of the sex linked inheritance of hæmophilia

The patient was in hospital under the care of Prof W I. C Morris, to whom we are indebted for constant coöperation and advice on the obstetric and gynæcological aspects We also wish to pay tribute to the highly skilled and devoted nursing

which this patient received in the St Mary's Hospitals, Manchester Without this it is doubtful if she would have recovered

REFERENCES

Bauer, H Mellor, J (1937) *Wien klin Wschr* **50**, 495
Birch, C L (1937) Hemophilia Clinical and Genetic Aspects Illinois vol i no 4
Brinkhous K M. (1939) *Amer J med Sci* **198**, 509
— (1950) see *Lancet* ii 409
Bulloch, W, Fildes, P (1912) Treasury of Human Inheritance London vol i, p 169
Dieter, D G Spooner M Pohle, F J (1949) *Blood*, **4** 120
Graham J B, Buckwalter, J A, Hartley, L J, Brinkhous, K M (1949) *J exp Med* **90** 97
Hewlett, J S, Haden, R L (1949) *J Lab clin Med* **34**, 161
Lee, R I, White, P D (1913) *Amer J med Sci* **145**, 495
Lempert, H (1935) *Lancet* i, 151
Lozner E L, Jolliffe, L S Taylor, F H L (1940) *Amer J med Sci* **199**, 318
Madison, F W, Quick, A J (1945) *Ibid* **209**, 443
Merskey C (1950) *J clin Path.* **3**, 301
— (1951) *Quart J Med* (in the press)
Owren P A (1947) *Lancet*, i, 446
Quick, A J (1943) *Amer J Physiol* **140** 212
— (1947) *Amer J med Sci* **214**, 272
— Favre Gilly, J E (1949) *Blood*, **4** 1281
Soulier, J P (1950) *Acta med scand* **137**, 1
Stefanini, M (1951) *Lancet*, i 606
— Crosby W H (1950) *Blood*, **5** 964
Taylor W K (1940) *Lancet*, ii 312

ABDOMINAL EMERGENCIES FROM SPONTANEOUS RUPTURE OF ENDOMETRIAL CYSTS

THOMAS DEAN
F R C S E, M R C O G
SENIOR OBSTETRICAL AND GYNÆCOLOGICAL REGISTRAR, ROYAL INFIRMARY, LEICESTER

DURING the past thirty years endometriosis has excited much interest and discussion In 1921 Sampson gave the first clear cut picture of this disorder, which of late years has been treated surgically

While no single theory seems to explain every case of endometriosis, two theories explain a very large proportion of them Sampson's (1921) original theory of retro grade tubal implantation of endometrium seems to explain satisfactorily the origin of many cases of pelvic endo metriosis, but not endometriosis in extragenital situa tions, such as the umbilicus, groin, and labia Today, the theory of metaplasia of cœlomic epithelium has been generally accepted as the only one adequately accounting for endometriosis in these situations

The four main symptoms of endometriosis are (1) acquired dysmenorrhœa, (2) dyspareunia, (3) relative or actual sterility, and (4) interference with the menstrual cycle—either menorrhagia or metrorrhagia, or both

Chronic and progressive dysmenorrhœa, mainly before or during the period, is extremely common in endo metriosis The pain is usually limited to the hypo gastrium, but may radiate to the sacro iliac joints or to one or both iliac fossæ Pain in the rectum during a menstrual period is an uncommon but reliable symptom of endometriosis of the rectovaginal septum Sterility is a common symptom and is especially significant when, after a normal pregnancy and labour early in marriage, a long period of sterility ensues for no obvious reason Commonly associated with this symptom is dyspareunia, which is usually progressive This is due to endometriosis of the rectovaginal septum with or without endometrial nodules in the posterior fornix of the vagina Menorrhagia and irregular bleeding are common symptoms, occurring in about half the cases

Endometrial cysts often perforate, even when quite small. If the cyst and the perforation are small, and the pelvic peritoneum relatively insensitive owing to past endometrial deposits, the patient experiences few symptoms Sharp hypogastric pain before or during menstruation may be the only symptom from these minute perforations If the cyst is large, perforation causes the severe symptoms of acute peritonitis, with acute generalised abdominal pain and rigidity of the anterior abdominal wall Possibly peritonitis is a misnomer as there is no positive evidence of bacterial infection, and peritoneal irritation or peritonismus might be a more accurate designation It is well known that even small leakages of "chocolate" fluid give rise to intense irritation, dense adhesions, and moderate pyrexia 6 such emergencies have arisen at the Leicester Royal Infirmary in the last two years—3 of them in the space of three months

CASE-RECORDS

Case 1 —A married woman, aged 48, was admitted on July 28, 1948, with a forty eight hour history of severe hypogastric pain and pain in both iliac fossæ The pain had been constant, and had not radiated She had vomited a dark fluid once

At the age of 20 years, she had had a normal pregnancy and delivery The periods, which began at the age of 14 years, had been regular (7/21), with moderate bleeding For the past ten years there had been progressive dysmenorrhœa, and for some years she had had leucorrhœa between periods with a yellow non irritant discharge Her last period had begun two days before admission. She had no urinary symptoms, and bowel action was normal

During an operation for herniorrhapy in September, 1948, endometriosis was noted on opening the peritoneal sac

Examination —Temperature 98 6°F Pulse rate 96 per min. There was tenderness on superficial and deep palpation all over the lower abdomen which was rigid in both iliac fossæ, no mass was felt On vaginal examination, the uterus was fixed and retroverted, and an indefinite mass replaced the left and right adnexa The cervix appeared normal, but was tender on bimanual palpation, the posterior fornix was also tender Speculum examination showed no evidence of endo metrial nodules, and the bleeding from the cervix was consistent with a normal menstrual flow

Investigations —The urine was normal Blood-count red cells 2,580,000 per c mm, Hb 46%, colour index 0 9 White cells 16,000 per c mm (polymorphs 84%, eosinophils 2%, lymphocytes 13%, monocytes 1%)

Endometriosis with superadded small bowel obstruction was diagnosed

Operation —At operation, free "chocolate" fluid was found in the peritoneal cavity The greater omentum and a loop of small bowel were adherent to the posterior surface of the broad ligament Both ovaries were replaced by endometrial cysts The right cyst was about 3 in. in diameter, and the left cyst about 2 in in diameter Both were adherent to the posterior aspect of the broad ligament and lateral wall of the pelvis The right cyst had ruptured, and the site of perforation could be seen The uterus was retroverted and fixed, and contained three small subperitoneal fibroids The rectum and pelvic colon were adherent to the posterior surface of the cervix and body of the uterus The appendix and gall bladder were normal A subtotal hysterectomy with bilateral salpingo oöphorectomy was performed

Convalescence was normal and she was discharged to a convalescent home on the 12th day after operation.

Pathological examination of the organs removed at operation showed the uterus and endometrium to be normal Scanty endometrium was present in the walls of the cysts in both ovaries (figs 1 and 2)

Follow up —On Jan 10, 1951, the patient stated that she felt well, but she had had moderate menopausal symptoms, which were easily controlled by small doses of stilbœstrol There had been no dyspareunia or leucorrhœa since the operation, nor had there been any vaginal bleeding On vaginal examination the pelvis was clear, with no tenderness on bimanual examination

Case 2 —A married woman, aged 48, was admitted on May 25, 1949, complaining of severe hypogastric pain which radiated to the right iliac fossa She had vomited several times before admission

The patient had been married for twenty years but had had no children Her periods began at 12 years of age, and had been irregular (7/14–7/21) She had heavy loss during her periods,

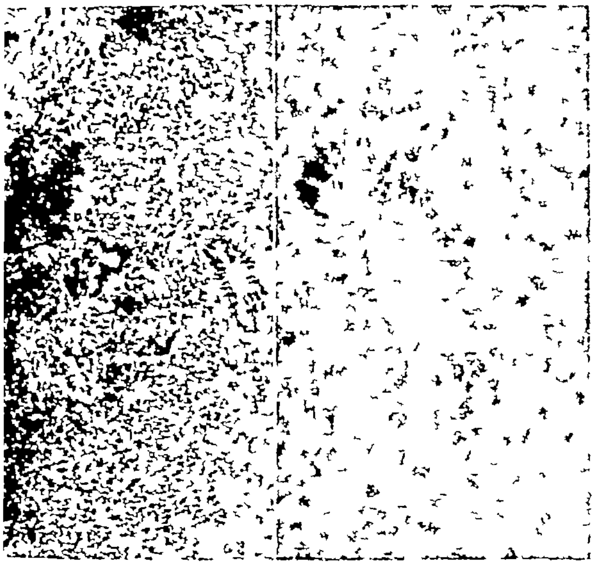


Fig 1 Fig 2

Fig. 1 (case 1)—Right ovary showing endometriosis (× 110)
Fig. 2—The same (× 500)

and there had been severe spasmodic dysmenorrhœa for many years; this had been getting worse. She complained of sterility; no contraceptives had been used throughout her married life. Dyspareunia had been present for some years, gradually becoming more severe. There was slight leucorrhœa between periods. The last period began twenty four hours before admission.

Examination.—Temperature 99·4°F. Pulse-rate 100 per min. There was generalised rigidity of the abdomen with muscular guarding, especially in the lower part, and tenderness on superficial and deep palpation, especially in the umbilical region and in the right iliac fossa. No mass was felt. On vaginal examination the uterus was bulky, retroverted, and fairly fixed. The right adnexa was replaced by an indefinite mass which appeared to be cystic. The left adnexa was not felt. The cervix was normal and nulliparous. On bimanual examination there was exquisite tenderness in the posterior fornix and on movement of the cervix. A speculum examination showed the cervix to be normal with no endometrial nodules in the posterior fornix. A normal menstrual flow was present.

Investigations.—The urine was normal. White blood-cells 17,000 per c.mm.

Acute appendicitis with generalised peritonitis was diagnosed.

Operation.—At operation a considerable amount of "chocolate" fluid escaped from the peritoneal cavity. The omentum was adherent to the posterior part of the broad ligament. The uterus was bulky and the size of a ten-week pregnancy; it was retroverted and fixed, and was adherent to the rectum posteriorly throughout its whole length. No subperitoneal fibroids were seen. The right ovary was replaced by a cyst adherent to the posterior surface of the broad ligament, the posterolateral surface of the uterus and the side wall of the pelvis. The cyst was partially collapsed, and a perforation was seen in its wall. The left ovary and tube were firmly bound down to the posterior surface of the broad ligament. Total hysterectomy with bilateral salpingo-oöphorectomy was carried out.

Postoperative progress was uneventful and the patient left hospital for convalescent home on the 13th day after operation.

Pathological examination showed that the right ovary contained a cyst, while the left ovary was relatively normal. Unfortunately microscopical sections were not examined.

Follow-up.—On Jan. 14, 1951, the patient stated that she had improved considerably since the operation, and complained only of menopausal symptoms. These were rather severe, but were alleviated to some extent by stilbœstrol given for several months. Vaginal examination showed the vagina to be adequate and well healed. On bimanual examination the pelvis was clear. She said that coitus was normal, and dyspareunia had disappeared.

Case 3.—A married woman, aged 38, was admitted on Aug. 8, 1950, with a twenty-four-hour history of continuous severe colicky pain in the umbilical region, and a six-hour history of pain in the tip of the right shoulder. She had vomited yellow fluid twice. Micturition was normal, but she was constipated.

At the age of 25 she had had a normal pregnancy and delivery. Her periods began at 13 years of age, and were regular (3/31), with scanty loss. She had not suffered from dysmenorrhœa or menorrhagia. The last menstrual period began, at the expected time, twenty-four hours before admission. In 1926 the patient had had an operation for drainage of an appendix abscess, and in 1943 appendicectomy; and in 1950 she was admitted to hospital with subacute intestinal obstruction, for observation, but she was not operated on.

Examination.—Temperature 100·4°F. Pulse-rate 100 per min. There was some tenderness and rigidity of the lower abdomen on superficial and deep palpation, but no real evidence of general peritonitis. On vaginal examination the cervix was firm and closed. The uterus was bulky, anteverted, and relatively mobile. Tenderness on bimanual examination prevented any clear definition of the adnexa. The right adnexa appeared to be replaced by an irregular mass; the left adnexa could not be outlined. Speculum examination showed the cervix to be normal, and there was no evidence of endometrial nodules in the posterior fornix. There was a normal menstrual flow.

Investigations.—The urine was normal. Blood-count: white cells 12,000 per c.mm.; red cells 4,130,000 per c.mm.; Hb 77%; colour-index 0·94. Radiography of chest and abdomen were normal.

Subacute intestinal obstruction was diagnosed.

Operation.—At laparotomy a moderate quantity of "chocolate" fluid escaped from the peritoneal cavity. An endometrial cyst approximately 4 in. in diameter replaced the left ovary; it seemed to be unruptured. An endometrial cyst, containing a minute but obvious perforation, replaced the right ovary. The uterus was bulky and anteverted, and in the region of the right cornu contained one visible subperitoneal fibroid about 1 in. in diameter. The tubes and ovaries were adherent to the posterior pelvic peritoneum, the posterior aspect of the broad ligament, and the side walls of the pelvis. Neither the small gut nor the greater omentum were adherent to the pelvic mass, although both were heavily contaminated by "chocolate" fluid. The cæcum and gall-bladder were normal. Total hysterectomy and bilateral salpingo-oöphorectomy was carried out.

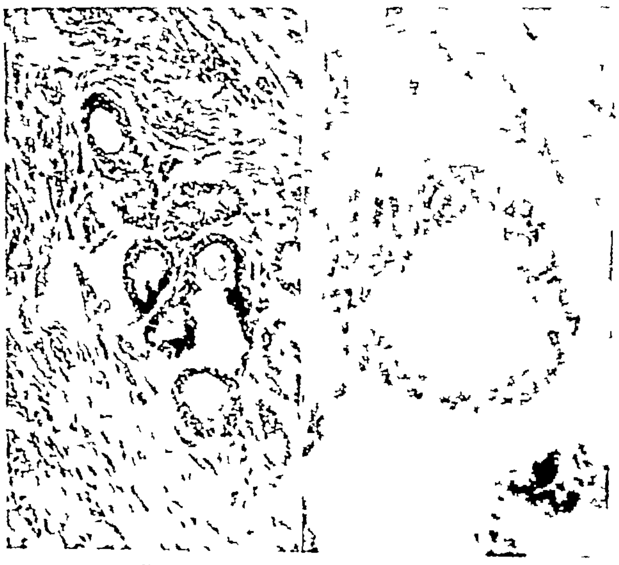


Fig 3 Fig 4

Fig 3 (case 3)—Right ovary showing endometriosis (× 110)
Fig 4—The same (× 500)

IMMUNISATION WITH INFLUENZA VIRUS A VACCINES

COMPARISON OF INTRADERMAL AND SUBCUTANEOUS ROUTES

J C Appleby
B Sc Lond , Ph D Reading
BACTERIOLOGIST, DEPARTMENT OF MEDICINE, UNIVERSITY OF SHEFFIELD

F Himmelweit
M D Berlin, Ph D Lond , M R C P E
DIRECTOR, DEPARTMENT OF VIRUS RESEARCH, WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, ST MARY'S HOSPITAL MEDICAL SCHOOL, LONDON

C H Stuart-Harris
M D Lond , F R C P
PROFESSOR OF MEDICINE, UNIVERSITY OF SHEFFIELD

Evidence has been brought forward in the U S A to show that influenza virus vaccines are better given intradermally than subcutaneously (Van Gelder et al 1947, Weller et al. 1948, Bruyn et al 1949, Rantz and Randall 1949) The advantages claimed for the intradermal route are that it (1) reduces the risk of serious general reactions , and (2) saves vaccine because an intradermal dose smaller than the usual subcutaneous one produces an equally good antibody response and should therefore be equally effective in immunisation against actual infection

Bruyn and co workers (1949) were dealing with the immunisation of children, in whom serious reactions are frequent when virus vaccine is given subcutaneously in the usual concentration This seems important from the theoretical standpoint of the factors known to be concerned in the antibody response to influenza vaccine It has been repeatedly shown that the amount of antibody formed in response to a particular quantity of influenza virus antigen partly depends on the person's pre immunisation level of antibody The response to a particular antigen, in terms of the change in titre, may be impressive in people with a low initial level of antibody and negligible in those with a high initial level (Hirst et al 1942, Eaton and Martin 1942, Henle et al 1946) In view of the low level of antibodies to the influenza viruses normally found in children, they may be regarded as particularly sensitive indicators of influenza virus antigens The amount of antibody response is also governed, within limits, by the quantity of antigen given , and theoretically, because of their lack of pre existing antibodies, children might therefore respond at least as well to a small dose of antigen as to a large one, whereas adults might respond to large amounts of antigen but not to small amounts This means that the small dose of vaccine given intradermally to children, which apparently can have as good an antigenic effect as the ten times larger subcutaneous dose, might be entirely ineffective in adults There is clearly a need, therefore, for a further comparative trial in adults of influenza virus vaccine given intradermally and subcutaneously

METHOD

The plan was to inoculate alternate volunteers intradermally and subcutaneously with a concentrated virus vaccine Previous experience had shown that the influenza virus vaccine adsorbed on aluminium phosphate* was an effective antigen with a low rate of general reactions, and this preparation was therefore chosen for the subcutaneous inoculations However, since vaccines containing aluminium phosphate cause mild irritation when injected into the skin, the intradermal inoculations were done with a concentrate prepared by red cell adsorption and elution of the virus, using a 5% suspension of fowl red cells The vaccines were made from similar pools of egg allantoic fluid, infected with the same A strain of virus The concentration of virus in each vaccine was equalised, the final level being some ten times as high as in the original allantoic fluids. The doses given were 0 1 ml intradermally or 1 ml subcutaneously Four vaccines were prepared two from the PR8 strain, and two from the NED/1/49 strain representative of the A prime group The hæmagglutinin titres were 1/12,800 for the PR8 eluate vaccine and 1/19,200 for the NED eluate The vaccines adsorbed on to aluminium phosphate were adjusted so that the concentration of hæmagglutinin was about the same as in the eluate vaccines Formaldehyde in a final concentration of 1 in 4000 was added to all vaccines to inactivate the virus

The volunteers were nurses of the United Sheffield Hospitals, medical students at the University of Sheffield, and men of the R A F The inoculations were done in April and October, 1950, when there were no recognised outbreaks of influenza A in Great Britain Three blood samples for the estimation of serum antibody levels were collected—before inoculation, two weeks after inoculation, and two months after inoculation

Antibodies were titrated by the Salk technique of agglutination inhibition, using a concentrated virus antigen with four final hæmagglutinating doses and fowl red cells (0 125% final concentration) The antigens were derived from single batches of red cell eluates from pooled allantoic fluids infected with the respective virus strains Titres were expressed as reciprocals of the appropriate serum dilution

REACTIONS

The PR8 virus vaccines were used for 40 nurses and 18 R A F men, half of each group receiving one vaccine,

TABLE I—ANTIBODY TITRES AFTER IMMUNISATION WITH INFLUENZA A VACCINES (PR8 STRAIN) (HOMOLOGOUS VIRUS)

Case no	Intradermal		Case no	Subcutaneous	
	Mean initial titre	Mean post-vaccination titre		Mean initial titre	Mean post-vaccination titre
22	313	213	25	13	1440
23	133	373	28	267	2133
24	27	640	29	360	400
26	120	200	31	93	2133
27	480	800	32	160	1920
30	240	1920	33	13	107
34	40	240	36	120	640
35	60	960	37	60	3840
38	20	160	46	160	320
39	100	1920	48	60	640
40	120	480	50	187	5120
41	27	2133	51	53	2133
42	20	160	54	120	1280
43	187	3413	55	100	1600
44	400	400	56	15	7680
45	60	480	57	80	8533
47	25	160	58	40	160
49	240	320	59	40	640
52	120	240	60	120	320
53	173	3413	61	133	6827
143	120	320	146	120	1920
145	160	480	148	60	2560
151	27	4267	150	60	960
155	120	120	152	15	7680
157	240	400	154	107	7680
158	80	240	156	40	640
160	160	2560	159	10	240
163	10	160	164	20	1920
165	160	960	166	20	960
Geometric mean titre	83	540		57	1350
Antibody rise	× 6 5			× 23 6	

---

* These vaccines were prepared by one of us (F H) by adsorbing the virus from allantoic fluids on to aluminium phosphate The final preparations were adjusted to contain 6 mg of aluminium phosphate per ml and 1 part of Merthiolate per 10 000 in addition to the required amount of virus (inactivated with formalin 1 in 4000) in neutral $M/10$ phosphate buffer solution

and half the other There were no febrile reactions in any of the nurses Of the 20 nurses inoculated subcutaneously, 6 complained of transient tiredness, aching, or dizziness in the next 24 hours, and 1 had a severe headache and was off duty for a day, 15 had trifling and 1 moderate local reactions with œdema and tenderness at the site of injection Of the 20 nurses inoculated intradermally, 2 complained of tiredness or aching in the next 24 hours, and 2 had trifling local reactions The 18 R.A.F men were not examined in detail, but none of them reported a severe general or local reaction

The NED-virus vaccines were given to 45 student volunteers, of whom 23 were injected intradermally and 22 subcutaneously No severe general reaction was encountered, but 1 student in each group complained of slight headache in the evening after the injection Mild local reactions, with redness and tenderness at the site of injection were noted in 9 students who had subcutaneous vaccine and in 2 who had intradermal vaccine The remainder of the 45 students either had no reaction at all or only trifling local changes

TABLE II—ANTIBODY TITRES AFTER IMMUNISATION WITH INFLUENZA A PRIME VACCINES (NED/1/49 STRAIN) (HOMOLOGOUS)

Case no	Intradermal		Case no	Subcutaneous	
	Mean initial titre	Mean post vaccination titre		Mean initial titre	Mean post vaccination titre
1	30	160	24	40	120
2	30	240	25	60	240
3	40	80	26	10	240
4	20	80	27	40	320
5	60	240	28	120	240
6	15	120	29	15	1920
7	20	80	30	20	960
8	20	160	31	30	50
9	40	80	32	15	80
10	25	60	33	30	240
11	20	80	34	60	240
12	60	80	35	20	853
13	60	120	36	50	120
14	40	160	37	80	160
15	20	80	38	50	120
16	37	320	39	80	640
17	20	47	40	40	160
18	80	80	41	10	80
19	40	80	42	80	320
20	40	160	43	40	240
21	60	120	44	10	160
22	30	80	45	20	640
23	40	40			
Geometric mean titre	33	104		33	242
Antibody rise	× 3 1			× 7 3	

ANTIBODY RESPONSE TO HOMOLOGOUS VIRUS

PR8 virus vaccines

The antibody responses were determined by comparing the antibody level before vaccination with that two weeks afterwards, both pairs of sera being titrated at the same time on more than one occasion Table I gives the arithmetic means of the duplicate or triplicate estimations for each serum Log mean titres are about normally distributed in a population, so the statistical analysis has been done on the logarithms of these averages, and the final results have been transformed back to the original units Accordingly it is the geometrical mean titre that has been given for each group in table I

The range of initial titres for those receiving vaccine either intradermally or subcutaneously was similar, and lay between 10 and 480 for the intradermal group and 10 and 360 for the subcutaneous group The geometric means of the initial titres were 83 for the intradermal and 57 for the subcutaneous group The range of post-vaccination titres lay between 120 and 4267 for the intradermal group and between 107 and 8533 for the subcutaneous group The geometric means were 540 and 1360 respectively, and the 95% confidence limits for the post-vaccination groups were calculated as shown in table III The post vaccination geometrical mean titre was significantly greater in the subcutaneous than in the intradermal group ('t' with 56 degrees of freedom was 3 07, and the probability of this being exceeded by chance is less than 1/100)

TABLE III—SUMMARY OF RESULTS

Vaccine	Vaccination group	No of cases	G.M initial titre	G.M post vaccination titre
PR8	Intradermal	29	83 (57 122)	538 (364 796)
	Subcutaneous	29	57 (41 82)	1352 (861, 2123)
NED/1/49	Intradermal	23	33 (27 40)	104 (83 123)
	Subcutaneous	22	33 (24 45)	242 (165 355)

The figures in parentheses give the 95% confidence limits for the geometric means being transformed from the expressions (arithmetic mean ± 2 s e) in the logarithmic units

Because a variation in antibody response to a vaccine has been ascribed to different initial antibody titres, the distribution of initial titres in the two groups was examined more closely There were 16 persons with initial titres of 80 or less in the subcutaneous group, compared with 11 persons in the intradermal group However, the antibody response in the intradermal group was far below that obtained in the subcutaneous group With the intradermal vaccine, 11 persons with a geometric mean initial titre of 30 gave a post vaccination mean titre of 433 The corresponding post vaccination figure for the 16 subcutaneously immunised persons with a geometric mean initial titre of 30 was 1234

Even in the persons with low initial titres a better antibody response was therefore induced by subcutaneous vaccine than by intradermal vaccine

NED virus Vaccine

Table II gives the antibody titres in the two groups receiving NED virus vaccine intradermally or subcutaneously The geometric mean initial titre for each group was 33, and the post vaccination was 104 in the intradermal group and 242 in the subcutaneous group—a difference which is again statistically significant ('t' for 43 degrees of freedom being 3 9, $P < 1/1000$) The antibody response was therefore greater in the volunteers receiving vaccine subcutaneously than in those inoculated intradermally The distribution of initial titres in both series was substantially the same, the numbers with low titres being actually slightly greater in the intradermal group, hence the greater antibody response in the subcutaneous group was unlikely to have been due to this factor

Decline in Antibody Response

The antibody levels two months after vaccination were compared with those found after two weeks in each of the four groups Sera were tested from 26 of the volunteers receiving PR8 vaccines intradermally and 24 receiving vaccine subcutaneously The tests were carried out on the same day with the pairs of serum from each person collected two weeks and two months after vaccination The serum pairs from 14 of the intradermal and from 10 of the subcutaneous group gave identical titres, but lower titres were found in the serum collected after two months in 8 intradermally and 14 subcutaneously immunised persons. The fall in titre was to a quarter or half of that encountered two weeks after vaccination, except in 1 case The serum titre of this person, who had received vaccine intradermally, declined from 1/3840 to 1/80 Possibly a mistake had occurred in the serum sampling in this case

In no case in the subcutaneous group did the titre increase but in 4 of the intradermal group the titre increased twofold in two months The geometric mean titre of the two month serum samples was still statistically greater in the subcutaneous group (750) than that in the intradermal group (290)

In the NED vaccinated series serum was obtained two months after inoculation from 16 of the intradermal and 20 of the subcutaneous group Identical titres were found in the pairs of sera from the same persons two weeks and two months after inoculation in 13 of the intradermal and 14 of the subcutaneous group 3 of the intradermal and 6 of the subcutaneous group showed a fall in titre to half of that present two weeks after inoculation No rises in antibody were found in either group

It was concluded that in most people the antibody titre present two months after vaccination was the same as that present two weeks after injection with either strain of virus In a few people, however, antibody levels had declined to a quarter or half of those present two weeks after inoculation It mattered but little whether the vaccine was given subcutaneously or intradermally

Response to Heterologous Virus

Tests were made of sera from people in the various groups with a virus strain other than that utilised in the preparation of the vaccine Thus pairs of sera from 25 people immunised with PR8 vaccine either intradermally or subcutaneously were tested against the NED virus The sera were chosen as being representative of the various ranges in antibody response to PR8, and the titre of the post vaccination specimens varied from 120 times the pre vaccination titre down to identical values The titres of the pre and post vaccination sera against the NED virus were identical with each other in 23 pairs and showed only a twofold increase in titre in the remaining cases These results agree with the published observations of other workers and indicate the ineffectiveness of PR8 antigen in stimulating antibody against the influenza A prime viruses (Sigel et al 1948, Loosh et al 1948, Salk and Suriano 1949)

Observations were made with sera from 26 people immunised either intradermally or subcutaneously with the NED virus PR8 antigen and a red cell eluate prepared from a recently isolated influenza A prime virus A/SWE/1950 were used in the tests

TABLE IV—SERA FROM PEOPLE IMMUNISED WITH NED/1/49 VIRUS

Route	Case no	NED/1/49		SWE/50		PR8	
		Initial titre	Post vacc titre	Initial titre	Post-vacc titre	Initial titre	Post vacc titre
Intradermal	1	20	160	80	160	320	320
	2	30	240	40	160	160	320
	4	20	80	80	160	320	640
	6	15	120	20	160	20	40
	8	20	160	80	320	40	40
	10	25	60	40	160	640	640
	11	20	80	40	160	40	80
	14	40	160	80	320	40	160
	15	20	80	80	160	320	320
	16	37	320	40	160	160	320
	17	20	47	20	80	10	10
	20	40	160	40	320	40	80
Subcutaneous	26	10	240	40	320	160	160
	27	40	320	80	640	160	320
	29	15	1920	20	320	320	2560
	30	20	960	40	640	80	320
	32	15	80	40	160	80	160
	33	30	240	20	160	80	80
	34	60	240			640	640
	35	20	853	20	1280	80	320
	39	80	640	80	320	40	160
	40	40	160	40	160	80	160
	42	80	320	40	160	80	1280
	43	40	240	40	160	80	320
	44	10	160	10	160	80	320
	45	20	640	10	320	160	320
Geometric mean titre		25 9	216 8	37 8	229 4	91 5	220 3
Antibody rise		× 8 2		× 6		× 2 4	

Table IV shows that, though the titres of antibodies against the PR8 virus underwent a change as a result of the vaccination in some people, the degree of change was quantitatively smaller than with homologous virus. In one person the antibody increase to PR8 was, however, greater than that to the homologous virus (case 42)

The results of tests with the Swedish virus were a little more difficult to interpret, but compared with the results with NED virus the differences were not large and seemed to be due to a high titre in the pre vaccination serum As already shown (Stuart Harris and Miller 1947) the influenza A prime virus strains are influenced by the exact source of the fowl red cells used in the test When the same fowl was used as a source of cells in tests made with NED virus and SWE virus strains the results were closely similar But the results with the pre vaccination sera varied when different fowl cells were used with the different virus A prime strains

The results with heterologous viruses did not seem to vary according to the type of vaccination used

Finally, the sera from people immunised subcutaneously with a vaccine concentrated by centrifugation and prepared from the A/SWE/1950 strain in Copenhagen (personal gift from Dr von Magnus) were also tested against the SWE and NED viruses Closely similar antibody titres were obtained with the two viruses, and it seems probable that any difference existing between the virus strains was insufficient to influence immunisation in man

DISCUSSION

Several prerequisites for a virus vaccine against influenza have become apparent in the past few years Of these the antigenic constitution of the vaccine has proved to be paramount Yet from a practical standpoint two other desirable features have emerged (1) the use of the vaccine should be attended by a low rate of reaction, and (2) the greatest possible economy should be achieved in the use of raw materials, particularly of the egg fluid necessary for each dose of vaccine. The red cell eluate vaccine suffers from two disadvantages (1) reactions following its use subcutaneously are significant in number and degree, and (2) a relatively large volume of infected allantoic fluid is necessary to provide the antigen needed for a single inoculum The incidence of reactions, particularly febrile or systemic ones, was shown by Salk (1948) to depend on the virus content of the vaccine In the trial carried out in Great Britain in 1945 (Stuart Harris 1947), 1406 persons received 1 ml. of tenfold concentrated eluate vaccine subcutaneously, and 31 (2 2%) of them had local reactions, 92 (6 57%) had general reactions, and 13 (0 92%) had fever These figures represent, if anything, a lower incidence of reactions than that recorded by other workers, particularly Sadusk et al (1949)

The decision in the present study to use virus vaccine adsorbed on to aluminium phosphate arose from previous experience of its low incidence of reaction coupled with satisfactory power to stimulate antibody formation Since previous workers have compared the antibody stimulating power of a vaccine given intradermally with that of a tenfold dose of the same [illegible] given subcutaneously, the two virus [illegible] brought to similar de[illegible] concentration com[illegible] was adopted b[illegible] field experiments [illegible] Influenza (1944) in U S A

The results given above indicate that 1 ml doses of tenfold concentrated virus vaccine adsorbed on to aluminium phosphate and given subcutaneously are attended by an insignificant degree of systemic reaction Nor did significant reactions follow 0 1 ml doses of eluate vaccine given intradermally, but the antibody response to this amount of vaccine intradermally is clearly inferior to that produced by the 1 ml. dose of adsorbed vaccine subcutaneously Thus the use of this amount of eluate vaccine intradermally cannot be relied on to produce in adults a maximal antibody response

The vaccine adsorbed on to aluminium phosphate, which must be given subcutaneously, is unfortunately as extravagant in eggs as the ordinary eluate vaccine given by the same route. It remains to be seen whether a smaller dosage or lesser concentration of adsorbed vaccine would be as effective a stimulant to antibody formation as that used by us

Vaccine adsorbed on to calcium phosphate was considered by Salk (1947) to exert an antigenic effect as great as that of a larger amount of unadsorbed vaccine given by the same route Similar observations were made by one of us (F H) with vaccines adsorbed on to aluminium phosphate given to mice. This superior antigenic effect was attributed by Salk in his investigations to a relatively slow release of antigen Such an effect might be responsible for the good results obtained by us with the vaccines adsorbed on to aluminium phosphate However, if a really longer antigenic effect was produced by adsorbed vaccine in our case, it seems likely that a divergence between the antibody levels at the interval of two months after inoculation in the subcutaneous and the intradermal groups would have been apparent

When the antibody response induced by vaccination is determined for heterologous viruses as well as the homologous strain, the results are complex. It has been shown conclusively by other workers and confirmed by us that the standard PR8-virus strain does not stimulate antibodies against the A prime group of strains. However, the A prime antigen does stimulate some antibody formation against the PR8 virus, but the response to inactivated virus is much less robust and more irregular than that produced by infection In infection (Stuart-Harris and Miller 1947, Stuart Harris et al 1949) the antibody response may be demonstrable more readily and more often by using the PR8 antigen in the in vitro tests with human sera than by using the homologous A prime antigen Further work is desirable with different strains of the A prime group not only from the standpoint of breadth of antibody response but also because these strains seem to be relatively poor antigens (Salk et al. 1949) The selection of an A prime antigen which is highly antigenic is of great importance for the future use of influenza vaccine

SUMMARY

Volunteers were inoculated subcutaneously with 1 ml doses of influenza virus vaccines adsorbed on to aluminium phosphate, or intradermally with 0 1 ml. amounts of virus vaccines prepared by red cell adsorption and elution All the vaccines were concentrated tenfold in terms of the original allantoic fluids The vaccines were prepared either from influenza A virus (PR8) or an A prime strain (NED/1/1949)

General reactions were insignificant, and local reactions, though frequent after subcutaneous immunisation, were trifling [illegible] original units According to the strain of virus incor titre that has been given for each [illegible]termined by comparing

The range of initial titres for thos[illegible]fter vaccination by either intradermally or subcutaneously [illegible]ficantly higher lay between 10 and 480 for the [illegible] immunisation in the 10 a[illegible] the [illegible] volunteers compared with those in the volunteers inoculated intradermally

The enhancement of antibody levels induced by the PR8 vaccines seemed to be greater than that following the A prime virus, irrespective of the route of immunisation

The antibody titres attained two weeks after immunisation were maintained in more than half the volunteers, as shown by serum samples collected two months after vaccination

Though the PR8 vaccines did not stimulate antibodies against the 1949 A prime virus, the vaccines made from the latter occasionally induced alterations in titre of antibodies to PR8 virus, and regularly produced a rise in antibodies to a second A prime virus (A/SWE/1950)

We wish to thank all the volunteers and those assisting with the inoculations particularly Dr P W W Gifford, Dr H. R Worth, and Dr D A J Tyrrell, of the University of Sheffield and the United Sheffield Hospitals, and Flight-Lieutenant J H B Urmston, R.A.F , the Director of Hygiene of the Royal Air Force for his coöperation and for permission to cite the results obtained in the Servicemen and Mr R F Wrighton, statistician to the department of social medicine of the University of Sheffield

REFERENCES

Bruyn H B Meiklejohn G Brainerd H D (1949) *Amer J Dis Child* 77 149
Commission on Influenza (1944) *J Amer med Ass* 124, 982
Eaton M. D Martin W P (1942) *Amer J Hyg* 36 255
Henle W Henle G Hampil B Maris E P Stokes J jun. (1946) *J Immunol.* 53 75
Hirst G K Rickard, E R Whitman L Horsfall F L jun (1942) *J exp Med* 75 495
Loosli, C G Schoenberger J Barnett G (1948) *J Lab clin Med* 33 789
Rantz L A. Randall, E (1949) *Stanford med Bull* 7 25
Sadusk J F jun. Bassett P C Meddaugh J S (1949) *Amer J Hyg* 49 143
Salk J E (1947) *J Immunol* 57 301
— (1948) *Ibid* 58 369
— Suriano P C (1949) *Amer J publ. Hlth,* 39 345
— — Laurent A. M. McGinnis R C (1949) *Fed Proc.* 8 410
Sigel M. M. Shaffer F W Kirber M. W Light A. B Henle W (1948) *J Amer med Ass* 136 437
Stuart Harris C H (1947) *Lancet* i 201
— Miller M. H (1947) *Brit J exp Path* 28 394
— Laird J Tyrrell D A. Kelsall M. H Franks Z C Pownall M. (1949) *J Hyg Camb* 47 434
Van Gelder D W Greenspan F S. Dufresne N E (1947) *Nav med Bull., Wash.* 47 197
Weller, T H. Cheever F S Enders J F (1948) *Proc Soc exp Biol N Y* 67 96

"MYOCARDITIS" AND AORTIC HYPOPLASIA IN ARACHNODACTYLY

REPORT OF A CASE

A G W WHITFIELD
M.D Birm., M.R C P
ASSISTANT PHYSICIAN UNITED BIRMINGHAM HOSPITALS

W MELVILLE ARNOTT
T D , M.D Edin., F.R C.P , F.R C.P.E
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF BIRMINGHAM

J L STAFFORD
M.B Birm.
ASSISTANT PATHOLOGIST UNITED BIRMINGHAM HOSPITALS

ARACHNODACTYLY was first described by Marfan (1896) under the name of dolichostenomelia and is consequently often called Marfan's syndrome. Méry and Babonneix (1902), who described Marfan's original case some six years later, called it hyperchondroplasia Poynton (1903) was the first in this country to refer to it and called it atavism, but Achard (1902), in France, suggested arachnodactyly, and this name has come into common use

Well over 200 cases have been recorded, and the abnormalities that characterise the condition are now well known. Briefly, they comprise abnormal height, poorly developed musculature, absence of subcutaneous fat, long slender extremities, particularly the fingers and toes, abnormal extensibility of joints, with a tendency to contractures, a funnel shaped chest or pigeon breast with kyphosis, scoliosis, and often winging of the scapulæ, a dolichocephalic skull with prominent supraorbital ridges, a high arched palate, and a tendency to malformation of the external ears, pes planus, spurring of the os calcis, and sometimes elevation of the patellæ, and in some instances congenital abnormalities of the lungs and a propensity to pneumonia

Over 60% of cases present ocular abnormalities (Rados 1942), usually dislocation of the lens, iridodonesis, and a small pupil which dilates poorly with mydriatics The high incidence of ophthalmic defects is the reason why so many cases have been published in ophthalmological journals

A somewhat smaller proportion of cases present cardiac abnormalities Seventy two of the recorded cases had some objective cardiac abnormality, but in only ten was its precise nature verified post mortem These and other cases which came to necropsy are summarised in the accompanying table, which shows that patent foramen ovale, dissecting aneurysm of the aorta, dilatation of the aorta, abnormally high origin of the coronary arteries, and mitral and aortic valvular defects have been the commonest abnormalities

In most of the cases that have not come to necropsy the published data have been insufficient to identify the cardiac lesion In many the presence of a murmur, usually systolic, or of enlargement, or simply of "vitium cordis" alone is mentioned, but cases of patent foramen ovale, patent interventricular septum, pericarditis, aortitis, pulmonary stenosis, and mitral disease have all been described

In the case described here a type of cardiac disorder was present that, so far as we are aware, has not hitherto been recorded in arachnodactyly

CASE RECORD

A man, aged 35, was seen by one of us (A G W W) on April 1, 1950 He had been in bed for a year, and had been away from school for eighteen months with a "strained heart" at the age of 8 or 9 years The only symptom of this childhood illness that he could recollect was vomiting In 1939 he had been examined for life insurance and passed as a first class life, the examination, however, seems to have been extremely cursory The doctor who had examined him and also attended him during his childhood illness had died some years ago, so no more detailed information is obtainable The patient had worked hard as a farmer, hunted regularly, and had a very good exercise tolerance until October, 1949, when he had noted that he was becoming unduly tired, and his family had remarked that he did not look well and was losing his usual rubicund colour In January, 1950, he had first become aware of exertional dyspnœa, which became progressively worse, and in March, 1950, he had begun to have pain under the right costal margin on exertion—a pain which disappeared when he had rested for a few minutes In addition he had lost all his usual energy, and his weight had decreased by a few pounds There were no other symptoms apart from some vomiting during the four days immediately before he was first seen His doctor, who had been in attendance for several weeks before we first saw the patient, state that there had been no pyrexia, and he had not observed an rise of blood pressure

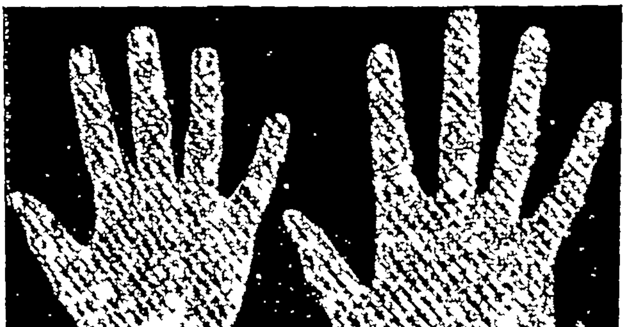


Fig 1—Patient's hand (on right) compared with hand of one of his physicians (height 6 ft. 3 in) Note disproportionate length of patient's ring finger

On examination the most striking initial impression was th patient's height, which he said was 6 ft 10 in He was no measured at the time, but at necropsy his height was foun to be 7 ft He was extremely thin, and there was virtuall no subcutaneous fat The supraorbital ridges were ver prominent, there was some dorsal kyphosis, the extremit were extremely long and slender, particularly the hands an feet, and the great toe appeared grossly abnormal in lengt partly because of contracture of all the other toes (figs 1 and 2 There was no œdema or dyspnœa, but the patient looked pal and was a little cyanosed, venous pulsation was evident in th neck, and a tender liver extended almost to the umbilicu The cardiac rhythm was normal, pulse rate of 124, bloo pressure 130–120/110 mm Hg, with alternation of 10 mm The apical impulse was in the fifth space in the anter axillary line, a grade II systolic murmur was audible a the apex, the pulmonary second sound was much accentu ated, and pronounced gallop rhythm was present, loudest i the tricuspid area The chest was clinically normal. Th clinical picture strongly resembled diphtheritic myocardit Radioscopy showed generalised cardiac enlargement withou prominence of the left auricle The lung fields were norma A blood count was normal, and the erythrocyte sedimentatio rate was 2 mm in 1 hr (Wintrobe) Repeated examinatio of the urine showed no albumin and no formed elements o microscopy A Wassermann reaction of the blood wa negative The electrocardiograms are shown in fig 3

Treatment—The patient was immediately admitted t hospital, and digoxin 0 25 mg was given four times dail by mouth No slowing of the pulse or diminution in venous pressure resulted, but ventricular extrasystoles became very frequent, so the digoxin was discontinued, and aminophylline and vitamin B_1 were tried The venous pressure rose steadily, pallor increased, and Cheyne Stokes breathing, hæmoptysis, œdema, albuminuria, and intractable vomiting developed Mercurial diuretics were given and digoxin therapy was resumed No improvement, however, resulted and, when the patient should have been fully digitalised, auricular fibrillation with a ventricular rate of 130–140 per min. developed Systemic congestion increased, and jaundice appeared. Venesection was done, but the patient's condition steadily deteriorated and he died seventeen days after admission. Throughout his stay in hospital he was afebrile, apart from three consecutive days on which pyrexia up to 100° was present. A blood culture was sterile

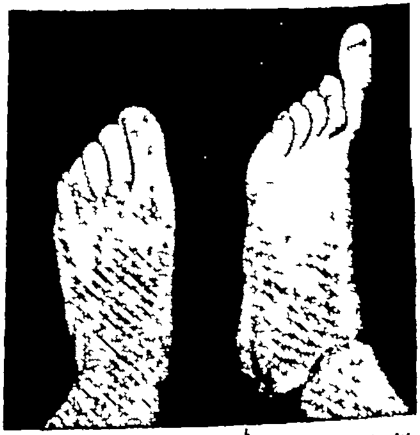


Fig 2—Patient's foot (on right) compared with foot of one of his physicians (height 6 ft. 3 in.) Note elongation of patient's great toe, contracture of all his other toes, and slight œdema of foot.

Necropsy Findings—The body weight was 94 6 kg Slight ascites was present, the pleural sacs contained 500 ml of straw-coloured fluid, and there was a pericardial effusion of 250 ml The *heart* was enlarged, weighing 910 g All the chambers of the heart were dilated, with ante mortem clot adherent to the right auricular wall the myocardium was firm and had some streaks suggesting fatty degeneration but no visible fibrous scars. The valves appeared normal, and the coronary arteries were free from atheroma, with their ostia dilated but in normal positions There was a valvular patency of the foramen ovale In the left auricular wall, over the area of MacCallum's patch the endocardium was thickened by a yellowish fatty deposit some 1 5 cm in dia

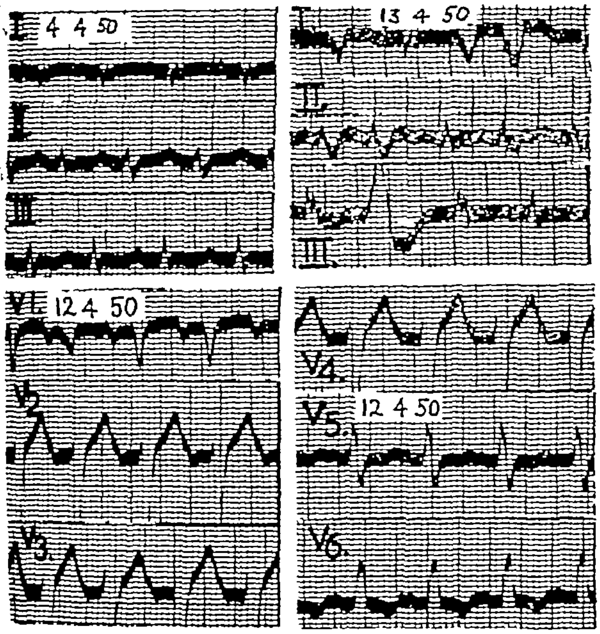


Fig. 3—Electrocardiograms showing right preponderance, low voltage ventricular extrasystoles TV, negative and auricular fibrillation supervening

meter. Histological examination of the myocardium revealed a fine diffuse fibrosis, most marked in the interventricular septum, with scattered areas where destruction of muscle fibres and replacement by collagen and fibrous tissue was evident (fig 4) Sections of the valve cusps showed no evidence of any post-rheumatic change The tissue from the area of MacCallum's patch consisted of scattered histiocytes in a loose myxomatous stroma, the appearances resembling the changes seen in an old mural thrombus The *aorta*, which showed only slight atheroma, had no localised constrictions but was relatively hypoplastic, with a circumference of 47 mm. (normal 52 mm.) The aortic intima contained diffuse fatty deposits without conspicuous atheromatous plaques, and the media showed mucoid degeneration and fine particulate calcification, changes of a degree within the range of normal for a person of the patient's age There was no evidence of the medio necrosis cystica of Erdheim Both *lungs* were congested, and basal peripheral hæmorrhagic infarctions were present with embolic clot occluding some of the smaller pulmonary arteries The *kidneys* were enlarged (670 g) and pale yellowish pink. The glomerular tufts were slightly enlarged, and debris was present in the spaces The tubules contained similar debris, and the tubular epithelium was uniformly granular There was no increase of supporting connective tissue, and the vessels were normal. The *liver* (2580 g), *spleen* (210 g), and *gastric mucosa* showed severe chronic venous congestion. No other significant changes were seen in these or other organs In particular the pituitary was of normal size and structure

DISCUSSION

The clinical picture in this case was that of an extremely severe myocardial insufficiency for which no cause was apparent other than arachnodactyly, whose association with various congenital and acquired abnormalities of the cardiovascular system is well known

Histological examination amply confirmed the "myocarditis," without abnormality of the coronary arteries

The aortic diameter of 15 mm has to be compared with a figure of 16 7 mm derived from the mean figure of 52 34 mm for the circumference of the aorta observed by Millar and Ross (1942) in 300 necropsies on adults It is therefore clear that in our patient, a man of exceptionally large stature, the aorta was smaller than the mean of normal people His blood pressure in the brachial artery was 130/110, and it may be inferred from his active habits and good exercise tolerance (farming and riding to hounds) before the onset of illness that his cardiac output was adequate His surface area (DuBois' formula) was 2 3 sq.m (normal 1 7 sq m), so it may be deduced as an approximation that his cardiac output was increased in the ratio of 2 3/1 7—i e , + 35% According to Poiseuille's law, pressure in a rigid tube varies directly as the first power of the volume flow, therefore, to deliver at the brachial artery an increased volume flow without reduction of pressure through a tube somewhat smaller than normal implies a 30–40% increase of ejection pressure by the left ventricle This factor alone calls for some slight hypertrophy of the left side of the heart, which in its dilated state was 15 mm thick (upper limit of normal 14 mm) compared with the right ventricular wall thickness of 4 mm (normal 5 mm) However, the cardiac weight (910 g) was nearly thrice the weight (326 g) regarded as normal for a male aged 30–40 (Bell and Hartzell 1924), hence other causes of cardiac enlargement must be considered There is nothing in the patient's clinical history to support a diagnosis of protracted hypertension. On the other hand, the kidneys weighed 670 g (normal 250 g) and the liver 2580 g (normal a fiftieth of the body-weight—i e , 1890 g), hence it seems there is a tendency to organ hyperplasia, which for want of a better explanation we regard as another aspect of the generalised dysplastic state It is perhaps appropriate to recall that great cardiomegaly in association with myocardial fibrosis, sudden death, and a familial incidence was described by Evans (1949) His cases, however, showed gross conduction defects and more extensive myocardial fibrosis So far as we have been able to ascertain, the

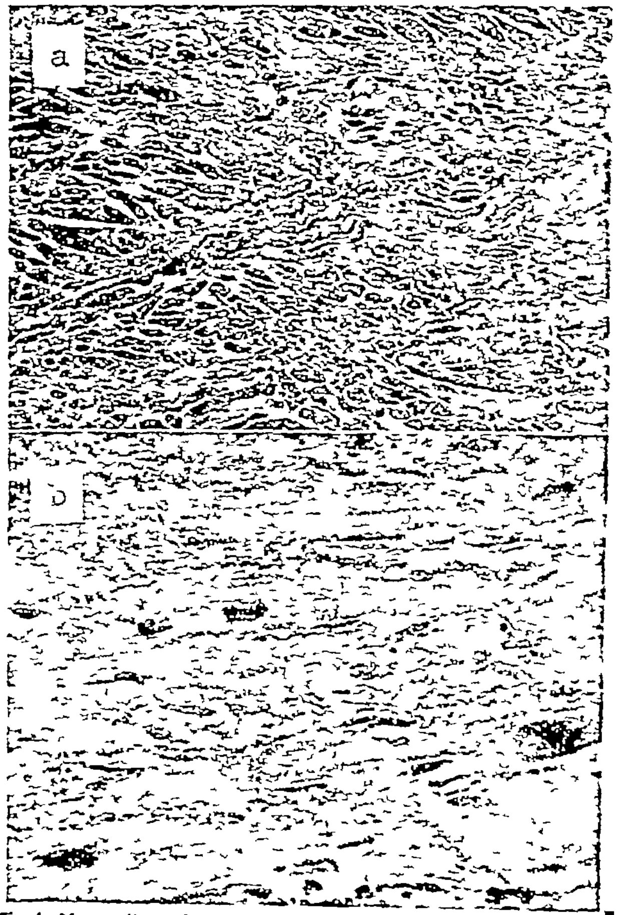


Fig 4—Myocardium of interventricular septum *a* **diffuse fibrosis with local replacement of muscle-fibres (× 90)** *b* **local destruction of muscle cells, with fine fibrosis (× 375) (Hæmatoxylin and van Gieson.)**

association of arachnodactyly with a pathological myocardium has not been previously recorded, and Uyeyama et al (1947) are the only workers who have referred to narrowing of the aorta, in their case the aorta was the seat of Erdheim's medionecrosis, and death resulted from a dissecting aneurysm

That our patient was the subject of arachnodactyly is, we think, beyond question None of the published cases have shown by any means all the manifold abnormalities that have been described as part of the syndrome, and in this case the abnormal height, poor musculature, lack of subcutaneous fat, prominent supra orbital ridges, long slender limbs, and particularly the appearance of the hands and feet left us in no doubt The actual hand/height and foot/height ratios were 12% and 17% respectively, both of which are above the normal ratios, which are given as 11% and 15% respectively by Gray (1945) The disproportionately long ring finger is well shown in fig 1, a similar condition was noticed by Marfan (1896) and by subsequent workers—e g, Burch (1936) Extreme elongation of the great toe (fig 2) was noted by Burch (1936) in two of his cases, and the contracture of the other toes has been described by many other workers (Marfan 1896, Weill 1932, Olcott 1940, Ellis 1940, Baer et al 1943) We did not find anything wrong with our patient's eyes, and he had no symptoms referable to them

There has been much speculation about the cause of arachnodactyly The abnormal height that is so commonly present suggests some disturbance of the pituitary gland Young (1929), Weill (1932), and Burch (1936) all reported abnormally small pituitary fossæ on radiography of the skull, and Rados (1942) demonstrated bridging of the clinoid processes in addition to diminution in the size of the sella turcica In o of Weill's (1932) cases that came to necropsy the pituita was small, and in Olcott's (1940) case cysts were foun in the posterior lobe and pars intermedia Our patient skull was not radiographed, but his pituitary showed n macroscopic or microscopic abnormality despite h grossly abnormal height

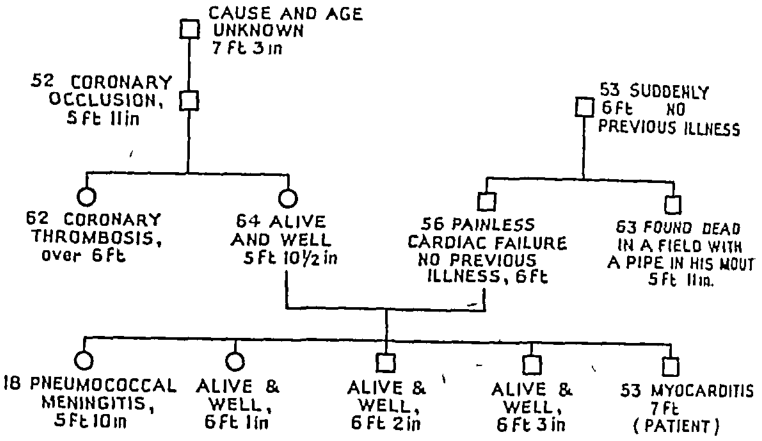


Fig 5—Patient's family tree, showing age, cause of death, and height.

The hereditary and familial tendencies of arachnodactyly were first noted by Achard (1902), and have sinc been emphasised by Young (1929), Weve (1931) Weill (1932), Burch (1936), Futcher and Southwort (1938), Harrison and Klainer (1939), and Ellis (1940 Rados (1942), in his comprehensive review of the publishe cases, found a family history present in 58, doubtful i 38, and absent or not mentioned in 113 We have no examined any of our patient's relations, but the famil history (fig 5) shows a tendency to abnormal height in all siblings and some forbears, and a high incidence o sudden death, possibly due to cardiac disease

NECROPSY FINDINGS IN ARACHNODACTYLY

Reference	Sex	Age at death	Cardiac abnormalities	Other findings
Salle (1912)	M	2½ mos	Patent foramen ovale, tricuspid and aortic valves showed reddish grey elevations (studded protuberances) near their margins	—
Boerger (1915)	M	1 yr	Small opening in valvula fossa ovalis	Middle lobe of righ lung vestigial
Piper and Irvine Jones (1926)	F	21 mos	Patent interauricular septum right auricle and right ventricle dilated	Left lung all one lobe, middle lobe of righ lung very small
Weill (1932)	M	47 yr	Old mitral endocarditis	—
Weill (1932)	F	27 yr	Old aortic endocarditis	Small pituitary
Rambar and Denenholz (1930)	M	30 mos	Heart normal macroscopically, myocardium histologically normal	—
Olcott (1940)	F	15 yr	Two (? congenital) perforations in centre of posterior cusp of mitral valve which was calcified and showed two vegetations on its line of closure, *Bact coli* grown on culture of cardiac blood	—
Etter and Glover (1943)	M	21 yr	Dissecting aneurysm of ascending aorta hæmopericardium, aortic incompetence	—
Bergstrand (1943)	F	19 days	Nil	Left lung consisted of a single lobe
Baer et al (1943)	F	24 yr	Foramen ovale patent, diameter 4 5 cm fusiform dilatation of ascending aorta high origin of coronary arteries histologically aorta showed atrophy of muscle and elastic tissue of the media, ? congenital	—
Baer et al (1943)	M	26 yr	Patent foramen ovale and a second opening in interauricular septum high origin of coronary arteries aortic ring and ascending aorta dilated, histologically aorta showed abnormality of muscle and elastic tissue of media ? congenital	—
Uyeyama et al. (1947)	M	22 yr	Dissecting aneurysm of aorta high origin of coronary arteries aortic valves fenestrated aorta narrowed 11 cm distal to valves, histologically aorta showed Erdheim's medionecrosis	—

SUMMARY

A case of arachnodactyly is described in which death took place from "myocarditis," and hypoplasia of the aorta and organ hyperplasia were found at necropsy

We thank Prof K. D Wilkinson and Dr O Brenner for their advice and help in the clinical care of this patient Professor Wilkinson for the electrocardiograms, and Prof J W Orr for stimulating and helpful criticism.

REFERENCES

Achard, C (1902) *Bull Soc. méd Hôp Paris* 19 834
Baer R. W Taussig H B Oppenheimer E H (1943) *Bull Johns Hopk. Hosp* 72 309
Bell, E T., Hartzell T B (1924) *J med. Res* 44. 473
Bergstrand, C G (1942-43) *Acta pædiatr Stockh* 30 345
Borger F (1915) *Ztschr f Kinderh* 12 161
Burch, F E (1936) *Arch Ophthal., Chicago* 15 645
Ellis, R W B (1940) *Arch Dis Childh.* 15 267
Etter, L. E. Glover L, P (1943) *J Amer med Ass* 123 88
Evans W (1949) *Brit Heart J* 11 68
Futcher P H. Southworth H. (1938) *Arch intern Med* 61 693.
[illegible] H (1945) *Ibid* 75 215
[illegible], J., Klainer M. J (1939) *New Engl J Med* 220 621
Marfan, A. B (1896) *Bull. Soc méd. Hôp Paris* 13 220
Méry H., Babonneix. L. (1902) *Ibid* 19 671
[illegible] W G Ross T F (1942) *J Path Bact* 54 455
[illegible] C T (1941) *Amer J Dis Child* 60 660
Piper R. K., Irvine-Jones E (1926) *Ibid* 31 832
Poynton, F J (1933) *Trans med. Soc. Lond* 26 338
Rados A. (1942) *Arch. Ophthal. Chicago* 27 477
Rambar A. C Denenholz E. J (1939) *J Pediat* 15 844
Salle V (1912) *Jb Kinderheilk.* 75 540
Uyeyama, H., Kondo B. Kamins M. (1947) *Amer Heart J* 34 580
Weill, G (1932) *Ann Oculist Paris* 169 21
Weve H. (1931) *Arch. Augenheilk* 104, 1
Young M. L (1929) *Arch Dis Childh* 4 190

PREPARATION OF HÆMOPOIETICALLY ACTIVE EXTRACTS FROM FÆCES

SHEILA T E CALLENDER
M.D B.Sc St And M.R.C.P
MAY READER IN MEDICINE, UNIVERSITY OF OXFORD

G H SPRAY
M.A. B.Sc, D.Phil Oxfd

From the Nuffield Department of Clinical Medicine Radcliffe Infirmary, Oxford

Two years ago we and our colleagues (Callender et al. 1949) prepared an extract from the fæces of an untreated case of pernicious anæmia and showed that when injected intramuscularly into another patient with untreated pernicious anæmia the extract provoked a hæmopoietic response The experiment has since been repeated with extracts prepared from the fæces of a normal person and of two more patients with untreated pernicious anæmia.

Preparation —The following method of preparing the extracts was found to be the most satisfactory

The fæces were homogenised, with the addition of enough water to give a fluid mixture This was heated to about 90°C in a water bath, then cooled and an equal volume of ethyl alcohol was added The mixture was filtered with suction and the filtrate was concentrated *in vacuo* at about 60 C Three volumes of ethyl alcohol were added, and the mixture was kept at 0 C for at least 24 hours, when some solids separated and were filtered off. The alcohol was distilled off, and the aqueous residue was treated with charcoal, until the filtrate was almost colourless. The charcoal was well washed with water, and was eluted with liquefied phenol Four volumes of ether were added to the phenol, the small amount of aqueous solution which separated was run off, and the ether was extracted twice more with a little water The combined aqueous layers were extracted with fresh ether, to remove residual phenol, and were concentrated *in vacuo* at 60°C, with repeated addition of a little alcohol to prevent frothing The solution was sterilised by filtration through sintered glass

TABLE I—CONCENTRATION OF HÆMOPOIETIC FACTORS IN EXTRACTS FROM FÆCES OF A NORMAL PERSON AND THREE PATIENTS WITH UNTREATED PERNICIOUS ANÆMIA (P.A.)

Extract no	Source of fæces	Wet weight of fæces extracted (g)	Volume of extract (ml.)	Contents of hæmopoietic factors (µg per ml)		
				Vitamin B_{12}	Folic acid	Folinic acid
1	P.A patient	200	6[illegible]	0·3*	0·06	—
2	Normal person	1570	10	7·5	17	7·8
3	P.A patient	694	6	2·2	—	—
4	P.A patient	457	10	5·0	19	7·3

* Extract 1 was used in the case reported by Callender et al (1949) It was then stated to contain 1 µg of vitamin B_{12} per ml., but this figure was based on a standard that was later shown to contain only a third of its supposed content of vitamin B_{12} (Shaw 1949).

TABLE II—RESPONSE OF PERNICIOUS ANÆMIA PATIENTS TO INJECTION OF FÆCAL EXTRACTS

Case no	Total vitamin B_{12} injected	No of days observed	Red-cell count (million per c.mm)		Hæmoglobin (g per 100 ml)		Maximum reticulocytes per 100 red cells (day observed)
			At start	At end	At start	At end	
1	7·5 µg (5 ml of extract 1 daily for 5 days)	35	1·66	3·53	4·7	11·3	17 (7th)
2	30 µg (4 ml of extract 2)	1[illegible]	1·40	2·33	6·4	9·1	27 ([illegible]th)
3	8·8 µg (4 ml. of extract 3)	1[illegible]	1·67	3·20	7·9	11·7	13 (6th)
4	10 µg (2 ml of extract 4)	13	2·00	2·54	8·4	9·7	8·8 (5th)
	10 µg (crystalline vitamin B_{12})	9	2·54	3·00	9·7	11·0	4·2 (5th)

The extracts were assayed for vitamin B_{12} with *Lactobacillus lactis* Dorner or *Lb leichmannii*, and in some cases also for folic acid with *Lb casei* ε and for folinic acid with *Leuconostoc citrovorum* The findings are shown in table I It is improbable that vitamin B_{12} is extracted quantitatively by the above process, though the fraction lost is not likely to vary greatly for different batches of fæces. Thus the amounts of B_{12} shown in table I do not necessarily correspond to the amounts in the original fæces, but the results do indicate that there is no significant difference between the amounts excreted by the two groups of subjects The weight of stools passed each day was not measured, but, assuming an average daily output of 200 g of wet fæces, the amounts of B_{12} extracted from each day's fæces would be 8 µg from the normal subject, and 19, 3·8, and 22 µg, with a mean of 15 µg, from the three patients with untreated pernicious anæmia The extracts did not contain enough folic acid or folinic acid to produce a hæmopoietic response, and no attempt has been made to quantitate the output of these factors

Suitable amounts of the extracts were injected intramuscularly into patients with classical addisonian pernicious anæmia in relapse The injections sometimes caused local tenderness and some pyrexia, but no more severe or lasting toxic effects were observed The responses of the patients, including a more detailed summary of the results on the patient described earlier (Callender et al. 1949), are shown in table II Injection of the fæcal extracts was followed by hæmatological responses similar to those provoked by liver extracts and vitamin B_{12} The fourth patient was given 10 µg of crystalline vitamin B_{12} thirteen days after the fæcal extract, there was only a slight secondary reticulocytosis, indicating that the response to the fæcal extract had been nearly optimal.

DISCUSSION

The results show that it is possible to extract from the fæces of normal people or of patients with untreated pernicious anæmia substances which produce hæmatological improvement when injected intramuscularly into patients with addisonian pernicious anæmia in relapse From these effects, and the growth stimulating actions of the extracts on micro organisms, it may be concluded that the active principle is vitamin B_{12} As much of this vitamin could be extracted from the fæces of patients with pernicious anæmia as from those of normal people and, though the proportion lost in the process of extraction is unlikely to be always the same, it seems from these results that there is no significant difference between the amounts excreted by the two types of subject It was hoped to extend this study by comparing the amounts of vitamin B_{12} taken in the diet with the amounts excreted in the fæces by normal people and patients with pernicious anæmia, but no satisfactory method could be found for estimating vitamin B_{12} quantitatively in crude extracts of food or of fæces

SUMMARY

A method is described for the preparation from fæces of non toxic extracts which provoke hæmopoietic responses when injected into patients with pernicious anæmia

The active substance in these extracts appears to be vitamin B_{12}

The amounts of this substance excreted in the fæces seemed to be much the same in a normal person and in three patients with untreated pernicious anæmia

We are grateful to Prof L J Witts for his advice and criticism in connection with this work

REFERENCES

Callender S T E , Mallett B J , Spray, G H Shaw G E (1949) *Lancet*, ii, 57
Shaw, G E (1949) *J Pharm Pharmacol* 1, 709

INFLUENCE OF THYROXINE ON THE DESENSITISING ACTION OF A C T H AND OF CORTISONE IN B C G -INFECTED GUINEAPIGS

D A LONG
M D Lond

A A MILES
M A Camb , F R C P

W L M PERRY
M.D St And

From the National Institute for Medical Research, Mill Hill, London

THE hypersensitivity to tuberculin of B C G infected guineapigs maintained on a diet supplemented by cabbage is diminished about three times by 'Cortisone' or adrenocorticotrophic hormone (A C T H), and trebled by moderate thyrotoxicosis (Long and Miles 1950) Thus there is a ninefold range of hypersensitivity between thyrotoxic animals and those treated with cortisone or A C T H

In this paper it is shown that when thyrotoxic animals are treated with A C T H or cortisone their sensitivity is decreased about nine times, bringing it to the same level as that in non thyrotoxic animals treated with A C T H or cortisone , and that neither cortisone nor A C T H has any desensitising action in animals treated with propylthiouracil

METHODS

In view of the many possible interactions between the factors investigated in these experiments, we have throughout used factorial designs of a kind previously described (Long et al. 1951) One experiment was designed to determine the relationship of thyroxine in large doses, to A C T H and cortisone , and a series of experiments to discover the relationships of propyl thiouracil, thyroxine, and cortisone , A C T H was omitted because in other, non factorial, experiments it behaved like cortisone The design of the experiments is evident from the tables, which show the analyses of the various combinations of treatments The number of albino guineapigs used for each treatment group varied from 5 to 15 in different experiments All animals were given 2 mg wet weight of B C G intramuscularly and were tuberculin tested twenty eight days later by the multiple dose method (Long and Miles 1950) They were maintained on the pelleted diet of Bruce and Parkes (1947) This diet is grossly deficient in ascorbic acid, which was provided by giving unlimited cabbage Propyl thiouracil 50 mg by mouth three times a week for four weeks, and a single injection of cortisone 2 mg or of A C T H 1 international unit, were given to appropriate groups Sodium thyroxine 0 1 mg or 0 2 mg was injected twice weekly for four weeks , the body weight and sensitivity to tuberculin were not affected by the smaller dose, but were by the larger dose The smaller dose was therefore considered to be a reasonable " replacement dose " for animals treated with propylthiouracil, and the larger as a mildly thyrotoxic dose in otherwise untreated animals As in our previous work, the diameter of the tuberculin lesions after twenty four hours was found to be proportional to the logarithm of the dose of tuberculin , and it was possible to estimate the degree of sensitivity by the relative positions of the dosage response lines fitted to the mean lesion diameters plotted against the logarithm of the dose

TABLE I(*a*)—COMPLETE ANALYSIS OF VARIANCE OF FACTORIAL EXPERIMENT EXPLORING THE RELATIONSHIP BETWEEN THYROXINE, A C T H , AND CORTISONE

Source of variation	Sum of squares	D F	Mean square	Variance ratio	P*
Between treatments	189 1312	7	27 087	7 562	<0 001
Thyroxine	7 7521	1	7 7521	2 164	—
Cortisone	63 0690	1	63 0690	17 606	<0·001
A C T H	44 4083	1	44 4083	12 397	<0·01
Cortisone/A C T H	55 3581	1	55 3581	15 454	<0 001
Thyroxine/A C T H	3 3333	1	3 3333	0 930	—
Thyroxine/cortisone	10 2083	1	10 2083	2 850	—
Thyroxine/cortisone/A C T H	5 0021	1	5 0021	1 396	—
Between doses	322 0511	2	161 0271	44 952	<0 001
Linear regression	322 0031	1	322 0031	89 898	<0 001
Departures from linearity	0 0510	1	0 0510	—	—
Between animals	114 6300	32	3 5822	(error)	—
Treatment dose interaction	18 0376	11	1 2880	—	—
Residual	22 5450	64	0 3523	—	—
Total	666 3929	119	—	—	—

*Only those effects which are significant at least at the P = 0·05 level are shown.

TABLE I(*b*)—COMPARISON OF THE INDIVIDUAL TREATMENT EFFECTS WITH THAT OF THE CONTROL ANIMALS (SAME EXPERIMENT AS TABLE I(*a*))

Treatment compared with control	Potency ratio	Variance ratio	P
Thyroxine	0 356	5 540	<0·05
Cortisone	3 366	8 450	<0 05
A C T H	3 950	5 160	0·05–0·10
Cortisone + A C T H	3 526	4 707	0 05–0 10
Thyroxine + cortisone	3 781	10 537	<0·05
Thyroxine + A C T H	2 910	5 376	<0·05
Thyroxine + cortisone + A C T H	2 823	7 475	<0 05

RESULTS

Relationship of Thyroxine to A C T H and Cortisone in their Effect on Hypersensitivity

In our first experiment we investigated the relationship of thyroxine to A C T H and cortisone in their effect on hypersensitivity The full analysis of this experiment is given in table I(*a*), and the results of the individual lyses comparing single treatment groups in table I(*b*) form of these analyses is that used by Long et al (1951)

Table I(*a*) shows that the effects of cortisone and A C T H were highly significant, and that these substances interact significantly Thyroxine, on the other hand, seemed to have no significant effect, and did not interact *significantly with either* A C T H *or cortisone* This result is difficult to interpret unless we also consider the results of the individual treatment comparisons given in table I(*b*), thyroxine did, in fact, treble the sensitivity of the animals compared with the controls On the other hand, A C T H and cortisone, singly or together, decreased the sensitivity of the animals and continued to do so even when thyroxine was given in addition The relationship is an unusual one, and the absence of significant interactions between thyroxine and cortisone or A.C T H is explained by the fact that the effect of cortisone or A C T H is neither enhanced nor diminished by thyroxine, although thyroxine itself, in the absence of these substances, produces a significant effect in the opposite direction

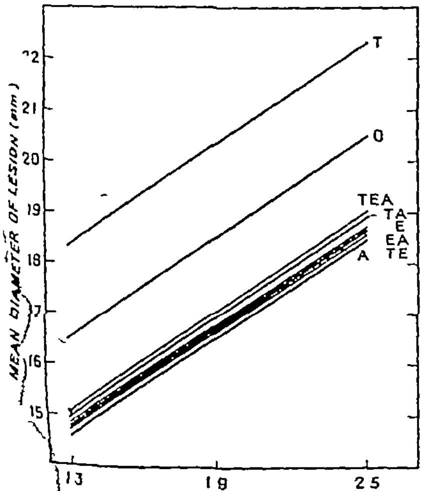


Fig. 1—Dose-responses to 20, 80, and 320 i u tuberculin in sensitive guineapigs: T thyroxine E, cortisone A A.C T H ; O controls

In fig 1 we have plotted the dosage response lines for each of the eight treatment groups, using the fitted common slope calculated from the analysis of variance This is legitimate, since the analysis showed that there was a significant common linear regression and that there were no significant departures from parallelism (table I[*a*]) This figure shows clearly the relationship just described The dosage response lines fall into three groups the thyroxine group with a high degree of sensitivity, the control group, and the remaining six lines clustered in a third group, in which sensitivity is three to four times less than in the control group

The following conclusions may be drawn from this experiment

1 Thyroxine injected subcutaneously in large doses for twenty eight days increases hypersensitivity about three times.

2 In animals treated with thyroxine there is no inhibition of the desensitisation produced by A C T H and cortisone which in control animals is *three to four fold in degree* In other words, the level of sensitivity after treatment with A C T H or cortisone is the same in non thyrotoxic or thyrotoxic animals As a result, sensitivity is reduced three times in the non thyrotoxic animals, but approximately nine times in the thyrotoxic animals

Effect of Propylthiouracil on Hypersensitivity

In view of the relationship of A C T.H and cortisone to thyroxine, we investigated the effect of propylthiouracil on hypersensitivity In the first experiment the dose of thyroxine was large enough to increase sensitivity, though to a somewhat smaller extent than in the experiments described above, and in the second, the dose of thyroxine was not large enough to produce this effect Analyses of variance of the factorial experiments were carried out in both cases, there was a significant common linear regression, and there were no departures from parallelism The results of the individual comparisons of single treatment groups are summarised for the first experiment in table II and fig 2, and for the second experiment in table III and fig 3

TABLE II—COMPARISON OF THE INDIVIDUAL TREATMENT EFFECTS WITH THAT OF THE CONTROLS IN THE FIRST EXPERIMENT EXPLORING THE RELATIONSHIP BETWEEN PROPYLTHIOURACIL, THYROXINE, AND CORTISONE

Treatment compared with control	Potency ratio	Variance ratio	P
Thyroxine	0 588	1 710	>0 2
Propylthiouracil	1 018	—	—
Cortisone	1 715	3 060	>0 1
Thyroxine/propylthiouracil	0 607	3 017	>0 1
Thyroxine/cortisone	3 968	13 571	<0 01
Propylthiouracil/cortisone	0 818	—	—
Thyroxine/propylthiouracil/ cortisone	2 643	5 606	<0 05

In the first, thyroxine doubled the sensitivity, though this increase is not significant Propylthiouracil did not modify this increase in sensitivity in any way, nor did propylthiouracil itself affect the tuberculin response in otherwise untreated animals Cortisone alone reduced sensitivity, though the effect was smaller than that usually obtained and was not significant The interesting fact emerges that the effect of cortisone is abolished by propylthiouracil and restored by thyroxine It should be noted that propylthiouracil and cortisone together appeared to increase the sensitivity slightly The results of this experiment are not conclusive, since the effect of cortisone alone was not significant In the second *experiment (fig 3), however, the results are quite unequivocal*

Here the dose response lines tend to cluster into three groups In one group (A) the sensitivity is increased, in the second (B) it approximates to that of the control group, and in the third (C) it is considerably diminished Within groups B and C the individual effects do not differ significantly from one another On the other hand, all the responses in group C differ significantly from the control responses (table III) The *single response in* group A is almost significantly lower than the control response Thus, neither the thyroxine nor the propylthiouracil, given alone or together, modified the sensitivity Cortisone alone produced a significant three to four fold decrease in sensitivity, but this decrease was completely inhibited by treating the animal with propylthiouracil, when combined, moreover, they actually increased the sensitivity by an amount which is

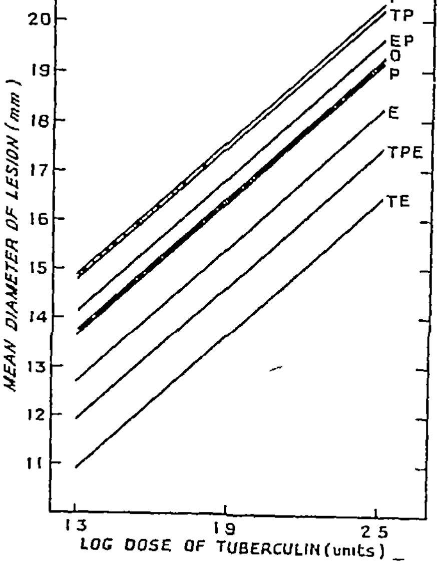


Fig 2—Dose-responses to 20 80 and 320 i u tuberculin in sensitive guineapigs T thyroxine E, cortisone A, A.C.T H ; O controls P propylthiouracil

should not be withheld because the fundus is in its normal position This view is upheld by the description of two cases by Spain (1946) Further, the term "crater like" suggests a much larger depression than the actual fundal dimpling which is usually found Any abdominal rigidity which follows attempts at placental expression will increase the difficulties of palpation, and the fundus may easily be passed as normal Regular abdominal pains and a bearing down sensation, as in case 3, may also point to the presence of the inverted fundus distending the vagina

Most workers agree that, in the absence of shock, the uterus should be replaced as soon as possible That this can be done safely with little or no danger to the patient is shown by case 5 The general practitioner who attended case 3 had attended another case of acute inversion and had replaced the uterus at once, with complete success When shock is present, resuscitation should first be attempted, but if it is not successful no time should be lost in replacing the uterus, because even incomplete reposition is followed by some improvement in the patient's general condition

Many methods of replacement have been suggested, and probably no one method will be successful in all cases We should like to record, however, the ease with which replacement was performed in 3 of these cases using the hydrostatic method described by O'Sullivan (1945) Even when shock is profound the method may be used with success without an anæsthetic The main disadvantage is that a large amount of sterile fluid is required (8–12 pints) because constant leakage occurs, but in an emergency the fluid need not be sterile as there is apparently little or no leakage into the peritoneal cavity (case 6)

After replacement the main concern should be to treat any further shock that may be present It should not be necessary to give an oxytocic drug since firm contraction usually follows reposition, and if the uterus has not been completely replaced the oxytocic drug may be dangerous since reinversion may follow, but if such a drug is given the hand should be kept within the uterus until it contracts, to prevent reinversion The level of the fundus is likely to drop because the structures surrounding the vault of the vagina are considerably stretched by the inversion, so the level of the cervix will fall after replacement This may lead to an incorrect diagnosis of recurrent inversion, as in case 6

Finally, while an obstetric "flying squad" should always be summoned to these cases, prompt diagnosis is likely to permit easy replacement of the inverted uterus before severe shock arises or œdema and constriction of the neck of the inversion makes operative treatment more difficult Once the uterus has become inverted, undue delay may kill the patient

SUMMARY

Six cases of acute inversion of the uterus have been described Reposition was successful in all, one case ended fatally

Cord traction is a dangerous procedure

Correct diagnosis of partial inversion may be delayed because of the following findings (*a*) the amount of blood lost may alone be sufficient to account for the shock, (*b*) the fundal abnormality on palpation is slight and the dimple small, and abdominal rigidity makes palpation difficult, and (*c*) the level of the uterine fundus is normal A vaginal examination should not be withheld if the patient does not respond to resuscitation

When the uterus becomes inverted it should at once be replaced, before the onset of shock

Treatment for established shock should precede replacement, but it is inadvisable to wait for much improvement in the general condition before carrying out replacement

The method of hydrostatic reposition has been fo most valuable In the one fatal case no fluid was fou in the peritoneal cavity following successful hydrost replacement

Our thanks are due to Dr R Newton for help in t preparation of the manuscript, to Dr F A Langley for t necropsy report, and to Dr A F Pearson, Dr E S Roge and Dr P G Seed

REFERENCES

Greenhill, J P (1947) De Lee s Principles and Practice of Obstetri Philadelphia p 730

O Sullivan J V (1945) *Brit med. J* ii 282

Spain, A W (1946) *J Obstet Gynæc* 53 219

Stander H J (1950) Williams' Obstetrics New York p 925

REDUCTION OF STRANGULATED INGUINAL HERNIA

CHARLES BOWESMAN

M D Dubl, F R C S E, D T M & H.

SURGICAL SPECIALIST, COLONIAL MEDICAL SERVICE, GO COAST

THE operative mortality of strangulated hernia wi gangrenous bowel treated by resection and anastomo is stated to be up to 60%, and that of strangulated hern without gangrene, when operated on within twelve hou of the onset of the strangulation, about 20% (Gre Turner 1943)

From the annual reports of the Gold Coast for th past few years it appears that strangulated hernia is th surgical condition causing the greatest number of death and also the one with the highest case mortality, abo 50%

For twelve years I adopted the orthodox policy immediate operation on all cases of strangulated herni as soon as the patient could be prepared and the theat made ready—usually an hour or two after admission hospital The case mortality where the bowel was no gangrenous was about 20%, and where the bowel wa strangulated with gangrene, necessitating gut resectio about 40%

During these twelve years postural treatment wa instituted after the patient had been prepared and wa waiting to go to the theatre, A few strangulated herni were thus reduced—perhaps 10% With increasi pressure of work in later years the time between admissi and going to the theatre tended to be longer, and wi the inevitable delay the number of herniæ which we reduced was noted to be much larger—about 25% subsequent cases notes were made of the duration of th herniæ and the time they took to be reduced Fro these it appeared that gangrene seldom, if ever, too place in less than twenty four hours from the time strangulation Hence it was considered permissible, cases where the history was less than twenty four hour to undertake postural treatment for up to eight hour if this time did not bring the total time from th strangulation to more than twenty four hours.

Herniæ that have been strangulated for twenty fo hours are better operated on at once, because the risk gangrene is high Richter's hernia is also better operate on without an attempt at postural reduction, because th risk of a small local area of gangrene is high

ROUTINE

The following routine was instituted if ordinary tax did not accomplish reduction

(1) Very high blocks (2 ft) under foot of bed
(2) Morphine gr $^{1}/_{2}$ for adults (not gr $^{1}/_{4}$)
(3) Cold compress to groin and scrotum
(4) General warmth to patient
(5) Flexion of both legs at hips and knees with thr pillows (it is necessary to put two pillows at the head the bed to prevent the patient's head from going throug the bars, since the bed's slope is steep)

RESULTS

e results have been most gratifying, the reduction- being 72%—in eighteen months 34 out of 47 strangu- herniæ were reduced by postural treatment

e advantages of reducing a strangulated hernia are (1) the patient can be operated on later in a better tion, (2) the local inflammation settles down in a days, (3) the tissues at the site of operation are in a r condition to ensure a more systematic and accurate r, and (4) the risk of sepsis in the wound is reduced timed operation at a later date

rniæ have been reduced in from one to eight s (average four hours) Consequently, if reduction not take place after six hours' postural treatment, chances of reduction are small. A few herniæ were ed at between seven and eight hours, but very ndeed One hernia was almost reduced at eight s and was by then soft so a further period was ed and the hernia was reduced completely at ten To wait more than eight hours for reduction is lly not justifiable.

e accompanying table shows that the over all lity for all cases of strangulated hernia in this

MORTALITY OF STRANGULATED INGUINAL HERNIA

Type of hernia	No of cases	Treatment	Re covered	Died	Mortality
ed under Re of posture ed by po- e Operation	34	Postural	34	Nil	Nil
	34	Herniorrhaphy	34	Nil	Nil
ed under Posture ment failed. table	10	Herniorrhaphy	9	1	10%
ed over Gut ction	3	Gut resection herniorrhaphy	2	1	33%
ed Irre-	13	—	11	2	15 4%
Total	47	Postural or operative	45	2	4 3%

es was 4 3%—2 deaths in 47 cases In the 34 cases hich the herniæ were reduced by posture but not ated on there were no deaths. In the 34 cases in h the herniæ were reduced and subsequently operated here were also no deaths In the 13 cases in which ural treatment had failed or strangulation had lasted twenty four hours operation was followed by 2 hs (mortality 15 4%)

CONCLUSIONS

stural treatment is an efficient method of reduction rangulated inguinal hernia in suitable cases, 72% rniæ were reduced by such means.

ses of strangulated inguinal hernia suitable for ural treatment are those in which the strangulation existed for less than twenty four hours.

guinal herniæ which have been strangulated more twenty-four hours should be operated on immedi- , because the risk of gangrene of bowel is too high arrant further delay

e average time taken for reduction with postural ment is four hours but varies from one hour to eight s. If reduction is not achieved in eight hours, ation should be undertaken.

a series of 47 strangulated herniæ treated at a ernment hospital in the Gold Coast there were 2 hs, a mortality of 4%

am indebted to the Director of Medical Services, Gold t, for permission to publish.

REFERENCE

er G G (1943) Modern Operative Surgery London vol. ii, p. 1160

Reviews of Books

Essentials of Urology

J C AINSWORTH DAVIS, M D F R.C S, urological surgeon, Bolingbroke Hospital London. Oxford Blackwell Scientific Publications 1950 Pp 734 50s

BRITISH urology retains very close links with general surgery and places strong emphasis on clinical matters It avoids extremes of specialisation and the narrow or partial view In the main Mr Ainsworth-Davis's book reflects these qualities admirably The first part deals with general principles from a practical and mainly clinical standpoint, and the succeeding sections follow the field of urology region by region and cover the ground thoroughly, though omitting rarities Being mainly the work of one author the book avoids contradictions and redundancies Not only does it incorporate the recent advances (such as the use of streptomycin) but it is free from the lumber often found in dark corners of late editions The approach to diagnosis is wisely balanced, and instructions about treatment are clear, detailed and definite. Indeed, in those instances where respectable authorities disagree Mr Ainsworth-Davis is *perhaps a little too definite and uncompromising—for example* in deciding the question whether the ureter as well as the kidney should be removed in renal tuberculosis A number of other contributors have provided short articles on special subjects Mr H. A. Daniel has written on his modification of the McCarthy electrotome, but even so endoscopic prostatic surgery is touched on rather lightly Over 500 photographs and drawings illuminate the text, the paper is of good quality, and the volume is of a handy size Altogether this is an excellent book and will be welcomed by students on all rungs of the ladder—practising surgeons among them.

The Physiology and Pathology of Hemostasis

ARMAND J QUICK, PH.D M D, professor of biochemistry, Marquette University School of Medicine Milwaukee Wisconsin. London Henry Kimpton. 1951 Pp 188 28s

THIS book is arranged in two parts, theoretical and practical. The theoretical section presents a new hypothesis to explain hæmostasis and its application to the classification and differential diagnosis of hæmorrhagic diseases This hypothesis is based on some well-established and some still controversial findings, it is, however, "not presented with any sense of finality, but is offered as a working blue print which will require changes and modifications as new knowledge becomes available." A short and interesting chapter on the history of the development of knowledge about hæmostasis precedes the detailed discussion of the hypothesis, in the course of which the most recent researches into the blood-clotting process are discussed, taking into account especially results obtained when siliconed surfaces are used to prevent premature coagulation. There follows a brief account of hæmorrhagic diseases with emphasis on the newer syndromes, useful tables are given to make differential points clear The final chapter of this section recapitulates Quick's views of the mechanism of venous thrombosis. All this takes up but 99 pages, including references. The remaining 81 pages of text are devoted to a really detailed description of the techniques that Quick employs, and this is a most valuable account because, as Quick rightly says, "the diagnosis, management of therapy and prognosis of hæmorrhagic diseases depends largely on laboratory methods." He emphasises the need for meticulous attention to detail if accurate results are to be obtained, and notes that it is equally important that the details should be correct seemingly minor modifications can, in this field, spoil a test completely *In addition to full descriptions of* techniques for the usual tests, the following are described assay of thromboplastinogen, properties and assay of thrombin, assay of heparin, assay of antithrombic activity of plasma, decalcification of blood with ion-exchange resin, assay of vitamin K, and determination of the potency of prothrombinopenia-inducing agents should not be withheld because the fundus is in its normal position This view is upheld by the description of two cases by Spain (1946) Further, the term "crater-like" suggests a much larger depression than the actual fundal dimpling which is usually found Any abdominal rigidity which follows attempts at placental expression will increase the difficulties of palpation, and the fundus may easily be passed as normal Regular abdominal pains and a bearing down sensation, as in case 3, may also point to the presence of the inverted fundus distending the vagina

Most workers agree that, in the absence of shock, the uterus should be replaced as soon as possible That this can be done safely with little or no danger to the patient is shown by case 5 The general practitioner who attended case 3 had attended another case of acute inversion and had replaced the uterus at once, with complete success When shock is present, resuscitation should first be attempted, but if it is not successful no time should be lost in replacing the uterus, because even incomplete reposition is followed by some improvement in the patient's general condition

Many methods of replacement have been suggested, and probably no one method will be successful in all cases We should like to record, however, the ease with which replacement was performed in 3 of these cases using the hydrostatic method described by O'Sullivan (1945) Even when shock is profound the method may be used with success without an anæsthetic The main disadvantage is that a large amount of sterile fluid is required (8–12 pints) because constant leakage occurs, but in an emergency the fluid need not be sterile as there is apparently little or no leakage into the peritoneal cavity (case 6)

After replacement the main concern should be to treat any further shock that may be present It should not be necessary to give an oxytocic drug since firm contraction usually follows reposition, and if the uterus has not been completely replaced the oxytocic drug may be dangerous since reinversion may follow, but if such a drug is given the hand should be kept within the uterus until it contracts, to prevent reinversion The level of the fundus is likely to drop because the structures surrounding the vault of the vagina are considerably stretched by the inversion, so the level of the cervix will fall after replacement This may lead to an incorrect diagnosis of recurrent inversion, as in case 6

Finally, while an obstetric "flying squad" should always be summoned to these cases, prompt diagnosis is likely to permit easy replacement of the inverted uterus before severe shock arises or œdema and constriction of the neck of the inversion makes operative treatment more difficult Once the uterus has become inverted, undue delay may kill the patient

SUMMARY

Six cases of acute inversion of the uterus have been described Reposition was successful in all, one case ended fatally

Cord traction is a dangerous procedure

Correct diagnosis of partial inversion may be delayed because of the following findings (*a*) the amount of blood lost may alone be sufficient to account for the shock, (*b*) the fundal abnormality on palpation is slight and the dimple small, and abdominal rigidity makes palpation difficult, and (*c*) the level of the uterine fundus is normal A vaginal examination should not be withheld if the patient does not respond to resuscitation

When the uterus becomes inverted it should at once be replaced, before the onset of shock

Treatment for established shock should precede replacement, but it is inadvisable to wait for much improvement in the general condition before carrying out replacement

The method of hydrostatic reposition has been fo most valuable In the one fatal case no fluid was fo in the peritoneal cavity following successful hydrost replacement

Our thanks are due to Dr R Newton for help in t preparation of the manuscript, to Dr F A Langley for t necropsy report, and to Dr A F Pearson, Dr E. S Roge and Dr P G Seed

REFERENCES

Greenhill, J P (1947) De Lee s Principles and Practice of Obstetric Philadelphia p 730
O Sullivan, J V (1945) *Brit med. J* ii 282
Spain A W (1946) *J. Obstet Gynæc* 53 219
Stander H J (1950) Williams' Obstetrics New York p. 925.

REDUCTION OF STRANGULATED INGUINAL HERNIA

CHARLES BOWESMAN
M.D Dubl, F R C S E, D T.M & H.
SURGICAL SPECIALIST, COLONIAL MEDICAL SERVICE, GOL COAST

THE operative mortality of strangulated hernia wit gangrenous bowel treated by resection and anastomosi is stated to be up to 60%, and that of strangulated herni without gangrene, when operated on within twelve hour of the onset of the strangulation, about 20% (Gre Turner 1943)

From the annual reports of the Gold Coast for the past few years it appears that strangulated hernia is the surgical condition causing the greatest number of deaths, and also the one with the highest case mortality, abo 50%

For twelve years I adopted the orthodox policy o immediate operation on all cases of strangulated hernia as soon as the patient could be prepared and the theatre made ready—usually an hour or two after admission t hospital The case mortality where the bowel was not gangrenous was about 20%, and where the bowel was strangulated with gangrene, necessitating gut resection about 40%

During these twelve years postural treatment was instituted after the patient had been prepared and was waiting to go to the theatre A few strangulated hernia were thus reduced—perhaps 10% With increasing pressure of work in later years the time between admissio and going to the theatre tended to be longer, and wit the inevitable delay the number of herniæ which wer reduced was noted to be much larger—about 25% I subsequent cases notes were made of the duration of th herniæ and the time they took to be reduced Fro these it appeared that gangrene seldom, if ever, too place in less than twenty four hours from the time o strangulation Hence it was considered permissible, i cases where the history was less than twenty four hours to undertake postural treatment for up to eight hours if this time did not bring the total time from th strangulation to more than twenty four hours

Herniæ that have been strangulated for twenty fou hours are better operated on at once, because the risk o gangrene is high Richter's hernia is also better operate on without an attempt at postural reduction, because th risk of a small local area of gangrene is high

ROUTINE

The following routine was instituted if ordinary taxi did not accomplish reduction

(1) Very high blocks (2 ft) under foot of bed
(2) Morphine gr 1/3 for adults (not gr 1/4)
(3) Cold compress to groin and scrotum
(4) General warmth to patient
(5) Flexion of both legs at hips and knees with three pillows (it is necessary to put two pillows at the head of the bed to prevent the patient s head from going through the bars, since the bed's slope is steep)

A new Glaxo
WHOOPING COUGH
VACCINE
for
MASS
IMMUNISATION

A PLAIN suspended vaccine is now made available as SUSPENDED WHOOPING COUGH VACCINE *Glaxo* Prolonged study of every detail of each stage of production provides the assurance of an efficient immunising agent, and the vaccine can be given by subcutaneous or intramuscular injection without untoward local or general reaction Incidence of whooping cough this past winter has been higher than for very many years Success in immunisation depends on the quality of the antigen employed, and it is now realised that a suitable vaccine can give a considerable *degree of protection (Brit Med J 1951, 1, 430)*

Suspended Whooping Cough Vaccine *Glaxo*

Saline suspension of 20 000 million H pertussis per cc 5 cc. & 10 cc vials.

ALSO AVAILABLE

Whooping Cough (Pertussis) Vaccine *Glaxo*	Diphtheria Pertussis Prophylactic *Glaxo*
Suspension of 20 000 million H pertussis per cc. adsorbed on aluminium phosphate 5 cc. & 10 cc. vials.	Lf 25 diphtheria toxoid and 20 000 million H pertussis per cc. adsorbed on aluminium phosphate 5 cc & 10 cc vials

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX BYRon 3434

---

a *NEW* treatment for vomiting in pregnancy

'APOLOMINE', a tablet containing three members of the Vitamin B complex, atropine, hyoscine and benzocaine, has proved most valuable in dealing with this wayward symptom of early pregnancy The early clinical work with it was done in Sydney, Australia.

Suggested dosage 1, 2 or 3 tablets a day

Literature and further information available on request.

BAYER

APOLOMINE

Trade Mark

BAYER PRODUCTS LIMITED, AFRICA HOUSE, KINGSWAY, LONDON, W C 2

This is a clear and valuable account by one of the most experienced workers in the field , but it is the practical section that will make every clinical pathologist and research worker want to have a copy on the shelf for constant reference

The Law relating to Mental Treatment and the Health Service

HAROLD BERRY London J & A Churchill 1951 Pp 121 8*s* 6*d*

WHILE the old poor law system was still operated, the relieving officer of a public-assistance committee had some important responsibilities in connection with the certification and removal of persons of unsound mind These duties have now been transferred to the "duly authorised officers of local health authorities" by the new sections 14 and 15 inserted in the Lunacy Act, 1890, by the National Health Service Act of 1946 Mr Harold Berry, the duly authorised officer of the Lancashire county council, has written a short manual on the law of mental treatment for the guidance of other similar officers, justices, practitioners, and students The book is practical and elementary, and does not compete with the more comprehensive legal treatises which experts usually consult

Occasionally Mr Berry leaves the law and offers a few generalisations Thus, in a page or two on psychiatric evidence in capital cases, he suggests that there is a real risk of a mentally sick man being hanged because prosecuting counsel (who may be "woefully ignorant of the elements of psychological medicine") rely on the report of the prison medical officer "who is seldom an adequately trained psychiatrist and is in any case never an independent one" Few counsel who prosecute in murder trials are ignorant of the case they have to meet when insanity is put forward , their professional experience has probably included briefs for the defence to put forward that very defence As for the prison medical officer, he is likely to be familiar with the law of criminal responsibility, and he must answer questions within the range of his opinions and his personal observation , he is not a partisan It is the law, not the persons who apply it, that Mr Berry should attack , he would find useful material in the statistics of persons found guilty at trial but certified as insane soon afterwards

Thyreotoxikosen und Antithyreoidale Substanzen

HANS WILHELM BANSI, professor of medicine, Hamburg University Stuttgart Thieme 1951 Pp 99 D M 11 40

THE antithyroid drugs were first used clinically by Astwood in 1943 News of the discovery reached Germany at the end of the late war, and the drugs themselves became available there towards the end of 1946 Professor Bansi's book shows that German physicians have now made up the lost leeway and are as familiar with the clinical use of these substances as their Anglo-American colleagues He himself has now treated some 300 patients with antithyroid drugs, including the recently introduced methylmercaptoimidazole His experience has obviously been similar to that of English doctors , though impressed by the new drugs he does not regard thyroidectomy as superseded There is a full review of both experimental and clinical work on the subject, including a generous proportion of references to American authors

Prostitution and the Law

T E JAMES, barrister at law, lecturer in laws in the University of London at King's College London Heinemann Medical Books 1951 Pp 160 21*s*

THE United Nations Convention of 1949 stigmatised prostitution as "incompatible with the dignity and worth of the human person" But a topic which lies on the borderline between law and morals must not expect a decisive lead from the legislature of Britain Governments will hesitate to introduce a Bill , it may be left to private members to reform the law Thus Mrs Castle's Criminal Law Amendment Bill, making progress amid general approval, may at last remove from the statute of 1885 certain surviving exceptions which upheld the view of former generations that an enactment for the protection of women and girls need do nothing for anyone described as "a common prostit or of known immoral character"

The ordinary citizen and his representatives in Parl ment are not excited by general ideas of law reform b only by particular incidents, like the Savidge case 1928 when the methods of the police were made the subje of independent inquiry The Macmillan Committee c Street Offences reported in the same year in favour (a single simple enactment—presumably not unlike tl Public Places (Order) Bill which Lady Astor introduc in 1925 and 1926—making it an offence to importu a person of the opposite sex for immoral purposes in street or public place There was to be another pr vision making it an offence to frequent a street or publ place for the purpose of prostitution or solicitation s as to create a nuisance, but the evidence of one or mor of the aggrieved persons was to be essential to a con viction The Macmillan Committee hoped thus to ge rid of the tangle of general and local enactments o which section 35 of the Town Police Clauses Act, 1847 is an elderly, and Defence Regulation 42C was a recent example

In this book Mr James tells us how the problem has been treated in France, the United States, and the U S S R , as well as in England He suggests that, if English society really sets its face against prostitution, the Criminal Justice Act, 1948, might be found useful Section 26 would facilitate inquiry into the physical or mental condition of the person charged , a probation order under section 3 could require residence in an institution, and an order under section 4 could ensure treatment under medical direction If the remedies lie outside the statute book, Mr James has nevertheless supplied us with a clear statement of the law Incidentally, his references to the Royal Park Acts are presumabl to the Parks Regulation Acts, which apply to man other open spaces besides a royal park That, however, is a trivial criticism to make of a book which collects in a small compass a great deal of information, ranging from the ritual of temple prostitution, to the medieval idea of courtly love, and the position of women in modern Russia

Yellow Fever

Editor GEORGE K STRODE, M D , director, international health division, the Rockefeller Foundation, New York London McGraw Hill 1951 Pp 710 81*s*

THE possibility that the mosquito disseminated yellow fever was first suggested just over a hundred years ago, but the serious scientific study of the problem really began in 1900, when Major Walter Reed was sent to Cuba as president of the Yellow Fever Commission of the U S Army Within three years the nature of the infective agent had been established, its mode of transmission defined, and methods for its control evolved , but, despite this swift progress, a vast amount remained to be done , and during the subsequent years yellow-fever research attracted large numbers of diligent and skilful workers all over the world This book has been written by members of the International Health Division of the Rockefeller Foundation as a tribute to those who lost their lives in advancing yellow fever research , in its pages is set out authoritatively the fascinating story of this research and a summary of our knowledge

A short introductory chapter giving some notable landmarks in the conquest of yellow fever is followed by informative chapters on the virus, pathology, and immunology Then follow sections on the arthropod vectors and the mammalian hosts of the infection There is a good section on clinical aspects and diagnosis, and finally valuable chapters on the epidemiology and control of the infection with a useful discussion of costs and man power requirements. The great figures who have played a leading rôle in the study and solution of the problems of yellow fever are shown in a series of photographs In the forefront of these is that humble but great benefactor Asibi the African patient from whom in 1927 was obtained the historic 17 D strain of yellow fever virus. From this strain has been made most of the world's supply of vaccine, by means of which millions of people have been protected

The book is admirably printed and well illustrated.

THE LANCET

LONDON SATURDAY JUNE 30 1951

The Borstal Puzzle

THE more we learn of the springs of adolescent delinquency the less willing we seem to use our knowledge—pardonably perhaps, since all we find out about this type of behaviour suggests that it is troublesome both to prevent and to cure The temptation to look for a short cut is therefore very great. This may explain some curious features in the report [1] on borstals just published by the committee * appointed in 1948 by the Secretary of State for the Home Department to review punishments in prisons, borstals, approved schools and remand homes

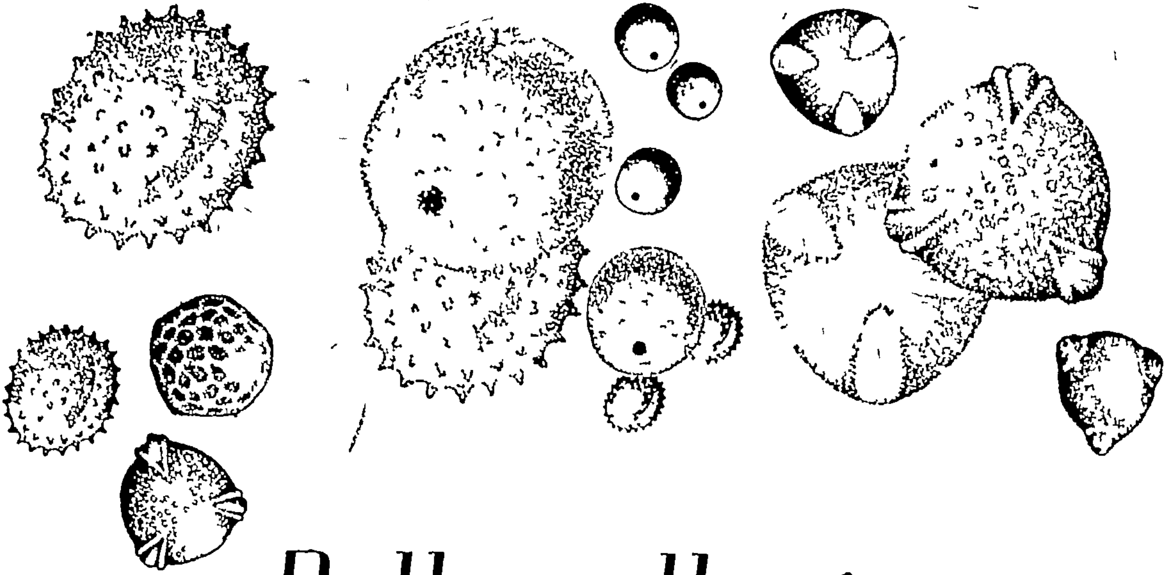
Up to 1939, the borstal institutions designed to reform certain young offenders between the ages of [illegible] and 21, were working well. More than half the young people who passed through them were not brought into court again. The war, however, meant loss of accommodation and staff, and the work for them was seriously disrupted and is is only now being restored to its former scope The committee, leaving the girls' borstals out of account, have reviewed the curriculum, discipline, system of promotion, and punishments in the boys' borstals The curriculum consists of compulsory physical training and eight hours' work daily in the shops or on the farm, with educational classes, handicrafts, or recreation in the evenings. In most of the institutions there is a system of promotion, and the privileges attaching to the higher grades are designed to encourage responsibility and self control. A common punishment, therefore, is loss of privileges, or loss of the grade of promotion carrying such privileges Other punishments are removal of a prisoner from his house, removal from the company of other inmates, stoppage of earnings, and confinement to a room All these may only be imposed for reasonable prescribed periods Formerly the offending young man could be put on bread and water (restricted diet no 1) for not more than three days at a time, or on a less restricted but very dull and inadequate diet (restricted diet no 2) for a longer period. These dietary penalties are at present suspended—properly, in our view, since restriction of diet is not a suitable punishment for a person who is still growing The committee recommend that all existing punishments should be retained and that the power to award restricted diet no 1 should be restored Restricted diet no 2 they propose should be abolished. If dietary punishments are to be used at all on growing people they should certainly be sharp and short-lived rather than prolonged and undernourishing The principle of maintaining the other existing punishments seems to us sound Lack of suitable official punishments encourages the use of unofficial punishments and this may have most undesirable results All punishments, however, if they are to serve their purpose of reform must be used constructively The delinquent must be brought to see that these are something he brings on himself—something he deliberately chooses, in fact—not merely the revenge of those who have power over him The committee do not discuss this important aspect of their subject

They were often dissatisfied with standards of discipline in the borstals visited. Good discipline they define as a right attitude in the individual and in the community to society, work, authority, decency, order and life and as embracing in addition, diligence, conduct, cleanliness, and deportment Since deficiency in some or most of these qualities brings the young people into the borstals in the first place, it was perhaps unduly optimistic of the committee to expect to find the borstal population displaying many of them However, it is easy to understand their human impatience at the sight of "lads with long matted hair, unkempt in their clothing, slouching without any form of respect past the officers of whatever rank whom they met or passed." This behaviour compares ill with the cheerful greetings offered by the boys in a good approved school, but the borstal youths are usually those with whom the approved school has failed. While the committee do not advocate a system of military discipline they think the authorities should try to foster a higher standard of smartness and deportment not as an end in itself but as a means of training character The idea is sound enough the recruit who begins by reviling spit-and-polish comes in a few weeks to think no polish too high for such a fine fellow as he is This rise in self respect, however, is not so easily achieved among people who are under punishment by society, and who regard defiance of customary standards almost in the light of a duty Doubtless an improved bearing could and perhaps should, be enforced, but unless it is an outward and visible sign of an inner change it will have only a convenience value Within the borstal system opinions on the standard of discipline conflict The Prison Officers' Association assured the committee that discipline had deteriorated since the war, that superior officers were pushing the 'policy of leniency' too far, and that reports of misconduct were sometimes suppressed by chief officers, housemasters, or governors The Prison Commissioners on the other hand, did not agree that borstal discipline had deteriorated, and refuted the allegation that reports of misconduct were suppressed The committee admit that there is nothing in any official documents or published statistics to support the criticisms of the Prison Officers' Association, and that an invitation to them to supply concrete instances of the suppression of reports 'was less fruitful than might have been anticipated from the emphatic language used." Nevertheless, bearing in mind that the success-rate has gone down somewhat since 1947, and that absconding has increased, they consider that discipline should be tightened, even at the cost of increased punishments, and that "the policy of leniency, appeasement, or soft treatment as at present interpreted is not having the success expected or desired" They do not review the impressive evidence on which the policy of 'leniency' is based,

---

[1] Parts I and II. Prisons and Borstal Institutions London H.M. Stationery Office 1951 Pp. 122 3s 6d

The members of the committee were Mr. H W F. FRANKLIN (chairman) Mrs. D M. BATES, M.B.E. Dr R. DESMOND CURRAN, Mr J C JOLLY (who died before the work was concluded) Sir LEO PAGE, and Mr E V WATERING



Pollen allergy

every summer brings unnecessary discomfort to many
Hay fever and other allergic conditions can be relieved by the administration of the outstanding antihistaminics

'ANTHISAN'
trade mark *brand*
mepyramine maleate

Tablets Containers of 25, 100 and 500 x 0.05 Gm
25, 100 and 500 x 0.10 Gm
Elixir Containers of 4 and 40 fl. oz
Solution (2.5 per cent) Boxes of 10 x 2 c.c. amps
Cream (2 per cent) Containers of 1 oz. and 1 lb

which combines selective antihistamine activity with rapidity of action

trade mark **'PHENERGAN'** *brand* **promethazine hydrochloride**

an antihistaminic with a prolonged antihistamine effect having in addition subsidiary pharmacological activities useful in certain cases

Tablets Containers of 25 and 500 x 0.01 Gm
25 and 500 x 0.025 Gm
Elixir Containers of 4 and 40 fl. oz
Solution (2.5 per cent) Boxes of 10 x 2 c.c. ampoules

M&B

manufactured by
MAY & BAKER LTD

MA48603

distributors
PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD DAGENHAM

ed fragility of the red cells in saline solution— red cells begin to hæmolyse in 0 45% solutions NaCl *and are completely hæmolysed in* 0 33%, reas in congenital hæmolytic jaundice hæmolysis ns between 0 7 and 0 5% of NaCl Many ingenious hods of displaying this increased fragility quanti rely have been devised, their particular aim being etect the less obvious changes in mild cases and in tives of the affected people These methods have been outstandingly successful, moreover, cases pherocytic anæmia have been described in which cell fragility was apparently normal Lately adi[3] has pointed out that abnormal fragility of the cells is exaggerated if the patient's blood is annised and allowed to stand for 24 hours at room-perature, whereas normal blood is not affected, method, based on this observation, may well help how up minor changes in red cell fragility

ickle cell anæmia has been recognised for 40 years, its clinical pictures are well described in the text-ks Under reduced oxygen tension, as when blood ollected from a finger that has been congested a rubber band for five minutes, the red cells ibit a series of typical deformities Several methods the rapid detection of this sickling have been sed[4] Investigations among the relations of ients with sickle-cell anæmia soon revealed many h sickling of their red cells but no anæmia, these ple are said to show the "sickle cell trait" In the A Neel[5] estimated that there is 1 case of the mia to about 50 of the trait The sickle cell maly has been connected particularly with Negroes the African Bantus and Nilotes the trait is much mmoner than among the American Negroes, but lly enough the sickle cell anæmia syndrome is ch less common, according to Raper,[6] in African groes the ratio of anæmia to trait is less than 1 in 0 On the current theory sickle cell disease is ited as a Mendelian dominant, when the minant gene is heterozygous the person shows only sickle cell trait, whereas if it is homozygous he elops the full sickle cell anæmia syndrome But, Lehmann[7] points out, it is difficult to fit this ory to the African figures, which suggest that anæmia should be much commoner, among the moid Baamba, for instance, the incidence of the le-cell trait is 45%, and this percentage must ude some homozygotes Raper suggests that some er factor, imported by intermarriage with other es, may be responsible for the high incidence of le cell anæmia in American Negroes The sickle anomaly is not entirely confined to Negroes ntrobe[8] cites 8 genuine cases in white families, these columns Choremis and colleagues[9] lately orted some cases in Greeks, and Dreyfuss and nyesch[10] found sickling of the red cells in 10 out 105 Yemenite Jewish children The curiously ped red cells have lately been linked with abnormal ms of hæmoglobin Pauling et al.[11] have found by physicochemical methods that in sickle cell anæmia all the hæmoglobin in the red cells is abnormal, whereas *in sickle cell trait* 40% is abnormal and 60% normal Perutz et al[12] have demonstrated similar abnormalities in their X ray and solubility studies And now Neel[13] seems to have established the existence of a mild form of sickle cell anæmia associated with a second abnormal hæmoglobin

Mediterranean anæmia, or "thalassæmia," as i now called, in its full blown form has a striking clinic picture The onset is usually in childhood, there after there is progressive anæmia with splenomegaly, a "mongoloid" facies, and characteristic X ray changes in the bones, especially the skull, familial incidence is the rule, and the disease is resistant to all treatment Such a remarkable syndrome could not escape recog nition for long, and it was described by Italian physicians in the 1880s, though owing to the bony changes it was then linked with rickets It was more clearly described in 1925 by Cooley and Lee, who noted its incidence among children whose parents came *from the Eastern Mediterranean regions,* especially Italy and Greece Later investigations have established that the syndrome is associated with thin red cells that are unusually *resistant* to saline solutions, complete hæmolysis being attained only below 0 3% of NaCl or in even more dilute solutions The red cells, however, seem to be easily fragmented, and blood films show extreme variation in their size and shape When the red cells are transfused into normal people they survive for only 15–50 days, compared with the normal 120 days The leptocyte often appears in stained films as a cell with a pale circle round a deeply stained central area—a so called "target cell" Examination of the relations of known cases has shown that, as in sickle cell disease, apparently healthy people may have target cells in their blood and red cells showing the typical increased resistance to hypotonic saline The situation is clearly presented in a monograph by Astaldi and others[14] and in Frontali's review[15]

Three forms of thalassæmia are now recognized (1) thalassæmia major, the fully developed Cooley's syndrome that appears in infancy and is always fatal, (2) thalassæmia minor, first noted in the second year of life and relatively chronic, with anæmia, icterus, and hepatosplenomegaly, described in Italy as the "Rietti Greppi Micheli syndrome of ictero-anæmia with increased erythrocyte resistance", (3) thalassæmia minima, in which the hæmatological abnormality is present alone—namely, increased red cell resistance, small cells, and sometimes a moderate polycythæmia with a normal hæmoglobin level Thalassæmia is now thought to be inherited like sickle cell disease, thalassæmia major represents the effect of homozygous inheritance, *and thalassæmia* minor and minima that of heterozygous inheritance Many affected families have been described in Italy, Greece, and America, and Fawdry[16] has reported the disease from Cyprus Though it is commonest among Eastern Mediterranean peoples, thalassæmia has been reported from many other places, though

---

aradi S *J clin Path* 1951 4 221

Annotation *Lancet* 1948 i 874

eel J V *Medicine* 1947 26 115

aper A B *J trop Med. Hyg* 1950 53 49

ehmann H *Nature, Lond* 1951 167 931

Vintrobe M. M. Clinical Hematology 2nd ed, London 1946 p 501

Choremis C Zervos N Constantinides V, Zannos L *Lancet* May 26 1951 p 1147

Dreyfuss F Benyesch M. *Nature Lond* 1951 167 950

Annotation. *Lancet* 1950 i 770

[12] Perutz M F Liquori A M. Eirich F *Nature Lond* 1951, 167, 920

[13] Neel, J V *Blood*, 1951, 6 389

[14] Astaldi G, Tolentino P Sacchetti C La Talassemia Pavia 1951

[15] Frontali G *Sem Hôp Paris* 1951 27 1209

[16] Fawdry A L *Lancet* 1944 i 171

nor do they mention any definite period over which it has been tried, or the forms which it has taken They do, however, note—elsewhere in the report—that the young men now in borstals are of the generation which " suffered most the unsettling conditions of the war years Evacuation, bombing, interrupted schooling, lack of proper parental control, all helped to produce boys and girls who are not able, or are not disposed, to count the cost of their actions and are therefore more difficult to train " A proportion of them, the committee assert, " are of a type so vicious and obdurate as to be incapable of influence by the good example and quality of the staff, or by any admonition or advice, however wise and wholesome " They are not here concerned, they add, with the reasons why these vicious young people exist, or with their numbers, but they recommend that a special closed institution should be established with all possible speed where they can all be sent, so that their persistent misconduct and subversive activities will not interfere with the training of others

It is not easy to see that this would really be a solution if the young people are as vicious and obdurate as the committee believe, they are surely not fit for any kind of borstal training, and it is doubtful whether they will pick up better habits in the unrelieved society of each other Nevertheless, such an institution would certainly help to prevent this more hardened type from corrupting others It would be interesting to know what proportion of the whole they are believed to form The offence records of 4 of the borstals for the years 1947 and 1949, which are set out in an appendix, suggests that they must be relatively few Serious offences are rare, and some are so trivial (the filching of 4 oz of sugar from the kitchen, a theft of apples from the orchard, and failure to have the face washed for tea) as to suggest an almost grandmotherly concern for behaviour Of the more serious offences the commonest are unsatisfactory conduct (usually insubordination or insolence, often coupled with swearing) and absconding or failure to return from leave Fighting among the boys seems to be a rare offence (only 7 instances out of 175 offences in the years 1947 and 1949 taken together), and assault on an officer rarer still (only 6 instances) In 1947 there was one attempted suicide and one case of stabbing with a table-knife, but there were no offences of comparable gravity in 1949 All the assaults on officers occurred in the earlier year, too, so in this respect at all events discipline seems to have improved The populations were similar in the two years (926 in 1947 and 931 in 1949), yet there were fewer offences in 1949 than in 1947 (77 as against 98) Though there may be reasons for this decline which the committee have not quoted, the figures do not suggest that behaviour in borstals had deteriorated in the later year

Of the 175 offences 5 were examples of homosexual behaviour, and—since few people regard this form of emotional arrest as impartially as they would, say, mental defect—there were witnesses who advocated that those addicted to homosexual practices should be eligible for the special corrective institutions designed for the vicious and obdurate The committee think that in the borstals there is probably " a very small percentage of untreatable practising homosexuals whose influence may be very pernicious and quite out of proportion to their numbers " They wisely advocate that each case should be judged on its merits, but add the counsel of defeat that when people have been convicted of offences of this kind, " removal to prison might provide in certain cases, the least unsatisfactory solution " It would, of course be quite a convenient solution as far as society is concerned, and probably widely acceptable, for the idea that people become homosexual by choice dies hard Whether we should be justified in dealing with a disabled criminal in quite this way is open to question We take credit that in this country the mental defective convicted of crime is received into an institution appropriate to his state The report is disappointing in this respect and some others the committee seem to have brought little vision to an important task

Inherited Red-cell Anomalies

THE accumulated facts and findings of 25 years have given us a clearer view of the inherited red cell anomalies and the diseases that sometimes accompany them Four of these anomalies are known In *elliptocytosis* the red cells are biconvex like the camel's In *spherocytosis* they are thicker than normal, this abnormality is associated with the hæmolytic anæmia known as acholuric jaundice or congenital hæmolytic jaundice In *drepanocytosis*, more familiar as sickle cell anæmia, some red cells adopt curious reaping hook (falciform) shapes if they are starved of oxygen, regaining their normal form if the oxygen supply improves, and this deformity is sometimes accompanied by recurrent hæmolytic crises In the fourth anomaly, *thalassæmia*, or leptocytosis, seen in cases of Mediterranean anæmia or Cooley's syndrome, the red cells are abnormally thin Thus of the four types of anomalous red cells only the elliptocytes can withstand the wear and tear of the circulation without any tendency to hæmolysis[1] Elliptocytosis seems to be inherited as a simple Mendelian dominant[2], it has been traced through families of several different races, including some of Negro descent The other three anomalies are easily demonstrated and each gives rise to a characteristic disease People who have one of these diseases in its fully developed form seldom survive to a marriageable age, or if they live long enough they rarely have children, the anomaly is passed on mainly by apparently healthy people who have it in a minor form which as a rule will not be detected unless it is specially sought

The best known and perhaps least rare of the anomalies is spherocytosis This chiefly affects people of European descent, only one or two cases have been detected in Negroes Many family trees extending over three or even four generations are now on record The anomaly is transmitted as a Mendelian dominant and can be transmitted by either parent The main clinical features of the disease—a persistent hæmolytic anæmia with crises of more grave anæmia, splenomegaly, and cure by splenectomy—are well known, abnormalities of bone structure may also occur but they are not a prominent part of the picture In the laboratory, spherocytosis is most easily detected by the cases of hepatic cirrhosis, 2 with hæmatemesis from oesophageal varices, and 4 with ascites, the splenic artery and the hepatic artery distal to the pancreatico duodenal branch were ligated All 6 cases have done remarkably well clinically with an apparent drop in the portal blood pressure Thus, despite the impairment of the hepatic circulation already present, complete and sudden occlusion of its arterial supply is withstood by the liver without any evidence of parenchymal necrosis

---

[1] Hedenstedt S *Acta chir scand* 1947, 95 suppl. 128

[2] Florman A L Wintrobe M M *Bull Johns Hopk. Hosp* 1938 63 209

Of even greater interest, perhaps, are the observations *of the Mayo Clinic workers on the production of* ascitic fluid The factors at present regarded as significant are the portal blood-pressure, the level of serum albumin, sodium retention, and impaired hepatic inactivation of an endogenous antidiuretic agent Of these factors the most important is usually thought to be raised portal venous pressure, due in most cases to reduction, by scarring, of the vascular bed within the liver, the ascitic fluid is then attributed to increased filtration pressure in the visceral serous membranes The results of ligations variously placed, singly or in combination, on the portal vein, inferior vena cava below the liver, and inferior vena cava above the liver have shown, however, that the main factor in determining ascites is not portal hypertension due to circulatory obstruction within the liver, but hepatic congestion due to interference with venous drainage from the liver The nature of the hepatic sinusoids is such that lymph is readily filtered off in large quantities Even in normal animals the liver is the main source of lymph from the abdominal viscera, and with hepatic venous congestion the flow of hepatic lymph may be increased thirtyfold with no associated increase of intestinal lymph-flow From its chemical composition ascitic fluid seems more likely to originate in the liver than as a transudate from portal visceral surfaces The clear, faintly yellow appearance of this fluid and its high protein content identify it more closely with hepatic lymph than with the colourless opalescent intestinal lymph, which has a low protein ontent This conception of excessive hepatic lymph s the source of ascitic fluid explains the lack of orrelation between the portal venous pressure and he development of ascites It is well known that atients with advanced cirrhosis and high portal ressures may be quite free from ascites, while in thers with relatively mild cirrhosis ascites may be onspicuous This seeming anomaly is understandable the ascites results, not from portal but from hepatic ongestion—an explanation which would also account r the ineffectiveness of serum-albumin transfusions controlling the accumulation of ascitic fluid The epatic sinusoids are unusually permeable to albumin, nd normal hepatic lymph has a protein level of over % If the liver is the source of ascitic fluid, then any ncrease in serum albumin will result in an increase the albumin content of the fluid Experimentally uch an increase has been observed by WHIPPLE and is colleagues[25], and a similar relation has also been eported in man[26]

The results of anastomosing the portal vein to the nferior vena cava in cases of hepatic cirrhosis also upport GRAY's hypothesis Follow up of 111 such cases[27] showed unmistakably the fall in portal pressure and the great clinical improvement associated with this procedure, and the reduction or disappearance of oesophageal varices is quite striking Nevertheless the effect on ascites is much less marked 'The operation is indicated primarily in patients who have had hæmorrhage from portal hypertension and varices It is almost an exclusive indication since ascites is not best treated by this method'[28] The pathogenesis of ascites is still not completely understood, but observations on both man and animals indicate that obstruc*tion to the outflow of blood from the liver is a more* important factor than impediment to venous outflow from the other abdominal viscera

---

5 McKee, F W, Hyatt, R E Wilt W G Tishkoff G H Whipple G H. *J exp Med.* 1949 90 447
6 Patek A. J Mankin H Colcher H, Lowell A Earle D P *J clin invest* 1948 27 135

Annotations

A CHEAP SUBSTITUTE FOR CORTISONE?

THE work of Dr A A Miles and Dr D A Long at the National Institute for Medical Research is a fascinating example of the methods of modern therapeutic research They started with a standard tissue reaction—that of guineapig skin to tuberculin toxin—and used this to investigate systematically the actions and interactions of various substances Thus they found that thyroxine increases tuberculin sensitivity and 'Cortisone' diminishes it[29] Furthermore, in their article on an earlier page of this issue, they report that thyroxine is powerless in the presence of cortisone, but cortisone is powerless if thyroxine is completely absent As so often happens in research an unexplained discrepancy led them to a new discovery—that cabbage contains a factor which modifies ascorbic acid metabolism.[30] When this cabbage factor was omitted results were different, and Dr Long and his colleagues were led to believe that the decreased tuberculin sensitivity of cabbage fed guineapigs which had received cortisone depended primarily on ascorbic acid—that is to say ascorbic acid, potentiated by cortisone, decreases tissue sensitivity to tuberculin

Speaking last Monday in a Festival symposium organised by the Royal Society of Medicine and the British Medical Association, Dr Long suggested by logical deduction, mixed with a certain amount of speculation, that the action of cortisone in the tissues is to facilitate the oxidation of ascorbic acid to dehydroascorbic acid And this substance, Dr Long reports, has actions indistinguishable from cortisone in the experimental procedures so far investigated Dehydroascorbic acid is known to be diabetogenic and may be dangerously so Nevertheless toxicity trials of this and the related substance alloxan are planned, and if successful will be followed by clinical trials Thus from the chance observation that cabbage is not the equivalent of the ascorbic acid it contains has come a new lead in the search for cheap antirheumatic drugs

SOCIAL WORK IN THE MENTAL HEALTH SERVICES

THE mental health services of England and Wales look after nearly 300,000 patients Probably no other group of patients is in such need of help from the social worker, yet a Government committee, which has been meeting for the past three years under the chairmanship of Prof J M Mackintosh, has to report[31]

---

27 Blakemore A H *J Amer med Ass* 1951 145 1335
28 Welch C S *Ibid* p 1338
29 Long D A Miles, A A *Lancet* 1950 i 492
30 Long D A Miles A A Perry W L M *Ibid*, May 19 1951 p 1085
31 Report of the Committee on Social Workers in the Mental Health Services London H M Stationery Office Cmd 8260 1951 Pp 58 1s 6*d* The members of the committee were Prof J M Mackintosh F R.C.P (chairman) Dr R M Bates Miss S Clement Brown Dr J B S Lewis Mrs K F McDougall Miss J M Mackenzie, Prof R H Parry F R C P, Mr Bryn Roberts Miss M J Roxburgh A M I A Dr Kenneth Soddy Miss Eileen L Younghusband Mr A Forbes (secretary)

these cases are mostly of the minor type with carriers of the minima type among the relations For instance, Silver[17] described 4 affected children in San Francisco—2 from Chinese families, 1 Mexican, while in 1 the mother was French and the father Filipino Dagradi et al[18] have reported the eighth case among American Negroes Not all the reported cases of thalassæmia can be accepted without reserve, since the diagnostic criteria are not so simple as with the sickle cell anomaly, in particular, target cells alone are not diagnostic Frontali[15] considers that for diagnosis the red cells must show increased resistance to hypotonic saline, excessive spontaneous fragmentation when kept in vitro, and true microcytosis, target cells should be present in fair numbers As in sickle cell anomaly, an abnormal hæmoglobin has been found in the red cells of thalassæmia, Astaldi and his co workers[11] say that fœtal hæmoglobin is still present in the red cells of major cases and to a less extent in minor ones, this finding has been confirmed by Liquori,[19] who found that in the red cells of patients with thalassæmia major over the age of 8 years at least half the hæmoglobin was of fœtal type, normally all the fœtal hæmoglobin disappears in the first 6 months of life

It will be seen that a considerable body of information has been gathered about these hereditary anomalies, but there are still many questions to be answered Are there really many sporadic cases of congenital spherocytosis, or are our methods for detecting spherocytosis too clumsy? It is now certain that hæmoglobin abnormalities may occur in elliptocytosis and spherocytosis, as they do in the other two conditions, Singer and his colleagues[20] have recently suggested that such abnormalities are less specific than was at first thought and can be detected in other anæmias Are new mutations a relatively frequent source of new cases, as they seem to be in hæmophilia, or will the major forms of the diseases be avoided by discouraging marriage between male and female carriers of the minor traits? At least we seem to be within reasonable distance of answering these questions

The Hepatic Circulation and Ascites

Sudden and unexplained deaths after operations on, or in the vicinity of, the liver are within the experience of almost all abdominal surgeons and pathologists Some at least of these deaths are due to interference with the hepatic circulation, and at the Mayo Clinic experimental investigation of this aspect has led to most interesting results, some of which have been discussed by Dr H K Gray[21] in a Moynihan lecture at the Royal College of Surgeons

It has long been known that in dogs ligation of the hepatic artery or one of its main branches results in the animal's death, owing to great bacterial proliferation in the ischæmic liver Administration of penicillin prevents this proliferation and with penicillin about half the animals survive ligation of the main hepatic artery, recovery is associated with the development of a collateral arterial supply, mainly derived from the diaphragm Gray strongly recommends the use of penicillin wherever operation has endangered the integrity of the hepatic artery, but the benefit is less certain than in dogs, since neither gross bacterial proliferation nor toxæmia is a feature of ischæmic hepatic necrosis in man It is, moreover, by no means certain that in man ligation of the hepatic artery or its branches results in infarction McMichael[22] has shown that in this respect there is considerable species difference, depending largely on the relative importance of the artery and of the portal vein in bringing oxygen to the liver In cats, for example, the portal vein contributes blood supplying about two thirds of the oxygen used by the liver, whereas in rabbits the artery has the major share In the rabbit ligature of the artery causes typical infarction, but in the cat only slight centrilobular degenerative changes It seems that here man more closely resembles the cat than the rabbit, the portal vein providing a high proportion of the hepatic oxygen requirement In man ligation of a branch of the hepatic artery rarely leads to infarction, unless shock or some other factor further impairs the intrahepatic blood flow The importance of the portal blood supply has also been studied with reference to its influence on hepatic regeneration after excision of 70% of the liver substance In a series of well planned experimental ligations, with and without portocaval anastomosis, Gray showed that the presence of the portal blood was essential for adequate regeneration, while "in those animals in which no regeneration had occurred, the only common factor that obtained seemed to be the absence of portal blood" This is reminiscent of the classical experiments of Rous and Larimore[23] on the effects of ligation of the left portal vein in rabbits The portion of the rabbit's liver supplied by this vein underwent progressive atrophy with simultaneous hypertrophy of the right lobe, which of course still retained its portal blood supply intact If, however, the hypertrophy of the right lobe was prevented by ligation of the right hepatic bile duct, atrophy of the left lobe did not ensue This experiment illustrates the dependence of structure on function, and the dependence of function on supply of appropriate metabolites Apart from oxygen, the bulk of the raw materials used by the liver is brought to it by the portal vein The gradual atrophy in any area of liver deprived of its portal supply may therefore be regarded as a form of disuse atrophy

After partial hepatectomy regeneration requires a better portal blood supply than does maintenance of the status quo Thus, in the dog with the establishment of an Eck fistula general hepatic atrophy is slight, but in such a dog regeneration after partial hepatectomy is greatly impaired It seems that the supply of raw materials to the liver, despite an Eck fistula, suffices to prevent disuse atrophy, but not for the synthesis of a large quantity of new hepatic tissue Presumably the blood supply to any organ normally provides the raw materials both for its work and its regeneration, it is only in organs with a dual blood supply that these two rôles can be distinguished The ability of the human liver to survive without its arterial blood supply is particularly well illustrated by the operation recently introduced by Rienhoff[24] In of the disease[13] In two, liver function tests were abnormal, and in both these patients the blood copper content was raised and urinary excretion of copper and of amino acid nitrogens was increased Dimercaprol (BAL) s known to produce increased urinary excretion of opper,[13] and several courses of this substance were dministered to these two patients In both the copper xcretion at first increased, but subsequent courses had ss effect, and there was no demonstrable effect on he amino acid nitrogen excretion More surprisingly, finite clinical improvement was noted in both patients ver a period of a few months In the other two patients iver function tests were normal, in one the urinary opper content was somewhat increased and the amino cid nitrogen was normal while in the other these findings ere reversed, in neither case did dimercaprol have any ffect on these biochemical findings, nor was there any linical improvement

---

[17] Silver H K *Amer J Dis Child* 1950, 80 765

[18] Dagradi A E Sollod N, Friedlander J H *J Amer med Ass* 1951 145 317

[19] Liquori A M *Nature Lond* 1951 167 950

[20] Singer K Chernoff A I, Singer, L *Blood*, 1951, 6, 413 429

[21] Gray H K *Ann R Coll Surg* 1951, 8 354

[22] McMichael J *Quart J exp Physiol* 1937 27 73

[23] Rous P Larimore L D *J exp Med* 1920 31 609

[24] Rienhoff W F *Bull Johns Hopk Hosp* 1951 88, 368

These various findings suggest that two biochemical bnormalities may occur in hepatolenticular degeneration —increased amino-acid excretion in the urine, and ccumulation of copper in liver and basal ganglia with an creased blood-copper content and increased urinary xcretion of this metal—and that in individual cases hese two abnormalities may be dissociated Further ork is necessary to clarify the meaning of these findings, nd it would be advisable to correlate the clinical picture arefully with the biochemical abnormalities since there re two clinical and pathological types of the disease[6] n the classical type of Kinnier Wilson dystonia and ntorted postures are the prominent clinical findings, hile cavitation and softening of the putamen are vident at necropsy, in the other type, to which the ame of pseudo sclerosis was given by Westphal[14] and y Strumpell,[15] tremor with little in the way of abnormal osturing is prominent clinically, while pathologically here is usually no naked eye abnormality but wide-pread glial charges microscopically[16] In both types here is hepatic cirrhosis and a Kayser Fleischer ring in the cornea. Possibly different biochemical abnormalities ay be present in these two types of hepatolenticular egeneration, at any rate in the earlier stages, while in he late stage of liver failure both abnormalities may be resent, as in Cumings's two cases with abnormal liver unction tests.

TOXIC SPRAYS IN AGRICULTURE

THE death reported on p 1419 draws attention once gain to the dangers of toxic chemical substances in griculture Since the cereal crop spraying season of 946 eight agricultural workers in Great Britain have ied of di nitro ortho cresol (D N O C) poisoning In ddition to the latest death there have been a number f cases of acute poisoning by D N O C in the present ason Instructions to users of D N O C include an ccount of the early signs and symptoms of poisoning, nd this is also printed on the labels of containers irculars giving particulars of spraying times, the risks agricultural workers and an account of the clinical gns and symptoms and treatment of poisoning by toxic hemical substances in agriculture were sent this year by he British Medical Association to all doctors,[17] and the arnings were repeated in circulars from the Ministry f Health and the Ministry of Agriculture The recom-endations of the Zuckerman working party, appointed o inquire into the safe handling of these substances, ave also been published The clinical picture of D N O C oisoning is quite different from that of poisoning by the organic phosphorus insecticides, and the conditions must be distinguished. In D N O C poisoning the rapid progress from apparent well being to death underlines the need for early diagnosis No antidote is known at the present time but prompt treatment by general measures, including absolute rest, cold sponging, and the administration of barbiturates, has proved effective even in severely affected patients A high environmental temperature increases the risk of absorption of D N O C, aggravates symptoms, and may precipitate symptoms as long as 48 hours after the last exposure to D N O C Poisoning may be cumulative

Spraying of D N O C on cereal crops is almost at an end for 1951, but the use of the new organic phosphorus insecticides has begun and will continue for 2-3 months Atropine is a specific antidote in poisoning by these phosphorus substances A great deal of information about the clinical features and treatment of poisoning by both D N O C and organic phosphorus insecticides has been collected by the Department for Research in Industrial Medicine at the London Hospital. Doctors are asked to notify this department (Bishopsgate 3255) of suspected cases of poisoning at the earliest possible moment

QUINCENTENARY AT GLASGOW

CELEBRATION of the Quincentenary of Glasgow University was to have been a royal occasion, and regret was expressed on all sides that the King and Queen had after all been unable to come

The presentation of addresses from other universities and learned bodies was a most colourful ceremony Lord Boyd Orr, chancellor of the university, said that they looked back with pride and thankfulness on what had been achieved, and looked forward with hope that the university would continue to contribute in ever-increasing measure to the world wide common fund of knowledge He emphasised the need for wisdom and understanding, to ensure the proper use of knowledge for the promotion of the welfare of mankind Sir Hector Hetherington, principal of the university, thanking the delegates, said that our universities had long ago ceased to cultivate a cloistered virtue, and that they were involved in all the practical issues of the modern world

Among those who received the honorary degree of doctor of laws, Medicine was represented by Prof E D Adrian, O M, F.R S (Cambridge), Prof Evarts Graham (Washington), Prof J M Holst (Oslo), Prof B A Houssay, For Mem R S, Prof. H F Humphreys, F D S (Birmingham), Sir John Parkinson (London), Prof Dorothy Russell (London) Prof Rene Sand (Brussels) and Prof G H Whipple (Rochester) The formal ceremonies concluded in St Andrew's Hall on June 21 with an oration by Lord Macmillan of Aberfeldy Before the address a message from the King was read in which His Majesty referred to the quincentenary as "a notable event in the history, not only of Scotland, but of the academic world generally" Lord Macmillan gave a brief review of the history of the university through the centuries and dwelt on the good fortune of the University of Glasgow in being situated in a great industrial zone The Prime Minister paid tribute to Scotland's interest in higher education—"realising that it would pay them better to cultivate their brains than their soil." He referred to the University Grants Committee as a characteristically British device in that it passed muster with the financial critics of the House of Commons while it left the universities almost completely free to run their own affairs "In a democracy," he continued, "it is fundamental that thought should be free, and the inquiring and critical university spirit should be brought to bear on all our affairs. The university must ever seek for truth, it must never be a mere instrument in the hands of a Government, a Church, or any political or economic group"

---

2 Cumings J N *Ibid* 1951 74 10
3 Mandelbrote B M Stanier M W Thompson, R H S Thruston, M N *Ibid*, 1948 71 212
4. Westphal C *Arch Psychiat* 1883 14 87
5 Strumpell, A. *Dtsch Z Nervenheilk.* 1898 12, 115
6 Hosslin C Alzeimer A. *Z ges Neurol Psychiat.* 1912 8 183
7 See *Lancet* March 31 1951 p 728

an acute shortage of trained workers in every branch of this essential work The reasons are not far to seek The work is exacting, it requires a long training, and it can be done successfully only by responsible and mature people Yet the salaries offered are small, and the committee believes that this is the most important single cause of the shortage of recruits Training is often taken when the candidate is older than most students, and the committee suggests an increase in the number of training grants, older women in other professions would often be willing to transfer to this work if their path was made smooth More men could take up this work with advantage, and part time workers, including married women, should be encouraged to share it

The cornerstone of social care in the mental health services must be the psychiatric social worker The committee has no doubt as to her proven value, and is anxious that the high standard of her training should not be sacrificed to immediate need There are so few psychiatric social workers that the demand for them has, as it were, gone underground, employers do not continue indefinitely to advertise for the unobtainable The committee estimates that about 1500 psychiatric social workers are needed at present, but that only 331 are in practice Nor are these scanty forces well deployed In 1949 there were 43 in the North of England and a mere 5 in Wales, compared with 231 in the South Training may be had only at the London School of Economics and the universities of Edinburgh and Manchester, which provide in all 65–70 places each year The committee insists that a register of these workers should be set up, and that training facilities should be increased—if possible at centres outside London, so as to encourage a more even distribution of the workers The committee proposes that the psychiatric social worker should be given greater theoretical training and experience of mental deficiency, especially community care, and a deeper insight into the administration of the mental welfare service of local health authorities More attention might also be given during her training to abnormal mental states One of the difficulties of the newly qualified psychiatric social worker, says the committee, is that the psychiatrist is sometimes unaware of how to make the best use of her help Of the basic courses in social science, held in 19 universities in England and Wales, the committee is more critical Most of these courses offer introductory studies rather than practical training, and "much remains to be done in linking theory with practice" Although practical work in the universities is increasing, most students obtain their practical experience in one or other of the specialised branches of social work—with an almoner for instance, or with probation officers A general background is thus lacking, and this leads to "overlapping in training and compartmental rigidity in practice" A further criticism is that students from the social science departments have insufficient grounding in psychology, so that they are unable to relate their knowledge to the living situations met in their daily work

The committee recognises that psychiatric social workers must remain the corps d'élite of the mental health services There is a much larger number of workers who will never take the full training The committee is concerned to make the best use of them, they must be "accounted for as they are and not made subordinate to some theoretical and unreal situation" Many, who were transferred from local authority services when the N H S started, are experienced in their work and highly skilled, and the committee proposes that for a specified period officers who have spent not less than five years in responsible social work should be eligible for recognition and registration For other workers who have had no formal training in mental health work and only limited practical experience the committee recommends in service training under the supervision of a psychiatric social worker, followed by opportunities for study at an extramural university department As an urgent but temporary measure for the next five years, the committee proposes a trainee scheme under which candidate would serve an apprenticeship of two years under an experienced worker, while receiving a salary or training grant At the end of two years the candidate would be able to apply for admission to a mental health course to train as a psychiatric social worker The committee believes that courses of this kind would attract both people who find a more formal academic training irksome and also younger people who have finished their university course but are not yet old enough to take the mental health course The committee suggests that this scheme should be organised by the regional hospital boards, and that a central committee should be set up to achieve common standards.

BIOCHEMISTRY AND HEPATOLENTICULAR DEGENERATION

HEPATOLENTICULAR degeneration, though rare, excites considerable interest The association of cirrhosis of the liver with pathological changes in the basal ganglia was reported in single cases by Ormerod,[1] Homen,[2] and Gowers,[3] [4] but it was Kinnier Wilson [5] who, in 1912, recognised that the association was more than a coincidence and established the clinical and pathological features of the disease to which his name has been attached In fact present ideas on the functions of these ganglia are partly derived from his study of this disease in which the cerebral changes are confined to the basal ganglia, and in particular the putamen Although symptoms due to the liver disorder are not common in the early stages of the disease, cirrhosis is thought to be present before there is clinical evidence of nervous dysfunction [6]

Recent biochemical studies have established some further facts which may help in determining the ætiology of the disease Uzman and Denny Brown [7] showed that the urine of a patient with hepatolenticular degeneration persistently contained a large amount of amino acid nitrogen—a finding that has been confirmed by Porter [8] Such excretion of amino acid nitrogen may occur in severe liver failure, but there was no clinical or laboratory evidence of this in Uzman's patient It has been suggested that this excess excretion may be due to lowered renal threshold rather than to liver dysfunction [9] Since manganese poisoning may cause cirrhosis of the liver with a Parkinsonian syndrome, metal metabolism has been studied in hepatolenticular degeneration, and in one case Luthy [10] found a greatly increased copper content of the liver and brain Cumings [11] estimated the copper and iron contents of the liver and of various parts of the brain in three fatal cases, and compared the findings with those in normal subjects and in patients with obstructive jaundice and multilobular cirrhosis of the liver In the cases of hepatolenticular degeneration he found an abnormally high copper content in the liver and in the brain, particularly in the globus pallidus and the putamen, there was no excess of iron in the liver or in the putamen, but there was some increase in the caudate nucleus, the thalamus, and the cortical grey matter He has lately extended these studies in four

---

1 Ormerod, J A *St Bart's Hosp Rep* 1890 26, 57
2 Homen E A *Zbl Neurol* 1890 9 514
3 Gowers W Diseases of the Nervous System London 1888
4 Gowers, W *Rev Neurol Psychiat* 1906 4 249
5 Wilson S A. K. *Brain* 1912 34, 295
6 Denny Brown D Diseases of the Basal Ganglia and Subthalamic Nuclei Oxford 1947
7 Uzman L Denny Brown D *Amer J med Sci* 1948 215 599
8 Porter H. *J Lab clin Med.* 1949 34 1623
9 Cooper A M Eckhardt, R D, Faloon W W Davidson C S *J clin Invest.* 1950, 29, 265
10 Luthy F *Dtsch Z Nervenheilk* 1931 123 101
11 Cumings J N *Brain,* 1948 71 410

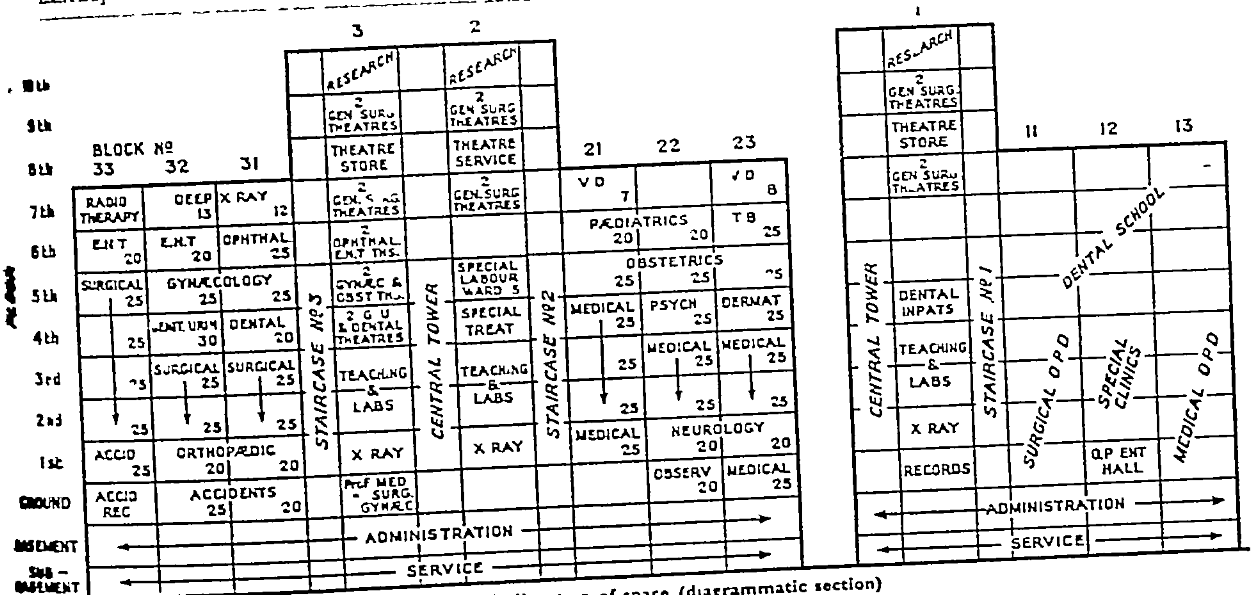


Fig 4—Proposed allocation of space (diagrammatic section)

The detailed disposition of the ward units has still to settled, but generally speaking it was assumed that the in surgical wards will be planned on a horizontal plane, close touch with the theatre floors, whereas possibly medical and special wards will be planned one above other Each ward will consist of a general ward of beds and 4 single bed wards To satisfy the shape e plan as a whole, and to arrange the wings of the ued length to fit the shape of the site, all the ward s (except the one on the extreme eastern boundary h has to be curtailed) are given a splayed outline planning on these lines the 24 bed wards can be divided into two 12 bed wards with a central space for the sister in charge and for supervision There will be eight ward units all of the same size and shape, the ninth unit being the exception also referred to

That then is the outline of the plan for the new Guy's, the advantages and disadvantages of the plan are given by the consultant architect[3] as

ADVANTAGES

1 Grouping of three wards around a vertical traffic artery —lifts, stairs, chutes &c —gives in effect separate hospitals of about 450–500 beds close to the optimum which can be serviced by such an artery

2. Each three ward group on each floor is immediately adjacent to a treatment and/or teaching unit of the central three pronged core of the building

3 There is a possibility of complete separation of teaching staff, student, and technician travel from the trolley and stretcher traffic of the lifts, and from the stairs used in patient service and by visitors This teaching and professional traffic becomes in a multi storey building and particularly in a teaching hospital a major item By the use of the central tower exclusively for this purpose no such traffic not used for actual patient contact need use the facilities in the towers serving the patient wings

4. Inspection of the plan shows excellent orientation for all wards and that all have a free outlook.

5 Each unit of area whether ward or clinical is in effect at the end of a line. Except for teaching access through the central wings to patient wards no area need become a traffic lane between other sections of the building an obvious necessity in all quadrangle or straight line planning

6 The plan lends itself to sectionalised building One- two or three ward units per floor, attached to a service tower and corresponding wing of the central core as indicated by need or resources, may be constructed. Units may be added adjacent to standing structures with a minimum of disturbance to the existing building or its occupants Under budgetary restrictions this is a major virtue of the plan, though the practical unit which can be built may be of a scale which is embarrassingly large to budget for

DISADVANTAGES

1 Decentralisation of lift services into four units involves more lifts than would be necessary were they grouped together This results from loss in diversification in use, since in most cases the number of lifts must be based on the frequence of service rather than the carrying capacity of the equipment The saving in horizontal travel and resulting time loss for personnel material, equipment &c, may justify the additional cost involved in providing the separate banks of vertical travel facilities

2 Once the entire pattern in plan has been constructed it will be a complete unit and no additions will be possible except to the extent that London County Council rulings will permit low buildings in the courts. The hospital would, therefore, be committed to a building which converted to patient housing in the nine outer "spokes," will have a final limit of about 1000 beds with treatment and teaching facilities available in the central core

3 When completed, the building will be a dominant mass in its own right without reference to the existing buildings and grounds It is acceptably related as to entry In so far as it faces ' at all it faces the park but it is not and, because of its size and height no matter how planned, cannot be an extension of the present group

We are grateful to the *Guy's Hospital Gazette* for figs 1–3, and to Mr Alner W Hall for fig 4

KING EDWARD'S HOSPITAL FUND FOR LONDON

The Duke of GLOUCESTER presided at the fifty fourth annual meeting of King Edward's Hospital Fund for London, at the House of Lords on June 20 He said that the fund is not today a mere grant distributing body It was very much in the mind of King Edward VII and his advisers that an active central body was needed in London to provide for the hospitals a means of organised cooperation among themselves, and to help the hospital world of London generally towards objectives that seemed to elude individual hospitals

It at once discouraged and brought to an end the obsolete and undesirable practice of requiring patients to get letters from subscribers it had to break down the prejudice against anybody visiting anybody else's hospital it had to see that hospitals did not ill advisedly open more beds than they could maintain, and so on. Times have changed There still remain innumerable matters where the hospitals need and welcome a lead from committees gathered together by the Fund for specific purposes For example in 1945 the Fund drew attention to the need for proper care of the health of

---

[3] *Ibid* p 31.

Special Articles

THE NEW GUY'S

WORK will soon begin on the new Guy's Hospital[1], part of the building will be completed within the next five years, at a cost of about £1 million, but the complete rebuilding is expected to be spread over fifty years

The new hospital,[2] has been planned by Mr A W Hall, the hospital's architect, in collaboration with Mr Paul G Burt, of Chicago, a consulting architect with wide experience of hospital construction The design is highly original and is a departure from English hospital conventions The plan adopted (fig 1) takes the form of a "multi star" or "snowflake" structure around a main central tower, with three subsidiary towers, the four being connected by three great blocks of buildings like "spokes" from a central hub From each of the subsidiary towers three wings project, all at right angles to each other and their own "spoke" These wings will house all the main wards, and the "spokes" will contain the research and teaching units, the operating theatres, and the administration offices The hospital will provide 800 beds, the maximum allowed by the Ministry of Health The new site is a war damaged area immediately adjacent to the present hospital, bounded by St Thomas Street, Weston Street, Snows Fields, and Great Maze Pond The general plan provides for a floor layout (fig 2) of (1) sub basement, (2) basement, (3) ground floor, (4) 6 floors of wards, (5) 1 floor, the 7th over ward blocks, for research, (6) 3 floors—the 8th, 9th and 10th —for operating theatres, &c , and (7) a further floor for tanks and engineering services There will be no beds above the 6th floor, the remaining units being housed (except for the 7th) in the great "spokes" connecting the central and subsidiary towers There will be about 10–12 operating theatres, sections for dental work and research, space for the research departments of the medical school, and 2 or more lecture rooms each holding 200 people The medical school will remain in its present building, but the dental school will be incorporated in the new building The outpatient and casualty departments will be built on the ground floor in close contact with the wards, and both departments will have separate entrances opening on to the street Part of the ground floor wi be taken up by entrances for staff, visitors, and patient porters' lodges, record offices, canteens, cloakrooms, an rooms for medical and administrative staff The basemen will house the kitchens and stores At some level, yet t be determined, an underground car park will be buil and subways will connect all parts of the hospital Th sub basement, which will extend over the whole of th building, will enable all the engineering services to b run wherever they are needed The new building will n encroach on any part of the present hospital so that th question of preserving Guy's House will remain ope

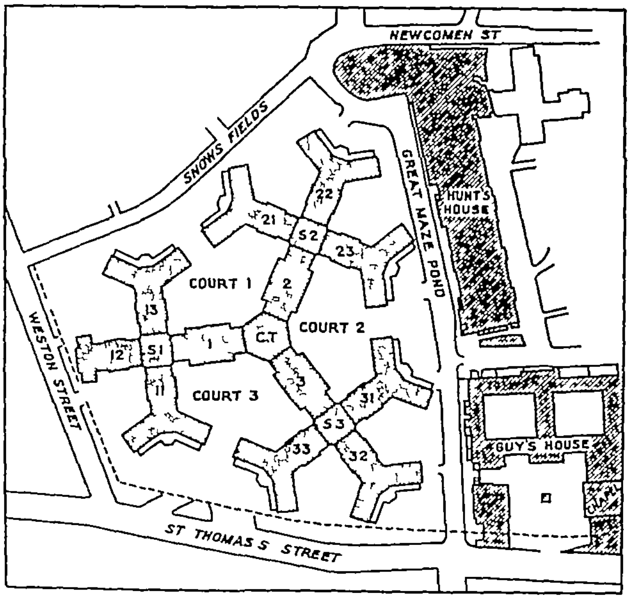


Fig 1—Ground plan of the new hospital and part of existing buildings on right.

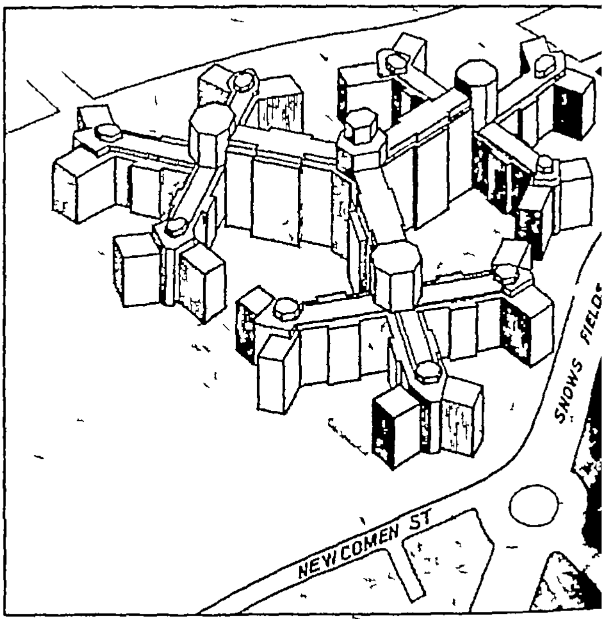


Fig 2—Model of the new hospital as seen from Newcomen Str

An important part of the plan for the new hospital i that the medical and research staff, students, and man of the administrative staff will use the staircases and lift in the central tower Patients, nurses, visitors, an services to and from wards will use the lifts and staircase in the subsidiary towers directly serving the wards I this way traffic across the hospital will be greatly reduced and practically all movement will be vertical, this wi make 20 or more lifts necessary In section, the buildin will satisfy all the conditions laid down governing angle of light and site cover, but the planning of the alternativ ways of escape, which have been accepted in principle b the London County Council has enabled a greatl increased height for the three main "spokes" beyon that usually allowed under the Building Act

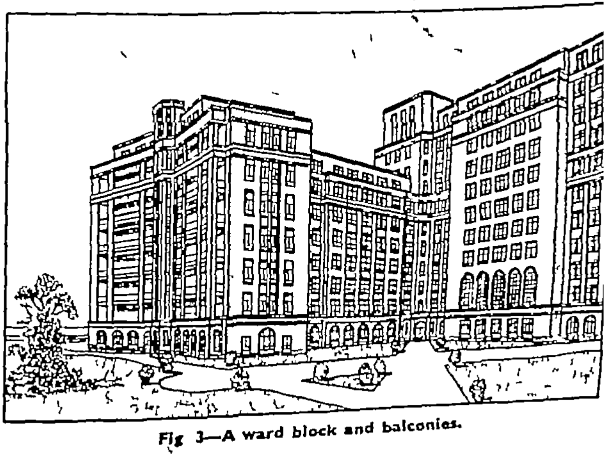


Fig 3—A ward block and balconies.

---

[1] *Lancet* June 16 1951 p 1329

[2] *Guy's Hosp Gaz* 1951, 45 110

ure A third patient, who had been operated on Paget's disease that had become sarcomatous, and had been fitted with an artificial palate and jaw a false face attached to her spectacles, was vincingly demonstrated in absentia

If Sir Stanford Cade's climax was dramatic Dr Walshe's was the outcome of inexorable logic His approach was orthodox, the careful history—no mere chronicle but an equal contribution by patient and doctor —and the meticulous physical examination pointed unmistakably to a tumour of the spinal cord Only a negative myelogram stood in the way This was itably disposed of, and the validity of the clinical dings was reaffirmed

BEDSIDE INSTRUCTION

Prof G W Pickering, discussing bedside teaching, insisted that the part of the teacher was to appraise and criticise while the student did the work The wards were essentially adapted to teach methods—methods of collecting and checking evidence and methods of interpretation This could only be done if students were given certain duties and responsibilities and made to take an active part in the management of patients They should be encouraged to make their own observa ns and to try and answer some of the problems which ise on ward rounds He always taught that treatment as essentially an experiment which demanded carefully ntrolled observation He favoured small classes with maximum of six and an optimum of one

Prof Robert Platt described a physiologicoclinical conference where preclinical students were shown selected patients whose diseases could be interpreted in terms of disordered physiological mechanisms The cases were presented by clinicians in the presence of physiologists, and students were encouraged to ask questions even though some could not be completely answered He illustrated the procedure by an account of a conference on a case of pernicious anæmia

Others welcomed this method because it took students up to the frontiers of knowledge and encouraged a critical outlook One speaker even valued it because it gave students a chance to tell their teachers that they were talking nonsense—a practice which he hoped would become universal The general sense of the meeting, however, was that this should be reserved for cases of obvious necessity

TEACHING IN THE OUTPATIENT DEPARTMENT

Mr A J Gardham and Sir James Spence gave an account of outpatient teaching Both appreciated the unique relationship between patient and doctor which was the essence of outpatient work Under modern conditions the outpatient department was the only place in a hospital where anyone could turn up as a sick person and have an individual consultation, this must take precedence over student teaching Each department had its own problems In some physical signs might be specially demonstrated, while in others students might be allowed to examine patients themselves or take histories, but the principles of teaching were the same In the outpatient department students learned by observing a trained person doing his ordinary work—seeing patients, diagnosing their complaints, taking decisions about treatment, and giving suitable explanations

TECHNICAL CLINICAL METHODS

Mr Julian Taylor also took a practical line when discussing the *training* of the young surgeon Each step must be learned empirically, the apprentice must try his hand under the master s eye and receive approval or correction of his work He should begin with simple tasks, and move on to more difficult ones only when he had proved his capacity Surgeons in the audience unanimously agreed that this was the true path to craftsmanship and condemned strongly the practice of teaching, or failing to teach, by giving unlimited responsibility to the untrained

PICTORIAL TEACHING

Discussing pictorial methods, Dr P W Cardew had much to say about bad slides with crowded diagrams, and often covered with illegible typescript These should have no place in teaching, for by a little thought, proper lettering, and skilful use of colour they could be transformed He preferred lantern slides to filmstrips and to the epidiascope, and he thought that there was a limited place for films in recording movements and surgical operations which could not easily be demonstrated in the theatre Miniature slides, which were easy to store and to transport, should be more widely used, and all illustrations should be filed in a central library Dr Cardew made a strong case for improved lecture theatres, and suggested the possible use of a diagonal construction scheme

THE YOUNG TEACHER

Prof W Melville Arnott remarked that the difference between the young and the old teacher was not so much of age as of mental outlook Young teachers had the advantage of being close to their students, and were in a position to establish an intimate relationship of give and take with their class They also lacked the philosophic doubts of their elders, and were able to leave students with a number of sharply defined images which they could remember Young teachers were the examination teachers par excellence, but they were often dogmatic, and that was dangerous The teacher's job was to maintain the inherited tradition of knowledge and to stimulate the intelligent to add to it There was no place for the average in medicine, nor for the kind of teacher who catered for them A research training and outlook were essential to the equipment of a teacher, and he would unhesitatingly reject those without them

This provoked considerable discussion on the general problem of teachers, including a defence of the dogmatist and a plea for encouragement of the urge to teach wherever it appeared

RESEARCH BY YOUNG GRADUATES

The training of the young research worker was discussed by Prof H J Seddon and Prof J McMichael Professor Seddon scrutinised the motives for research, which were not always academic He distrusted the man who "just wanted to do research," but would always look carefully at someone with an idea or a piece of work which he had already done Others less original might feel an urge to take part in some specific project and could prove useful members of a team Research was a laborious discipline and meant the exchange of the immediate satisfaction of clinical medicine, and of many pleasant social pursuits, for a life of much frustration and uncertain rewards It provided valuable training in the scientific method, and there was still a wide field for clinical studies of the natural history of disease and of the problems of epidemiology

Professor McMichael discussed the initiation of the young worker He preferred to give him facilities and little help until he saw how he handled his problems The real test of a man came when he had to surmount difficulties If he did this with energy and initiative, then he should be helped to the maximum extent

COMMENT

Judged by the interest which it aroused and the high standard of the discussions, this conference was an undoubted success, but its real value, as Professor Aird modestly pointed out, could be assessed only by the effect which it would have upon the teaching of those who took part If there was little said that was new, much was said to clarify the old Although the audience contained many experienced teachers already producing good results, there can have been few who failed to gain nurses Since then there has been a great advance, and our memorandum has been revised and re issued The Ministry made sure that copies reached all the appropriate people in hospitals, and between twenty and thirty thousand copies have been distributed or sold in the last month or two To take another example, everybody has known how important convalescence is and paid lip service to the great value of convalescent homes But, until the Fund instituted a real inquiry into the extent of the need and the way in which it is being met, nobody really had any accurate information at all The results of this inquiry will shortly be published

' That part of our new programme concerned with training schemes is well established and beginning to bear fruit We have now three centres from which this work is being carried on The nurses' staff college was established two years ago at 147, Cromwell Road, and you will see from the new prospectus from what a wide range of hospitals it is drawing its students In a way it is following an old tradition of the Fund by helping to spread experience from one hospital to another Our second undertaking, known as the Hospital Administrative Staff College, is now in operation Many of the wiser heads in the hospital world have long felt the need for such a college, and some most encouraging things have already been said about the first courses held there in the last two or three months Linked with this is the work we have been doing in the training of medical records officers, whose responsibilities are really much wider than the title suggests All the men trained last year have been snapped up for posts, and there is abundant evidence that the scheme is meeting a real need

The School of Hospital Catering at St Pancras Hospital is now ready This lies cheek by jowl with the large St Pancras Hospital kitchen, itself re equipped with the help of a grant of £11,000 from the Fund Here and in the catering advisory services linked with the school we are breaking new ground, and encountering one difficulty after another But we are sure much still remains to be done before hospital catering generally can be said to be on a satisfactory footing "

The Duke reported that in 1951 some £180,000 was being allocated in direct grants to hospitals and convalescent homes both within and without the health service Besides helping the existing hospitals outside the health service the fund had been called upon to look into many excellent voluntary projects and to decide whether they fell just within or just outside the scope of the Fund The old traditional procedure of visits and reports by subcommittees wherever capital grants were included was being maintained "At present there is probably no direction in which help can more usefully be given than in providing homes for the aged sick who would otherwise have to stay in hospital The quarter of a million which we set aside is now nearly all earmarked One after another the homes are being opened "

Sir **Edward Peacock**, the treasurer, in moving the adoption of the accounts said that the total expended during the year 1950 was £337,796 Grants to hospitals and convalescent homes absorbed £197,100, and £102,303 was spent in setting up and administering the special services An interim payment of £200,000 had been received from the estate of the late Lord Wakefield, and since the end of the year a further £80,000 had come in The days of the very large bequests might be drawing to a close, but the idea that money should be left to hospitals would not quickly die away, and it might be that many who in the past would have left bequests to individual hospitals would feel that their purpose would now be best achieved by making the Fund their legatee

Sir **Ernest Pooley**, chairman of the management committee, in presenting the annual report, referred to the evidence submitted by the Fund to various bodies, including the Committee on Charitable Trusts presided over by Lord Nathan of Churt The Fund was generally in agreement with the view that some modification was desirable in the law relating to charitable trusts It believed that means should be devised whereby the objects and scope of a charitable trust could—subject to proper safeguards—be varied more readily than was the case today, without the need to wait for the technical failure of the original trust But any legislation should be restricted to the minimum necessary to secure the needs in view, since it would be easy to damage the charitable impulse beyond repair if the confidence of the testator or other benefactor were undermined With the spread of the activities of the State into many more departments of the life of the community the importance of the independent charity was vastly increased

CONFERENCE ON MEDICAL TEACHING

Criticism of teachers and educational methods has by now an established place at student conferences and in the educational numbers of medical journals Recently it has taken a more constructive form, and teachers themselves have begun seriously to examine their practices and to seek ways of improving them Shortly before his death Sir Thomas Lewis illuminated the problem with a lucid analysis, and stimulated interest in a more scientific approach Since then enthusiasm has grown steadily, and last year a committee of the Royal College of Physicians was set up to consider the subject The time was clearly ripe for a conference, and the Postgraduate Medical School of London deserves to be congratulated for its enterprise in sponsoring such a conference, which was held on June 22 and 23

AIM OF THE MEDICAL TEACHER

With only two days available for discussions, the organisers confined themselves to the more concrete aspects of teaching methods None the less, both Dr R D **Lawrence**, who has been a pioneer in the movement, and Sir **Francis Fraser** insisted in their opening addresses on the need for a broad philosophical approach rather than a technological or instructional one Sir **Francis Fraser** particularly emphasised the university ideals of the conservation and interpretation of knowledge and the search for truth. Subsequent speakers, although discussing with virtuosity the conventional methods of teaching, were all keenly aware of this background

THE FORMAL LECTURE

Prof **Ian Aird** called for a more careful consideration of programmes, lectures on a single subject should be given consecutively and not scattered haphazardly over a period in a way detrimental to continuity of thought Classes as well as subjects should be studied the knowledge, for instance, that postgraduates tended to read their subject before, and undergraduates after a lecture must influence its content He touched lightly on the maladies of bad lecturers, both introvert and extrovert, and pleaded for their removal as positive impediments to learning In the matter of address he left little to chance and laid down for himself a rigid code He avoided extravagances of delivery and of dress, eschewing equally the light suit, the gaudy tie, and the gardenia, but encouraging a sophisticated use of mannerisms His preference for a focus of vision in the middle of the third row from the back—except when quelling a hostile stare, when he looked steadily at the root of the offender's nose—suggested that he had studied perspective and had achieved his own *golden section* This was an admirable performance in which the lecturer was seldom seen to deviate from his own standards

THE LECTURE DEMONSTRATION

Both Sir **Stanford Cade** and Dr F M R **Walshe**, F R S, displayed their mastery of the clinical demonstration Sir **Stanford Cade** demonstrated two patients, one showing the life history of a pimple on the forehead which had developed after twenty five years into an extensive rodent ulcer, and the other the different consequences of radical mastectomy and local excision of a tumour in each breast With forensic skill he extracted the answers he needed from his patients, and left his audience waiting tensely for the dramatic amount was 80,000–120,000 units Penicillin was in doses of 50,000 units intramuscularly every four in all moderate and severe cases, as well as in mild cases which required tracheotomy In all fatal penicillin was given until the patch subsided, or took place

AGE DISTRIBUTION

The age distribution of the 115 cases was as follows

Age-group	No of cases	Percentage
6 mos.–1 year	22	19·1
1 year–2 years	34	29·5
2–3 years	23	20·0
3–4 years	15	13·0
4–5 years	6	5·2
5–6 years	3	2·6
6–12 years	12	10·4
Total	115	

The percentage of patients aged less than 2 years was and less than 3 years 68·6

CLINICAL FEATURES

The clinical conditions are analysed in table I Laryngeal obstruction has been the most prominent feature in the cases Tracheotomy had to be done in [illegible]8% of the cases, which is an abnormally high figure [illegible] out of 23 patients who died also required tracheotomy, [illegible]t the cause of death in a large proportion of these was something else (see below) The death rate was extremely high (20%) Antitoxin given within forty eight hours of the onset of the illness gave good result, none of the patients admitted so early died, although 8 of them needed tracheotomy

TABLE II—INCIDENCE OF COMPLICATIONS

Day of disease	No of cases	Laryngeal	Cardiovascular	Pulmonary	Neurological	Adenitis and periadenitis	Primary laryngeal	Hæmorrhagic
[illegible]	27	10	3	5	1	3	3	0
[illegible]	18	11	5	3	2	1	1	0
[illegible]	26	7	7	3	2	1	1	0
[illegible]	27	16	11	9	2	3	1	1
Later	17	12	8	5	3	3	1	0
Total	115	56	34	25	10	11	7	1
%		*48·7*	*29·6*	*21·7*	*8·7*	*9·6*	*6·0*	*0·8*

The incidence of complications is shown in table II Here again laryngeal complications were the most important feature Contrary to expectation, the cardiovascular system was affected in 29·6% of the cases Such involvement was clinically assessed by the presence of some sign of involvement of the heart—e g, cyanosis, a displaced apex-beat, disproportionately fast heart rate, embryocardia, gallop rhythm heart-block (confirmed in many cases by electrocardiography), and unprovoked vomiting—or of the peripheral circulation such as ashen cyanosis (where the complexion was fair), cold clammy extremities, a feeble rapid pulse, pallor, collapsed veins, prostration, and asthenia with muscular hypotonia

The incidence of neurological complications was also high (8·7%) The commonest were paralysis of the soft palate and pharynx and generalised polyneuritis Bronchopneumonia and primary laryngeal involvement were encountered in 21·7% and 6·0% of cases respectively

CAUSES OF DEATH

Deaths in the early cases (up to the third day of disease) were due to extension of the membrane down the trachea In later cases circulatory failure, often complicated by polyneuritis, was the main cause of death In 5 cases where extension of the membrane down the trachea caused death tracheotomy did not relieve the obstruction completely In 1 such case the membrane was found at necropsy to have extended to the bifurcation of the trachea It is impossible to state whether such extension continued after the administration of serum, since all these patients lived from two to four days after tracheotomy

TABLE III—COMPLICATIONS CAUSING DEATH

Day of disease	Cardiovascular	Bronchopneumonia	Extension of membrane	Neurological	Total
3rd	0	1	3	0	3
4th	2	1	1	0	4
5th	5	4	0	2	8
Later	5	1	1	3	8
Total	12	7	5	5	23
%	52	*30·4*	*21·7*	*21·7*	

DISCUSSION

McLeod (1943) showed that the death rate from mitis infection was only 2–3% of all cases published up till then Unusually high death rates had been reported only three times Anderson et al (1936), in Australia, had reported 8%, Perry et al (1936), in America, had reported 8·2%, and Hilgers and Thoenes (1936), in Germany, had reported 19%

Although the mortality in the present series was 20%, if the cases admitted more than five days after the onset of diphtheria are excluded, the mortality was 15·3% This is in accord with the high fatality from mitis infection in diphtheria recorded by Hilgers and Thoenes (1936) This high death rate occurred in spite of the usual doses of serum and penicillin

In assessing our results, due consideration should be given to the comparatively few cases studied and to the inevitable difficulty of obtaining correct information of the date of onset

Another factor responsible for the high case-mortality may be the fact that in this country many of the patients with mild diphtheria do not seek hospital treatment, consequently there is always a tendency for the death-rate of diphtheria to be high

Nevertheless we are of opinion that mitis infection in Calcutta is not so benign as suggested by most workers in other countries Apart from the high death rate, the cardiovascular system was involved in 29·6% and was responsible for death of 52% of the patients coming to hospital on or after the fourth day of the disease Neurological complications were also present in 8·7% of the cases, which is a comparatively high figure for mitis infection

At the same time we wish to point out that almost all the important characteristic features of mitis infection described by previous workers were observed in our series For example, as expected in mitis cases, laryngeal obstruction was the most prominent complication, being present in 48·7% In early cases it caused death by extension of membrane Tracheotomy was also found necessary in 21 out of 23 fatal cases, although death in late cases was due to toxæmia Primary laryngeal diphtheria had accounted for 6% of the cases Bronchopneumonia, which is another common complication in mitis infection, was found in 21·7% In spite of the high death rate we did not encounter any malignant type of diphtheria with severe early toxic symptoms

This investigation tends to show that mitis infection, apart from its characteristic features, can produce a grave condition when it has established itself for a long enough period It seems to take a longer time than the other two types to produce severe toxæmia

SUMMARY

115 strains of *Corynebacterium diphtheriæ* isolated from diphtheria cases in Calcutta were found to be mitis only

enormously from the rational analysis of what is so often an intuitive performance The main function of the conference was to put what Sir James Spence called the instruments of teaching in their proper perspective But underlying each discussion could be sensed more than a little of that wider educational purpose which Sir Francis Fraser demanded From a consideration of the means there began to emerge a pattern of the end, the student turned doctor at the close of his undergraduate career

The conference readily accepted Mr Gardham's objective of the ideal resident, the totipotential cell of medicine, the doctor able to treat patients safely and with sympathy, the humanist scientifically trained, the artist equipped for research Such a man must acquire a technique of collecting facts and a method of scientific thought, and yet not lose the common touch He has to learn many facts, some of them empirically, before he can understand them Professor Arnott was perhaps a little hard upon the dogmatic teacher and a little optimistic in his intellectual demands Many of the best doctors learn by simple precept, and the teachers whom they appreciate do not always possess dogmatic minds What is important is that factual learning and understanding should follow one another, and that somehow a theme should be enunciated and constantly sustained throughout its numerous variations Professor Pickering and Professor Platt went a long way in this direction when they insisted on the basis of anatomy, physiology, and pathology of disordered structure function and of disease processes that underlies inevitable short cuts of clinical medicine The clu physiological and the clinicopathological confere could surely be profitably developed as a means integrating clinical and preclinical training, and inculcating a critical outlook

In the background was the question of the teac himself and his training In the presence of so m masters it was difficult not to feel that the best quali of a teacher are innate and incapable of precise definit Some have natural handicaps which make them teachers, and which they can never overcome But ther provided they are enthusiastic, could undoubtedly pi from instruction A single conference can only m them aware of faults and limitations, but in senior teacl it can awaken a sense of their responsibility for training and selection of their successors Even exp enced pedagogues might ponder Professor Aird's remin that an attentive audience is not always interested in lecturer's discourse, whilst some might profitably seci a candid friend in the theatre

This conference will have its repercussions, and oth will follow If many who went were already convert they will have acquired a fresh stimulus to pre their views Much remains to be discussed, and it be surprising if the substance of teaching, the curricul and examinations do not figure prominently in programme of future meetings

---

Public Health

DIPHTHERIA IN CALCUTTA

A DAS
M B Calcutta, M R C P
PROFESSOR OF MEDICINE,
NILRATAN SIRCAR MEDICAL
COLLEGE

S C GHOSAL
M B Calcutta, D Bact
PROFESSOR OF BACTERIOLOGY
AND PATHOLOGY, SCHOOL OF
TROPICAL MEDICINE,
CALCUTTA

IN 1931 Anderson et al showed that, by using a special tellurite medium, *Corynebacterium diphtheriæ* could be classified into three types—gravis, mitis, and intermedius These types, they found, had characteristic cultural and biochemical reactions, and it was possible to correlate the severity of the illness with the type present Gravis, as the name implies, was associated with a high fatality rate, and mitis mostly with mild cases Intermedius corresponded rather to gravis than to mitis as regards the severity of the disease

Since then, the results of many other investigations, in England and elsewhere, have supported the contention that gravis and intermedius types are mainly responsible for severe cases with a high fatality rate, and hence predominate where diphtheria is severe, whereas mitis is usually encountered more in places where the disease is mild

On the other hand, a few workers, such as Wright and Rankin (1932), Menton (1932), and Parish et al (1932), have either been unable to classify the strains properly into three types or have found the mitis type commonly associated with severe infection

We have, in India, very little information on this subject One of us, using the technique of Anderson et al (1931), has shown (Ghosal 1944) that mitis greatly preponderated in Calcutta, gravis and intermedius being rare Soman and Naik (1949) have also noticed a high incidence of mitis in Bombay

The present investigation was undertaken in 1949 to determine the incidence of types prevalent in Calcutta at that time, and to find out whether the type of organism could be correlated with the severity of the disease Our report is based on 115 bacteriologically positive cases of diphtheria admitted into the Calcutta Medical College

METHOD

Swabs were plated on McLeod's blood tellurite mediu The colonies were examined after 24 and 48 hours a subcultured on Lœffler's medium Morphological exa nation was done after overnight incubation All stra were then tested for action on saccharose, gluco maltose, glycogen, and starch Broth cultures and te for hæmolysis and pathogenicity were made only wh necessary

BACTERIOLOGY

Most of the strains could be typed on the basis appearance of the colonies on blood tellurite mediu morphology, and action on sugar without much difficul and were found to be mitis In some instances furt tests had to be done to confirm the diagnosis No ot types were encountered in this series

TYPES OF CASES

Cases were divided into mild, moderately severe, a severe according to the following criteria

(1) *Mild* —Exudate not fully covering area of both tons heart rate below 120 a minute, periadenitis exceptional, pallor or prostration, no fœtor no other signs of toxæmia

(2) *Moderate* —Exudate on both tonsils and extending to ot areas of the fauces heart rate about 140 a minute slight fa or periadenitis slight pallor or prostration

(3) *Severe* —Extensive membrane on both tonsils and on palate uvula, and pharynx often around fauces periadeni often fœtor, heart rate above 160 a minute, pallor and prostrat both evident often other signs of toxæmia

In mild cases the patient was given 40,000 units antitoxin intramuscularly, in moderate and severe ca

TABLE I—CLINICAL CONDITIONS IN 115 CASES

Day of dis case	No of cases	Mild	Moderately severe	Severe	Hæmorrhagic	Tracheotomy	Tracheotomy death	No of deaths
2nd	27	22	2	3	0	8	0	0
3rd	18	8	5	5	0	8	3	3 (16 8
4th	26	12	8	6	0	7	4	4 (15 4
5th	27	6	11	10	1	12	7	8 (29 6
Later	17	0	5	6	0	12	7	8 (47 0
Total %	115	54 46 9	31 26 9	30 26	1 0 8	47 40 8	21 18 3	23 20

In England Now

Running Commentary by Peripatetic Correspondents

WEEK before, I had stood in pouring rain gazing on lights and reflections from the South Bank, the flood- of St Paul's, and Middle Temple Hall in its de Now I was passing them again in brilliant ght Is St Paul's floodlit more beautiful than Paul's by day surrounded by the remains of burnt- warehouses, and waste ground golden with weeds, across the idle barges and busy tugs of the river? man proud of his sense of direction will be humbled the waterbus It chugs from side to side of its , throwing pictures of Tower Bridge up at you you least expect them You are almost certain Limehouse Church has walked across the river, find yourself amazed that the *Prospect of Whitby* look so small But it is not the illusions of size of position that are most startling on the river journey that this journey, on a midsummer day, can be so 'y beautiful And I am not referring to the well- architecture above Tower Bridge, but to the Pool, the Isle of Dogs, Greenwich Windows scintillate reflected sun, roofs are mirrors glittering with ns wholly different from their "local" slatey grey corrugated iron The river itself defeats the impres- , the barges are every colour except black, their ic lines, horizontal or perpendicular, reminding of some of Ingres' curves The bridges, seen against sun, retain some of their basic blackness, but it is inconstant black shot through with patines of pure like Belmont Garden or the Globe Theatre

* * *

I did not realise what a back number I am until I t in" on the viva voce part of a prize examination on child health for sixth-year students

The candidate was asked how he would feed a breast-fed baby whose mother had had a severe accident and could no longer feed it My answer would have been "Make sure that the person who was looking after the baby knew all about the hygiene of keeping bottles and teats Advise her to go to the chemist and buy a glass measure graduated in fluid ounces, bottles, teats, and a packet of any reputable brand of dried milk and follow the instructions on the packet Tell her to let me know f she has any trouble" But what the candidate said was "The baby must have so many calories per kilogramme of body-weight, so many c cm of water, and o many grammes of protein, carbohydrate, and fat in he 24 hours" The only thing he was not certain about was how much sodium chloride to give it Milk was never mentioned in the discussion—as though the subject was lightly improper

* * *

That wretched problem of the 20 foot ladder leaning gainst a wall and touching a 4 foot-cube box carelessly eft underneath (1950, i, 462, 514) cropped up again he other day and disorganised the department The Director was on leave, and the locum "sitting in" for um (as locums will when they haven't the courage to ead Agatha Christie) was browsing through the bound olumes of *The Lancet* The Media King was the first to e involved Calling to protest against some useless fancy nedium that the locum had ordered (as locums will) he vas soon leaning on the desk drawing triangles. The olution eluded the pair of them, and they enlisted the ld of the latest junior, a Distinctions-in-Higher-Certifi- ate type who pretended to know something about rigonometry In a short time Mary Queen of Spits, vas also involved The party was rudely interrupted by he Chief Technician, who always surfaces and looks for rouble at 11 A M precisely A chastened Media King nd subdued juniors went about their respective occa- ions, while the Chief Technician, whose scorn for locums s well known but suitably restrained, proceeded to solve he problem At 12 10 P.M., however, he muttered omething about agglutinations and disappeared into us sanctum, whereupon, so the Office types allege, he out through a trunk call to his brother who turns a lishonest penny by teaching mathematics in one of our less reputable scholastic institutions Whatever the outcome of this, it is further reported that he was seen during the lunch hour in the "Gardeners' Arms," drinking Guinness with the Deputy Chief Sanitary Inspector, two FIMTAs, and the local bookie, and drawing triangles on copies of the *Daily Express* By 2 30 the Milk Lab had claimed a solution, while the locum had interested two itinerant sampling officers, the MOH, and a midwife who came to the wrong lab for a blood-count

Fortunately all locums go home at 4 o'clock, and the whole business died suddenly when the Chief Technician, on his afternoon snoop, found triangles chalked on the wall of the animal house and blew his main fuses A junior who was foolish enough to mention the affair later was awarded five gross of Dreyer's tubes to clean

* * *

I am spending Sunday nursing my horse rake leg Readers of Westerns and American thrillers in general will agree that "riding the rods" (getting a free lift underneath a railroad freight car) must be the most uncomfortable mode of travel known to man It has no counterpart in England, but we have something that runs it pretty close—to wit, riding on a horse drawn hay rake What's more, the immediate discomforts of the actual journey by rake are nothing to the pains of horse rake leg, the occupational complaint that invariably develops next day This year, to speed up haymaking, we adapted our horse rake so that the tractor could pull it, and it was my lot to ride on the rake for the main part of a fine June Saturday Like most hybrids, this outfit had all the vices of both its parents, and the bad winter has left the ground unusually rough The tractor driver drove on inexorably, with me riding the rods behind, as helpless as no 2 on a tandem bicycle All I had to do was to trip the rake and keep my seat But it is pushing down the trip pedal about every 20 seconds for eight hours at a stretch (less time off for refreshment) that gives the amateur horse rake leg, and I got it all right That is why I am spending Sunday on the sofa

* * *

When the South Africans beat England in the first Test, at Trent Bridge, we had a discussion over tea on "Why we don't beat other Countries at Games like we used to" Sidney was pretty sure we had won the World Croquet Championship, and I seemed to remember reading about our beating all comers at archery Was there, we wondered, a clue in these particular successes? Were we, as a nation, yearning to return to our Tudor and Victorian periods of expansion? Was this a symptom of regression to racial childhood? Sidney was inclined to look on it as a cyclical phenomenon, controlled by the national hypothalamus, and he believed that all would be well in a few years George, on the other hand, insisted that it was all a result of the decline in breast-feeding He was sure the statisticians could satisfy everybody (except, of course, rival statisticians) on this point He urged us to begin training our 1968 Olympic champions now (Sidney had to be restrained from leaving to begin right away) John saw our decline in cricket as a symptom of inevitable national deterioration The only hope, in his view, lay in a few atom bombs to ginger up our genes It seemed a high price to pay, but (Gad, Sir!) whatever the cost, we agreed, the Old Country must pay it

It was a bit of a relief, though, to hear that we'd won the second Test without a single bomb being dropped

* * *

The Professor of Hispanic Studies had mislaid a contingent of distinguished Spanish and Portuguese visitors He was searching for them in vain at the main doors of the university's hall when the Professor of Natural Philosophy, having solemnly considered his difficulties, sternly rebuked him for "putting all his Basques in one exit"

* * *

Aphorism of the Week

It is often better to do nothing than to do one's best

Excluding cases admitted after the fifth day, the death rate was 15 3%

Laryngeal obstruction (48 6%) was the most prominent feature Cardiovascular and neurological involvement was found in 29 6% and 8 6% respectively Death in the early stage was caused by extension of the membrane, and later by toxæmia

The disease caused by the mitis type of *C diphtheriæ* in Calcutta seems to be much more serious than the disease it causes in England

REFERENCES

Anderson J S Happold F C McLeod J W Thomson, J G (1931) *J Path Bact* 34 667

Anderson, P M Goldsworthy, N E, Ward H K (1936) *Med J Aust* ii 350

Ghosal S C (1944) Proceedings of the 31st Indian Science Congress Abst of papers, p 102

Hilgers W Thoenes, F (1936) cited by McLeod (1943)

McLeod J W (1943) *Bact Rev* 7 1

Menton J (1932) *J Path Bact* 35 651

Parish H J, Whatley E E, O Brien R A (1932) *Ibid* p 653

Perry C A, Whitley O R Petran, E (1936) *Amer J Hyg* 23 580

Soman, D W, Nail S K (1949) *Indian med Gaz* 84 488

Wright H A Rankin A L K (1932) *Lancet*, ii, 884

Salmonella typhimurium Infection

On June 1, a 12-year old schoolboy in Paddington, London, became ill with abdominal symptoms His doctor diagnosed acute appendicitis, and he was admitted to hospital Laparotomy was performed, and the appendix was removed, but some 48 hours later the child had well marked sickness and diarrhœa Examination of the fæces showed *Salmonella typhimurium*, and the child died 2 days later

Investigation failed to show any article in the family diet that could be suspected Bacteriological examination of the fæces of all members of the family was negative, and all the family are well except for an infant sister, who is now in hospital with gastro enteritis In this case bacteriological examinations so far have proved negative The mother reported that from time to time mice had been seen on the premises Up to date only one mouse has been trapped, and a bacteriological examination has been negative Although mice have also been reported in the neighbouring houses there are no reports of dead mice being found, and further efforts are being made to obtain specimens for examination

B C G Vaccination in Denmark

In Copenhagen systematic tuberculin-testing of school-children has been carried out ever since 1937, and in 1943 as many as 74% of the tuberculin-negative children of school leaving age were vaccinated with B C G Later this measure was extended to younger school-children, and in 1948 the senior school medical officer of Copenhagen advocated B C G vaccination of every tuberculin-negative school-child Five doctors were appointed to carry out this recommendation, and between Oct 1, 1948, and March 31, 1949, they vaccinated some 39,000, representing about 70% of all the tuberculin-negative school children

Winge[1] has sought evidence of the effects of this measure in the most recent notifications of pulmonary tuberculosis in children aged 5–14 years, and in the number of children admitted to tuberculosis hospitals He found that for this age group the number of cases notified in 1948 was 158, while in 1949 it was 84, and in 1950 it was 52 In none of these 52 cases had B C G vaccination been undertaken During the same period there was a pronounced reduction in the number of children admitted to tuberculosis hospitals, and in the course of 1950—i e, between nine and twenty-one months after the completion of the mass vaccination campaign—the number of hospital beds required for tuberculous children was appreciably reduced Tuberculin negative children under school age are now being vaccinated with B C G on a large scale, and this measure is also recommended for all babies born in the municipal maternity hospitals in Copenhagen

Dr Winge adds that not one case of tuberculou meningitis, miliary tuberculosis, or pulmonary tuberculosis has been observed throughout the period 1935–5 among the children known to the central tuberculos station and vaccinated with B C G Yet some of them lived in homes to which one or more patients with open pulmonary tuberculosis belonged

---

[1] Winge, K *Nord. Med* May 16 1951 p 774

Parliament

Supplies of Cortisone

Sir Thomas Moore asked the Minister of Health what quantity of the new American drug 'Cortisone' had been imported during the quarter ended March 31, 1951, and how far this amount had fallen short of medical requirements.—Mr H A Marquand replied *1500 g of cortisone were* purchased by my department from the American manufacturers during the quarter As the use of this scarce drug is still experimental, requirements cannot be estimated, but we are importing all the manufacturers can make available

Bone-conduction Hearing-aids

Mr Ralph Morley asked the Minister the reasons for the long delay in the production and supply of bone conduction hearing aids.—Mr Marquand replied Research resources had at first to be concentrated on the production and improvement of the air conduction aid, the different models of which have now been found to meet the needs of the great majority of people requiring an aid The production of a satisfactory bone conduction aid raises difficult technical problems involving considerable research, but encouraging progress is now being made I think we are now at the point when the production of models for clinical trials is possible, and if those trials are satisfactory we shall certainly press on with rapid production

Tuberculosis in Scotland

Mr Malcolm MacPherson asked the Secretary of State for Scotland whether the improvement which took place in the tuberculosis situation in 1950 had continued in 1951—Miss Margaret Herbison replied Yes In the first quarter of 1951 there were 723 deaths from all forms of tuberculosis as compared with 826 in the first quarter of 1950 For the first 23 weeks of 1951 there were 4489 new cases notified as compared with 4678 in the corresponding period of 1950 Apart altogether from beds in Swiss sanatoria, the number of beds available in Scottish hospitals for the treatment of tuberculosis increased by 176 in the first quarter of 1951 But while this trend is most encouraging, it is no reason whatever for relaxing our efforts in any way, and I am still most anxious that all concerned should give first priority to the improvement of services for the prevention and treatment of tuberculosis in Scotland

Unfit for Service

Mr Heathcoat Amory asked the Minister of Labour the total number of men registered for national service since 1945 and the number found medically unfit—Mr Fred Lee replied 1 588,000 men were registered under the National Service Acts from January 1, 1946, up to May 5, 1951 Between Jan 1, 1946, and May 29, 1951, 186,000 men were found medically unfit for service

Misuse of Surgical Spirit

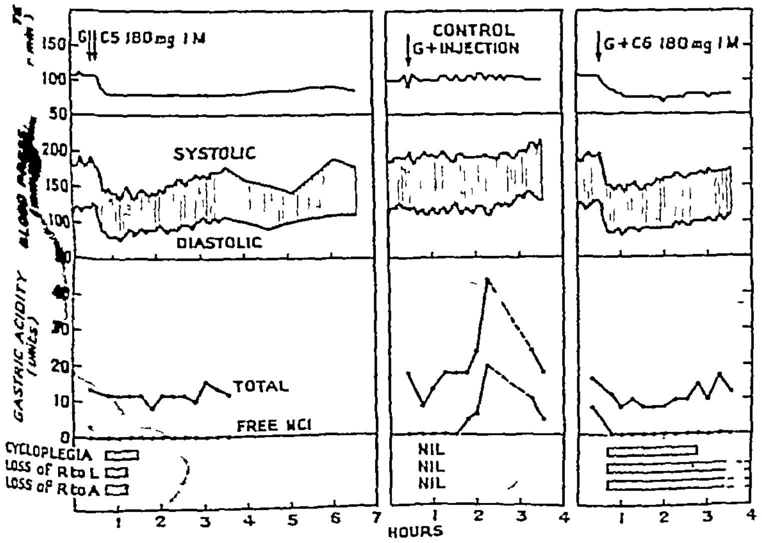
Mr Donald Scott asked the Home Secretary if he was aware of the misuse of surgical spirit, and if he would consider taking steps to enable him to prevent its sale by a chemist other than on a doctor's certificate—Mr Chuter Ede replied I am aware that there is some misuse of this spirit on a very small scale, but the only way in which I could control its sale in the manner suggested would be to list it as a poison under the Pharmacy and Poisons Act I do not think that it would be appropriate to use the powers conferred by that Act merely to prevent the misuse of surgical spirit by a few abnormal people I understand, however, that the commissioners of customs and excise have certain powers with regard to the sale of methylated spirit and I have asked the Chancellor of the Exchequer to consider whether these powers can be used to prevent this abuse ised that the disorder was caused by washing of the system almost all the available B vitamins by using up the rest to metabolise the glucose tion of alcohol to the glucose drips without supple ting these with B vitamins might increase the risk this complication

don W 1 Z A LEITNER

COMPARISON OF PENTAMETHONIUM AND HEXAMETHONIUM BROMIDE

SIR,—Since the demonstration by Paton and Zaimis[1] the ganglionic blocking effect of the pentamethonium hexamethonium salts, various reports of their macological action and of their effect in hypertensive e and peptic ulceration have appeared In some the drugs have been used for their sympathetic n and in others for their parasympathetic ganglionic king action In each instance the synaptic blocking that part of the autonomic nervous system upon which effect is desired may be a nuisance

Some of the early reports suggested that a particular drug might have a predominant effect on one or other the two divisions of the autonomic nervous system us Kay and Smith[2] stated that hexamethonium had a found effect on the gastric secretion and motility, in therapeutic doses it had no marked effect on the pressure More recently both drugs have been in the treatment of arterial hypertension[3 4 5] Hexamethonium has been favoured in the management of patients with duodenal ulceration[2 6 7 8] In a recent report on the use of the hypotensive action of these drugs to reduce bleeding in surgery Enderby and Pelmore[9] have suggested the administration of hexamethonium, whereas Hughes[10] has obtained uniformly satisfactory results with pentamethonium



Effects on the pulse-rate blood pressure and gastric acidity and certain ocular features produced by intramuscular injection of equal amounts of pentamethonium and hexamethonium bromide 2 mg per kg body-weight. G = gruel meal R to L = reaction to light. R to A = reaction to accommodation

SUMMARY OF EFFECTS OF PENTAMETHONIUM BROMIDE (C5) AND HEXAMETHONIUM BROMIDE (C6)

(1) Feature Observed	(2) No of cases	(3) Effect of injection of C5 (cases)			(4) Effect of injection of C6 (cases)			(5) (6) Effect of C5 and C6	
		Rise	Fall	No significant change	Rise	Fall	No significant change	Concordant (cases)	Discordant (cases)
Pulse rate	7	4	3	0	4	3	0	7	0
Systolic B P	7	0	6	1*	0	7	0	6	1
Diastolic B P	7	0	4	3*	0	6	1	5	2
Gastric acidity	6†	0	5	1†	0	5	1†	6	0
Intra ocular tension	6‡	0	6	0	0	6	0	6	0
		Present		Not present	Present		Not present		
Cycloplegia	7	3		4	3		4	7	0
Loss of reaction to light	7	4		3	4		3	7	0
Loss of reaction to accn	7	4		3	4		3	7	0

* One patient with labile hypertension was normotensive on day of injection of C5 and in another patient the diastolic pressure was lower on the day of injection of C5

† One patient had achlorhydria and thus no effect of C5 or C6 on gastric secretion could be observed

‡ One patient was orthopnoeic and it was not possible to measure the intra ocular tension

In view of this uncertainty some observations on this point were made before a trial of the methonium compounds in patients with severe hypertension Each patient received on different days intramuscular injections of pentamethonium bromide, hexamethonium bromide, and distilled water—the sequence being varied In all cases the dosage of the active compound was 2 mg per kg body weight Observations were made of the pulse rate, systolic and diastolic arterial blood pressures, gastric acidity in response to a gruel test meal procedure, presence of cycloplegia, change in reaction to light and accommodation, and, in certain cases, intra ocular tension The observations made during one investigation are shown in the accompanying figure, and the investigations are summarised in the table

It will be seen that in certain respects the response varied from case to case However, provided the original conditions were comparable, the responses to the pentamethonium and hexamethonium compounds were qualitatively similar in each individual patient (columns 5 and 6 of table) The only discordant results concerned the effect on the blood pressure in two patients One of these patients was hypertensive on the day when hexamethonium was injected, and normotensive on the day when pentamethonium was injected In the other patient, in whom the hypotensive effect was not well marked, the pre injection diastolic blood pressure was lower on the day of the injection of the pentamethonium bromide There was no significant difference in the quantitative effects of the two drugs

It was concluded that with the dosage and mode of administration described, there was no evidence of any superiority of one compound over the other in respect of sympathetic or parasympathetic ganglionic blocking activity, or avoidance of side effects

Pentamethonium and hexamethonium bromide were supplied through the courtesy of May & Baker Pty Ltd

Clinical Research Unit
Alfred Hospital
Melbourne Australia

A J BARNETT
Assistant Director

---

1 Paton W D M Zaimis E J Nature, Lond 1948 162 810
2 Kay A W Smith A N Brit med J 1950 i, 460
3 Campbell A Robertson E Ibid ii 804
4 Turner R Lancet 1950 ii 353
5 Saville S Ibid p 358
6 Kay A W Smith A N Brit med J 1950 ii, 807
7 Scott L D W Kay A W O Hare M. M. Simpson J A Ibid p 1470
8 Douthwaite A. H. Thorne M. G Ibid Jan. 20 1951 p 111.
9 Enderby G E H Pelmore J F Lancet March 24 1951 p 663
10 Hughes C Ibid p 666

Letters to the Editor

TEACHING THE TEACHER

Sir,—I was interested in your leading article of June 9 Some months ago I was shown round an officer cadet training unit, in which a large amount of detailed instruction has necessarily to be compressed into a short time The arrangements for this were most impressive, as was the extensive use of visual aids of all types

I was particularly impressed by one detail A specially trained and chosen junior officer is given the duty of attending all lectures and demonstrations for the purpose of subsequently criticising the lecturer or instructor, and especially with a view to correcting faults such as those you mention—addressing the floor or ceiling, turning away from the audience, fidgeting, staring with apparent surprise at a diagram one has just put up, mumbling, hesitating, and so on He also notes the degree of attention inspired in the audience, the lighting and ventilation of the room, and any other relevant factors He is the *universal candid friend* I was told, as an example of the system, that after the commandant's opening address this young man had asked to see him and said " I think your address was too quickly delivered and too complicated, sir These are only cadets, and I don't think they took it all in "

Most, almost all, who lecture could benefit from the help of the candid friend, and this excellent plan provides such help officially, and so without the possibility of ill feeling It is difficult to imagine the sort of person who might undertake a similar function in medical education, but the idea is perhaps worth considering

Reading J J Kempton

PNEUMOCONIOSIS IN COALMINERS

Sir,—The correspondence in your columns has shown how dangerous it can be to approach this question in a manner tinged with emotion Whilst we find on one side the miners' attitude described as " apprehensive and querulous," we find it on the other hand called " understandable and justifiable " Surely, Sir, this is pure emotionalism

I suggest that the questions raised should be submitted to a simple but exact analysis, and I suggest the following two simple statistical experiments, which could be easily checked and repeated

1 Let a few general practitioners in the Welsh coalfield (preferably in various parts of it) make a note of the next 100 new patients who come into their surgeries expressing concern about their chest condition and voicing a fear that it may be due to dust disease These patients should then be fully investigated, irrespective of age or industrial history, and the percentage of likely dust sufferers determined If the percentage were consistently very small this would obviously support the assumption of a " mass psychosomatic disorder ", but if the percentage should prove to be more or less substantial the assumption of an understandable and justifiable attitude " would appear to be correct I realise, of course, that to carry out this suggestion would entail a certain amount of effort and expense, but I believe such a pilot experiment would be worth while

2 Every certified sufferer from dust disease comes to necropsy It would be interesting to know the percentage of certified cases confirmed after death, compared with the percentage of certified cases not so confirmed As certification is made on the basis of clinical and radiological examinations performed by experienced observers, these figures would provide a suitable check on the efficiency of these methods I am, of course, aware of the possible sources of error of this method, but I do not think they are important enough greatly to vitiate the results

As far as I know, these figures have never been published, when they were asked for some time ago in Parliament the Minister of National Insurance replied that they were not available But perhaps some effort could now be directed towards producing them I fe that they would contribute greatly to the solution of t problems under discussion

Abertillery, Mon K Triger.

THE TREATMENT OF PSYCHONEUROTICS

Sir,—In his article last week Dr Neustatter deplor the " press button outlook " I agree with him, b am surprised to find the patient's natural fear of t treatment still being regarded as an obstacle T average patient does not know (and often should n know) that he has had convulsion treatment at all hyoscine gr $^{1}/_{100}$ plus morphine gr $^{1}/_{6}$ is given hyp dermically one to two hours before the treatmen L C Cook suggested this premedication in t 'Cardiazol' days of 1938, when giving the treatme was everything but pressing a button

In over a thousand treatments (with cardiaz 'Triazol,' and electricity) given in the thirteen yea since then, I have always used this premedicatio It abolishes apprehension, promotes sleeping on (n unimportant therapeutically), and does away wi excitement on waking Thanks to this premedicatio and the postoperative amnesia, the patient has r recollection of the actual treatment Some rememb the initial injection, those who should not know th they have had convulsion treatment at all readily accep the explanation that the injection was given to promot sleep

Anything that might help these patients to reconstruc the event should be avoided by nurses and doctor With so simple, safe, and effective a premedication, does not seem justifiable to inflict convulsion treatme upon the conscious patient

Isleworth Middlesex H Pullar Strecker.

INTRAVENOUS ADMINISTRATION OF ALCOHO

Sir,—I was interested in your annotation (June 16) o this procedure, which I am confident will be of some hel in the postoperative management of geriatric patients

You refer to the possibility of precipitating an acut vitamin B complex deficiency by giving large amount of carbohydrate in the glucose alcohol drip Th danger seems still not to be sufficiently recognised in a its aspects—e g, in giving excessive amounts of glucose containing drips during the postoperative period i debilitated or elderly patients In this connection th following case history may be of interest

A man, aged 84, underwent prostatectomy following acut urinary retention Apart from severe emphysema he wa physically fit The first few days after operation passe uneventfully On the 5th postoperative day he had anorexi and nausea, but when he was seen at 6 P M he was quiet an slightly somnolent, and answered questions well. Abou 8 P M he became suddenly restless and confused and talke nonsense, with confabulation. Gradually he became mor and more agitated and disorientated, and he wanted to pul out the drip and the catheter When seen again at 11 P M he was unable to answer questions From the surgical sid the provisional diagnosis of uræmia was suggested, bu because slow bilateral nystagmus and loss of knee reflexe were noticed the possibility of Wernicke's encephalopathy wa also considered

It was then found that the patient had been given 22 litre of glucose saline within 5 days Thereupon 100 mg thiamin 30 mg riboflavine, and 300 mg nicotinamide was administere intravenously, and the same doses were repeated intramuscu larly three times daily for the next few days Within 72 hour he became reasonable and coöperative, and he lost all neurological signs after 1 week's treatment The blood urea level at the height of the confusional state was 22 mg per 100 ml

Similar case histories have occasionally been published with detailed description of the development of Wernicke's encephalopathy, but it has not been sufficiently

---

1 Pullar Strecker H *Med Pr* 1943 210 25 *Ibid* 1945, 214, 102

ologically could we find hepatic tumours in the animals 3rd—i e , untreated—group It is noteworthy that the in content of the diet did not prevent the cirrhogenic of tannic acid cirrhosis seemed even to occur more only on a high casein diet.

hese results indicate that the carcinogenic activity tannic acid can be influenced by dietary factors tis work will be published in detail in the *Acta Morphologica ranca*

partment of Morbid Anatomy
University Medical School
Szeged Hungary

B KORPASSY
M. MOSONYI

CONCENTRATION OF PENICILLIN IN THE LUNGS

ir,—We are very interested in the article of June 9 Dr Heathcote and Dr Nassau on the effects of penicillin esters in chronic pulmonary infections ough the courtesy of Messrs Glaxo Laboratories Ltd , have also been studying the properties of one of these r penicillin L G 1 "

ver 70 specimens of sputum have been examined from patients under the care of Prof D M Dunlop in the al Infirmary, Edinburgh They all had chronic chitis or bronchiectasis, and had been admitted to pital because of an exacerbation of the infection y were given crystalline sodium penicillin or penicillin 1, either therapeutically or for the purposes of estigation In estimating penicillin in sputum the r-disc assay method with seeded plates was used method was considered adequate for the detection penicillin in the sputum, but not for the quantitative tion of penicillin in bronchial secretions We have able to confirm that L.G 1 appears more often, and ibly in greater concentration, than does sodium icillin after injection of equivalent doses Penicillin ost readily detected about three hours after injection single dose, and it is rarely possible to detect any r a dose of less than 300,000 units of either L G 1 or ium penicillin

From the therapeutic aspect we have found that icillin L.G 1 produces similar effects to sodium penicillin chronic suppurative lung infections These are reduction in systemic disturbance, a change from a low purulent to a white mucoid sputum, and a inution in sputum volume However, using dosage tems of either 100,000 units four-hourly or 500,000– ,000 units twelve hourly we have not yet found that therapeutic effects of L G 1 differ from those obtained h sodium penicillin

epartment of Therapeutics
University of Edinburgh

J D MATTHEWS

epartment of Bacteriology
The Royal Infirmary
Edinburgh.

T B M. DURIE

UNICELLULAR SEBACEOUS GLANDS

ir,—I have shown that the nucleus and protoplasm the cells which I described in the basal layer of the man epidermis undergo the remarkable and charac istic changes of the cells of an ordinary sebaceous nd, and also that the fat *stained the same way* , that se cells are most *numerous just* where ordinary sebace glands are *absent or* rudimentary, namely in the palm, e, and the inner or nasal side of the eyelid that the ier side of the eyelid is shinier and greasier than the ter and contains a great number of the cells under cussion , that xanthelasma palpebrarum arises as a wn growth of the basal *layer of the* epidermis, which is dually converted into foam cells, and that in the crete form of the disease the localised masses of cells k almost exactly like a sebaceous gland ?

These interrelated facts, unless they can be refuted, ove that the cells I have described are indeed uni- llular sebaceous glands, and that the shine of the skin of the palm is due to them They also give an excellent reason why xanthelasma palpebrarum is so common on the inner side of the eyelid

Dr Lloyd (May 5), commenting on my article of April 21, does not attempt to refute any of the above observations , he merely states that the cells described above are dendritic melanoblasts Now everybody knows that actual or potential melanoblasts occur in the basal layer of the epidermis, but they are different from the cells in question in the epithelium of the corneal limbus, where melanoblasts are common, there are no unicellular sebaceous glands And in any case, what would be the function of a melanoblast stuffed with fat ?

London W 1

EUGENE WOLFF

ANTITOXINS AND ANTIBIOTICS

SIR,—I am in entire agreement with Dr Frank Marsh (March 17) In our enthusiasm for antibiotics we have forgotten antitoxic treatment It was with this in mind that I pointed out, regarding treatment of plague by streptomycin " It would be profitable to combat initial tox emia with anti plague serum "[1]

Poona, India

P V KARAMCHANDANI

ÆTIOLOGY OF DUPUYTREN'S CONTRACTURE

SIR,—Dr Herzog's article (June 16) reminds me that many years ago, during the South African War, I was asked to see a well known general on account of his having progressive contracture of the fingers of both hands There was well marked Dupuytren's contracture on both sides

He had never used an oar or any carpenter's tool , nor had he played tennis The ætiology was not apparent until I watched him at lunch holding both knife and fork with the butt end pressed into the hollow palm of each hand He told me he had done so all his life , his age then was about 60 years Inquiry was not made as to possible hereditary predisposition Evidently the only possible cause was slight trauma spread over many years.

Farnborough Hants.

M P HOLT

THE TRAGIC PARADOX

SIR,—Last week a *peripatetic correspondent* lamented the tragic paradox that abler boys who wish to be doctors must devote their last years at school to science and so forgo their only chance of a real education May I join him by the waters of Babylon and relate an instance of this pernicious dispensation

A boy, aged 14, entered a public school that has a very high classical tradition , in fact it was largely because of this tradition that he went there He had had a good grounding in Greek at his preparatory school and was prepared to take advantage of the opportunity to learn more. During his first three terms he did exceptionally well, and after each term easily got his remove , he was considered to be one of those who go right through to the top of the school Then, when he was about 15, his parents received a postcard from him saying I want to be a doctor and so I must give up greek. It seemed fantastic, but on inquiry they found it was true It appeared that because he was of scholarship standard he must start science at once, for no college at Oxford or Cambridge would accept a boy as a medical scholar unless he had passed his 1st M.B Very reluctantly they agreed that he should give up greek The subsequent decline in his scholarship which was quite phenomenal may not be relevant to the point in question but under the circumstances would it be remarkable if his parents regretted his choice of a profession ?

In *Liberties of the Mind* Charles Morgan says " No fact that a teacher can teach has meaning or value except in association with *other facts* " How true this is, especially of Medicine, for no fact that Science can teach has meaning or value except in association with a knowledge of humanity

XYZ

Paper read at the dermatology section of the Royal Society of Jan. 19 1951

[1] *Lancet* 1949 i 96

CURES OF PEPTIC ULCER

SIR,—I should like to express my gratitude for the kind personal reference in your leading article last week to a most embarrassing position in which I have been placed by the publication of Mr Parr's book I should like to assure you that I could not prevent its publication, and trust that you will accept this disclaimer

It is not possible to explain in a short letter the essential points of my theory of ulcer formation, but it is not quite as simple as it is made to appear It is primarily based on physiological and pathological considerations which establish the new principles which I believe to be of fundamental importance in the understanding of gastric pathology

Your leading article, while giving a very fair exposition of the confused state of the ulcer problem, is also affected by the general confusion

This confusion may be easily gauged from a large American book[1] in which the authors come to the disappointing conclusion that one of the most important elements in the causation of peptic ulcer is a *locus minoris resistentiæ*—which sounds well but does not mean much. They refuse to recognise that the acute and the chronic ulcer are two unrelated disease entities and are satisfied that the so called subacute ulcer (of doubtful existence) " is not an acute ulcer , *yet one hesitates to call it a chronic ulcer It is really an* acute ulcer of ' slight chronicity ' ' (p 16) Although they admit that ' under ordinary conditions erosions and acute ulcers of the stomach and duodenum heal rapidly, in fact so rapidly that it is remarkable that a chronic ulcer ever occurs," they nevertheless reject the suggestion that chronic ulcer does not originate from an acute ulcer because " it is difficult to conceive and no one has explained adequately, how a chronic ulcer could arise, like Minerva *springing* fully armed from the forehead of Jove, without its being initially an acute lesion of the mucosa " (p 174), thus ignoring the probability that the chronic ulcer only represents the end stage of a previously chronically inflamed mucous membrane which has finally broken down

Although your leading article denies me the credit of having first suggested that fat is the food factor responsible for the mechanism which ultimately leads to the production of a chronic ulcer, and assumes that others have tried a low fat diet but failed to confirm my results, you give no evidence in support of this assertion While conceding that bile has a destructive effect on the gastric mucous membrane, you offer the experimental acute metabolic lesions which follow the elimination of bile and their prevention by the administration of bile salts as proof against the argument that bile has a locally destructive effect when it acts outside its usual milieu in a susceptible place where it has no normal function to perform You quote Kaye, who observed that uncooked and cooked fats have a different effect on gastric motility and secretion, but omit reference to Card's[2] observation that saturated fats (produced by cooking of unsaturated fats) also inhibit gastric motility , and you completely ignore the investigations of Morrell Roberts and the experimental work of Pavlov, Earl Thomas, and their associates who differentiate between the early and the late effects of oil on both gastric motility and secretion While cautious enough not to attempt to justify the elimination of the acid factor in the orthodox treatment of ulcer, you also omit to say that my approach to the ulcer treatment is not empirical, but has at least the virtue of a physiological basis, that it hinges round an original interpretation of the function of the pyloric sphincter which I postulated 20 years ago in refutation of Cannon's law, and that it is now accepted by most physiologists

May I take this opportunity to draw your attention to a point of clinical interest ? It is generally overlooked that many causes may be responsible for the deformity of the duodenal cap Of the many cases of duodenal ulcer which have been referred to me, not more than 20% could be confirmed in their diagnosis , and one may, therefore, be justified in questioning the accuracy of the statistics dealing with the incidence of peptic ulcer

Finally, may I say that while I agree with your concluding remarks, nevertheless there will no doubt be many who will agree with Glenn[3] in believing " that by continuing the studies which are going on in the various clinics at the present time we probably will have an answer—not by 1960 but by 2000 "

London W 1 J JACQUES SPIRA

CUTANEOUS ANTHRAX

SIR,—I read with interest your annotation of May 5 Many years ago, as district physician and chief of a hospital in West Bosnia, I saw about 60 cases of anthrax within three years In these parts of the country it was the custom among some of the population to kill an infected animal and to use most of it Most of the people, including women and children, were infected with anthrax, even though they had nothing to do with the slaughter or evisceration of the animals , so one assumes that the infection was transmitted by flies The commonest sites of infection were the neck, the cheek, and sometimes the upper eyelid Among my cases there was no infection of the lung or bowels Locally gangrene of the skin quickly developed (hence the German *Milzbrand*), sometimes over an area the size of a child's palm The skin became black and hard like leather Healing took weeks, according to the size of the defect

The death rate was about 10% The illness lessened dramatically on the 6th day after the onset of the first inflammatory signs, with abrupt fall of temperature and disappearance of the toxic symptoms , after this time no death was observed

Zagreb, Yugoslavia VITOMIR DIJAMANT

INFLUENCE OF DIETETIC FACTORS ON CARCINOGENIC ACTIVITY OF TANNIC ACID

SIR,—We have *lately demonstrated the* cirrhogenic[4] and carcinogenic[5] activity of tannic acid in rats, by prolonged parenteral administration The induced tumours were always formed in the liver and they closely resembled those induced by azo dyes It is well known that the carcinogenic activity of azo dyes can be influenced by dietary factors, and it therefore seemed worth while to investigate the effects of diet on the carcinogenic action of tannic acid

120 young white rats were used, of the same strain as in our earlier experiments The animals were divided into 3 groups, each group comprising 17 males and 23 females.

The first group was fed on a high casein/low fat diet (25% casein, 5% sunflower oil) The 2nd and 3rd groups received a diet low in casein and high in fat (3% casein, 20% sunflower oil) and also each day 1 25 mg of pyridoxine (' Benadon ')

The animals of the 1st and 2nd groups were injected sub*cutaneously every 5th day* with at first 150 mg , then 200 mg , and finally 250 mg of tannic acid per kg body weight in a 1 5–2 5% aqueous solution The 3rd group served as untreated controls

By the 180th day of treatment 25 animals in the 1st group and 21 in the 2nd group had died , no animal in the 3rd group had died Macroscopically we *found* liver tumours much more commonly in the 2nd group (low casein/high fat diet), than in the 1st (high casein/low fat diet) The surviving animals were submitted to laparotomy before the 180th day Among the animals which survived for more than 100 *days* the findings were as follow of the 1st group 11 animals had tumours, and of the 2nd group 25—*that is*, in the 1st group 29 7% and in the 2nd group 67 5% Neither macroscopically

---

[1] Ivy A C Grossman M. I , Bachrach W H Peptic Ulcer Philadelphia 1950

[2] Card W I *Amer J digest Dis* 1941 8 47

[3] Glenn, F *J Amer med. Ass* 1951 145 802

[4] Korpássy B Kovács, K *Brit. J exp Med.* 1949, 30 266

[5] Korpássy B Mosonyi M. *Brit J Cancer* 1950 4 411

EATH FROM DI-NITRO-ORTHO-CRESOL

—In the following case the patient died after
re to di nitro ortho cresol (D N O C)

ung man aged 21, was sent to this hospital by his own
at 11 A.M on June 21 His hair, eyebrows, and pubic
ere so coated with the yellow substance as to appear
all of his skin was faintly yellow but the palms of
ds and the soles of his feet were deeply stained He
e to walk and to give a reasonable account of himself
d that he had been spraying D N O C for some days,
felt perfectly well until June 20 when he sweated a
deal and noticed some constriction of the chest He
t slept well on the night of June 20–21

mination confirmed that he was sweating heavily
from the face, his respiration rate was 40 per min,
hallow movements, but no other abnormal sign was
in the chest His pulse rate was 130 per min and
ature 98 4°F

was put to bed and washed, to remove the excess of
, but not much came off His respiration rate
despite administration of oxygen The patient
comatose and unable to swallow and a stomach
nly entered the trachea

patient was treated by sponging with tepid water,
1 P.M his temperature had increased to 104 8°F
eathing then became irregular and laboured, and his
ate increased to 160 per min the pulse was of poor
At 1 30 P.M he had a generalised convulsion with
pasms at the rate of about 3 per sec, lasting about
He then collapsed and became cyanosed artificial
ion was performed only to be interrupted by another
convulsion, accompanied by a mass reflex and
tion. After this the heart fibrillated, and, despite
rdiac adrenaline, it stopped beating

ediately after death post mortem lividity was notice-
bout the neck and rigor mortis was well marked,
lly in the back within $^3/_4$ hour At necropsy the
ng day, the chief findings were that the blood had
t clotted and showed no sign of doing so and that there
increase of red bone marrow at the distal end of the
Dr P Lesley Bidstrup of the M.R C Department
earch in Industrial Medicine, reported that a sample of
aken immediately after death contained 75 µg
per g whereas a sample taken at necropsy showed
µg per g and D N O C levels in other tissues were
ble with the latter figure

indebted to Dr R Y Young for the post mortem
gs, and to Dr M Long for permission to report
ase

n General Hospital
Banbury

C STEER

THEORY OF CEREBRAL LOCALISATION

—Our knowledge of localisation of function in the
al cortex presents a confusing picture It would
hat Dr Jefferson (March 17 and April 28) accuses
oddy and Mr McKissock (March 3) of trying to
about some order by abandoning whatever material
res with their theory

of the things rejected by Dr Gooddy and Mr
sock appears to be the experimental method
are of the opinion that the more refined experimental
ques are further removed from reality, which would
o suggest that Adrian s technique of following the
of a nerve impulse through the intact nervous
is of less value than cutting lumps out of a
or observing the effects of the destruction of an
wn amount of tissue by a tumour Furthermore,
onsider that the conclusions derived from experi
are artificial constructs, having no basis in the real

But if, as they suggest, localisation of function is an
al creation of the investigator, having no reality
subject and his behaviour, then so also is the
on of structures into muscles, nerves, or pairs of
es

Gooddy and Mr McKissock indicate clearly that
n work has shown that the old doctrine of topo-
ical project invalid It is to be regretted, however, that they did not really tackle the problems raised by modern research, which, as they are aware, covers a good deal more than therapeutic hemispherectomy Dr Jefferson refers to the discovery of secondary and tertiary projection areas in the cortex, and it is known that these have important homolateral projection A supporter of the old theories of localisation can point to the existence of these areas as nullifying the conclusions derived from hemispherectomy For example, Allen [1] who investigated in dogs the effects of bilateral ablation of the three auditory projection areas on conditioned differential responses, found that bilateral removal of one of the areas had no effect, bilateral removal of areas I and II caused loss of conditioned responses, but these could be re acquired perfectly after re training, complete bilateral destruction of all three areas led to a complete loss of such responses, and these could not be re acquired Furthermore, after removal of areas I and II he could find no difference in the difficulty of reconditioning between untrained dogs and previously trained dogs

Discussions on the effects of damage to the central nervous system unfortunately take no note of the important concept of physiological reserve All other organs have such a reserve, so that minor damage does not affect their function The fact that nerve cells are never renewed in the central nervous system apparently has obscured the fact that the central nervous system too has its physiological reserve This reserve takes the form of alternate pathways or, if one prefers it, alternate ' centres ' Once this notion is accepted, it becomes easy to understand that localisation is functional" rather than "anatomical"—i e, that the original cortical structure permits more or less of connections to all parts, but that constant use "wears out" channels that come to form the localised "centre" This theory explains many apparently unrelated facts For example, Adrian was puzzled by the large representation of the muzzle area of the face, and suggested [2] that "we are descended from animals without hands, animals using the snout and the long vibrissæ of the face as their most delicate tactile guides" Such a hypothesis, which is contrary to what we know, becomes unnecessary if we postulate that a "centre" is developed by usage, for this area of the face, together with the tongue, larynx &c, forms the all important mechanism of communication Neither is it surprising that the representation of the upper limb is reversed in the cortex, so that the thumb and fingers come adjacent to this area of the face, for the handling of tools and communication are both socially derived functions which are closely interlocked

Dr Jefferson relates this problem to the conflicting views and data on whether movements or structures are represented in the cortex He suggests that both are represented, however illogical this may seem There is no difficulty in reconciling these two theories The motor cortex does not normally function isolated from the rest of the central nervous system It is connected to two systems—the basal ganglia and the cerebellum—by both afferents and efferents, which can be regarded as "feed back" systems The cerebellum forms part of a feed back system that links the proprioceptive sense organs with the motor cortex. It is the cerebellar system that converts the represented movements into nerve impulses running to individual muscles, and this modification takes place in the cortex itself It must take place there, because the modification is responsive to impulses from other senses, such as the eyes and even the ears as anyone can tell who has tried to play the violin

---

[1] Allen, W F *Amer J Physiol* 1945 144 415
[2] Adrian E. D Physical Background of Perception. London, 1947 p 43

STRYCHNINE AND ASPIRIN POISONING

SIR,—I should like to report the following case, seen in a medical student, aged 22

On the eve of an examination he had a headache, so he took twelve 0 5 g aspirin tablets in two hours and went on studying through the night Next morning, feeling slightly tired and wishing to make himself more alert, he gave himself two injections of strychnine sulphate, each of 0 001 g Noticing a beneficial effect, he gave himself a third injection and went to the examination,

Sixteen hours after the aspirin and five hours after the last injection, severe symptoms suddenly appeared a sense of suffocation, cyanosis, excessive perspiration, and itching over the whole body There were no convulsions but he had slight muscular twitching in the extremities There were colicky pains in the abdomen and continuous vomiting, but no bowel action

His eyes were congested and lacrimation was profuse, the pupils were dilated and fixed Temperature subnormal, pulse feeble, rate 130 per min He was violent and hallucinated A fine vesicular rash was apparent, especially on his face and extremities

Treatment consisted of morphine hydrochloride gr $^{1}/_{4}$, stomach wash out with warm water containing sodium bicarbonate, 10% glucose with nikethamide subcutaneously, and calcium gluconate intravenously every four hours

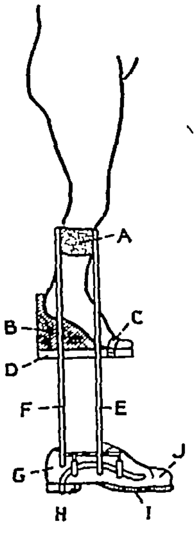
The young man felt better eight hours later and in seventy two hours was able to resume the examination

Cairo AHMID H WAHBA

STRUTS FOR ACHONDROPLASIACS

SIR,—Have you ever wondered what it would be like to be an achondroplastic dwarf ? Of this phenomenon Noble Chamberlain writes that it is less of a disease than a clinical curiosity, nor is there any means of remedying nature's defective development—even plastic surgery can do nothing

Since shortness of the legs is the most noticeable feature, I have been toying with the idea of making small stilts (fig 1) on an artificial foot (fig 2), which, if used with a walking stick, would do a great deal to conceal the abnormality The patient would have padded instep and heel, of the type common in women's fashions today, and would walk as if in a high heeled shoe This would have a wooden platform horizontal and light aluminium alloy struts of suitable length—about 1 ft perhaps, until the patient became accustomed to walking on them The shoe should be pliable in front and stiff behind to make a mechanical hinge The structure within the shoe is designed to make it spring back straight and not allow the toe to drag on the ground Probably, however, there are already artificial feet in existence which are more perfect in this respect, and which could be used instead



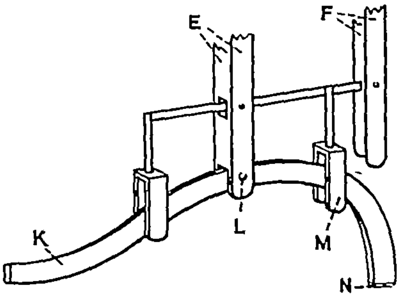


Fig 2—Mechanism in shoe K, aluminium alloy L ball grip M grip moving with weight of body N tip moved by contact of heel with ground

Fig 1—Stilt in use. A leather band B, velvet-covered rubber cushion; C supporting strap D wooden platform E and F front and rear aluminium struts G hard leather H, hard heel I crepe rubber J soft leather

I should be interested to know the opinion of doc and patients Would a slight stiffness in wal be offset by the almost entire concealment of deformity ?

Dublin MICHAEL DILLO

FORECASTING THE COURSE OF LABOUR

SIR,—I would like to record an obstetrical sign I have found valuable in forming a prognosis as tc likely course of labour, and especially in selecting (where induction of labour should be avoided

This observation has been under trial since the year when my assistant mastership at the Rot Hospital came to an end Since then, with one break, I have been in charge of a unit which deals some 3000 deliveries each year I mention this becau the very understandable scepticism which the enunci of "the sign of the deep natal cleft" is likely to pro

My main contention is that if we could make a prognosis upon the likelihood, or even the certaint disordered uterine action, we might be on the wa reducing the number of cases of obstetric shock, preventing stillbirths

Briefly, the test applies most dramatically to pati who present the outward signs of the "dyst dystrophy" syndrome The stocky build, short n thick thighs, and male distribution of hair are fam enough Nevertheless, there are some women in category who do deliver themselves spontaneously are delivered with the aid of forceps Those who require Cæsarean Section can be identified during antenatal period by means of this simple test

The patient is placed in the left lateral position with k well drawn up With the left hand the upper buttoc raised so that the genitalia can be seen The right har now placed flat, well into the natal cleft, so that the th rests against the skin of the perineum The upper but is then lowered into its normal position

If the entire right hand is thus hidden major incoördina of uterine action will be certain, and induction shoul avoided, if not ruled out altogether

If three fingers and thumb are obscured some incoördina or a labour terminated with difficulty by forceps, ma anticipated, induction should be avoided

If two fingers and thumb only are hidden by the cleft spontaneous delivery may be expected, and induc if required, will be safe, and labour certain in its onset

The majority of women enter the last category, inclu *many who are obese and have had large families wit* apparent difficulty Obesity by itself, therefore, is of prognostic value so far as disordered uterine acti concerned In some of the patients with deep c —whole or three quarter hand—the fœtus is in occipitoposterior position This merely adds should be a further deterrent to induction I infinitely preferable to allow such women to fall labour in their own time, and, if there is unwilling to accept the validity of the sign, to allow ther declare their disordered activity It is unwise to in labour in these women on whatever pretext, for will compromise the operative delivery which follow There should be no place for trial inductio a deep cleft is present

It should clearly be understood that the test nothing whatever to do with outlet contraction, disproportion, or with any form of pelvic measurem not excluding even X ray pelvimetry Some pati with deep clefts do have android pelves, but I regard association as almost accidental I would rather that, if it be conceded that women differ in the degr polarity shown in their respective labours, then this of the deep natal cleft will give adequate warning w ever polarity is destined to be minimal or absent

WENTWORTH TAYLO
Director Obstetrical an
Gynaecological Unit

Dudley Road Hospital
Birmingham

Notes and News

ALICE GREGORY AND TWO OTHERS

a world teeming, in Dr Johnson's phrase, with guilt ..sery, the history of social medicine stands as a refreshing ss o man's humanity to man Alice Gregory, whose life gbert Morland (formerly editor of THE LANCET) outlines cent book,[1] was daughter of the Dean of St Paul's ed as a midwife in the 'nineties when that was still an mmon thing for a young lady of birth and education to nd worked for eight years among the mothers in the xt villages round Midsomer Norton Lelia Parnell the d of the three pioneers about whom this book is written e to train as a maternity nurse, and was in charge of the ton Hospital when Alice Gregory came there to gain her experience of nursing Those were not the days of a nary training school Alice plunged into the new life a diver

"21.ix.93 To Paulton via Bath ' her diary runs Arrived Hospital about 6 Found Mrs Parnell working all alone and [illegible] D T Unpacked in passage and settled in. Slept very [illegible]

3rd member of the trio, Maud Cashmore, to whom Morland is indebted for much of his material, and whose h prevented her from helping to write this graceful and ly tribute to her friends, was another Victorian young who preferred a life of hard service to one of genteel re. These three women—Lelia Parnell with the good s and the flair for organisation, Alice Gregory with the , wisdom, and strength, and Maud Cashmore with her on to the task, her good memory, and her great personal ty, were to help to set a new standard in the care of bearing women

ce Gregory, believing that if midwifery offered even the st livelihood women of character would take it up, charged case at first, but was reluctantly obliged to raise the fee in her second year of district work her fees for the first had amounted to £27 10s In those days enthusiasts were ing hard to get the Midwives Act passed and Alice y and her friends had a training scheme in mind No al would accept it, and they realised that they would o found a training school of their own. While Maud more took over the district work, Alice Gregory ranged country looking for a place where such a school would be me. There was no welcome anywhere but at last she her story to the Rev Charles Escreet in Woolwich No er had he heard it than he reached for his hat He knew ery place for her, he said and a few months later the e that he pointed out in Wood Street became the Home others and Babies Later it was to receive an Exchequer t of £20,000, and to grow up into a new building, and a new —the British Hospital for Mothers and Babies. It has ved two wars and has trained innumerable midwives. Parnell died in 1931, the first of the three and her loss d for a time to dim the inspiration of the work but it after all, its own inspiration The other two members team worked on until 1945 and then retired together house at Alfriston which for many years had offered uary to any of the Woolwich staff who needed rest of or mind

CHILDREN'S FEET

t is surprising with what complacency the authorities the public accept the fact that four people out of every have foot defects severe enough to interfere with their fort and efficiency It is perhaps not so well realised the great majority of these defects arise during child d and are largely preventable Though it lies within the er of the authorities to effect the remedies they will r act except under the pressure of public opinion.

r. Pratt[2] has set out to tell the man in the street—or er the parent—how the common foot troubles arise how ook after their own children's feet and what could and ld be done on a wider national basis He presents the s clearly and intelligibly avoiding technical jargon and fusion of the main issues by unnecessary detail When nbing methods of examination he might have laid a little e stress on the importance of good mobility of the joints he foot and toes But his book can be recommended to all se who have anything to do with the care of the child's foot

---

[1] lice and the Stork. London Hodder & Stoughton. 1951 Pp [illegible] 7s 6d.

[2] our Children's Feet By CHARLES A. PRATT M.C.S.P London [illegible] 62 7s 6d.

University of London

Mr P H Mitchiner, F.R.C.S., has been appointed deputy vice-chancellor for the year 1951–52

University of Bristol

At recent examinations the following were successful

M D (State medicine)—M M. Lewis

M B, Ch.B—D R Coles June K Lloyd (with second-class honours) Margaret M Ashton W G Benson A C Brown C T Brown Ruth E Coles T E Dada, C E Dickson Dorothy R Douglas M. S Dunnill M. A Feldman D H Fox B. W Hill Doreen E D Hillier J A Jefferies S J Lloyd Ruth M. Martin, S J Palmer M. F Parry D S Paton Margaret R Salisbury J H Scudamore M. N Simmonds R E D Simpson R D Stride A M Sweeting, Deborah Vardy P G J Willcock

D P M (part II)—Oliver Lyth W D C Thomas

University of Liverpool

The title of professor of orthopædic surgery has been conferred on Mr Bryan McFarland director of orthopædic studies in the university Dr S Barton Hall has been appointed director of studies in psychological medicine

Royal College of Physicians of Ireland

On June 14 Prof E J Conway, D.Sc F.R.S., was admitted to the honorary fellowship of the college Professor Conway afterwards delivered a lecture entitled Science and the Physician

Order of St John of Jerusalem

The King has sanctioned the following promotions in, and appointments to this order

As Knight—C E Salt M B.

As Commanders—W J Vickers C.M.G M.R.C.S W E Hutchinson, M D M M. Scott M.R.C.S, Sir Arthur Porritt K.C.M.G C.B.E F.R.C.S Surgeon Rear Admiral K. A I Mackenzie C B. M.R.C.S K.H.P Sir Harold Graham Hodgson K.C.V.O F.R.C.P

As Officers—J B Mackie M.B Walter Radcliffe M.B. Major-General W E. Tyndall C B. C.B.E. M C M.B. K.H.S Major-General Frederick Harris C.B. C B.E. M.C M.B K.H.S E. R A. Merewether C.B.E M.D Dr J T P Handy M.R.C.S Dr Khoo Peng Seng Brigadier H C Edwards C.B.E. F.R.C.S George Swapp D C.M M.M. M.B. H M Golding D.F C M.B. Major R. R. M. Porter M.C I.M.S retd L. W Hefferman M.D F.R.C.S M. V Roberts L.M.S.S.A. E M. B West O B.E. B.M Squadron leader D S Grant M.R.C.S Surgeon Captain J Hamilton C.B.E. M.B. R.N Surgeon Captain W P E. McIntyre M.D R.N

As Associate Officers—Ip Kam Wa, M.B Dr Pah Chien Kwan. Dr Shaik Ismail Mohamed Ibrahim.

International Dental Congress

The eleventh International Dental Congress will be held in London from July 19 to 26, 1952 Further particulars may be had from the secretariat of the congress, 13, Hill Street, London, W 1

More Pay for Medical Auxiliaries

The Industrial Court has awarded an annual increase of £50 at all points of all scales in the salaries of the following medical auxiliaries who are employed in the National Health Service almoners, occupational therapists, orthoptists, physiotherapists, psychiatric social workers, remedial gymnasts, speech therapists, and therapeutic dietitians. The award is to date from April 1 this year, and about 6200 workers will receive a rise

Osler Club of London

The annual dinner of this club will be held on Thursday, July 12 at the South Kensington Hotel Queen's Gate Terrace S W 7 at 7 45 P.M. to celebrate the 102nd anniversary of Osler's birth. Mr S C Roberts, master of Pembroke College will deliver the Oslerian oration on the Rev James Beresford (1764–1840) Further particulars may be had from the hon. secretary Dr W R. Bett, 11, the Avenue Bedford Park W 4

Toxic Chemicals in Agriculture

The Working Party on precautionary measures against toxic chemicals used in agriculture, whose first report was published in April, has been reappointed to investigate the risks to the consumer of the final product arising from the use of toxic chemicals in agriculture and in the storage of food The members include Prof S Zuckerman, C.B., M.D., F.R.S. (chairman) Dr J M. Barnes, Dr R H. Barrett, Dr B. S Lush, and Dr R J Peters Organisations who wish to submit evidence should write to Mr W K. Melrose, Ministry of Food Portman Court London, W 1

Our ideas of the function of the central nervous system have veered between theories based on specialisation and localisation, and theories based on equipotentiality We shall not make progress until we cease to regard these theories as contradictory, for they are based on different aspects of the one phenomenon If our theories are to lead forward they must synthesise these antithetical aspects, not ignore one in favour of the other May I suggest a simple analogy when a man walks, he does so with his legs It is not the legs that walk but the man, yet he cannot walk without them (unless he learns to walk on his hands) In the same way, we may say that movements do not originate in the motor cortex, but in the brain as a whole, yet this cannot happen in the brain without the precentral cortex, unless under abnormal conditions when it can "learn" to use some of its physiological reserve for the purpose

King's College Hospital
London S E 5

MAX HAMILTON
Senior Registrar
Department of Psychological Medicine

ADDICTION TO AMPHETAMINE

SIR,—An increasing number of patients addicted to amphetamine are coming to my notice Severe cases are not attributable to overdosage with amphetamine tablets Inhalers, which in themselves cause little trouble when used in the normal way, can cause distressing symptoms when their contents are extracted and chewed. Hyperkinesis with visual hallucinosis and delusions, cerebellar signs, and hypertension, may cause difficulty in diagnosis Sleeplessness, of course, is a concomitant, and the addiction is severe and persistent

I am bringing this to your notice in the hope, not only that sales of the inhalers may be controlled, but also that the possibility of this noxious habit may be considered in the diagnosis of some obscure nervous disorders

London W 1 J GORDON MATHIAS

⁂ The inhaler is packed with blotting paper impregnated with about 250 mg of amphetamine base The American military prisoners who first drew attention to the habit (Monroe, R R, Drell, H J *J Amer med Ass* 1947, **135**, 909 See annotation, *Lancet*, 1948, i, 221) said that they took the drug to make the time pass more quickly—ED L

THE WRONG WAY

SIR,—The Kingston and Malden Victoria Medical Foundation exists to create a new G P hospital in our boroughs in order to make good the loss of the old Victoria Dr Stark Murray, in his letter last week, says that we should be better employed by using the old Surbiton annexe—an ill favoured building in the wrong place made no less useless by its new name than by its now being "pleasantly decorated and furnished"—to "prove the case for G P beds" This case of course needs no proving anywhere, least of all in Kingston where the old Victoria served its purpose well for more than fifty years in all and for nearly three years within the National Health Service

Dr Stark Murray further states that at the Claremont Hospital doctors can have all the consultant opinions they require Just as any doctor can in any patient's own home, that is no doubt true, but it is a very different matter to having regular attendances by consultants both in outpatient departments and in the wards as we had at the Victoria

He says that we seek to "delay or thwart" the local hospital programme Nothing could be further from the truth of our intentions I find it astonishing that a member of a regional board of an area in which there is an admitted and large shortage of beds should object to any plan which may relieve that shortage We seek only to fill a gap, and to continue to serve our patients with local facilities as we have done in the past We have weighed the difficulties, and we find them outbalanced by the gains that will accrue from our plan

Let it be quite clear, we have certain principles a propose to stick to them In addition, 41,000 of local friends (65% of the electorate, and theref individuals of all political faiths) have signed a petit pledging support to us We do not propose to them down May I, as honorary treasurer of the foundation, add that donations should be sent to Kingston Victoria Fund, c/o Barclays Bank, Kings Hill, Surrey, and that every gift will be gratef acknowledged

L D DE LAUNA

SIR,—Dr Stark Murray says "The question general practitioner hospitals will not be settled in country for a long time to come" He must not desp At the present rate of "progress" it should not t long to bring about the total extinction of these hospit His "pleasantly decorated and furnished unit" I am sure, gladden the hearts of all general practition —a tea room with a nice view would be a welco addition

Dr Murray says that this group is "handling a h pital programme in the right way both at the speci and the G P level" This opinion is not shared to knowledge by many medical men in this group, inste they think that progress has been retarded by plann who appear to have no experience of practice or hosp administration, and to have no idea of what type hospital the general practitioner wants

Surbiton Hospital
Surrey

RALPH G SMITH

Obituary

JOHN CHISHOLM

M B Edin, F R C S E, F R C O G

Prof John Chisholm, who died on June 12 at the of 68, retired last year from the chair of obstetrics a gynæcology in the University of Sheffield

Born in Inverness, he was educated at the Ro Academy there and at the University of Edinbur where he graduated in 1905 During some years general practice in South Wales he became increasin interested in obstetrics and finally decided to special in this branch of medicine He accordingly accepted appointment as gynæcological house surgeon at M chester Royal Infirmary, and later he became resid obstetrical officer to the St Mary's Hospitals, Manchest In 1914 he took a holiday as a ship's surgeon, was wreck off the coast of Arabia, and returned to England to f the country at war He at once joined the R A M. with which he served in France till the end of the war

When he returned to take up the threads of his car he settled in Sheffield, where he was offered the post registrar at the Jessop Hospital In 1920 he took F R C S E, and the same year he joined the staff of Jessop Hospital as assistant surgeon In 1935 he elected F R C O G, and he also became senior surgeon his hospital, and was appointed professor of obstet and gynæcology in the University of Sheffield Th posts he held until 1950, continuing to serve both hospital and university for some years after he norma should have retired

C G P writes "As a doctor Chisholm earned gratitude of countless patients by his kindliness courtesy, and by his sound, if unspectacular, surg work He instinctively mistrusted innovations, and success was built on the basis of wide and critical clin experience, garnered over the years In his teaching showed the same care and conscientiousness, but he at his best in informal talks at the bedside and in o patient sessions Many generations of residents, n practising obstetrics and gynæcology both here a abroad, will remember gratefully his part in their edu tion Outside his home and his hospital he had few int ests, in his too short retirement he often returned visit us, and he was always interested in all the everyd occurrences of a busy hospital"

Professor Chisholm leaves a widow and five daughte

INDEX TO VOLUME I, 1951

REFERENCES AND ABBREVIATIONS

Institutions and Corporations with the right to the prefix Royal will be found under that prefix, with the exception of Medical Societies, which are separately indexed under Societies. All Universities are indexed under the word Universities. (A) = Annotation, (C) = Correspondence, (LA) = Leading Article, (ML) = Medicine and the Law, (NI) = New Invention, (O) = Obituary, (P) = Parliament, and (R) = Review

A Concordance of page numbers and dates of issue will be found on opposite page

A

bdul Z H chloramphenicol in pertussis (C) 1370
bdomen false acute (Jones) (C) 113 (Colston) (C) 638
bercrombie M Dictionary of Biology (R) 778
bnormal Pneumoencephalogram (Davidoff and Epstein) (R) 724
bortion Law Reform Association 416
bortion medical secrecy and (A) 676
brahams A—aspiration of empyema thoracis (C) 1127 calling all athletes (C) 1020 physical exercise 1133 1157
bscesses chronic non tuberculous arising at site of injections (Fielding and Norris) 556 (Chapman) (C) 642
ccident—in the home (LA) 97 railway mortality for (P) 168 traffic charge for treatment in (P) 633
ccommodation for medical staff in hospitals (Goodall) 847 (Hardman) (C) 1016
cetylsalicylic acid—and urinary excretion of adrenocortical steroids (Van Cauwenberge and Heusghem) 771 sensitivity to (A) 595 (Das Gupta) (C) 1327 strychnine and aspirin poisoning (Wahba) (C) 1418
chondroplasiacs stilts for (Dillon) (C) 1115
crodynia (LA) 1216
cromegaly and diabetes (LA) 847
crosclerosis (Littler and Canter) 153 (Tait) (C) 290
A C T H see Adrenocorticotropic hormone
ctidione (LA) 596
ctinomycosis of spine (Winston) 315
damantinomas 330
dams A V prospect of war (C) 232
dams E B aplastic anæmia 657
daptation syndrome (LA) 277
ddendum to British Pharmacopœia 1948 (A) 837
ddendum to Kings and Some Kings Men (Lyle) (R) 836
ddiction to amphetamine (Mathias) (C) 1420
ddison Lord (A) 677
ddison's disease liquorice in (A) 953
denitis tuberculous cervical (Morris and Prosser Evans) 1193
dey W R connection between prefrontal cortex and hippocampal formation (C) 532
dler F H Physiology of Eye—Clinical Application (R) 777
dministrative failure (A) 730
drenaline urticaria following (Herxheimer) 615
drenocortical hormones—(LA) 157 acetylsalicylic acid and urinary excretion of adrenocortical steroids (Van Cauwenberge and Heusghem) 771
drenocorticotropic hormone (Morris) 161 (Parrott) (Bornstein and Gray) (C) 237 (LA) 277 977 1211 and lymphopenia (LA) 674 bibliography of 697 effect of on renal glucose threshold (De Filippis and Iannaccone) (C) 556 in dermatomyositis (Suzman and Rudolph) 660 (Williams and Bowler) 1053 in diagnosis of gout (Kersley Mandel and Jeffrey) (C) 637 (Bayly) (Kersley Mandel and Jeffrey) (C) 738 infection and (LA) 349 influence of thyroxine on desensitising action of in B C G infected guineapigs (Long Miles and Perry) 1392 in *hæmatology* (LA) 453 intravenous infusion of (Jolliffe Stewart and Beaumont) 1260
dvances in Carbohydrate Chemistry (Hudson and Cantor) (R) 836
edes scutellaris (Manson Bahr) 49
fibrinogenæmia congenital (Prentice) 211
frica—endemic syphilis of Southern Rhodesia (Willcox) 558 medical school for non Europeans in South Africa 357 medical services of South Africa, 561
ge average age at death (P) 743 [illegible] in Scotland (P) 132
ged—beds for (P) [illegible] biochemistry of (LA) 157 care of (P) 36[illegible] Conference on Problems of Aging (Shock) (R) 1036 [illegible] for (A) 62[illegible] 616 Incontinence in Old People (Brocklehurst) (R) 1[illegible] in U S A (LA) 101 (LA) 504 medical care of [illegible] 436 radical cure of inguinal hernia in (Dodd) 1192 [illegible] in mixed institutions (Grant and [illegible] homes) 25[illegible] results of sanatorium treatment in (Paul) 167 sick hospital beds for (P) 234 (P) 167 (P) 524 sick treatment of (Fleetwood) (De Largy) 471 sick use of hospital in treatment of (Amulree Exton Smith and Crockett) 123 (Brown) (C) 533 (Amulree and Exton Smith) (C) 63 treatment of fractures in (Flemming) 798
Agene in flour (ML) 711 [illegible] 314
Agranulocytosis due to amidopyrine 389 thiouracil (Holliday) 265
Ahumada syndrome (Wingate) (C) 412
Aiken D fat absorption (C) 1073
Ainsworth Davis J C Essentials of Urology (R) 1397
Air embolism 15[illegible]
Air travel 687 (Clifford) (C) 1021
Alarm reaction (LA) 277
Albee F surgeon's Fight to Rebuild Man (R) 724
Albuminuria orthostatic (Abrahams) 1159 (Watson) 1136
Alcock S fate of a group (C) 810
Alcohol—and motorist (A) 1265 (Pullar Strecker) (C) 1369 intravenous (A) 1313 (Feltner) (C) 1414 whisky (Karrer) (C) 365
Alcoholism—education on (Cheston) 753 increase in (P) 503
Alexander J O D chloramphenicol in dermatitis herpetiformis (C) 532
Alice and Stork (Morland) 1121
Alkali reserve estimation of (Lehmann) 718
Alkaloids (Manske and Holmes) (R) 33
Allergy—comparative (A) 723 Pediatric Allergy (Chobot) (R) 1162 therapeutic effect of allergic reaction to food on rheumatoid arthritis (Polymnakos) 831
Alliborne E C streptomycin in *Hæmophilus influenzæ* meningitis 610
Allonal causing agranulocytosis 530
Allowances—income tax (Besterman) (C) 744 marriage of National Service medical officers (P) 467
Alloxan in hyperinsulinism (Gilchrist and Lynch) 440 (correction 806) (Martensson) (C) 365 (Lynch) (C) 1151
Almoners (A) 785 906 (A) 953 uncertificated 536
Alroy M surgery of mitral disease (C) 1363
Alston E F Cytologic Diagnosis of Lung Cancer (R) 672
Altmann A serum proteins in malignant malnutrition 203
Altounyan E H R inter innomino abdominal amputation (C) 1017
Altschul R. Selected Studies on Arteriosclerosis (R) 1308
Alvarez DeChoudens J A torulosis of central nervous system 1253
Ambulation early postoperative—early movement early rising and early discharge (LA) 95 effect of on venous blood flow (Wright Osborn and Edmonds) 22 survey of hospital practice (Goodall) 43 (Henderson) (C) 173
America—North care of sick in (Simmonds and Peers) 844 *see also* Canada U S A
American Medical Association 537 1373
American Society for Study of Fertility 1362
Amidone (LA) 156 overdosage in child (Roxburgh and Munro Faure) (C) 174
Amidopyrine agranulocytosis 389
Amino acids—Symposia on Quantitative Biology (R) 452
Aminophyllin in emphysema (Whitfield Arnott and Waterhouse) 490
Aminopterin in acute leukæmia (Williamson and Gardikas) 325
Amira A.— Cortisone and fat metabolism (C) 641 effects of cortisone on early fibrosis of liver in rats (C) 55
Ammi visnaga (Valdecasas and Glanzmann) (C) 1325
Amœbiasis—indigenous in Britain (Morton Neill and Sage) 766 treatment of (LA) 1153 (Boyd) (C) 1233
Amphetamine addiction to (Mathias) (C) 1420
Amputation—inter innomino abdominal (Altounyan) (C) 1017 stump epidermoid cysts arising in (Young) 716
Amulree Lord use of hospital in treatment of aged sick 123 (C) 63
Anæmia—(LA) 213 A C T H in (LA) 453 aplastic (Adams) 657 Cooley's (A) 572 (LA) 1400 due to sulphone (Lowe) 13 hæmolytic during treatment of leprosy with diaminodiphenylsulphone (Ramanujam and Smith) 21 (Lowe) (C) 163 (Cochrane) (Scott) (C) 739 in pregnancy (LA) 351 Mediterranean (A) 572 (LA) 1400 megaloblastic response of to penicillin (Foy Kondi and Hargreaves) (C) 410 of pregnancy intravenous iron in (Scott and Govan) 367 (Nath) (C) 474 (French) (C) 641 (Scott and Govan) (C) 6[illegible]1 pernicious thymidine in (Hausmann) 329 pernicious treated with *Leuconostoc citrovorum* factor (Davidson and Girdwood) 372 pernicious vitamin B_{12} in (Gill and Hemsted) (C) 237 sickle-cell (A) 572 (LA) 1400 in Greece (Choremis Zervos Constantinides and Zannos) 1147 (Lehmann) (C) 1273 thalassæmia (A) 572 (LA) 1400
Anæsthesia—and bleeding at operations (A) 677 cardiac arrest under (A) 62 death under 151 general for gastroscopy (Colligher and Thornton) 632 in coronary thrombosis (Mason) 362 procaine with hyaluronidase as local anæsthetic (Thorpe) 210 safety endotracheal connection (Bell) (NI) 619 spinal and kidney 993 spinal complications of (A) 516 (Sophian) (C) 556 (Calley) (C) 653 spirometer tidal (Barry) (NI) 214
Anæsthetist damages against (ML) 405
Analgesia—analgesics compared (LA) 156 local hyaluronidase in (A) 1095 Lumbar Puncture and Spinal Analgesia (Macintosh) (R) 1033
Anatomy—Anatomy of Man and Other Animals (Murray and Jeffrey) (R) 672 Atlas of Human Anatomy (Anson) (R) 835 Atlas of Human Anatomy (Woerdeman) (R) 451 Functional Anatomy of Limb and Back (Hollinshead) (R) 1305 Living Anatomy (Lockhart) (R) 620 Osteology for Dissectors (Howat) (R) 331 shape and size of female pelvis 535 Visual Anatomy (Friedman) (R) 1107
Anderson A vaccine-lymph 1067
Anderson A F curettage in diagnosis of cervical cancer 1152
Anderson A W prevention of tuberculosis in young people 1116
Anderson T memorial to John Brownlee (C) 1371
Anderson T A smallpox 1248
Andrewes C H experiment on transmission of colds 25
Androgens influence of on sexuality of women (Foss) 667
Androgyny scale (Tanner) 574
Anencephalus (McKeown and Record) 192 (LA) 218
Aneurysm dissecting neurological complications of (A) 222
Angel R E operating table arm rest (NI) 511
Angina pectoris (A) 895
Angor animi (A) 895 (Bourne) (C) 962
Aniline causing methæmoglobinæmia in newborn (Howarth) 934
Animal Evolution (Carter) (R) 1108
Annotated Bibliography of Cortisone A.C.T.H and Related Hormonal Substances [illegible]
Annual Review of Medicine (Cutting and Newman) (R) 332
Anopheles and Malaria in Near East (Leeson Lumsden Yofe and Macan) 536
Anoxia in man effects of oxygen in (Latham) 77
Anson B J Atlas of Human Anatomy (R) 835

culty of Radiologists

At a recent examination for the fellowship the following re successful F M. Hooper (radiodiagnosis), Margaret Snelling (radiotherapy)

sociation of Workers for Maladjusted Children

A general meeting of this newly formed association is being ld at Red House School, Tadworth, Surrey, at 11 15 A.M., day, Saturday, June 30 Information may be obtained from Otto L Shaw, the hon secretary (Sutton Valence 3104)

A F Medical Technician Branch

Airmen, between the ages of 35 and 40, with the necessary alifications serving in the medical and dental trades of the yal Air Force are now eligible for commissions as flying cers in the newly formed medical technician branch. This ch will comprise medical and dental secretarial officers quartermaster and medical adjutant duties, and medical ician officers in the categories of hygiene inspector, oratory technician, pharmacist, physiotherapist, and radio apher These officers will be employed at hospitals, medical abilitation units, the Medical and Dental Training Estab hment, and the Central Medical Establishment, and in staff sts Candidates for these appointments must hold civil ofessional qualifications, and airmen may be granted special ve to study for qualifying professional examinations

CORRIGENDUM *Vitamins and Hormones*—This book, uch was reviewed on April 28 (p 948), is vol VIII in the ies

Appointments

SON S W M B Lond F R C S D L O, consultant E N T rgeon Boston General Hospital London Road Hospital ston Skegness and District Hospital, Holbeach Hospital, d Johnson Hospital Spalding

N S M B Leeds D L.O consultant E.N T surgeon, Scun rpe War Memorial Hospital and the Brigg Infirmary

S ENID M D Lond D O.M S, D P H ophthalmologist to Powys and Mawddach H M C

SIMEON M B Leeds C P H tuberculosis physician trincham Mid-Cheshire and Crewe

N R S, L.R C P E consultant venereologist, Stockport d East Cheshire

BE J M., M.B Lond., D PHYS MED assistant M O in physical edicine Edgar Allen Physical Treatment Centre, Sheffield

R, L D M R C S tuberculosis physician Stockport Macclesfield and East Cheshire

pointed Factory Doctors:

BUCKLER F R M R C S Shepton Mallet district Somerset

GIBSON, W I M, M B Leeds Leeds North district, Yorkshire

PARKER ROBERT, M B Glasg Kilsyth district Stirlingshire

ROOKE, C J M B Camb Yealmpton district Devonshire

SHAW H A M B Birm Oldbury district Worcestershire

SOMERS G DE N U M B Birm West Bromwich district Staffordshire

WILLIAMS A L, M R C S Toddington district Bedfordshire

spital for Sick Children Great Ormond Street, London

DUNN H G M A M B Camb, M R C I D C H assistant medical registrar

PUGH R O B M D Lond assistant morbid anatomist

lonial Service

ALDERICE, A A. M B Sydney M R C P medical superintendent, Mulago Hospital Uganda

ARMSTRONG H C M B Belf B A.O D P H A D M.S Gold Coast

BECKETT D W M B Dubl M O, Zanzibar

BRAWN, E, M R.C.S M O (temporary) pathology Nigeria

CHRZASZCZ A, M B Polish School of Medicine Edin. M O Nigeria

CURRIE ANDREW M B Aberd M O (temporary) Nigeria

ALY W M M B N U I M O General Hospital Barbados

OHERTY E M L R.C S I M O Nigeria

DLON, D S M.R C S D L O medical superintendent (temporary), Barbados

UPTA, N R L R C P E M O, Aden

OLGATE J E M.R C S M O, Nigeria

RSHAM G B, M B. F R F P S M.O Aden

NDRETH SMITH Mrs D M L.R C P E M O, Grade B Trinidad

REDITH J S M B Glasg medical specialist Tanganyika

OHAMED MAZHAR M B D T M D O.M.S M O Aden

UTH MISIR R C M.B M O British Guiana

RICHARDSON R K. L.R C P E M O, Grade 'B' Trinidad

TAYLOR, JAMES M B Glasg D P H D T M & H senior M O Seychelles

TUCKER, W A. L F R.C.S D T M surgeon specialist Aden.

Terms and Conditions of Service of Hospital Medical and Staff apply to all N H S hospital posts we advertise unless se stated. Canvassing disqualifies, but candidates may normally he hospital by appointment

Diary of the Week

JULY 1 TO 7

Monday, 2nd

INSTITUTE OF NEUROLOGY, National Hospital Queen Square, W
5 P M Dr F Grewel (Amsterdam) Acalculia

Tuesday, 3rd

CIBA FOUNDATION
6 P M (Royal Institute of British Architects 66, Portland P W 1) Prof B A Houssay For Mem R.S (Bu Aires) Sex Hormones in Diabetes

INSTITUTE OF NEUROLOGY
5 P M Prof R Leriche (Paris) Treatment of Cerebral Embo and Thrombosis

WEST END HOSPITAL FOR NERVOUS DISEASES, 40 Maryle Lane, W 1
2 30 P M Mr K I Nissen Orthopædic Treatment in Neurol

EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
4 30 P M (University New Buildings Edinburgh) Prof H Harris Bone Growth with Special Reference to Epiphyses

Wednesday, 4th

ROYAL COLLEGE OF SURGEONS, Lincoln s Inn Fields W C 2
5 P M Mr A Wilfrid Adams Range and Results of Tra urethral Surgery (Hunterian lecture)

YORKSHIRE SOCIETY OF ANÆSTHETISTS
8 P M (Leeds General Infirmary) Dr Laurence Mountfo —Methods of Anæsthesia in Chest Surgery

Thursday, 5th

ROYAL COLLEGE OF SURGEONS
5 30 P M Prof Kenelm Digby Carcinoma of the Nasophary

GUY S HOSPITAL MEDICAL SCHOOL, London Bridge S E.1
5 P M Prof F G Young F R S Thomas Addison and Background to Cortisone (Fifth Addison lecture)

INSTITUTE OF NEUROLOGY
5 P M Dr Honor Smith Intrathecal Tuberculin Reactions

Friday, 6th

ROYAL COLLEGE OF SURGEONS
5 P M Prof H H Stones Oral Manifestations of Syste Disease (Charles Tomes lecture)

DIABETIC ASSOCIATION
11 30 A M (Postgraduate Medical School of London Duc Road, W 12) Prof C N H Long (Yale Medical Schoo Endocrine Control of Carbohydrate Metabolism (Bant lecture)

Saturday, 7th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
10 30 A M (Royal Pavilion Brighton.) Sir Geoffrey Tod Treatment and End results of Tuberculous Pyo-pneum thorax Dr J F Jameson Laboratory Aspects of Tuberculosis Problem

Births, Marriages, and Deaths

BIRTHS

BARRON—On June 18 in Edinburgh the wife of Mr Art Barron, F.R C S E—a daughter

CRAIG—On June 17 at Bristol the wife of Dr R A Craig daughter

DAVIES—On June 17, at Burton-on Trent, the wife of Mr. F W Davies, F R.C S E—a son

GILFORD—On June 18 at Tonbridge Kent the wife of Mr W Gilford F R C S—a son.

HERIOT—On June 18, in London the wife of Mr A. J Her F R.C S—a son

STALKER.—On June 23, the wife of Dr Harry Stalker of E Croydon—a daughter

WIGGINS—On June 21 in London the wife of Dr W R Wiggins—a daughter

MARRIAGES

DOIG—BERRY—On June 23 at Winchester William Grant D M B of Colac Victoria Australia, to Doris Lydia Berry

FAGAN—MANSON—On June 15, at Giffnock Renfrewshire Ja Hugh Wallace Fagan, D O M S to Margaret Elizabeth Man

HALL—PICKSTONE—On June 20 in Birkenhead, John L.R C P E to Rose Pickstone

HEBER—SAVILL—On June 23 at Coulsdon Kenneth Re Heber M B to Nina Greenaway Savill.

NEWSAM—CAPE—On June 16 in London, John E Newsam M to Virginia Cape

DEATHS

BELLAMY—On June 22, at Winterbourne Stickland, Dor Henry Francis Bellamy, M D Lond

FRANCIS—On June 16 in London Louis Arthur Francis, M R.C aged 84

LEMON—On June 18 at Hove, Edward Henry Lemon M.R C aged 85

LYONS—On June 17, Charles John Lyons F R.C.S I of Isipi Beach, South Africa aged 88

NORMAN WALKER.—On June 18 at Streatley Berks John Norm Norman Walker O I E. M R C P Lond colonel, I.M.S re aged 79

RICHARDSON—On June 19 at St. Andrews Hugh Richard D S O M D Edin. colonel R A M C (T) retd

WILLIAMS—On June 17 at Chatham Edward Rex Pascoe Willia O B E M R C.S surgeon commander R N aged 40

ochemistry (King) (R) 672 of old age
A) 157 Textbook of Physiology and
ochemistry (Bell Davidson and
arborough) (R) 33
luna e Terapia Sperimentale 1185
gy—Anatomy of Man and Other
nimals (Murray and Jeffree) (R) 672
ll Physiology and Pharmacology
aufeld) (R) 216 Dictionary of
ology (Abercrombie Hickman and
hnson) (R) 775 History of Biology
inger) (R) 152 Symposia on Quanti
tive Biology (R) 152
hysics—Progress in Biophysics and
ophysical Chemistry (Butler and
andall) (R) 1213
h C A—bodys from (C) 1017 Emer
ncies in Medical Practice (R) 274
Munchausen's syndrome (C) 112
C W G auto agglutinins 97
ell J B Races (R) 671
s that count 1128
ingham breast milk bureau 805
n F Color Psychology and Color
erapy (R) 836
hmarks (A) 158 (Walter) (C) 475
bs in prisons (L) 193
op I M F stilbœstrol sulphate
trone and equilin 815
muth in early syphilis (Jefferiss Willcox
d McElligott) 53
kham R J (O) 235
lder see Urinary bladder
ding see Hæmorrhage
ch T H fingerprint detection and
ercury poisoning 378
d—employment of 418 welfare of
Kew and Colligan) (C) 111
ker T C burns 135
d K liver (Blend and Baker) (C) 172
d—(LA) 219 ACTH and Cortisone
hæmatology (LA) 453 adrenocortico
opic activity of blood plasma extracts
ornstein) (C) 750 afibrinogenæmia
ngenital (Prentice) 211 Bakteriologie
nd Serologie (Hallmann) (R) 332
lood Clotting and Allied Problems
lynn) (R) 1162 cell embolism and
etastasis (LA) 96 chemistry post
erative changes in (Wilkinson Billing
agy and Stewart) 315 circulation of
nd De la Reyna (Keevil and Payne)
1 drepanocytosis (A) 572 (LA)
100 elliptocytosis (LA) 1400 erythro
astosis neonatorum vitamin K in
evention of (Hay Hudson and
odgers) 423 (A) 455 (Hay and
udson (C) 533 erythropoiesis 330
enoch Schonlein purpura ACTH in
A) 453 inherited red-cell anomalies
A) 1400 in vivo survival of rabbit's
d cells recovered after freezing
oulter) 1350 leucocyte-counts
thiouracil therapy (Holliday) 265
raser) (C) 353 (Young) (C) 111
olliday) (C) 528 leucocytes in burnt
atients 390 lymphocytosis acute
fections in adult (Malamos and
tamatelakis) 148 lymphopenia and
ituitary gland (LA) 674 myeloid
eticulosis (Israëls) 976 plasma labile
ctor (Stefanini) 606 platelet counts
90 preparation of hæmopoietically
ctive extracts from fæces (Callender and
pray) 1391 pulmonary and peripheral
irculation times in hæmorrhagic shock
Mukherjee and Rowlands) 1041 recov
ry of human red cells after freezing
Sloviter) 823 salicylate gentisate and
osinophils (Meade and Smith) (C) 236
Meade and Smith) 773 (Kelemen and
Majoros) (C) 962 separation of
mechanical (A) 1060 serum protein
evels of Samoans Fijians and Indians
n Fiji (Wills and Bell) 820 serum
roteins in malignant malnutrition
Anderson and Altmann) 203 sphero
ytosis (LA) 1400 see also Anæmia
Hæmoglobin Hæmophilia Hæmorrhage
Leukæmia Methæmoglobinæmia
ood-culture—contaminants in (LA) 334
Taking a Blood-culture (film) (LA) 334
ood donors awards for 179 862
ood flow—peripheral arterial effect of
venous occlusion on (Thompson and
Vane) 380 venous effect of post
operative rest in bed and early ambula
tion on (Wright Osborn and Edmonds)
22
ood pressure—hypotensive action of
Veratrum viride (Kauntze and Trounce) (C) 691 see also
549 (L) 568 (Dawes)
Hy g adults Hypotension
oc story sion—fluid mechanics and
dynamics of (Melrose and Shackman)
of liver in shock
1144 perarterial (Clarkson) (C) 747
(Delorme) 259 —aortic hypoplasia and
lood vessels— in arachnodactyly
myocarditis Arnott and Stafford) 1387
(Whitfield damage produced by
cardiovascular preparations (Selye)
anterior pituitary estimation of resistance
483 collateral
of during obstruction of main artery to
limb (Dornhorst and Sharpey Schafer)

51 great surgery of 342 mortality from circulatory diseases in Norway 1940–45 (Strøm and Jensen) 126 nerve (A) 158 of human gastric mucosa (Doran) 133 retinal changes in aortic coarctation (A) 1220 selected studies on Arteriosclerosis (Altschul) (R) 1305 see also Coronary disease Embolism Temporal arteritis Thrombosis
Bloss J F E vaccination against smallpox (C) 633 (correction) 800
Boake W C recurrent Kaposi's varicelliform eruption in adult 383
Boards of governors of provincial teaching hospitals 1222
Bodecker C F Movable Removable Bridgework (R) 332
Bodian M Hirschsprung's disease 302
Bodman F delinquency (C) 56
Bogdin A modification of whooping-cough in contacts by means of chloramphenicol 764
Bolam R J Munchausen's syndrome (C) 743
Bonatti B salicylate (C)
Bond C J memorial to 14
Bone marrow aspiration universal needle for (Hill) (NI) 1214
Bones—costal chondritis (Deane) 583 digital osteitis (Lowden) 136 hip congenital dislocation of 94 1316 hyperostosis in vitamin A poisoning (LA) 534 Neoplasms of Bone (Coley) (R) 565 osteoarthritis of hip 296 Osteology for Dentists (Howat) (R) 331 osteomyelitis and overgrowth of long bones 1316 osteomyelitis due to Friedländer's bacillus (Muskat and Findlay) 1151 see also Fractures
Bonnin J G Complete Outline of Fractures (R) 1056
Book of the It (Groddeck) (R) 153
Boon T H—complete inversion of appendix 1304 gastroscopy 641
Booth W G notification of food poisoning (C) 53
Borist M—Cortisone and fat metabolism (C) 641 effects of Cortisone on early fibrosis of liver in rats (C) 55
Bornholm disease (Goldstone) (C) 635
Bornstein J—ACTH (C) 237 adrenocorticotrophic activity of blood plasma extracts (C) 750
Borstals (A) 335 (LA) 1333 for girls (A) 518 (Bell) (C) 795 (Elkin) (C) 515
Bourdillon R B infection of surgical wounds 537
Bourne G—heart size 17 methonium compounds in hypertension (C) 527
Bourne I H J personal hygiene 232
Bourne W L angor animi (C) 362
Bousfield G—diphtheria antitoxin in cord blood (C) 855 paralyses following immunising injections 1028
Bovet L Psychiatric Aspects of Juvenile Delinquency (A) 624
Bowel see Intestines
Bower H I general practitioner and consultant (C) 363
Bowesman C inguinal hernia 1396
Bowlby J Maternal Care and Mental Health (LA) 1165
Bowler D I ACTH in dermatomyositis 1054
Box, C R (O) 859
Boyd J D appointment 1075
Boyd J S K amœbiasis (C) 1243
Boys see Children
Brackett, A S treatment of smallpox (C) 690
Bradley S E Renal Function (R) 1108
B.R.A. Homes Ltd 1284
Brailsford J F—unusual syndrome with tobacco (C) 1128 will we never learn? (C) 591
Brain—anencephalus (McKeown and Record) 192 (LA) 218 bullet wound through both frontal lobes with recovery (Slorach) 1349 cerebellar damage in acute rheumatism (Cruickshank) 1052 cerebral localisation (Gooddy and McKissock) 481 (McDonald) 627 (Jefferson) (C) 635 (Gooddy) (C) 745 (Jefferson) (C) 966 (Whitty) (C) 1070 (Hamilton) (C) 1419 cerebrospinal fluid after cisternal streptomycin (Beynon) 322 connection between prefrontal cortex and hippocampal formation (Adey) (C) 532 control of autonomic nervous system by hypothalamus (McDonald) 627 electrical stimulation of (LA) 455 electro-encephalograms of cretins (A) 784 encephalitis in Australia 644 encephalitis postinfectious 859 Essay on Cerebral Cortex (Von Bonin) (R) 273 hemispherectomy (Gooddy and McKissock) 481 (LA) 514 hepatolenticular degeneration (A) 1404 Hirndurchblutungsstörungen (Brobeil) (R) 1352 hydrocephalus (McKeown and Record) 192 metabolic disorders in head injury (Higgins Lewin O'Brien and Taylor) 1295 polioencephalitis following appendicectomy (Warren) 313 Problems in Cerebellar Physiology (Moruzzi) (R) 672 trochar and cannula for tapping lateral ventricle (Cathie and Tizard) (NI) 623 see also Electroconvulsive therapy Leucotomy Meningitis Pneumoencephalography Poliomyelitis
Brain R H F sequelæ of radical gastric resections 1137 (correction) 1286
Brain W R mind and matter 863
Brandt S Werdnig Hoffmann's Infantile Progressive Muscular Atrophy (R) 777
Breakey V K St C familial idiopathic methæmoglobinæmia 955
Breast cancer in mouse and man (A) 1114
Breast milk—breast feeding and morbidity and mortality of infants (Robinson) 755 breast feeding in Bristol (Ross and Herdan) 630 (Dobson) (C) 746 (Simon) (C) 801 bureau in Birmingham 805
Bremer K appointment 480 (correction) 516
Brewis E C acute obstructive laryngotracheitis (C) 314
Bridie James (A) 251
Brighton smallpox at 59 108 169 233 256
Brindle H fingerprint detection and mercury poisoning 378
Bristol—breast feeding in (Ross and Herdan) 630 (Dobson) (C) 746 (Simon) (C) 801 problem families of (A) 100
British Columbia mental hospital in (Moss) 1120
British Empire Leprosy Relief Association 1131
British Empire Society for Blind 1236
British Encyclopædia of Medical Practice (Horder) (R) 332 (R) 1056
British Epilepsy Association 478
British Federation Against Venereal Disease 970
British Medical Association (LA) 35 399 596 1131 1271 representative meeting 1353
British Red Cross unit for Korea 150 (P) 833
British Rheumatic Association 1284
British Standards Institution 298 1053
British Surgical Practice (Carling and Ross) (R) 273
British United Provident Association 751
Broadcasting and doctors 1359
Broadmoor patients discharged from (L) 365
Brobeil A Hirndurchblutungsstörungen (R) 1352
Brockbank E M John Ferriar (R) 566
Brockington C F appointment 1155
Brocklehurst J C Incontinence in Old People (R) 1262
Bromage P R ætiology of chronic gastric ulcer (C) 408
Bromism on low-salt diets (Rosenheim) (Holt and Litchfield) (C) 347
Bronchi—bronchial asthma treated by bilateral resection of vagus (Clarke) 438 (C) 737 Bronchoesophagology (Jackson and Jackson) (R) 566 bronchogenic carcinoma treated with nitrogen mustard (Frankel and Workman) (C) 1231 (Droller) (C) 1326 bronchography delayed pulmonary complications of (Robertson and Morle) 357 (Lichter) (C) 528 tuberculosis of treated with streptomycin 253 (A) 250
Brooke B N total colectomy in one stage for ulcerative colitis 1197
Brooke C O S B prevention of tuberculosis in young people (C) 1181
Broom R (O) 915
Brown I M aged sick (C) 353
Brown J W Congenital Heart Disease (R) 33
Brown P S rutin (C) 52
Brown R Physiological Mechanisms in Animal Behaviour (R) 620
Browne R C, experimental nystagmus 721
Brownlee John memorial to (Anderson) (C) 1371
Brucellosis—control of (A) 459 neurological complications of undulant fever (Nelson Jones) 495 treated with antibiotics (A) 1006
Brussels Treaty Public health Committee 752 (P) 1014
Budget (LA) 840 (P) 913
Bullet wound through both frontal lobes with recovery (Slorach) 1349
Bullough W A personal hygiene (C) 744
Burkitt D P primary hydrocele 1341
Burn J H methonium compounds and hypertension (C) 642
Burne J C myocarditis with renal necrosis 446
Burnet Sir M recurrent Kaposi's varicelliform eruption in adult, 383
Burns—in large numbers treatment of 449 (correction) 646 (Patey) (C) 532 leucocytes in cases of 390 management of (Cram) 263 (Clarkson) 460 open-air treatment of (Blocker) 498 (Wallace) 501 tetanus in prophylaxis against (Colebrook) (C) 586 (Clarkson) (C) 690, (McLaren (C) 1325 ultraviolet delayed effects of (A) 280, (Thomson) 1347

Anthrax (A) 513 (Doig and Gemmill) 1011 cutaneous (A) 1004 (Dijamant) (C) 1116
Anthropology—Races (Coon Garn and Birdsell) (R) 671
Anthropometry—photogrammetric and androgyny scale (Tanner) 574 Prehistoric Man in Health and in Sickness Exhibition (A) 1004 research in (Clements) (C) [illegible]
Antibiotics—and antitoxins (Marsh) (C) 642 (Karamchandani) (C) 1417 cost of 750
Antibody Duffy and hæmophilia (James and Plaut) [illegible]
Anticoagulant (LA) 276 (LA) 456 in cardiac infarction (LA) [illegible] Thrombo-embolic Conditions and their Treatment with Anticoagulants (Marple and Wright) (R) 392
Antihistamine drugs—and tar in skin diseases (A) 1358 Antihistamines (Feinberg Malkiel and Feinberg) (R) [illegible] control of 916
Antitoxins and antibiotics (Marsh) (C) 642 (Karamchandani) (C) 1417
Anuria treatment of (LA) 1109
Anus tuberculosis of streptomycin in (Marcus) [illegible]
Any Wife or Any Husband (Malleson) (R) [illegible]
Aortic coarctation retinal changes in (A) [illegible]
Aortic hypoplasia and myocarditis in arachnodactyly (Whitfield Arnott and Stafford) 1387
Appendix—appendicectomy followed by poliomyelitis (Warren) 213 (Simpson) (C) 350 (Warren) (C) 412 appendicitis (A) 18, complete inversion of (Boon and Sibley) 1304
Appleby J C influenza A vaccines 1384
Appliances economy in 787
Appointed factory doctors charges of (P) [illegible]
Arachnodactyly with myocarditis and aortic hypoplasia (Whitfield Arnott, and Stafford) 1387
Archives of Middlesex Hospital 594
Arden G P Plasmosan 1090
Armitage G H Munchausen's syndrome (C) 743
Arm rest operating table (Wilson, Murphy and Angel) (NI) 511
Arnott W M—aminophyllin in emphysema 490 arachnodactyly 1387
Aronson R P streptomycin in Letterer Siwe's disease 859
Artane in parkinsonism (Garai) 429 (Ellenbogen) (C) 640 (Garai) (C) 800
Arteries *see* Blood vessels
Arteriosclerosis—Selected Studies on Arteriosclerosis (Altschul) (R) 1308
Arteriotomy to prevent bleeding at operations (A) 677
Arteritis temporal treated with Aureomycin (Rice Oxley and Cooke) 89
Arthritis—management of flexion deformities in (Howell) (C) 1017 postdysenteric streptomycin in (Chaudhuri Chakravarti and Rai Chaudhuri) 510 *see also* Gout Rheumatoid arthritis
Artificial limbs *see* Prosthetics
Ascites (LA) 1058 (LA) 1402
Ascorbic acid *see* Vitamin C
Ashby D W erythema multiforme 1091
Asher P prospect of war (C) 293
Asher R—empyema thoracis 924 Munchausen's syndrome 339
Askew W welfare of blind (C) 111
Asphyxia Neonatorum (Windle) (R) 332
Aspiration of—bone marrow universal needle for (Hill) (NI) 1213 empyema thoracis (Asher and Davies) 924 (A) 954 (Elliott and Young) (C) 1016 (Abrahams) (C) 1127 (Tait) (C) 1179 perforated ulcers (Taylor) 7
Aspirin *see* Acetylsalicylic acid
Association of British Pharmaceutical Industry 917
Association of Occupational Therapists 1373
Association of Optical Practitioners 243
Association of Sea and Air Port Health Authorities 1373
Association of Special Libraries and Information Bureaux 972
Association of Workers and Schools for Maladjusted Children 645
Asthma—Asthma (Francis) (R) 94 bronchial treated by bilateral resection of vagus (Clarke) 438 (C) 797 induced in man (Herxheimer) 1337
Atherosclerosis and cholesterol (Olbert) (C) 174
Athletes calling all (Abrahams) (C) 1020
Athletics—Medical Handbook for Athletic and Football Club Trainers (Jarvis) (R) 332 physical exercise (Abrahams) 1133 1187 tennis thumb (Oldfield) 1151
Atkins H J B Hilton's Rest and Pain (R) 512
Atlas d'electrocardiographie (Fattorusso and Ritter) (R) 332
Atlas of Human Anatomy (Anson) (R) 835
Atlas of Human Anatomy (Woerdeman) (R) 451
Auld W H R, fat absorption in chylothorax 991
Aureomycin—in cutaneous anthrax (A) 1004 in erythema multiforme (Sneddon) (C) 53 (Ashby and Lazar) 1091 (Jones) (C) 1280 in temporal arteritis (Rice Oxley and Cooke) 89 intramuscular (A) 843 prescription of, 1237 supplies of (P) 748 therapy bacteriological control of (Topley Lowbury and Hurst 87)
Auscultation (A) 1005
Australia encephalitis and rabbit myxomatosis in 644
Auto agglutinins (Bird) 997
Avomine (Harper) 1111 (correction) 1286
Aylworth Anthony 1077

B

Babies—Asphyxia Neonatorum (Windle) (R) 332 bowel rhythm in (Gordon) 1203 hypoprothrombinæmia of newborn (Stefanini) 606 immunisation of against diphtheria (Bousfield) 1028 Infant Feeding and Feeding Difficulties (Evans and MacKeith) (R) 1214 infant morbidity and mortality (Robinson) 785 neuromuscular incoördination of swallowing in (Macaulay) 1208 premature baby unit 1010, primary streptomycin resistant tuberculosis in (Timme and Henderson) (correction) 64 Über Blutfarbstoffwechsel gesunder Säuglinge und Kinder (Künzer) (R) 1214, vaccination of (P) 633 vitamin K in prevention of hæmorrhagic disease of newborn (Hay Hudson and Rodgers) 423 (A) 458 (Hay and Hudson) (C) 533 *see also* Methæmoglobinæmia
Bach F Recent Advances in Physical Medicine (R) 451
Bachrach D induced eosinopenia (C) 802
Bachrach W H Peptic Ulcer (R) 331
Bacillæmia due to *Shigella sonnei* (Tatham Williams and Stewart) 997
Bacilli *see* Bacteria
Bacitracin (LA) 1163
Back I G (O) 1371
Bacteræmia pneumococcal effect of Cortisone on (White and Marshall) 891
Bacteria—Bacterial Toxins (van Heyningen) (R) 619 bacterial variants produced with chloramphenicol (Vouroka) 27 (Vouroka) 28 (LA) 38, (Rogers) (C) 587 (Vouroka) (C) 857 bacterium versus virus (A) 39 (Wooster) (C) 51 (LA) 569 Bakteriologie und Serologie (Hallmann) (R) 392 Enterobacteriaceæ (Kauffmann) (R) 1108 Friedländer's bacillus causing osteomyelitis (Muskat and Findlay) 1154 *Leuconostoc citrovorum* (LA) 623 meningococcus, dissemination of (A) 41 oldest known (A) 1004 Textbook of Bacteriology (Dougherty and Lamberti) (R) 452 *see also* Staphylococci
Bacteriophages (A) 39 (Wooster) (C) 51 (LA) 569
Badenoch J Tween 80 508
Baensch W E Lehrbuch der Röntgendiagnostik (R) 154
Bailey Walter 1077
Baird I M myocarditis with renal necrosis 416
Baker C G diaphragmatic flutter 985
Baker D wrong way (C) 1370
Banister J M R M B F clothes room (C) 1231
Bankart A S B death of 813 (O) 915
Banks A L office manners (C) 1233
Banks H S staffing of infectious diseases hospitals (C) 288
Bansi H W Thyreotoxikosen und Antithyreoidale Substanzen (R) 1398
Banton A H methonium compounds in hypertension (C) 527
Barbour R G H penicillin resistant and streptomycin resistant staphylococci 435
Barclay A E (A) 1006
Barcroft H noradrenaline in hypotensive states (C) 854
Barlow F E ætiology of chronic gastric ulcer (C) 470
Barlow W economic value of doctor (C) 1019
Barnard J prospect of war (C) 354
Barnard R D streptomyces fermentation derivatives in acute leukæmia 1157
Barnett A J comparison of pentamethonium and hexamethonium bromide (C) 1415
Barnie Adshead W F death of 295 (O) 356
Baron C secrecy of Service medical reports (C) 472
Barr M diphtheria antitoxin in cord blood 713
Barran G F tuberculosis figures (C) 352
Barry, C T—decamethonium iodide,
tidal spirometer (NI) 214
Bartholomew R J, determination
hæmoglobin 1014
Barton L A Doctor Remembers (R)
Baths (A) 573
Batten L W prospect of war (C) 354
Batty Shaw, A diaphragmatic flutter
Baur H L Lecture Notes on Emerg
Diagnosis (R) 1262
Bayley Walter 1077
Bayliss R I S, pulmonary hyperte
in mitral stenosis (C) 350
Bayly M B diagnosis of gout (C) 79
B C G—influence of thyroxine on des
tising action of A C T H and 'Corti
in B C G infected guineapigs (Long
and Perry) 1392, vaccination (
ganathan) (C) 520 in Denmark
vaccine (P) 407 as research tool
1217
Beare J M epileptiform fits d
calciferol therapy 884
Bearn F A coronary disease (C) 85
Beaumont G E A C T H by intrave
infusion 1260
Bed rest in—aged sick and (Amul
Exton Smith and Crockett)
(Brown) (C) 353 (Amulree and Ext
Smith) (C) 533, postoperative effect
on venous blood flow (Wright, Osb
and Edmonds) 22
Beddard F D mass radiography (C)
Bedford P D diuretic effect of vita
B_{12} (C) 1232
Bedpan exercise (A) 222 (Churchill) (C)
Beds—British standard cot for child
356 Emergency Bed Service 10
for aged in Scotland (P) 1322 for m
tally defective (P) 1014 for tubercu
(P) 294 (P) 344 in Norway (*Lillingst*
(C) 173 (Sita Lumsden) (C) 799
pital (A) 223, 357 in U S A (A)
hospital, for aged sick (P) 294, (P)
(P) 524 hospital for chronic sick
853, (P) 968 in London (P) 914
pital in Kent (P) 294 in Swiss sa
toria for tuberculous (P) 294 (P)
(P) 592, (P) 913 pay, in hospital
1012
Bedson S P Virus and Rickett
Diseases (R) 215
Beerstecher L Biochemistry of B Vi
mins (R) 274
BEFORE OUR TIME—Francisco de
Reyna and circulation of blood (Ke
and Payne) 851—THE LANCET'S a
lytical sanitary commission of 1
(Dopson) 580
Begg R C urethral caruncles 824
1181
Beit fellowships for medical research,
Bejel (Willcox) 558
Bell E T Renal Diseases (R) 778
Bell G H Textbook of Physiology
Biochemistry (R) 93
Bell H E safety endotracheal connect
(NI) 619
Bell M E serum protein levels
Samoans Fijians and Indians in Fiji
Bell O borstals for girls (C) 708
Bender A E food and energy (C) 1
Benioff M A Cytologic Diagnosis of L
Cancer (R) 672
Bentham E improvised vaccine lym
ejector (C) 1326
Bentley F H ætiology of chronic gas
ulcer (C) 470
Bentley J F R treatment of perfora
peptic ulcer (C) 109
2 *Benzyl* 4 5 imidazoline hydrochlor
(LA) 1203 in obstetrics (Forster) (C)
Berens C Encyclopedia of Eye (R) 1
Berry H Law relating to Mental Tre
ment and Health Service (R) 1398
Bertolani F salicylates (C) 51
Beryllium toxicity of (A) 1357
Besterman E M M income tax all
ances (C) 744
Beta naphthyl di 2-chloroethylamino (
1111, (Spigliati) (C) 1128 in leukæ
Hodgkin's disease and allied disord
(Gardikas and Wilkinson) 137
Beta radiation of stomach produces hy
chlorhydria (Douglas Ghent and R
lands) 492
Bevan Aneurin (A) 223 (P) 967
Bevis D C A acute puerperal invers
of uterus 1391
Beynon D cerebrospinal fluid a
cisternal streptomycin 322
Bibliographic Index 62
Bickerstaff E R changes in cerebrosp
fluid after pneumo-encephalograp
1209
Bicknell F food and energy (C) 592
Bile pigments in urine test for (Ingha
[illegible] (Smith) (C) 237
Biliverdin (Lemberg) (C) 1018
Billing B H postoperative blood ch
istry 315
Binning R prospect and retrospect (C) 2
Biochemistry—Biochemistry of B Vitami
(Williams Eakin Beerstecher and Shi
(R) 274 Microanalysis in Medic

—carcinomatous obstruction of (LA)
, (Grahame) (C) 803 Hirschsprung s
ase (Bodian Carter and Ward) 302
) 337, sensibility of (Goligher and
ughes) 513 total colectomy in one
o for ulcerative colitis (Brooke) 1197
ntal Medical Service (P) 107 (P) 568
r Psychology and Color Therapy
Birren) (R) 516
ur-vision see Eye
well A R Types of Diabetes Mellitus
and Their Treatment (R) 566
fort A , prospect of war (C) 291
mission The Lancet's analytical
sanitary of 1851 (Dop on) 580
missurotomy in mitral stenosis, finger
nail knife for (Sellors) (NI) 118
mmittee on general practice 1360
mon Cold Research Unit 122
mon Skin Diseases (Roxburgh) (R) 31
munity care teams 17
pensation for pneumoconiosis (P) 1129
mplaints against doctors 1361
mplete Outline of Fractures (Bonnin) (R) 1056
pound F, synthesis of (A) 12

NFERENCES AND CONGRESSES—Conference of Institute of Public Administration 632 conference of prison medical officers 1247 conference of public health section of Royal College of Nursing (A) 160 conference on medical teaching 1108 Conference on Problems of Aging (Shock) (R) 1056 conference on school punishments 1330 5th congress of Societe Internationale de Chirurgie Orthopedique et de Traumatologie 1374 Health Congress of Royal Sanitary Institute 1010 1st International Congress of Clinical Pathology 1328 5th International Congress of Orthopaedics 1315 1st International Congress on Diseases of Chest 213

ngenital defects—Congenital Heart Disease (Brown) (R) 33 congenital malformations of central nervous system seasonal incidence of (McKeown and Record) 192 (Hick) (C) 317 (Wallis) (C) 348 genetics and (LA) 215 rubella and (LA) 218
Conn H F Current Therapy (R) 1161
Connolly N K infection of clean surgical wounds (C) 713
nquest of Malaria (Jaramillo Arango) (R) 777
nstantinides V sickle-cell anæmia in Greece, 1147
Consultants and general practitioners (Robertson) (C) 854 (Finer) (C) 910 (Bower) (C) 963 (Lalonde) (C) 1020
—at hospitals number of (P) 345
Consultations domiciliary 403
Contraceptive Technique (Wright) (R) 1161
Contracture Dupuytren's (Herzog) 1305 (Holt) (C) 1117
Contractures apparatus for reducing (Russell and Schuster) (NI) 1351
Contribution of Surgery to Preventive Medicine (Learmonth) (A) 812
Convulsions in purulent meningitis in children (Ounsted) 1245
onybeare Sir J unfair questions (C) 637
ook, P J Munchausen's syndrome (C) 743
ook Sir A (O) 1021
ooke A M temporal arteritis 89
ooke, W T potassium deficiency in idiopathic steatorrhœa (C) 413
ookery cleaner (LA) 333
ooley's anæmia (A) 572 (A) 1400
oon C S Races (R) 671
ooper D J B National Health Service Acts 1946 & 1949 (R) 332
ope Committees reports (LA) 895 904 (P) 968
ope E, extraperitoneal cæsarean section (C) 250
opeman W S C chronic non-tuberculous abscess arising at site of injections (C) 692
opper content of tissues in hepatolenticular degeneration (A) 1404
orner B Textbook for Health Visitors (R) 1352
orner G W menstrual cycle 919
oronary disease—and modern stress (Platt) (C) 51 (Geiringer) (C) 109 (Stewart) (C) 239 (Stocks) (C) 351 (Rentoul) (C) 587 (Hill) (Lowy) (C) 694 (Stewart) (C) 801 (Bearn) (C) 855 in young adults ([illegible]an) 1045 recent history of ([illegible] , 1 69 (Gordon) (C) 240 (Disc[illegible] (C) 411
oroners [illegible] L) 406
orporal [illegible]ment in approved schools (P) 59[illegible]
or pulmonale—(LA) 621 from recurrent pulmonary embolism (Petch) 1346 lethal effect of morphine in (Roussak) 1156
Cortisone —972 cheap substitute for (A) 1403, effect of on pneumococcal bacteræmia (White and Marshall) 891
effects of on early fibrosis of liver in rats (Cavallero Sala Amira and Borasi) (C) 55 fat metabolism and (Sala, Amira Borasi and Cavallero) (C) 611 in acute lymphoblastic leukæmia (Suzman Goldberg and Hirsch) 760 infections and (Cavallero and Sala) (C) 175 (LA) 913, (Laurie) (C) 1325 influence of thyroxine on desensitising action of in B C G infected guineapigs (Long, Miles and Perry) 1392 in hæmatology (LA) 453 in rheumatism (LA) 750 (Clayton) (C) 858 price of 298 supply of (P) 1412
Cos plane tree 1023
Cot British standard for children 356
Cotswold School 102
Cotton wool (A) 1205
Council on Child Care 50
Cowie V A atypical phenylketonuria 272
Cox G I definition and notification of tuberculosis (C) 559
Cox L W prolapsed cord 561
Crabb W J nursing infectious diseases (C) 555 (C) 736
Croft A W J Ministry of Pensions artificial limb service 400
Craig C F, Clinical Parasitology (R) 1056
Cram R H burns 263
Cretins intelligence of (A) 751
Crime see Borstals Cotswold School Delinquency
Crockett G S, use of hospital in treatment of aged sick 123
Cruickshank E K hyperpyrexia with cerebellar damage in acute rheumatism 1052
Cryptococcosis (A) 158
Culdoscopy 1362 1363
Currency for treatment abroad (Williams) (C) 413
Current Therapy 1951 (Conn) (R) 1161
Curwen M P central defect (C) 171
Cuspidotomy (Levy) (C) 1152
Cutting W C Annual Review of Medicine (R) 332
Cyanosis see Methæmoglobinæmia
Cylinder gas identification of (P) 167 478
Cyriax J protruded intervertebral discs (C) 351
Cysts—endometrial rupture of (Dean) 1350 post-traumatic epidermoid (Young) 716
Cytologic Diagnosis of Lung Cancer (Farber Rosenthal Alston Benioff and McGrath) (R) 672
Cytological Diagnosis of Cancer (R) 724

D

D A D P S see Diaminodiphenylsulphone
Dale report (A) 519 (LA) 567
Dalton H W automatic pipette (NI) 273
Dangerous Drugs Bill (P) 968
Danielli J F—Cell Physiology and Pharmacology (R) 216 Physiological Mechanisms in Animal Behaviour (R) 620
Das A diphtheria in Calcutta 1110
Das Gupta S B aspirin sensitivity (C) 1327
Davidoff L M Abnormal Pneumoencephalogram (R) 724
Davidsen H G chronic renal potassium deficiency 375
Davidson J N—nucleic acid content of cell 1287 Textbook of Physiology and Biochemistry (R) 93
Davidson L S P pernicious anæmia treated with *Leuconostoc citrovorum* factor 722
Davies D empyema thoracis 924
Davies I G Textbook for Health Visitors (R 1)352
Davies J V S A risks of gastroscopy (C) 856
Davies L P syncope during injections (C) 1020
Davis E Munchausen's syndrome (C) 910
Daw R H mortality from circulatory diseases in Norway (C) 289
Dawes, G S *Veratrum viride* in hypertension (C) 691
Dawson J O infection of surgical wounds (C) 798
Day G psychosomatic approach to pulmonary tuberculosis 1025
D D T—D D T and Newer Persistent Insecticides (West and Campbell) (R) 216 shortage of 538
Dean T rupture of endometrial cysts 1350
Deane E H W costal chondritis 883
Death—rapid dual cause of (Mackintosh) (C) 238 sudden natural causes of (A) 500 unexpected after operation 151
de Beaufort L F Zoogeography of Land and Inland Waters (R) 1000
Decamethonium iodide cumulative action of (Barry Stratton and Sutherland) 507
Defæcation autonomic control of (McDonald) 627
De Filippis V effect of A C T H on renal glucose threshold (C) 856
Deglutition neuromuscular incoordination of in newborn (Macaulay) 1208
Dehydroascorbic acid (A) 1403
De la Reyna and circulation of blood (Keevil and Payne) 851
De Largy J treatment of aged sick (C) 176
De Launay L D wrong way (C) 1120
Delbecq E Traite du pneumothorax extra pleural (R) 31
Delinquency—(Bodman) (Edelston) (C) 56 (Stott) (C) 111 adolescent delinquent boys (A) 1267 Order of the Court (Pank) (R) 1000 (Climo) (C) 1370 Psychiatric Aspects of Juvenile Delinquency (Bovet) (A) 624 punishment of (A) 1004 (Casson) (C) 1015 *see also* Borstals
Deller P, fibrosarcoma of tongue after interstitial irradiation 1159
Delorme E J arterial perfusion of liver in shock 259
Dempsey T G (O) 62
De Navasquez J S lipoid pneumonia 1206
Denmark—B C G vaccination in 1412 toxoplasmosis in hares in (Christiansen and Siim) 1201
Dental Board 1121
Dental caries and fluoride (A) 393 (A) 1356
Dental fellowships 357
Dental nurses (LA) 155
Dental services—cost of (P) 715 school (P) 315
Dental students annual intake of (P) 748
Dental treatment 594
Dentist, £1000 to be recovered from 479
Dentists—foreign qualifications of (P) 1013 local authority pay of 751
Dentists Act amendment of (P) 1129
Dentists Register 1079
Dentistry see Teeth
Dentures—charges for (LA) 810 (LA) 1001 (P) 1012 1156 for Servicemen (P) 1014 free cost of (P) 968, free numbers of supplied (P) 1013
Deoxycortone acetate and ascorbic acid in rheumatoid arthritis (MacLean) 144
Deoxyribonucleic acid (Davidson Leslie and White) 1287
Deoxyribonucleoprotein (Simpson) (C) 110
DePalma A F Surgery of Shoulder (R) 93
Depression treatment of (LA) 726 (Scott) (C) 911
Dermatitis see Skin diseases
Dermatology see Skin diseases
Dermatomyositis treated with A C T H (Suzman and Rudolph) 660 (Williams and Bowler) 1053
Design for Sanatoria (R) 1214
de Soldenhoff R extraperitoneal cæsarean section (C) 236
Developments in Diphtheria Prophylaxis (Holt) (R) 392
Dewberry E B Food Poisoning (R) 452
Dewhurst C J acute puerperal inversion of uterus 1394
Dextran (LA) 456
Diabetes mellitus—ætiology of (LA) 837 Grundsätzliches zur Diabetestherapie (R) 512 prevention of complications of (LA) 1354 regional centres for treatment of (Lawrence) 1318 (Paul) (C) 1370 Types of Diabetes Mellitus and Their Treatment (Colwell) (R) 566
Diagnosis—Diagnosis of Smallpox (Dixon) (R) 1055 diagnostic aids in general practice (A) 954 diagnostic centre (Farrer Brown) (C) 584 Lecture Notes on Emergency Diagnosis (Baur) (R) 1262
Dialysis—Treatment of Uremia by Dialysis and Other Methods with Special Regard to Principles and Scope of Intestinal Dialysis (Twiss) (R) 154
Diaminodiphenylsulphone — in leprosy (Lowe) 18 (Ramanujam and Smith) 21 (Cochrane) (C) 289 (Lowe) (C) 469 (Cochrane) (Scott) (C) 799 toxic hepatitis caused by (Jelliffe) 1343
Diamorphine hydrochloride (P) 406
Diaphragmatic flutter (Baker and Batty Shaw) 985
Diaphragmatic paralysis and suppurative hepatitis (Todd) 1210
Dible and Davie's Pathology (Dible) (R) 1000
Dicoumarol—(LA) 276 hypoprothrombinæmia (Stefanini) 606
Dictionaries—Dictionary of Biology (Abercrombie Hickman and Johnson) (R) 778 English German Medical Dictionary (Schoenewald) (R) 274 Freud Dictionary of Psychoanalysis (Fodor and Gaynor) (R) 1000 Medical Dictionary (Veillon) (R) 672
Diet—circulatory diseases and (Strom and Jensen) 126 fitness and (Abrahams) 1135 for invalids, 752 influence of, on carcinogenic action of tannic acid (Korpássy and Mosonyi) (C) 1416 in treatment of Laennec's cirrhosis (LA) 1058 tuberculosis and (Cameron) 807
Dietitians 907
Digital see Fingers
Digitalis and other Cardiotonic Drugs (Moritt) (R) 94
Dijamant V cutaneous anthrax (C) 1416

Burns B H results of surgery in sciatica and low back pain 215 (*correction*) 158
Busvine J R Insects and Hygiene (R) 999
Butler J A V Progress in Biophysics and Biophysical Chemistry (R) 1213
Button L P transparent film envelopes for syringes (C) 964
Byssinosis prescribed under National Insurance 593

C

Cabbage factor modifying metabolism of ascorbic acid (Long, Miles and Perry) 1085
Cæsarean section extraperitoneal (Stansfield and Dribble) 71 (Higgins) (C) 173 (de Soldenhoff) (C) 236 (Cope) (C) 290 (O Sullivan) (C) 291
Cafestol in rheumatoid arthritis (Myers and Ross) (C) 640
Calciferol *see* Vitamin D_2
Calcium metabolism in hyperthyroidism (Green and Lyall) 828 (*correction*) 972
Calcutta diphtheria in (Das and Ghosal) 1110
Calder R Men against Desert 178
Calendar of Country Receipts (Heaton) (R) 515
Callahan A Surgery of Eye Injuries (R) 331
Callender S T E hæmopoietic extracts of fæces 1391
Call up of Z reserve medical students exempt from (P) 633
Cameron C fads and fancies 807
Campani M mast-cells (C) 802
Campbell A hexamethonium bitartrate (C) 597
Campbell G A D D T and Newer Persistent Insecticides (R) 216
Campbell H Plasmosan 1006
Canada—care of sick in (Simmonds and Peers) 844 mental hospital in British Columbia (Moss) 1120
Cancer—1009 bronchogenic treated with nitrogen mustard (Frankel and Workman) (C) 1231 (Droller) (C) 1326, Cancer Where We Stand (Russ) (R) 619 cervical curettage in diagnosis of (Anderson) 1152 Cytological Diagnosis of Cancer (R) 724 Cytologic Diagnosis of Lung Cancer (Farber Rosenthal Alston Benioff and McGrath) (R) 672, gastric unsuspected perforation and hæmorrhage from (Jemison) 1036, hypercalcæmic uræmia with nephrocalcinosis due to carcinomatosis (Fulton and Paget) 886 (McGowan) (C) 967 (Herson) (C) 1016 (Lloyd) (C) 1070 influence of diet on carcinogenic action of tannic acid (Korpássy and Mosonyi) (C) 1116, Malignant Disease of Female Genital Tract (Way) (R) 1107 mammary in mouse and man (A) 1114 nasopharyngeal treated with nitrogen mustard and urethane (Stock) 612 obstruction of colon by (LA) 726, (Grahame) (C) 803 Primary Carcinoma of Vagina (Livingstone) (R) 215 publicity in (Russ) (C) 688 (Joules) (Hilton) (C) 797 (Robbins) (C) 856 (Gilmour) (C) 911 (Donaldson) (C) 962 (Patey) (C) 1021 (Sauer) (C) 1074 (Walter) (C) 1180 Radiation Therapy in Management of Cancer of Uterine Cervix (Cantrill) (R) 153 research (P) 345 Results of Radium and X Ray Therapy in Malignant Disease (Paterson Tod and Russell) (R) 565 smoking and (Parnell) (C) 963 Terminal Care for Cancer Patients (Peterson) (R) 1056 uterine cervical classification of (A) 159
Canicola fever—diagnosis of 390 first fatal case of (Wolff van Dam and Minkenhof) 1100
Canter S acrosclerosis 130
Cantor S M Advances in Carbohydrate Chemistry (R) 836
Cantril S T Radiation Therapy in Management of Cancer of Uterine Cervix (R) 153
Capon A W hermaphroditism 563
Carbarsone (LA) 1163
Carbohydrates—Advances in Carbohydrate Chemistry (Hudson and Cantor) (R) 836
Carbon Dioxide Therapy (Meduna) (R) 778
Carbon tetrachloride fatal poisoning by (Love and Miller) 1306
Carcinoma *see* Cancer
Cardiac *see* Heart
Cardiology *see* Heart
Cardiovascular *see* Heart
Caries dental and fluoride (A) 399 594 (A) 1356
Carling Sir E R British Surgical Practice (R) 273
Carter C O Hirschsprung s disease 302
Carter G S Animal Evolution (R) 1108
Cartwright A Medresco hearing aid 1170
Caruncles urethral (Begg) 824 (Mills) (Taylor and McLaren) (C) 963 (Begg) (C) 1181
Casson, F R C psychiatry and law (C) 1015
Catalogue of Lewis s Medical Scientific and Technical Library (R) 894
Cataract—Surgery of Cataract (Kirby) (R) 566
Catering—Catering Trade Working Party (LA) 333 (Irvine) (C) 636 Hygiene in Catering (A) 1005 Hygiene in Catering Establishments (LA) 333
Cathcart C C death of 100 (O) 177 (*correction*) 115
Cathie I A B, trochar and cannula for tapping lateral ventricle (NI) 723
Cavallero C—Cortisone and fat metabolism (C) 641 Cortisone and infections (C) 175 effects of Cortisone on early fibrosis of liver in rats (C) 55
Cawadias A P mind and matter (C) 1019
Cell—Cell Physiology and Pharmacology (Danielli) (R) 216 embolism (LA) 90 (Marshall) (C) 173 nucleic acid content of (Davidson Leslie and White) 1287
Census (LA) 673
Central Council for Health Education 595
Central defect (Curwen) (C) 171
Central Health Services Council (LA) 35 (A) 98 104 1270
Central Medical War Committee 850
Central Midwives Board 900
Cerebellar *see* Brain
Cerebral *see* Brain
Cerebrospinal fever *see* Meningitis
Cerebrospinal fluid—after cisternal streptomycin (Beynon) 322 changes in produced by pneumo encephalography (Fleck and Stein) (C) 1126 (Bickerstaff) 1209 in brucellosis (Nelson Jones) 495
Certificates medical (A) 784 (Pinsent) 786
Chakravarti, H streptomycin in post dysenteric arthritis 510
Chalvey 697
Chambers s Encyclopedia 521 (*correction*) 596
Chapman, P D H prospect of war (C) 111
Chapman P J observers errors in taking medical histories, 1007
Charnley J orthopædic signs of protruded intervertebral discs 186
Chaudhuri R N streptomycin in post dysenteric arthritis 510
Cheatle Sir L (O) 115
Chemistry—Advances in Carbohydrate Chemistry (Hudson and Cantor) (R) 836 Chemistry and Therapeutics of Synthetic Drugs (Keyser) (R) 893 Chemistry of Inositol (Weidlein) 972 Eighteenth Century Lectureship in Chemistry (Kent) (R) 1108 Enzymes (Sumner and Myrbäck) (R) 721 Organic Chemistry (Karrer) (C) 965, Progress in Biophysics and Biophysical Chemistry (Butler and Randall) (R) 1213 *see also* Biochemistry
Chemotherapie der Tuberkulose mit den Thiosemikarbazonen (Domagk) (R) 33
Chest—clinics (Ellman) (C) 57 X ray apparatus for (P) 524 empyema thoracis treated with penicillin and aspiration only (Asher and Davies) 924 (A) 954 (Elliott and Young) (C) 1016 (Abrahams) (C) 1127 (Tait) (C) 1179, fat absorption in chylothorax (Auld and Needham) 991 (Aiken) (C) 1073, infection and oral sepsis 391, laryngotracheitis and laryngotracheobronchitis acute obstructive (Forfar Keay and Thomson) 181 (Brewis and Neubauer) (C) 349 Thoracic Surgery (Sweet) (R) 620 *see also* Asthma Bronchi Lungs
Chester Beatty Research Institute 1184
Cheston F education on alcoholism 733
Chicory in coffee (Dopson) 580
Childbirth safer in Newcastle upon Tyne (A) 1266
Children—boys clubs medical scheme for (Falkner) (C) 111 care of (P) 633 in Israel (A) 517 child welfare 1010 convulsions in purulent meningitis in (Ounsted) 1245 cot British standard 356 Cotswold School 102 cyclical vomiting in 330 Emergencies of Childhood (Gamlin) (R) 1000 feet of 1421 fulminating Sonne dysentery in (Lewis and Claireaux) 769 gall bladder disease in (Jones) 324 Glasgow weights and heights of 1012 Handbook of Child Health (Furniss) (R) 672, handicapped reablement of 1078 health of study of in Newcastle upon Tyne (A) 221 hospital schools for (Williams) 1269, illegitimate (A) 1113 intravenous fluid therapy in (Todd) 982 (Matheson) (C) 1128 (Mann) (C) 1230 (Gunn) (C) 1278 (McNicholl) (C) 1368 invalid training of (Field) (C) 476 (Franklin) (C) 588 London at La Bourboule 970 mental health of (LA) 1165 Modern Trends in Pædiatrics (Parsons) (R) 512 National Dried Milk for 179 obesity in (A) 841 overdosage of amidone in child (Roxburgh and Munro Faure) (C) 174 Pediatric Allergy (Chobot) (R) 1162 Psychoanalytic Study of Child (Eissler Freud Hartmann and Kris) (R) 671 school for handicapped, 614, sub normal (P) 633 uneducable (trainin for (P) 1282 United Nations Inter national Children's Emergency Fun (P) 167, tuberculin sensitivity in i hospital (Lunn) 370, (Engler) (C) 964 *see also* Babies, Borstals Delinquency Diphtheria
Childs P Spigelian hernia, 1290
Chiropodists 907
Chisholm J death of 1358, (O) 1420
Chloramphenicol—bacterial variants pro duced with (Voureka) 27 (Voureka) 28 (LA) 38 (Rogers) (C) 587 (Voureka) (C 857, cost of prescriptions of 750 El Tor vibrio in estimation of (Doornbo and Kop) (C) 691 in cutaneous anthra (A) 1001 in dermatitis herpetiform (Thorne) (C) 410 (Alexander) (C) 53 in pertussis (Lassen and Grandjean) 76 (A) 787 in treatment of urinary carrie of paratyphoid fever (Kennedy an Millar) 92 modification of pertussis i contacts by means of (Bogdan) 764, (Khalil and Abdin) (C) 1370, prescrip tion of 1237
Chloride metabolism in head injury (Hig gins Lewin O Brien and Taylor) 129
Chloroquin (LA) 896 (LA) 1163
Chobot R Pediatric Allergy (R) 1162
Cholesterol and circulatory diseases (Strom and Jensen) 126 (Olbert) (C) 174
Chondritis costal (Deane) 883
Chordates (Rand) (R) 1214
Choremis C sickle cell anæmia in Greece 1117
Choriomeningitis lymphocytic (Duncan, Thomas and Tobin) 956
Christiansen M toxoplasmosis in hares in Denmark 1201
Christie, R V radiological diagnosis of emphysema 881
Chronic sick—beds for (P) 407 (P) 853 (P) 968, in London (P) 914 care of (P) 1282 in Canada (Simmonds and Peers) 844
Churchill S bedpan exercise (C) 475
Churchill Davidson H C noradrenaline in hypotensive states (C) 851
Chylothorax fat absorption in (Auld and Needham) 991 (Aiken) (C) 1073
Ciba Foundation, 916
Cibalgin causing granulopenia, 389
Circulatory diseases *see* Heart
Cirrhosis—hepatic attributed to methyl chloride (Wood) 508 Laennec s diet in treatment of (LA) 1058
Citrovorum factor (LA) 623 967
Claireaux A F, fulminating Sonne dysentery in children 769
Clamps for—gastrectomy (Stevenson) 1300 hysterectomy (Howkins) (NI) 1107
Clark C J M measurement of digital swelling in rheumatoid arthritis 775
Clark L H Physics in *Medical Radiology* (R) 835
Clarke C A bilateral resection of vagus in bronchial asthma 438 (C) 797
Clarke O miniature radiography (C) 1179
Clarkson P—burns 460 periarterial blood transfusion (C) 747 prophylaxis against tetanus in burns (C) 690 training of dressers in tissue-craft 1242
Clayton, B E, *salicylates and* Cortisone in rheumatism (C) 858
Clements, E M B, research in anthropometry (C) 237
Clifford A air travel (C) 1021
Clinical Orthoptic Procedure (Smith) (R) 672
Clinical Parasitology (Craig and Faust) (R) 1056
Clinical Use of Radioactive Isotopes (Low Beer) (R) 274
Clubs boys medical scheme for (Falkner) (C) 111
Clymo B J Order of the Court (C) 1370
Coalminers *see* Miners
Coca (A) 307
Cochrane, A I—observers' errors in taking medical histories 1007 pneumoconiosis in coalminers (*C*) *1278*
Cochrane R G diaminodiphenylsulphone in leprosy (C) 289 (C) 799
Coffee, adulteration of (Dopson) 580
Coghill N F tick borne relapsing fever, 604
Colby F H Essential Urology (R) 33
Colds experiment on transmission of (Andrewes Lovel[illegible] mmerville) 26
Colebrook L prophylaxis in cerebrotanus in burns (C) 580
Colectomy total in one stage for ulcerative colitis (Brooke) 1197
Coley B L Neoplasms of Bone (R) 565
Colitis *see* Colon
Collected Papers by Sigmund Freud (Strachey) (R) 31
Collected Papers on Psychoanalysis (Sharpe) (R) 724
Colligan J C welfare of *blind* (*C*) 111
Colombo plan (A) 626

ne and Tropical Medicine, 1155 kal Art Society 795 Ministry of th Art Club and Hygeia Camera b 108 Prehistoric Man in Health Sickness (A) 1004 Royal Academy 3, Sherlock Holmes exhibition 229 South Bank Exhibition 1066
ring the Unconscious (Groddeck)) 153
on Smith A N, use of hospital in treatment of aged sick 123 (C) 533
e—autonomic control of pupil (McDonald) 627 bags under eyes (A) 1311 blind, employment of 116 blind welfare of (Askew and Colligan) (C) 111 Clinical Orthoptic Procedure (Smith) (R) 672 cost of ophthalmic services (P) 718 disturbance of pupillary reactions (Dogart) 1081 Documenta Ophthalmologica (Fischer Schaeffer and Sorsby) (R) 216 Empire campaign against blindness 1236 Encyclopedia of Eye (Berens and Siegel) (R) 1108 Essentials of Ophthalmology (Pritikin) (R) 1055 Individual Differences in Colour Vision (Pickford) (R) 1308 nystagmus experimental (Browne) 721 ophthalmoscopic detection of microfilaria of *Onchocerca volvulus* (Sarkies) 1205 opsoclonia in polioencephalitis (Warren) 213 (Simpson) (C) 350 (Warren) (C) 412 Physiology of Eye—Clinical Application (Adler) (R) 777 Recent Advances in Ocular Prosthesis (Prince) (R) 891 Recent Advances in Ophthalmology (Duke Elder and Goldsmith) (R) 392 Researches in Binocular Vision (Ogle) (R) 452 retinal changes in aortic coarctation (A) 1220 Surgery of Cataract (Kirby) (R) 566 Surgery of Eye Injuries (Callahan) (R) 331

F

ctory doctors' charges (P) 407
culty of Anæsthetists—dinner 698 elections 752
culty of Ophthalmologists 1132
culty of Radiologists pass lists 63 1122
ds and fancies (Cameron) 807
eces preparation of hæmopoietically active extracts from (Callender and Spray) 1391
t emotional (Greenfield) 1302
ner F medical scheme for boys ibs (C) 111
pian tubes—diagnosis of patency of 383 physiology of 1362 salpingostomy 1363
mily *Doctor* (A) 677
AO (A) 459
rker S M Cytologic Diagnosis of Lung Cancer (R) 672
arquhar H C congenital indifference to pain 827
arrer Brown L specialisation (C) 584
at—absorption and distribution of (LA) 1007 absorption in chylothorax (Auld and Needham) 991 (Aiken) (C) 1073 and circulatory diseases (Strom and Jensen) 126 embolism 152 Lipidoses Diseases of Cellular Lipid Metabolism (Thannhauser) (R) 216 metabolism and Cortisone (Sala Amira Borasi and Cavallero) (C) 641 obesity (A) 782 (Lowy) (C) 858 1100 in children (A) 841
ttorusso V Atlas d electrocardiographie (R) 332
ust E C Clinical Parasitology (R) 1050
vism (A) 572
et—children's 1421 Foot Health Educational Bureau 596 1285 Foot Mechanics (Smart) (R) 332 Feet and Footwear 1285
lling, A Modern Trends in Neurology (R) 894
inberg R and Feinberg S M Antihistamines (R) 154
llowship for Freedom in Medicine—dinner to Lord Horder 104 memorandum on registrars 178
llowship of Postgraduate Medicine 918
llowships—Beit for medical research 1329 Crichton 801, dental 357 in clinical research 536 travelling 418 479 698 William Julius Mickle 594
moral shaft recent fractures of intramedullary nailing in (Lloyd Roberts) 711, (LA) 780
nestration operation—reduction of bleeding in (Hughes) 666
rguson D A bleeding peptic ulcer 814
rriar J—John Ferriar (Brockbank) (R) 566
rritin (LA) 838
rtilisation of mammalian ova 1263
stival of Britain medical symposia 1131
brinogen—congenital afibrinogenæmia (Prentice) 211
brosarcoma of tongue after interstitial irradiation (Deller) 1159
brosis, early of liver in rats effects of Cortisone on (Cavallero Sala Amira and Borasi) (C) 55
Field C F training of invalid children (C) 176
Fielding J abscess at site of penicillin injections 556
Fiji—19 congenital syphilis in Fijian (Manson Bahr) (C) 638 serum protein levels of Fijians and Indians in Fiji (Wills and Bell) 820
Films—Der Film als Experiment und Heilmethode (Ihotsky and Potzl) (R) 31 medical, 517 918
FILMS—Life Cycle of Malaria Parasite 1281 Lymphatic System 614 Œsophageal Speech after Laryngectomy 62 Out of True 1078 Snake Pit 1078 Taking a Blood-culture (LA) 334 Taking a Swab 972 The Undefeated 62
Findlay M osteomyelitis due to Friedländer's bacillus 1154
Finer D I general practitioner and consultant (C) 910
Fingerprints detection of and mercury poisoning (Blench and Brindle) 378
Fingers—infection of digital pulp space (Fowden) 196 measurement of digital swelling in rheumatoid arthritis (Hart and Clark) 775 *see also* Arachnodactyly
Fire accidents from in the home (LA) 97
Fischer F P Documenta Ophthalmologica (R) 216
Fisher, V E Meaning and Practice of Psychotherapy (R) 1162
Fits epileptiform during calciferol therapy (Beare and Millar) 881 (Cremeaux) (C) 1016
Fitzpatrick K slimming by television (C) 692
Fitzpatrick R J response of uterus to drugs 250
Fleck, I C S F changes with pneumoencephalography (C) 1126
Fleetwood J F, treatment of aged sick (C) 476
Fleming G W T H *Recent Progress in Psychiatry* (R) 1202 (correction) 1371
Flemming C treatment of fractures in aged 758
Fletcher C gastroscopy 617
Fletcher C M pneumoconiosis in coal miners (C) 1278
Flexion deformities in arthritis management of (Howell) (C) 1017
Flindt M laryngeal vertigo (C) 636
Florey M E relation of penicillin sensitivity in staphylococci to clinical manifestations of infection 309
Flour agenised (ML) 741 (P) 914
Floyd W F function of erectores spinæ 133
Fluorescence in gynæcology (A) 1061
Fluoride and dental caries (A) 399 591, (A) 1350
Flynn J E Blood Clotting and Allied Problems (R) 1162
Fodor N Freud Dictionary of Psychoanalysis (R) 1000
Folinic acid (LA) 623
Food—charts 62 clean 287 (LA) 333 (P) 344 (P) 633 (Irvine) (C) 636 (A) 1005 1010 comparative merits of animal and vegetable (A) 222 control of in Norway 917 energy and (Bicknell) (C) 592 (Bender) (C) 1070 Food and Agriculture Organisation (A) 459 Food Rationing (Special Diets) Advisory Committee (P) 1283 preservatives in 244 pure and nutrition (A) 570 THE LANCET's analytical sanitary commission of 1851 (Dopson) 580
Food poisoning—(LA) 333 (P) 344 Food Poisoning (Dewberry) (R) 452 in Kendal, 50 notification of (Booth) (C) 53
Foot *see* Feet
Foote J B thigh neck clearance 868
Foot operated w c seat (Bourne) 232
Foreign dentists qualifications of (P) 1013
Foreign workers pulmonary tuberculosis in (P) 968
Forensic medicine—Lehrbuch der gerichtlichen Medizin (Ponsold) (R) 671
Forfar J O laryngotracheitis 181
Forrest F P training of dressers in tissue craft (C) 1370
Forsell G (O) 860
Forster A proprietary preparations (C) 1181
Foss G L influence of androgens on sexuality of women, 667
Foster C A sensitivity to mercurial diuretics 614
Foster P A Priscol in obstetrics (C) 802
Foulis M A *smallpox* 1248
Foulkes, S H psychosomatic approach to pulmonary tuberculosis (C) 1180
Fox, H penicillin in megaloblastic anæmia (C) 410
Fractures—Complete Outline of Fractures (Bonnin) (R) 1056 medullary nailing (LA) 780, recent of femoral shaft treated by intramedullary nailing (Lloyd Roberts) 711 treatment of in aged (Flemming) 758
Franchise and certified lunatics (P) 345
Francis C, Asthma (R) 94
Frankel F—bronchogenic carcinoma treated with nitrogen mustard (C) 1231 methonium compounds in hypertension (C) 108 Munchausen's syndrome (C) 911
Franklin A W training of invalid children (C) 585
Franklin L M rationalised general practice 1226
Franklin P (O) 177
Fraser R—leucocyte counts in thiouracil therapy (C) 154 trophic and tropic (C) 52
Fraser I (O) 119
Frazer W M History of English Public Health (R) 671
Freeman A C electrocardiographic findings during operative manipulation of viscera and vagi 926
Freis E D methonium compounds in hypertension (C) 909
French D C intravenous iron (C) 811
French H death of 62 (O) 120
French, J C death of 900 (O) 969
Freud A Psychoanalytic Study of Child (R) 671
Freud Dictionary of Psychoanalysis (Fodor and Gaynor) (R) 1000
Freud Sigmund—Collected Papers by Sigmund Freud (Strachey) (R) 34
Friedl I Lehrbuch der Röntgendiagnostik (R) 154
Friedman S M Visual Anatomy (R) 1107
Friedmann's turtle vaccine (Cameron) 809
Friend J glucose tolerance 207 (C) 592
Fulton J F appointment 479
Fulton R M hypercalcæmic uræmia with nephrocalcinosis due to carcinomatosis 886
Fumagillin (LA) 1183
Functional Anatomy of Limbs and Back (Hollinshead) (R) 1308
Funktionelle Organisation des vegetativen Nervensystems (Hess) (McDonald) 627
Furniss A *Handbook of Child Health* (R) 672

G

Gaisford W hyaluronidase 1253
Gale A H, poliomyelitis in semi closed communities 735
Gall bladder disease in childhood (Jones) 324
Galley A H—*complications of spinal anæsthesia* (C) 689 *prospect of war* (C) 292
Galpine J F vaccine lymph ejector (C) 910
Gamlin R Emergencies of Childhood (R) 1000
Garai O Lysivane and Artane in parkinsonism 429 (C) 800
Gardikas C—aminopterin in acute leukæmia 325 β naphthyl di 2 chloroethyl amine 137
Garn S M, Races (R) 671
Garson J Z prospect of war (C) 235
Gas cylinders, identification of (P) 467 478
Gask G E (O) 240 295
Gastrectomy *see* Stomach
Gastric *see* Stomach
Gastro jejuno-colic fistula (Holman) 1348
Gastroscopy *see* Stomach
Gaynor F Freud Dictionary of Psychoanalysis (R) 1000
Geiringer E coronary disease and modern stress (C) 109
Geiser, M determination of hæmoglobin 1041
Gemmill J S—anthrax 1011 vaccination against smallpox (C) 352
General adaptation syndrome (LA) 277
General Clinical Counseling in Educational Institutes (Hahn and MacLean) (R) 948
General Medical Council 579 861 1077 1174 (A) 1218 1223 (corrections) 1286
General Medical Services Committee (A) 1311 (LA) 1353
General practice—31, (A) 98 104 682 committee on 1360 diagnostic aids in (A) 954 in Scotland 1174 rationalised (Franklin Paulett Tepper and Tuckman) 1226
General practitioners—consultants and (Robertson) (C) 854 (Finer) (C) 910 (Bower) (C) 963, (Lalonde) (C) 1020 distribution of 861 lists of patients of 179, checking of (P) 633 number of, in N H S (P) 345 pay of (A) 785 (A) 1220 1285 (A) 1311 (LA) 1353 1360 self improvement of discouraged (Jackson) (C) 585
Genetics—congenital defects and (LA) 218 *Hirschsprung's* disease (Bodian Carter and Ward) 302 viruses and (A) 99
Gentisate—and eosinophils (Meade and Smith) (C) 236 (Meade and Smith) 773, (Kelemen and Majoros) (C) 962 in rheumatism (LA) 780
German measles and congenital defects (LA) 218
Germany—Health and Human Relations in Germany (R) 620
Gerson diet (Cameron) 807

Dilantin sodium action of on suprarenal glands (Staple) (C) 1074
Dillon M stilts for achondroplasiacs (C) 1418
Di nitro-ortho cresol poisoning (A) 1405 (Steer) (C) 1119
Dinners and luncheons—Buckston Browne dinner of Harveian Society of London 1132 dinner of Association of Occupational Therapists 1373 dinner of Chelsea Clinical Society 1132 dinner of Faculty of Anæsthetists 698 dinner of London Hospital Clubs Union 1373 dinner of Medical Society of London 615 dinner of Royal Cancer Hospital 1184 dinner of Royal College of Surgeons to mark John Hunter's birthday [illegible] dinner of Royal College of Surgeons to Sir William Fry 595 dinner of Society of Chiropodists 1077 dinner to Dr F W Price 971 dinner to Lord Horder 101 luncheon of Anglo Argentine Society and Hispanic Council for A I Pavlovsky 538 U F A W jubilee dinner 1023
Diphenylhydantoin sodium action of on suprarenal glands (Staple) (C) 1074
Diphtheria—alkali dissolved toxoid antitoxin floccules adsorbed on aluminium carriers in immunisation of adults (Mason) 501 (correction) 646, antitoxin in cord blood (Barr Glenny and Walsh) 713 (Bousfield) (C) 855 campaign against 859 Developments in Diphtheria Prophylaxis (Holt) (R) 392 immunisation against 1177 immunisation of infants against (Bousfield) 1028 in Calcutta (Das and Ghosal) 1110 in immunised children (P) 406
Directory of International Scientific Organisations 478
Discombe G recent history of coronary disease (C) 411
Diseases of Heart and Circulation (Wood) (R) 565
Dislocation of hip congenital 945 1316
Display sets from Ministry of Health 697
Divorce—for incurable insanity (ML) 1077 Royal Commission on (P) 695
Dixon C W—Diagnosis of Smallpox (R) 1055 vaccination against smallpox (C) [illegible] (C) 532
D N O C *see* Di nitro ortho-cresol
Dobson J N breast feeding in Bristol (C) 746
Doctor Remembers (Barton) (R) 724
Doctors—broadcasting and 1359 called up arrangements for 1361 calling 752 checking lists of patients of (P) 633 complaints against 1361 distribution of (P) 747, doctor's friend (A) 398 Doctors of Mind (Ray) (R) 1056 economic value of (Roberts) 675 (Hughes) (C) 856 (Rabson) (C) 909 (Martin) (C) 961 (Barlow) (C) 1019 houses for 63 National Insurance and (P) 914, on boards and committees 1361 opportunities for in Britain (Smith and Smith) (C) 1069 training of 1362 Z reservist appeal of against call up 594
Documenta Ophthalmologica (Fischer Schaeffer and Sorsby) (R) 216
Dodd H inguinal hernia 1193
Dodson, A Urological Surgery (R) 154
Doggart J H pupillary reactions 1081
Doig A T anthrax 1011
Doll R—gastroscopy 647 prospect of war (C) 170 (C) 415
Domagk G Chemotherapie der Tuberkulose mit den Thiosemikarbazonen (R) 33
Domiciliary care (A) 783
Domiciliary consultations 403
Donaldson M publicity in cancer (C) 962
Donaldson R determination of hæmoglobin 874 1044
Donnelly J M kwashiorkor (C) 588
Donovan, G E radiography in colour 832
Doorenbos W El Tor vibrio in estimation of chloramphenicol (C) 691
Dopson L THE LANCET's analytical sanitary commission of 1851 580
Doran F S A—ætiology of chronic gastric ulcer (C) 532 (C) 635 blood supply of gastric mucosa 109
Dornhorst A C—estimation of collateral resistance during obstruction of main artery of limb 81 pulmonary hypertension in mitral stenosis (C) 57
Dougherty J M Textbook of Bacteriology (R) 452
Douglas D M—appointment 917 production of hypochlorhydria by β radiation of stomach 492
Downie A W—smallpox 419 Virus and Rickettsial Diseases (R) 215
Drabble L W D extraperitoneal cæsarean section 74
Drepanocytosis (A) 572 (LA) 1400
Dressers training of in tissue craft (Clarkson) 1242 (Forrest) (C) 1370
Drinking water cyanosis in infants from nitrates in (Ewing and Mayon White) 931 (Harrison and Gibson) (Jones) (C) 1071 (Heather) (C) 1324
Droller H bronchogenic carcinoma treated with nitrogen mustard (C) 1326
Dromoran (LA) 156
Drugs—addiction to in U S A (A) 1356 administration of (Trillwood) 1221 allowed to merchant ships 616 approved names for 178, Chemistry and Therapeutics of Synthetic Drugs (Keyser) (R) 893 cost of per patient in N H S (P) 467 Dangerous Drugs Bill (P) 968 Digitalis and other Cardiotonic Drugs (Movitt) (R) 94 narcotic 1330, oxytocics (Stansfield and Drabble) 71 proprietary (Forster) (C) 1181 *see also* Pharmacology
Drunkenness increase in (P) 853
Dry T J Manual of Cardiology (R) 216
Dublin famous surgeon anatomists of (A) 338
Du Boulay G H alarming names for hospitals (C) 353
Dudgeon J A recurrent Kaposi's varicelliform eruption in adult 383
Duffy antibody and hæmophilia (James and Plaut) 150
Duke Elder Sir S Recent Advances in Ophthalmology (R) 392
Dumoulin J G tetraethylammonium bromide in toxæmia of pregnancy 1257
Duncan P R lymphocytic choriomeningitis 956
Duodenum—intubation of with magnet tipped tubes (James) 209 *see also* Peptic ulcer
Dupuytren's contracture (Herzog) 1305 (Holt) (C) 1417
Durham County Council and trade union membership (P) 695 (P) 1014 1362
Durie T B M concentration of penicillin in lungs (C) 1417
Dust cells in lungs of albino mouse (Macklin) 132
Dwarfism renal causing disparity of growth in uniovular twins (Milne) 204
Dwarfs achondroplasiac stilts for (Dillon) (C) 1418
Dyke S C, hæmatinics (C) 1368
Dysentery—amœbic in Britain (Morton Neal and Sage) 766 amœbic treatment of (LA) 1163 (Boyd) (C) 1233 Sonne, fulminating in children (Lewis and Claireaux) 769
Dysmenorrhœa ureteric (Read) 312

E

Eakin R E, Biochemistry of B Vitamins (R) 274
Ear—Ménière's disease (A) 783 (Mitchell) (C) 909 (Passe) (C) 1280 Sonex ear defenders 971 *see also* Hearing aids
Eastwood N B heartburn (C) 1072
Edmonds D G effect of postoperative rest in bed and early ambulation on venous blood flow, 22
Education of medical students, 1367 (C) 1417
Eighteenth Century Lectureship in Chemistry (Kent) (R) 1108
Eire—department of health of (A) 399 scheme for free medical care of mother and child in 907
Eissler, R S Psychoanalytic Study of Child (R) 671
Elderly *see* Aged
Electricity cuts and hospitals (P) 467 (McIntosh) (C) 475
Electrocardiography—Atlas d'électrocardiographie (Fattorusso and Ritter) (R) 332 electrocardiographic findings during operative manipulation of viscera and vagus nerves (Freeman) 926 in hypokalæmia (LA) 393
Electroconvulsive therapy—heightened perception after (Todd) (C) 965 of psychoneurotics (Neustatter) 1331
Electro-encephalograms of cretins (A) 784
Elgood C Medical History of Persia and Eastern Caliphate (R) 1262
Elkin W A borstal for girls (C) 858
Ellenbogen B K Artane in parkinsonism (C) 640
Elliott W A empyema thoracis treated with penicillin and aspiration only (C) 1016
Elliptocytosis (LA) 1400
Ellis M—outpatient treatment of injured hand 1038 penicillin and sulphonamides in suppuration 774
Ellman P, alarming names for hospitals (C) 57
Embolism—air 152 cell (LA) 96 (Marshall) (C) 173 fat 152 pulmonary 151 recurrent causing cor pulmonale (Petch) 1346
Embryology—Human Embryology for Medical Students (Nair) (R) 894
Emergencies in Medical Practice (Birch) (R) 274
Emergencies of Childhood (Gamlin) (R) 1000
Emergency Bed Service 1065
Emphysema—aminophylline in (Whitfield Arnott, and Waterhouse) 490 radiological diagnosis of (Knott and Christie) 881
Empire Rheumatism Council 243
Empyema thoracis treated with penicillin and aspiration only (Asher and Davies) 921 (A) 954, (Elliott and Young) (C) 1016, (Abrahams) (C) 1127 (Tait) (C) 1179
Encephalitis, *see* Brain
Encyclopedia of Eye (Berens and Siegel) (R) 1108
Enderby G E H controlled hypotension and postural ischæmia 603
Endocarditis subacute bacterial caused by coagulase negative *Staph albus* (Matthew) 146
Endometriosis (Dean) 1380
Endometrium—human tissue culture of (A) 42 rupture of cysts of (Dean) 1380 tuberculosis of (Haines) 446
Endotracheal connection, safety (Bell) (NI) 619
Engler G tuberculin sensitivity in hospital children (C) 964
English German Medical Dictionary (Schoenewald) (R) 274
Enteric carriers (A) 518
Entamœba histolytica—detection of (Ross) (C) 912 *see also* Amœbiasis
Enterobacteriaceæ (Kauffmann) (R) 1108
Entzündungsbestrahlung (Glauner) (R) 1162
Enuresis (C) 803
Envelopes transparent film, for syringe service (McCartney) 509 (Heggie) (C) 580
Enzymes (Sumner and Myrbäck) (R) 724
Eosinophils—and salicylates and gentisates (Meade and Smith) (C) 236, (Meade and Smith) 773 (Kelemen and Majoros) (C) 962, mechanism of induced eosinopenia (Oláh, Majoros Varró Bachrach, and Kovács) (C) 802
Epidemiology—development of influenza epidemics (Logan and MacKay) 281 of canicola fever 391 World Health Organisation and (A) 457
Epidermoid cysts post traumatic (Young) 716
Epileptiform fits during calciferol therapy (Beare and Millar) 884, (Gromeaux) (C) 1016
Epsom College 298 917
Epstein B S Abnormal Pneumoencephalogram (R) 724
Epstein E Regional Dermatologic Diagnosis (R) 93
Equilin (Bishop Richards and Perry) 81[illegible]
Erectores spinæ function of in flexion of trunk (Floyd and Silver) 133
Ergometrine action of on uterus (Schild, Fitzpatrick and Nixon) 250
Erysipeloid of Rosenbach (MacDougall) 1345
Erythema multiforme (Sneddon) (C) 53 (Ashby and Lazar) 1091 (Jones) (C) 1230
Erythema nodosum leprosum (Lowe) 20
Erythroblastosis neonatorum vitamin K in prevention of (Hay Hudson and Rodgers) 423 (A) 458, (Hay and Hudson) (C) 533
Erythropoiesis 390
Esophagus and Pharynx in Action (Leche) (R) 1000
Essay on Cerebral Cortex (Von Bonin) (R) 273
Essentials of Ophthalmology (Pritikin) (R) 1055
Essentials of Urology (Ainsworth Davis) (R) 1397
Essential Urology (Colby) (R) 33
Essex Lopresti P C L (C) 1372
Esterman A prospect of war (C) 170 (C) 415
Eternal Eve (Graham) (R) 836
Ethopropazine hydrochloride in parkinsonism (Garai) 429
Ethylene oxide—Handling and Storage of Ethylene Oxide, 1330
Evans, D G hyaluronidase 1253
Evans F T—laryngoscope (NI) 1161 shoulder piece attachment for operating table (NI) 1307
Evans C Medical Treatment (R) 33
Evans P R Infant Feeding and Feeding Difficulties (R) 1214
Evans W phonocardiography 1083
Evolution—Animal Evolution (Carter) (R) 1108 Anatomy of Man and Other Animals (Murray and Jeffree) (R) 672, Chordates (Rand) (R) 1214
Ewing M C, cyanosis in infancy from nitrates in drinking water 931
Examinations unfair questions in (Conybeare) (C) 637 (Kirby) (C) 715 (Holroyd) (C) 746 (Jaffe) (C) [illegible]
Exercise, physical (Abrahams) 1133 1187
Exhibitions—contemporary French art 346 *Daily Mail* Ideal Home Exhibition 634 exhibition of history of pharmacy, 1078 exhibition of sculpture by mental patients 1181 Festival Exhibition of Science 1066 London School of

Gestation period of (ML) 1276
Ghent W R production of hypochlorhydria by β radiation of stomach 492
Ghosal S C diphtheria in Calcutta 1410
Gibson Q H familial idiopathic methæmoglobinæmia 935 (C) 1071
Gilbertson E hæmophilia in female 1375
Gilchrist W S I alloxan in hyperinsulinism 440 (correction) 806
Gillet J A health services bureau 404
Gilliland I C—insulin implants 143 prospect of war (C) 170 (C) 115
Gilmour M publicity in cancer (C) 911
Gilson J C pneumoconiosis in coalminers (C) 1278
Girby A—unfair questions (C) 715 prospect of war (C) [illegible]
Girdlestone G R—death of 62 (O) 117 infection of surgical wounds 597 memorial to 178
Girdwood R H pernicious anæmia treated with *Leuconostoc citrovorum* factor 722
Girls—borstals for (A) [illegible] (Bell) (C) 798 (Elkin) (C) 858 school for handicapped 644
Glands—sebaceous unicellular in human skin (Wolff) 858 (Lloyd) (C) 1010 (Wolff) (C) 1417 *see also* Adenitis
Glandular fever anginose type of (Librach) 1105
Glatzmann S *[illegible]* (C) 1325
Glasgow children's weights and heights 1012
Glasses *see* Spectacles
Glauner H R Entzundungsbestrahlung (R) 1162
Glenny A T—diphtheria antitoxin in cord blood [illegible] immunological protest (C) 1072
Glochinotomy (Levy) (C) 1182
Glomerulonephritis *see* Kidney
Glover R F human infection with virus of ovine contagious pustular dermatitis [illegible]
Glynne S R pneumoconiosis 810
Glucose—threshold renal and A C T H (De Filippis and Iannaccone) (C) 856 tolerance investigation of (Friend) 207, (Lawrence) (C) 471 (Friend) (C) 592
Gold S rôle of sulphonamides and penicillin in pathogenesis of systemic lupus erythematosus 269 (C) 641
Goldberg B cortisone in acute lymphoblastic leukæmia 760
Goldsmith A J B Recent Advances in Ophthalmology (R) 392
Goldstone B false acute abdomen (C) 638
Goligher J C—gastroscopy 652 (C) 796 sensibility of rectum and colon 343
Gonadotropin pituitary 1362
Gonorrhœa danger of penicillin in (Reckie) 327
Goodall J W D—accommodation for medical staff in hospitals 847, early ambulation 43 single rooms in hospitals 1063
Gooddy W cerebral localisation 481 (C) 715
Goodenough Sir W (A) 1313
Gordon I—bowel rhythm in healthy infant 1203 coronary disease (C) 240
Gout A C T H in diagnosis of (Kersley Mandel and Jeffrey) (C) 637 (Bayly) (Kersley Mandel and Jeffrey) (C) 798
Govan A D T intravenous iron in anæmia of pregnancy 367 (C) 691
Gow J G genito-urinary tuberculosis 1033
Graham H Eternal Eve (R) 836
Graham S (O) 1328
Grahame E W carcinomatous obstruction of colon (C) 803
Grandjean L C chloramphenicol in pertussis 763
Grant C residents in mixed institutions 282
Grant J typhoid fever in general hospital (C) 112
Grants for medical research in U S A. (LA) 1109
Granulopenia due to—amidopyrine 389 thiouracil (Holliday) 265 (Pollard) 388
Gray C H A C T H (C) 237
Gray F, maternity and administration (C) 858
Gray P C Medresco hearing aid 1170 (C) 1369
Greater London Red Cross Transfusion Service 696
Greece sickle-cell anæmia in (Choremis Zervos Constantinides and Zannos) 1147 (Lehmann) (C) 1279
Green J, calcium metabolism in hyperthyroidism 828 (correction) 972
Greenfield A D M—emotional faint 1302 yogi priest's feat (C) 56
Greenlees J R C death of 1169 (O) 1235
Gregory Alice 1421
Gremeaux A. E epileptiform fits during calciferol therapy (C) 1016
Grenville Mathers R prevention of tuberculosis in young people 1118
Grieve J spastic ileus 1104
Grist N R smallpox 1218
Groddeck G—Book of the It (R) 153 Exploring the Unconscious (R) 153
Grossman M I Peptic Ulcer (R) 331
Group practice (Alcock) (C) 910 (P) 1013
Group psychiatry (A) 839
Growth—in uniovular twins disparity of due to renal dwarfism (Milne) 204, longevity and (LA) 157 mental contentment and (Widdowson) 1316 Neurosis and Human Growth (Horney) (R) 1161
Grundsätzliches zur Diabetestherapie (R) 512
Grundy F, Preventive Medicine and Public Health (R) 835
Gunn W—intravenous fluid therapy in children (C) 1278 nursing infectious diseases (C) 796
Gunshot wound through both frontal lobes with recovery (Slorach) 1349
Gurd C W (O) 205
Guymer R F industrial health services (C) 857
Gynæcology—*fallopian tubes* 1362 fluorescence in (A) 1061 gestation period of (ML) 1276 influence of androgens on sexuality of women (Foss) 667, Malignant Disease of Female Genital Tract (Way) (R) 1107 Medical Gynæcology (Janney) (R) 274, ovarian physiology 1362 pelvis female shape and size of 835 pseudocyesis (A) 1312, streptomycin in latent genital tuberculosis in women (Halbrecht) 85 Textbook of Gynæcology (Young) (R) 836 *see also* Abortion Childbirth Labour Maternity Menstruation, Obstetrics Pregnancy Uterus, Vagina Vulva

H

H3 (LA) 1163
Hæmatinics injudicious use of (Dyke) (C) 1368
Hæmatology *see* Blood
Hæmoglobin—estimation of (Welch and Walther) 548 (Donaldson Sisson King Wootton and Macfarlane) 874 (King Bartholomew Geiser Ventura Wootton Macfarlane Donaldson and Sisson) 1044 Über Blutfarbstoffwechsel gesunder Säuglinge und Kinder (Künzer) (R) 1214
Hæmophilia—and Duffy antibody (James and Plaut) 150 female carrier of (Merskey and Macfarlane) 487 in female (Israëls Lempert and Gilbertson) 1375
Hæmophilus influenzæ meningitis treated with streptomycin (Allibone Pickup and Zinnemann) 610 (Ounsted) (C) 800
Hæmorrhage—at operations control of (Enderby and Pelmore) 663 (Hughes) 666 (A) 677 due to congenital afibrinogenæmia (Prentice) 211 into pituitary gland causing hypopituitarism (Robertson and Kirkpatrick) 1048 Physiology and Pathology of Hemostasis (Quick) (R) 1397
Hæmorrhagic disease—and plasma labile factor (Stefanini) 606 of newborn vitamin K in prevention of (Hay Hudson and Rodgers) 423 (A) 458 (Hay and Hudson) (C) 533
Hæmostasis—Physiology and Pathology of Hemostasis (Quick) (R) 1397
Hahn M F General Clinical Counseling in Educational Institutes (R) 948
Hahn P F Manual of Artificial Radioisotope Therapy (R) 1262
Haines M tuberculosis of endometrium 436
Halbrecht I streptomycin in latent genital tuberculosis in women 85
Haler D Liver (Blond and Haler) (C) 172
Hall S B Munchausen's syndrome (C) 858
Hall Sir A (O) 116 177
Hall Sir B death of 1169 (O) 1283
Hallmann L Bakteriologie und Serologie (R) 392
Hamilton M cerebral localisation (C) 1419
Hammersmith cocktail (LA) 1109
Hámori, A experimental glomerulonephritis (C) 586
Hand—injured outpatient treatment of (Ellis) 1038 *see also* Fingers
Handbook of Child Health (Furniss) (R) 672
Handling and Storage of Ethylene Oxide 1330
Handwriting—Strichbild (Pophal) (R) 948
Hardman F C accommodation for medical staff in hospitals (C) 1010
Hardy L I prospect of war (C) 414
Hardy T L potassium deficiency in pyloric stenosis 318
Hardy Roberts C P office manners 1119
Hares toxoplasmosis in in Denmark (Christiansen and Siim) 1201
Hargreaves A penicillin in megaloblastic anæmia (C) 410
Harold J T Munchausen's syndrome (C) 475
Harper J promethazine chlorotheophyllinate in seasickness 1141, (correctio 1280
Harrington, A B, paralytic poliomyelit following injury 987
Harris, R S Vitamins and Hormon (R) 948 (correction) 1422
Harrison D C familial idiopathic meth moglobinæmia, 935, (C) 1071
Harrison, E N.A.P.T Handbook Tuberculosis Activities in Great Brit and Commonwealth (R) 1108
Harrison T R Principles of Intern Medicine (R) 512
Harsant A C, will we never learn? (C) 9
Hart, F D—measurement of digit swelling in rheumatoid arthritis 77 myxœdema from resorcinol (C) 330
Hartmann H Psychoanalytic Study Child (R) 671
Haseeb M A, purification of vacci lymph with phenol (C) 114
Hassall A H (Dopson) 580
Hastings, Sir Charles, memorial festival Worcester 1271
Hauge M F health of hospital nurses 5
Haun P Psychiatric Sections in Gene Hospitals (R) 216
Hausmann, K thymidine in pernicio anæmia 329
Hawkins, C F potassium deficiency pyloric stenosis 318
Hay J D vitamin K in prevention hæmorrhagic disease of newborn 4 (C) 533
Head—injury metabolic disorders (Higgins Lewin O'Brien and Taylo 1295 Tumors of Head and Ne (Ward and Hendrick) (R) 1308
Health—Health and Disease in Tropi (Willcocks) (R) 215, Health and Hum Relations in Germany (R) 620 Healt of the People (Leff) (R) 34, in Scotlan 794
Health centres—(A) 571 (P) 1013 staffing of (P) 407
Health service for Oxford students (A) 13
Health services—bureau (Gillet) 404 industrial (A) 519 (Guymer) (C) 857
Health visitors—Textbook for Healt Visitors (Roberts Davies, and Corne (R) 1352
Hearing aids—bone conduction (P) 1412 Medresco (P) 633 (A) 1168, (Gray an Cartwright) 1170 (Stevens) (C) 1 (Gray) (C) 1369 unsuitable (P) 1013 waiting list for (P) 1282
Heart—angina pectoris (A) 898 an coagulants in cardiac *infarction* (L 675 cardiac arrest under anæsthes (A) 625, cardiovascular damage pr duced by anterior pituitary preparatio (Selye) 483 Congenital Heart Diseas (Brown) (R) 33 cor pulmonale (LA) 62 from recurrent pulmonary embolis (Petch) 1346 Digitalis and oth Cardiotonic Drugs (Movitt) (R) 94 Diseases of Heart and Circulation (Woo (R) 565 employment effect of o heart disease (A) 1358 Manual Cardiology (Dry) (R) 216 mitr disease surgery of (LA) 890 (Jóry) (C 1182 (Alroy) (C) 1369 *mitral stenosi* finger nail knife for commissurotomy (Sellors) (NI) 448 morphine leth effect of in cor pulmonale (Roussa 1156 mortality from circulatory disease in Norway 1940–45 (Strom and Jensen 126 (Daw) (C) 289 (Strom and Jense (C) 528 myocardial ischæmia and it surgical relief (Mason) 359 myo carditis and aortic hypoplasia arachnodactyly (Whitfield Arnott an Stafford) 1387 myocarditis with ren necrosis (Baird and Burne) 440 Phar macology of Failing Human Hear (McMichael) (R) 893 phonocardio graphy (Evans) 1083 physical exercis and (Abrahams) 1135 pulmonary hypertension (LA) 622 in mitral stenosi (Dornhorst) (C) 57 (Bayliss) (C) 350 rubella in (A) 99 size measurement o (Bourne and Wells) 17 sounds (A 1005, suppression of digitalis induc ventricular premature beats by Pron estyl (Munzer) (C) 637, surgery of 892 thiouracil compounds in preventio of paroxysmal cardiac arrhythmi (Ruskin) 134 *see also* Coronary disease Electrocardiography Endocarditis
Heartburn (Eastwood) (C) 1072
Heathcote A C S concentration o penicillin in lungs 1255
Heathcote R S A death of 1169 (O 1234
Heaton N, Calendar of Country Receipt (R) 948
Heggie, J F Cellophane envelopes fo syringe service (C) 589
Heller R Munchausen's syndrome (C 744
Hemispherectomy (Gooddy and McKissock) 481 (LA) 314
Hemsted E H vitamin B, in pernicious anæmia (C) 237

Immigrants tuberculous 356 (C) (Posner) 529
Immunisation—immunological protest (Glenny) (Holt) (C) 1072 paralysis after (P) 345 (Bousfield) 1028 with influenza A vaccines (Appleby Himmelweit and Stuart Harris) 1384 *see also* Diphtheria
Immunity development of in smallpox (Downie) 419
Imperial Cancer Research Fund 1009
Income tax allowances (Besterman) (C) 744
Incontinence in Old People (Brocklehurst) (R) 1262
India—diphtheria in Calcutta (Das and Ghosal) 1410 *Surgeons Twoe and a Barber* (McDonald) (R) 451 visit to (Hingorani) (C) 473
Indians in Fiji serum protein levels of (Wills and Bell) 820
Individual Differences in Colour Vision (Pickford) (R) 1308
Industrial Health Monthly 1186
Industrial Hygiene Newsletter 1186
Industry—industrial health services (A) [illegible] (A) [illegible] (Cuvmer) (C) 857 Industrial Injuries Act and tuberculous nurses (P) 523 *see also* Miners
Inebriates Acts 293

IN ENGLAND NOW—Air travel 687—Anæsthetics giving 1014—Army release ion 524—Ass's milk 1367—Authors income of 1177—Baby starving a new born premature 234—Battery inspect the 961—Bird table 688—Bull photographing a 795—Captain Cook 169—Chimney sweep 742—Christmas mail 50—*Daily Mail* Ideal Home Exhibition 634—Diaries pocket 50—Dinner Scotch 50—Doctor asking the 634—Dominion Day in Canada 1229—Education of medical students 1367—Elephant's milk 1367—Exhibition of French art 346—Exhibition of Ministry of Health Art Club and Hygeia Camera Club 108—Feet cold 50—Festival 1014—First aid 742—Flies killing in operating theatre 1015—Foreign body in stomach 68—General practitioners acknowledgment to 853—Glow worms 329—Horse rake leg 1413—Hospital Scandinavian 109—Hotels 960—Housewife's fatigue 1068—Indispensability 1277—Investigations special, 524—Influenza cure 1277—Italian visit 1322—Lectures 908—'Lifemanship' 169 234 285 346 407 525—London from the river 1413—Medical Art Society 795—Medicine slot machine 742—Milk 1177 1277 1307—Milkman's syndrome 108—Ministerial changes 287—National Health Service 1125—Newspapers in trains 1277—Paper waste 1125—Penicillin and pneumonia 524—Phenobarbitone 908—Plural shock 961—Private patients 908—Prosthesis 1277—References, 583—Registrars, 108 407—Reindeer's milk 1277 1367—Royal Academy 1068—Sherlock Holmes exhibition 1229—Spring cleaning, 908—Suppositories 1277—Surface area of body 1229—'Surgiarchy' 287—Telephone doctor's 583—Trespassing animals 468—Vaccination 108 525—We are the Boards appointed 795—We cannot eat but little meat 108—What can ail thee babe in arms? 634—When bicycles stand by the wall 742—Work hours of 345—Wriddle me wree 853

Infantile *see* Babies
Infants *see* Babies
Infection—A C T H and (LA) 949 Cortisone and (Cavallero and Sala) (C) 175, (LA) 949 (Laurie) (C) 1325 hospital (LA) 1310 of lungs and oral sepsis 391 of surgical wounds (Girdlestone Bourdillon and McFarlan) 597, (Thomas) (Connolly) (Hunter) (C) 713 (Dawson) (C) 798 *see also* Hygiene
Infectious diseases—monthly lists of 108 355 593 859 1067 1276 publication of information about (P) 406
Infectious diseases hospitals staffing of (Kennedy) (C) 175 (Banks) (C) 288 (Neale) (C) 412 (Pearce) (C) 472 (Crabb) (C) 585 (Linehan) (C) 694 (Gunn) (Crabb) (C) 796
Inflammation—Entzündungsbestrahlung (Glauner) (R) 1162
Influenza—59 107 168 (LA) 217 233 286 355 405 476 533 593 632 741, claims under National Insurance (P) 592 epidemics development of (Logan and MacKay) 264 immunisation with influenza A vaccines (Appleby, Himmelweit and Stuart Harris) 1384 influenzal pneumonia (A) 335, virus (LA) 1057
Ingham J, test for bile pigments in urine 151
Inoculation T.A.B.T in R A F (P) 592
Inositol—Chemistry of Inositol (Weidlein) 972
Insanity—divorce and (ML) 1077 franchise and (P) 345 intention and (ML) 1124
Insecticides—(A) 728 1079 D D T and Newer Persistent Insecticides (West and Campbell) (R) 216 D D T shortage of 538 toxic sprays 178 (A) 1105 1121
Insects and Hygiene (Busvine) (R) 999
Institute of Almoners 178 598
Institute of Hospital Administrators 122
Institute of Psycho Analysis 1284
Institutions mixed residents in (Grant and Thomas) 282
Insulin—hyperinsulinism treated with alloxan (Gilchrist and Lynch) 440, (correction) 806 (Mårtensson) (C) 965 (Lynch) (C) 1181 implants, effects of on rabbits (Gilliland and Martin) 143
Insurance—against sickness in Sweden (A) 1220 *see also* National Insurance
International Council of Ophthalmology 1330
International Research Centre for Chemical Microbiology, 1330
Intervertebral discs—(LA) 275 laterally placed cervical (Jefferson) 129 (Cyriax) (C) 351, late results of operations on 947 protruded orthopædic signs of (Charnley) 186 (Cyriax) (C) 351, (Meyer) (C) 352
Intestines—bowel rhythm in healthy infant (Gordon) 1203 deflation of distended bowel at operation (Lowdon) 1103 duodenal intubation with magnet tipped tubes (James) 209 Enterobacteriaceæ (Kauffmann) (R) 1108 gastro jejuno colic fistula (Holman) 1348, generalised scleroderma with intestinal involvement (Prowse) 989 Hirschsprung's disease (Bodian Carter and Ward) 302 (A) 337 sensibility of rectum and colon (Goligher and Hughes) 543 spastic ileus with mechanical obstruction of small intestine (Crieve) 1104 Treatment of Uræmia by Dialysis and Other Methods with Special Regard to Principles and Scope of Intestinal Dialysis (Twiss) (R) 154 *see also* Appendix Colon Steatorrhœa
Intravenous fluid therapy in children (Todd) 982 (Matheson) (C) 1128, (Mann) (C) 1230 (Gunn) (C) 1278 (McNicholl) (C) 1368
Introduction to Medical Photography (Hunt) (R) 94
Introduction to Study of Viruses (Smith) (R) 215
Introduction to Theory of Statistics (Yule and Kendall) (R) 672
Intubation of duodenum with magnet tipped tubes (James) 209
Invalid Children's Aid Association 537
Ireland—department of health of Eire (A) 399 Northern Ireland General Health Services Board annual report 416 scheme for free medical care for mother and child in Eire 907
Iron—body's (LA) 838 (Birch) (C) 1017, (Moore) (C) 1280, intravenous (Klopper) (C) 531 in anæmia of pregnancy (Scott and Govan) 367 (Naish) (C) 474 (French) (C) 641 (Scott and Govan) (C) 691 metabolism 391 (LA) 838
Irradiation *see* Radiotherapy
Irvine E D food-workers and infectious diseases regulations (C) 636
Irwin D application of psychology to dermatology (C) 348
Ischæmia postural to reduce bleeding in surgery (Enderby and Pelmore) 663 (Hughes) 666 (A) 677 (Korkis) (C) 801
Isle of Man—charge for prescriptions in 698 health services 971
Isotopes radioactive—Clinical Use of Radioactive Isotopes (Low Beer) (R) 274
Israel child care in (A) 517
Israëls M C G—hæmophilia in female, 1375 myeloid reticulosis 978
Ivy A C Peptic Ulcer (R) 331

J

Jackson C and Jackson C L Bronchoesophagology (R) 566
Jackson, L N self improvement discouraged (C) 585
Jacobs A retropubic prostatectomy 1088
Jaffé G V unfair questions (C) 855
James A H duodenal intubation with magnet tipped tubes, 209
James E typhoid fever in general hospital (C) 290
James J D Duffy antibody and hæmophilia 150
James T E, Prostitution and Law (R) 1398
James Lind Founder of Nautical Medicine (Roddis) (R) 999
Janney J C Medical Gynæcology (R) 274
Jaramillo Arango J Conquest of Malaria (R) 777
Jarman T F pneumoconiosis in coal miners (C) 1326
Jarvis W D Medical Handbook for Athletic and Football Club Trainers (R) 332
Jefferiss F J G treatment of early syphilis 83
Jefferson M—cerebral localisation (C) 635, (C) 966 laterally placed cervical intervertebral discs 129
Jeffree G M Anatomy of Man and Other Animals (R) 672
Jeffrey, M R A C T H in diagnosis of gout (C) 637, (C) 798
Jolliffe, A M A C T H by intravenous infusion 1260
Jemson, J perforation and hæmorrhage from unsuspected gastric cancer, 1036
Jenkins D H pilonidal sinus in barber (C) 746
Jenner medallist (A) 1169
Jensen R A mortality from circulatory diseases in Norway 1940–45 126 (C) 598
Jewesbury E C O vitamin B deficiencies after gastric operations (C) 1128
John Ferriar (Brockbank) (R) 566
Johnson B office manners (C) 1325
Johnson M L Dictionary of Biology (R) 778
Johnston R N prevention of tuberculosis in young people (C) 1369
Joints—osteo arthritis of hip 206 Surgery of Shoulder (DePalma) (R) 93, *see als* Arthritis
Joint Tuberculosis Council, 356
Jones F A—gastroscopy 647 medica research in regional hospitals (C) 961
Jones, H E cyanosis in infants from nitrates in drinking water (C) 1071
Jones H M R, false 'acute abdomen' (C) 113
Jones I, Stevens Johnson syndrome (C 1280
Jones R N gall bladder disease i children 324
Jordan A cation-exchange resins (C) 96
Joules H—prospect of war (C) 170 (C 115 publicity in cancer (C) 797
Journals—list of periodicals in library o Royal College of Physicians of London 750 new *Family Doctor* (A) 67 *Industrial Health Monthly* 1186, *Journa of Oslo City Hospitals* 611, *Notiziario dell Istituto Vaccinogeno Antitubercolare* 118
Juhn, B familial leukæmia (C) 1369
Juvenile *see* Children

K

Kaposi's varicelliform eruption 390 recurrent in adult (Boake-Dudgeon and Burnet) 383
Karamchandani P V antitoxins an antibiotics (C) 1417
Karrer, P Organic Chemistry (C) 965
Kauffmann F Enterobacteriaceæ (R) 110
Kauntze R *Veratrum viride* 519
Kay W W milk of some mammals (C) 136
Keay K. R laryngotracheitis 181
Keevil, J J De la Reyna and circulatio of blood 851
Keizer D P R congenital indifference t pain (C) 1020
Kelemen E salicylate gentisate an circulating eosinophils (C) 962
Kelham R L Ministry of Pensions artificial limb service 400
Kelleher, W N bulbar poliomyelitis, 97
Kelsall A R methonium compounds an hypertension (C) 585
Kempton J J teaching the teacher (C 1414
Kendall M. G, Introduction to Theory o Statistics (R) 672
Kennedy J M.—paratyphoid urinary carrier treated with chloramphenicol 92 staffing of infectious diseases hospital (C) 175
Kent A. Eighteenth Century Lectureship in Chemistry (R) 1108
Kersley, G D A C T H in diagnosis o gout (C) 637 (C) 798
Kessler H H. Principles and Practice o Rehabilitation (R) 154
Keysor J W Chemistry and Therapeutics of Synthetic Drugs (R) 893
Khalil A chloramphenicol in pertussi (C) 1370
Kidd J G Pathogenesis and Patholog of Viral Diseases (R) 215
Kidney—A C T H and renal glucose threshold (De Filippis and Iannaccone) (C 856 acute tubular necrosis (LA) 1109 chronic renal potassium deficiency (Davidsen Kjerulf Jensen, and Krarup 375 circulatory system and 998 cortical necrosis of with myocarditis (Baird and Burne) 416 glomerulonephritis experimental (Humori and Oláh) (C) 586 obstetric shock and 998 renal damage by anterior pituitary preparations (Selye) 483 Renal Diseases (Bell) (R) 778 renal dwarfism causing disparity of growth in uniovular twins (Milne) 204, renal failure (Platt) 1239 Renal Function (Bradley) (R) 1108 spinal anæsthesia and 999 *see also* Tuberculosis Uræmia
King E J—determination of hæmoglobin 874 1041 Microanalysis in Medical Biochemistry (R) 67

mation about (P) 100, Law relating to Mental Treatment and Health Service (Berry) (R) 1398 Leeds Regional Hospital Board (P) 1322 lists of patients of general practitioners 179 local health authorities 681, Manchester health centre (A) 571, medical auxiliaries in (LA) 895 904, Medical Practices Committee 1371, medico social services, 681 mental health services 681 midwifery service in Scotland (P) 1322, Ministry of Health (LA) 513 (P) 523 Ministry of Pensions artificial limb service (Magee Kelham Ritchie, McKenzie and Craft) 400 Ministry's liability for hospital staff's negligence (ML) 168 National Health Service Acts 1916 and 1919 (Scott, Cooper and Seuffert) (R) 332 National Hospital Service Reserve (P) 1076 Newcastle Regional Hospital Board (A) 337 ophthalmic services 243 (P) 718 patient removed from lists of four doctors 1281 planning and coördination, 686 prescriptions, cost of (P) 294, 297 problems of 682 Report of Comptroller and Auditor General (LA) 1057 residents in mixed institutions (Grant and Thomas) 282 review of (L) 35 Sheffield health centre (P) 1076 social workers in mental health services (A) 1403 specialists in Scotland 1322 spectacles charges for (LA) 810 (LA) 1001 (P) 1012, (P) 1014 1186 spectacles free number supplied (P) 1013 spectacles prescribing of 61 superannuation rights under 179 Supplement of National Health Service Act 1916 Annotated (Speller) (R) 778 tuberculosis medical officers number of (P) 294 tuberculous treatment of (P) 344 *see also* Aged Almoners Beds Central Health Services Council Hearing aids Hospitals Nurses Pay Registrars

National Health Service Bill, 1051 (P) 967 1075

National Health Service Tribunal, 1122

National Hospital Service Reserve (P) 1076

National Insurance—claims (P) 592 doctors and (P) 911, prescribed diseases (P) 593, sickness benefits for contacts 1079 tuberculosis benefits (P) 718

National Service—medical officers marriage allowances of, 167 number of men and proportion unfit registering for (P) 1112

Nautical medicine—James Lind Founder of Nautical Medicine (Roddis) (R) 999

Naylor P F D, sensitivity to mercurial diuretics 614

Neal, D ultrasonic waves 655

Neal R A indigenous amœbiasis in Britain 766

Neale A V—nursing infectious diseases (C) 412, specialisation in teaching (C) 1182

Near East—Anopheles and Malaria in Near East (Leeson Lumsden Yofe and Macan) 536

Neck—Tumors of Head and Neck (Ward and Hendrick) (R) 1308

Needham C D fat absorption in chylothorax 991

Needles—hypodermic standard 298 new lumbar puncture needle (Matthews) (NI) 777 universal needle for bone marrow aspiration (Hill) (NI) 1213

Negligence—complaint of (P) 1282 finding of against doctor and hospital (ML) 1233 verdict of against Ministry of Health (ML) 524

Nelson Jones A undulant fever 495

Neoarsphenamine in—early syphilis (Jeffcriss Willcox and McElligott) 83 tick borne relapsing fever (Coghill) 604

Neoplasms of Bone (Coley) (R) 565

Nervous system—aneurysm dissecting neurological complications of (A) 222 angor animi (A) 898 (Bourne) (C) 962 autonomic control of by hypothalamus (McDonald) 627 bronchial asthma treated by bilateral resection of vagus (Clarke) 138 (C) 797 central, torulosis of (Mosberg and Alvarez DeChoudens) 1259 congenital malformations of central nervous system seasonal incidence of (McKeown and Record) 192 (Hick) (C) 317 (Wallis) (C) 348 detection of spinal block (A) 1113 electrocardiographic findings during operative manipulation of vagi (Freeman) 926 epileptiform fits during calciferol therapy (Beare and Millar) 884 (Gremeaux) (C) 1016 Hirschsprung's disease (Bodian, Carter and Ward) 302 (A) 337 Modern Trends in Neurology (Feiling) (R) 894 nerve supply to rectum and colon (Goligher and Hughes) 543 Neural Crest (Hörstadius) (R) 392 neurological complications of undulant fever (Nelson Jones) 495 neuromuscular incoördination of swallowing in newborn (Macaulay) 1208 Neurosis and Human Growth (Horner) (R) 1161 neurosurgery and

sive stimulation therapy (Milligan) 938 phenylketonuria atypical (Cowie) 272, Practical Neurological Diagnosis (Spurling) (R) 154 serum neuritis (A) 40 sleep (McDonald) 627 (McDonald) (C) 1071, *see also* Brain Electroconvulsive therapy Pain, Sciatica

Neubauer C acute obstructive laryngotracheitis (C) 319

Neural, *see* Nervous system

Neurology *see* Nervous system

Neustatter W L treatment of psychoneurotics 1331

Newborn *see* Babies

Newcastle Regional Hospital Board (A) 337

Newcastle upon Tyne—safer childbirth in (A) 1266, study of health of children in (A) 221

NEW INVENTIONS.—*Apparatus for reducing* contractures (Russell and Schuster) 1351—Automatic pipette (Dalton) 273—Clamps for hysterectomy (Howkins) 1107—Finger nail knife for commissurotomy in mitral stenosis (Sellors) 148—Instruments for suprapubic exposure of prostate and bladder neck (Winsbury White) 153—Modified laryngoscope (Evans) 1161—New lumbar puncture needle (Matthews) 777—New oscillometer (Moore) 670—Operating table arm rest (Wilson, Murphy and Angel) 511—Safety endotracheal connection (Bell) 619—Shoulder piece attachment for operating table (Evans) 1307—Tidal spirometer (Barry) 214—Trochar and cannula for tapping lateral ventricle (Cathie and Tizard) 723—Universal needle for bone marrow aspiration (Hill) 1213

Newman H W Annual Review of Medicine (R) 332

Newman M coronary occlusion in young adults 1015

New Zealand—dental nurses in (LA) 155 research and teaching in 733

Nitrates in drinking water cyanosis in infancy from (Ewing and Mayon White) 931 (Harrison and Gibson) (Jones) (C) 1071 (Heather) (C) 1321

Nitrogen mustard—in bronchogenic carcinoma (Frankel and Workman) (C) 1231 (Droller) (C) 1326 in nasopharyngeal carcinoma (Stock) 612, substitutes for (LA) 1111

Nixon J A (O) 718

Nixon W C W—maternity and administrator (C) 746 response of uterus to drugs 250

Njovera (Willcox) 558

Nobel The Man and His Prizes (R) 1162

Noradrenaline—and suprarenal medulla (West and Hunter) (C) 471, in hypotensive states (Barcroft Churchill Davidson and Swan) (C) 854

Norris A abscess at site of penicillin injections 556

North America—care of sick in (Simmonds and Peers) 814 *see also* Canada U S A

Norway—beds for tuberculous in (Lillingston) (C) 173 (Sita Lumsden) (C) 799 control of food in 917 mortality from circulatory diseases in 1940-45 (Strom and Jensen) 126 (Daw) (C) 289 (Strom and Jensen) (C) 528

Notiziario dell Istituto Vaccinogeno Antitubercolare 1185

Novalgin causing granulopenia 389

Nucleic acid content of cell (Davidson, Leslie and White) 1287

Nuffield Foundation (A) 1312 dental fellowships 357

Nuffield Orthopædic Centre 178

Nuffield Trust for Special Areas 121

Nurses—160 administration of drugs by (Trillwood) 1221 dental (LA) 155 hospital health of in a Norwegian hospital (Hauge) 520 tuberculosis number of (P) 294 tuberculous and Industrial Injuries Act (P) 523

Nursing infectious diseases (Kennedy) (C) 175 (Banks) (C) 288 (Neale) (C) 412 (Pearce) (C) 472 (Crabb) (C) 585 (Linehan) (C) 694 (Gunn) (Crabb) (C) 796

Nutrition—and pure food (A) 570 Teaching Better Nutrition (Ritchie) 697 *see also* Malnutrition

Nutrition Society (A) 222

Nylon effect of phenol on (Thomas) (C) 743 (Dawson) (C) 798

Nystagmus experimental (Browne) 721

O

Obesity (A) 782 (Lowy) (C) 858 1160 in children (A) 841

OBITUARY

Back I G 1371—Bankart A S B, 915
—Barnie Adshead W E 306—Black
ham R J 295—Box C R 859—
Broom R 915
Cathcart C C 177 (correction) 418—
Cheatle Sir L 115—Chisholm J
1420—Cook Sir A 1021
Forsell, G 860—Franklin P, 17
Fraser T 119—French H, 12
French, J G 969
Gask, G E 240 295—Girdlesto
G R, 117—Graham, S 13
Greenlees J R C, 1235—Gurd C
295
Hall Sir A, 116 177—Hall Sir B, 1
—Heathcote, R S A, 1234
Kleine, F K 969
Macleod P J, 534—Martin, J G, 12
—Miller C G 1183
Nixon J A 748
Olive, E J P 1022—Oliver C P
Panton Sir P 60 120—Parsons Sir
62 120—Pennell A M 696—Philli
S P, 242—Poston, R I 749
Ramsbottom A, 534—Reddingto
M P 1283—Rencastle A G 534
Smith G M 643—Souza G H de
1130—Stallybrass C O 415—Sta
A J 477—Swain J, 176
Tewsley C H, 61—Tomlinson Sir P 6
Vernon H M 477—Verrall P J, 10
West C E 119, 177 242—White
749—Wilkinson K D 914 969
Wilson G H, 749—Woodroff
A J W 535
Yearsley, P M, 1130

O Brien D methæmoglobinæmia (C) 1

O Brien J R P metabolic disorders head injury 1295

Obstetrics—oxytocics (Stansfield an Drabble) 74, Priscol in (Foster) (802 renal changes in obstetric shock 998 umbilical cord, prolapsed, treatment of (Cox) 561 *see also* Cæsarean section

Obturator hernia (Rose) (C) 112

Occupational therapists 907

Occupational therapy (Krauss) (C) 17 (Herford) (C) 348 804

Ocular, *see* Eye

Œsophagus—Bronchoœsophagology (Jackson and Jackson) (R) 566 *Esophagus and Pharynx in Action* (Leroche) (R) 1000 Œsophageal Speech after Laryngectomy (film) 62 perforation of during gastroscopy (Jones Doll Fletcher and Rodgers) 647

Œstrogens (Bishop Richards and Perry) 818

Œstrone (Bishop Richards and Perry) 81

O Farrell M B social case work 955

Office manners (Hardy Roberts) 1119, (Banks) (C) 1233 (Johnson) (C) 1375

Ogilvie Sir H will we never learn? (C) 526

Ogle K N Researches in Binocular Vision (R) 452

Olah F—experimental glomerulonephritis (C) 586, induced eosinopenia (C) 803

Olbert T atherosclerosis and cholesterol (C) 174

Old age *see* Aged

Oldfield M C tennis thumb 1151

Oldham P D observers errors in taking medical histories 1007

Olecky S excretion of methonium compounds 889

Oligospermia 1362

Olive, E J P (O) 1022

Oliver C P (O) 477

Olwin J H venous thrombosis (C) 1231

Onchocerca volvulus ophthalmoscopic detection of microfilaria of (Sarkies) 1205

O Neill D psychosomatic approach to pulmonary tuberculosis (C) 1230

Operating table—arm rest for (Wilson, Murphy and Angel) (NI) 511 shoulder-piece attachment for (Evans) (NI) 1307

Operating theatre—electric hazards in 1372 responsibility in (ML) 1321

Operation of Central Syringe Service, 972

Operations code of 356

Ophthalmic *see* Eye

Ophthalmologists, pay of, 479 536

Ophthalmology *see* Eye

Oppé T E methæmoglobinæmia due to sodium nitrite, 1051

Opsoclonia in polioencephalitis (Warren) 213 (Simpson) (C) 350 (Warren) (C) 412

Order of St John of Jerusalem [illegible] 1421

Order of the Court (Pank) (R) 1000 (Clymo) (C) 1370

Orf (Lloyd Macdonald and Glover) 790

Organic Chemistry (Karrer) (C) 965

Ornithosis (A) 518

Orthopædic surgery in past fifty years (A) 338

Orthoptics—Clinical Orthoptic Procedure (Smith) (R) 672

Osborn S B effect of postoperative rest in bed and early ambulation on venous blood flow 22

Oscillometer new (Moore) (NI) 670

Osler Club of London 861

Osteitis digital (Lowden) 196

Osteo arthritis of hip 596

Osteology for Dissectors (Howat) (R) 331

Osteomyelitis—and overgrowth of long bones 1316 due to Friedländer's bacillus (Muskat and Findlay) 1151

O Sullivan J V extraperitoneal cæsarean section (C) 291

nition of (Stewart) (C)
n dispensaries (Ellman)
rial (Haines) 436 1363
(Cameron) 507 , figures
genito urinary tract
low, and St Hill) 1033
erculous, 306 (Posner)
968 in neighbouring
1311 in Scotland (A)
latent genital, in women
treptomycin (Halbrecht)
erculosis scheme 1161
number of (P) 291 ,
erculous streptokinase as
tment of (Forbes) 1134
berculous treatment of
(Thursby Pelham and
55 Ministry s statement
P T Handbook of Tuber
les in Great Britain and
a (Williams Hughes and
1105 National Insurance
) 748 notification of (Cox)
ses, number of (P) [illegible]
incidence of (A) 281 of
duct (Konstam and Mey
crowding and (Nash) (C)
sed as industrial disease
(P) 635 prevention of in
le (Anderson Grenville
Trenchard) 1116 (Brooke)
hnston) (C) 1369 , primary
resistant in newborn
Henderson) (correction) 61 ,
extrapleural pneumothorax
t of (Murstad) 291 pul
foreign workers (P) 968
psychosomatic approach to
(Foulkes) (C) 1150 (O Neill)
egisters number of cases on
elation to pneumoconiosis
10 sanatorium treatment
in middle aged and elderly
service, prospects in (A) 160 ,
ties of (A) 39 (Barran) (C)
ptomes de la tuberculose
et ses complications (Rist)
acheal and bronchial treated
ptomycin 253 (A) 280 ,
s cervical adenitis (Morris and
ans) 1193 waiting lists (P)
pensioners with (P) 167 , *see*
nothorax, Tuberculin
, nationalised general practice,

damantinomas 330 Neo
Bone (Coley) (R) 565 Steroid
and Tumors (Lipschutz) (R)
umors of Head and Neck
d Hendrick) (R) 1308
methonium compounds in
n (C) 408
ae (Cameron) 809
in patients with loss of weight
rtial gastrectomy (Badenoch
and Ward McQuaid 508
vular showing growth disparity
nal dwarfism (Milne) 201
E Treatment of Uræmia by
and Other Methods with
Regard to Principles and Scope
inal Dialysis (R) 154
Diabetes Mellitus and Their
(Colwell) (R) 566
ever—carriers (A) 518 in general
(Grant) (C) 112 (James) (C)
orld survey of 657
accine preservation of (Hender
acock, and Richley) 618

U

arbstoffwechsel gesunder Säug
nd Kinder (Künzer) (R) 1214
E Lehrbuch der Röntgen
ik (R) 154
Peptic ulcer Rodent ulcer
-waves (A) 399 in detection of
of texture in living tissues (Wild
) 655
let burns, delayed effects of (A)
Thomson) 1347
cord prolapsed treatment of
561
d (film) 62
fever neurological complications
n Jones) 495 (C) 637
questions (Conybeare) (C) 746
) (C) 745 (Holroyd)
(C) 855
Nations International Children s
y Fund (P) 167
ities—Aberdeen degrees, 861—
appointments 479 537
h degrees 537—Bris
booklet 570 1241—Cambridge
pass lists 917 chair of anatomy
ment 614 357, 479, 644 805 1078
degrees 1372 pass list 594 report
ent of medicine 536—Dublin
1234 pass list 751—Edin
1078 conference

bacteriology 505 degrees 178 1078
1372 quincentenary (A) 1301—Leeds
appointments, 537 751 1237 Liverpool
appointment 1121 chair of orthopædic
surgery 1121 pharmacology 1237 pass
lists 63 117 505—London appoint
ments 537 1237 1372 1121 chair of
clinical pathology 63 chair of com
parative anatomy 1155 diploma 63
pass lists 178 644 1131 1237 recog
nised teachers 751 1 travelling
fellowships 179 , William Julius Mickle
fellowship 531—Malaya chair of mid
wifery and gynæcology 117—Man
chester appointment 7 chair of
social and preventive medicine 1155—
New Zealand chair of obstetrics and
gynæcology 1078—Oxford appoint
ments 1023 1131 clinical [illegible] 117
degrees 178 297 531 1078 1131
elections, 537 health service for
students (A) 1155 mortality and pro
longed illness among undergraduates
(Parnell) 731—Queen s Belfast degrees
and diplomas 121—St Andrews chair
of child health 117, surgery 117
inquiry into (P) 1078 1231 pass list
178—Sheffield appointment 179 115
137—State University of New York
chair of medicine 1330—Yale chair of
history of medicine, 179
Universities—introduction to 750 , Year
book of Association of Universities of
Commonwealth 757
Universities Federation for Animal Welfare
1023
Upholstery clean (P) 632
Uræmia—(Platt) 1233 hyperkalæmic
with nephrocalcinosis due to carcinoma
tosis (Fulton and Paget) 858 (McGowan)
(C) 967 (Hebson) (C) 1016 (Lloyd) (C)
1070 Treatment of Uræmia by Dialysis
and Other Methods with Special Regard
to Principles and Scope of Intestinal
Dialysis (Twiss) (R) 154
Urea excretion of (Platt) 1233
Ureteric dysmenorrhœa (Reid) 312
Urethane in nasopharyngeal carcinoma
(Stock) 612
Urethral caruncles (Begg) 821 (Mills)
(Taylor and McLaren) (C) 963 (Begg)
(C) 1181
Urinal holder 296
Urinary bladder—instruments for supra
pubic exposure of bladder neck
(Winsbury White) (NI) 153 , *see also*
Tuberculosis
Urine test for bile pigments in (Ingham)
151 (Smith) (C) 237
Urology—Essentials of Urology (Ains
worth Davis) (R) 1397 Essential Uro
logy (Colby) (R) 33 genito urinary
tuberculosis (Ross Cow and St Hill)
1033 Urological Surgery (Dodson) (R) 154
Urticaria following adrenaline (Herx
heimer) 616
U S A—a city in the middle west 1175
aged in 801 American Medical Associa
tion, 537 call up of doctors 1023 care
of sick in (Simmonds and Peers) 844
cost of medical care in 243 drug
addiction in (A) 1356 grants for medical
research in (LA) 1105 hospital beds in
(A) 42 medical schools in (A) 1218
medical services of Armed Forces of,
178 number of doctors in 645
Physicians Forum 537
Uterus—acute puerperal inversion of (Dew
hurst and Bevis) 1394 cervical cancer
classification of (A) 159 curettage in
diagnosis of cervical cancer (Anderson)
1152 , prothrombin and menstruation
(Lewitus) (C) 51 , Radiation Therapy in
Management of Cancer of Uterine Cervix
(Cantril) (R) 153 response of to drugs
in early pregnancy (Schild Fitzpatrick,
and Nixon) 250 rupture of endo
metrial cysts (Dean) 1380 tissue culture
of human endometrium (A) 42 tubercu
losis of endometrium (Haines) 436 1363
see also Hysterectomy

V

Vaccination—and smallpox (Millard) 104
(Dixon) (C) 171 (McClean) (C) 236,
(Watts) (C) 288 (Woolman) (Gemmill)
(C) 352 (Viant) (C) 411 (Millard) (C)
471 (Dixon) (C) 532 (Taylor) (Rao) (C)
590 (Woolman) (Bloss) (C) 639 (cor
rection) 806 (Lycett) (C) 689
Vaccine lymph—ejector (Galpine) (C) 910
improvised (Bentham) (C) 1326 potency
of (Anderson) 1067 purification of
(Haseeb) (C) 114 (Krishnamurthy) (C) 172
Vaccines—B.C.G (P) 407 as research tool
(LA) 1217 influenza A immunisation
with (Appleby Himmelweit and Stuart
Harris) 1384 tuberculosis (Cameron)
809 typhoid preservation of (Hender
son Peacock and Richley) 618
Vagina—discharge from 92 Primary

Vagus bilateral resection of in bronchial
asthma (Clarke) 435 (C) 791
Vahrman J staphylococcal infections 12
Vakil R J yogi priest s feat (C) 533
Valdecasas F G *Inmunología* (C) 132
Vallet L coagulability of irradiated
plasma 1102
Van Cauwenberge H acetylsalicylic aci
and urinary excretion of adrenocortica
steroids 771
Van Dam R canicola fever 1100
Vane J R effect of venous occlusion o
peripheral arterial blood flow 180
Van Heyningen W E Bacterial Toxi
(R) 619
Van Pelt S yogi priest s feat (C) 173
Varró V induced eosinopenia (C) 502
Vasopression action of on uterus (S hil
Fitzpatrick and Nixon) 250
Veillon I Medical Dictionary (R 6
Venereal disease—new move against 97
Textbook of Venereal Diseases (Will c
(R) 1105 *see also* Gonorrhœa Syphi
Ventricle lateral trocar and annul
tapping (Cathie and Lizard) (NI) 72
Venturi S determination of hæmoglobi
1044
Veratrum viride (Kauntze and Troun
34 (LA) 565 (Davies) (C) 631
Verilod (Kauntze and Trounce) 3
(LA) 565
Vernon H M (O) 177
Verrill P J (O) 1022
Vertebrate—diseases transmitted by to
man (A) 318 , Life of Vertebrates (Young
(R) 671
Vertigo—laryngeal ([illegible]) (C) 63
Menière s disease (A) 781 (Mitchell) (C)
903 (Pa[illegible]) (C) 1289
Veterinary hygiene 1010
Viant, S P vaccination against smallpox
(C) 111
Vibrio El Tor in estimation of chlor
amphenicol (Doorenbos and Kop) (C)
691
Vickers H F prospect of war (C) 291
Vines H W C hospital economics (C) 1023
Viomycin (A) 952
Viruses—bacterium versus virus (A) 9
(Wooster) (C) 51 (LA) 569 Coxsackie
(A) 457 (A) 1061 genetics and (A) 99
influenza virus (LA) 1057 Introduction
to Study of Viruses (Smith) (R) 215
myxomatosis virus 644 ovine pustular
dermatitis (Lloyd Macdonald and
Glover) 720 Pathogenesis and Pathology
of Viral Diseases (Kidd) (R) 215 , Virus
and Rickettsial Diseases (Bedson
Downie MacCallum and Stuart Harris)
(R) 215 *see also* Influenza Poliomyelitis,
Smallpox
Vision *see* Eye
Visual Anatomy (Friedman) (R) 1107
Vital statistics—average age at death in
1939 and 1945 (P) 748 births and deaths
in England and Wales in 1950 233
births and deaths in war and peace 959 ,
births in England and Wales estimated
for first quarter of 1951 355 births in
England and Wales estimated for second
quarter of 1951 1276 death rates and
sickness rates of married and single
women in 1948 (Brooke) 1272 deaths in
1950, 1276 England and Wales in
1950 859 first quarter of 1950 900 ,
for 1946–47, 1176 for Eire 1950 1234
for Northern Ireland 1067 London in
1950 401 mortality in 1950 1177
sexes compared (A) 781 , third quarter
of 1950 in England and Wales 169
third quarter of 1950 in Scotland 108
Vitamin A poisoning (LA) 394
Vitamin B complex—Biochemistry of B
Vitamins (Williams Eakin Beerstecher
and Shive) (R) 274 deficiencies after
gastric operations (Welbourn Hughes
and Wells) 939 (Jewesbury) (C) 1128
Vitamin B_{12}—diuretic effect of (Bedford)
(C) 1232 in pernicious anæmia (Mills
and Hemsted) (C) 237 possibly
extracted from fæces (Callender and
Spray) 1391
Vitamin C—action of on tuberculin
sensitivity in guineapigs (Long Miles
and Perry) 1085 and deoxycortone
acetate in rheumatoid arthritis (MacLean)
444 in methæmoglobinæmia (Breakey
Gibson, and Harrison) 935
Vitamin D_2—therapy epileptiform fits
during (Beare and Millar) 884 (Gre
meaux) (C) 1010
Vitamin K—and plasma labile factor
(Stefanini) 606 in prevention of
hæmorrhagic disease of newborn (Hay
Hudson and Rodgers) 123 (A) 458, (Hay
and Hudson) (C) 533
Vitamins—and physical exercise (Abra
hams) 1135 food charts of 62 Vitamins
and Hormones (Harris and Thimann)
(R) 948 (correction) 1422
Vomiting—after morphine (A) 398 auto
nomic control of (McDonald) 627
cyclical in children 330
Von Bonin G Essay on Cerebral Cortex

Vote and certified lunatics (P) 315
Vourcka A—bacterial variants in patients treated with chloramphenicol 27 (C) 357 production of bacterial variants in vitro with chloramphenicol and specific antiserum 28
Vowles K D J treatment of perforated peptic ulcer (C) 175
Vulva fluorescent (A) 1061

W

Wahba A H strychnine and aspirin poisoning (C) 1115
Wakeley Sir C Spigelian hernia 1290
Walker J methonium compounds in hypertension (C) 173
Wallace A B burns 501
Walli H R E seasonal incidence of congenital malformations (C) 348
Walls L W Hilton's Rest and Pain (R) 512
Walter J—birthmarks and moles (C) 475 publicity in cancer (C) 1180 Short Textbook of Radiotherapy for Technicians and Students (R) 34
Walther W W estimation of hæmoglobin 548
War—pensioners with 100° disablement (P) 467 pensioners with tuberculosis (P) 467 prospect of (Doll Esterman Gilliland Joules Levy Pollock and Penrose) (C) 170 (West) (Garson) (Sheldon) (Cirby) (C) 235 (Vickers) (C) 291 (Hodge) (Sambrook) (Gaffey) (Adams) (C) 292 (Asher) (McClean) (Comfort) (Binning) (C) 293 (Hilton) (C) 353 (Lambert) (Batten) (Barnard) (C) 354 (LA) 395 (Chapman) (Hardy) (Mohun) (C) 414 (Doll Esterman Gilliland Joules Levy Penrose and Pollock) (C) 415 804 Psychological Factors of Peace and War (Pear) (R) 619
Ward B C H Hirschsprung's disease 302
Ward G E Tumors of Head and Neck (R) 1308
Ward McQuaid J N—Munchausen's syndrome (C) 474 Tween 80 508
Warner E C wrong way (C) 1327
Warren C M pilonidal sinus in barber (C) 912
Warren M D poliomyelitis after appendicectomy 213 (C) 412
Water—cold immersion in (A) 675; of swimming baths, purification of (A) 573 see also Drinking water
Waterhouse J A H, aminophyllin in emphysema 490
Watkin J H, new deal for defectives (C) 1231
Watson A orthostatic albuminuria 1196
Watson C J porphyrin metabolism and porphyria 539 644
Watson Jones R results of surgery in sciatica and low back pain (C) 413
Watson Williams E will we never learn? (C) 857
Watts A S vaccination and smallpox (C) 288
Watts Sir T death of 1268
Way S, Malignant Disease of Female Genital Tract (R) 1107
Wayte A B lipoid pneumonia, 1206
W c seat foot-operated (Bourne) 232
Weedkillers (A) 728
Weidlein E R Chemistry of Inositol 972
Weil's disease—diagnosis of 390 penicillin in (Suchett Kaye) 90 (Suchett Kaye) (C) 690
Welbourn R vitamin B deficiencies after gastric operations, 939
Welch G K estimation of hæmoglobin 548
Wellcome Research Institute 1078
Wells B G heart size 17
Wells C vitamin B deficiencies after gastric operations 939
Werdnig Hoffmann's Infantile Progressive Muscular Atrophy (Brandt) (R) 777
West C E (O) 119 177 242
West G B noradrenaline and suprarenal medulla (C) 471
West, R prospect of war (C) 235
West T F D D T and Newer Persistent Insecticides (R) 216
Wexler I B, rhesus factor nomenclature (C) 693
What is Hypnosis? (Salter) (R) 893
Whatmough W A, Poisons Guide (R) 1000
Whisky (Karrer) (C) 965
Whitaker's Almanack 1951 (R) 216
White J C, nucleic acid content of cell 1257
White R G effect of 'Cortisone' on pneumococcal bacteræmia, 891
Whitfield A G W—aminophyllin in emphysema 490 arachnodactyly 1387
Whitley Council Medical Committee (C) 58
Whitty C W M, cerebral localisation (C) 1070
W H O see World Health Organisation
Whooping cough—533 632, 741 chloramphenicol in (Lassen and Grandjean) 763 (A) 783 modification of in contacts by means of chloramphenicol (Bogdan) 764 (Khalil and Abdin) 1370
Whyte D (O) 749
Win (LA) 1163
Widdowson E M mental contentment and physical growth 1316
Wilcocks C, Health and Disease in Tropics (R) 215
Wild J J ultrasonic waves 655
Wilkinson A W postoperative blood chemistry 315
Wilkinson J F—aminopterin in acute leukæmia 325 β naphthyl di 2 chloroethylamine 137
Wilkinson K D (O) 914 969
Wilks J Munchausen's syndrome (C) 475
Willcox R R—endemic syphilis of Southern Rhodesia 558 Textbook of Venereal Diseases (R) 1108 treatment of early syphilis 83
Williams A A ACTH in dermatomyositis 1053
Williams B Munchausen's syndrome' (C) 527
Williams H currency for treatment abroad (C) 413 N A P T Handbook of Tuberculosis Activities in Great Britain and Commonwealth (R) 1108
Williams J H, hospital schools 1269
Williams R J, Biochemistry of B Vitamins (R) 274
Williams, T P bacillæmia due to *Shigella sonnei* 997
Willis R A Principles of Pathology (R) 948
Wills, L, serum protein levels of Samoans Fijians and Indians in Fiji 820
Will we never learn? (Ogilvie) (C) 526 (Rutherford) (Brailsford) (MacLellan) (C) 591 (Shepherd) (C) 612 (C) 691, (Latta) (C) 717, (Riggall) (C) 790 (Watson Williams) (C) 857 (Harsant) (C) 911
Wilson A appointment 1237
Wilson E F operating table arm rest (NI) 511
Wilson, G H (O) 749
Wilson O, conservative surgery [illegible] duodenal ulcer (C) 526
Wilson S R miniature radiogr[illegible] (C) 1323
Windle W F Asphyxia Neonat[illegible] (R) 332
Wingate P 'Munchausen's syndrome' (C) 412
Winsbury White H P, instrument for suprapubic exposure of prostate and bladder neck (NI) 153
Winston, M E actinomycosis of spine 945
Woerdeman, M W Atlas of Human Anatomy (R) 451
Wofinden R C Problem Families of Bristol (A) 100
Wolff, E unicellular sebaceous glands in human skin, 888, (C) 1417
Wolff J W, canicola fever 1100
Women see Gynæcology
Wood J S, specialisation (C) 584
Wood, M W, W cirrhosis of liver attributed to methyl chloride 508
Wood, P Diseases of Heart and Circulation (R) 565
Woodmansey A C, paraffin in syringes (C) 1018
Woodroffe [illegible] (C) 535
Woods Lionel, memorial to 53
Woolman A M vaccination smallpox (C) 352 (C) 639
Wooster N bacteria to cont (C) 51
Wootton I D P determin hæmoglobin 874, 1011
Worcester, Sir Charles Hastings festival at 1271
Workman, J M bronchogenic c treated with nitrogen mustard
World Health Assembly 1079 11
World Health Day (A) 730
World Health Organisation 24 417, (A) 457 (A) 459 180 59 861 1021 1078, 1079 1131 (L (A) 1169 1238 1329 1373
Wortis J Soviet Psychiatry (A)
Wright, H Contraceptive Techni 1161
Wright H P, effect of postoperat in bed and early ambulation on blood flow 22
Wright I S Thrombo-emb ditions and their Treatment coagulants (R) 392
Wright S tropic or trophic (C) 1
Wrong way (LA) 1261 (Lake) (Warner) (C) 1327, (Baker) (Murray) (C) 1370 (de Launay) (C) 1120
Wyman, A L bleeding peptic ul

X

X factor (LA) 277
X ray apparatus for chest clinic
X ray films standardisation of (correction) 646
X rays see Radiography Ra Radiotherapy

Y

Yaws (Willcox) 558 (Manson Ba 638 (Wills and Bell) 820
Yearbook of Association of Univer Commonwealth 787
Yearsley P M (O) 1130
Yellow Fever (Strode) (R) 1398
Yofe W H R Anopheles and in Near East 536
Yogi priest's feat (Crutchfield) (M (C) 56 (Van Pelt) (C) 173 (Vakil
Young A G Munchausen's s (C) 711
Young B A empyema thorac with penicillin and aspiration 1016
Young, C J leucocyte counts in t therapy (C) 411
Young F post traumatic ep cysts 716
Young J Textbook of Gynæco 836
Young J Z Life of Vertebrates (
Young R H, results of surgery in and low back pain 215 (correc
Young S, myxœdema from resor 798
Your Children's Feet (Pratt) 11
Yule, G U Introduction to T Statistics (R) 672

Z

Zannos L sickle cell anæmia i 1147
'Zeo Karb 225' (Morton) 825
Zervos N, sickle cell anæmia i 1147
Zinnemann, K. streptomycin i *philus influenzæ* meningitis 61
Zoogeography of Land and Inlan (de Beaufort) (R) 1000
Zoology—Chordates (Rand) (R Life of Vertebrates (Young) (R
Zoonoses (A) 518
Z reserve—doctors appeal of ag up 504 medical students exc call up of (P) 634
Zwischenhirn (Hess) (McDonald)